1,1′-Binaphthyl Dimers, Oligomers, and Polymers: Molecular Recognition, Asymmetric Catalysis, and New Materials†

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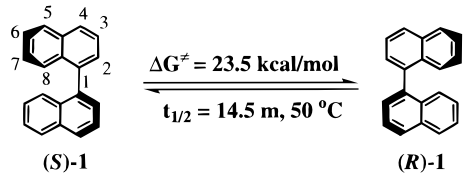
1. Introduction

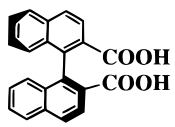
The atropisomerism of biaryl molecules has been studied extensively.[1] Increased hindrance to rotation at the pivotal 1,1′-bond can make these molecules resolvable as optically active enantiomers. One particularly interesting class of such biaryl compounds is that of 1,1′-binaphthyls. The racemization kinetics of optically active 1,1′-binaphthyl [(*R*)- or (*S*)-**1**] was studied by Cooke and Harris in 1963.[2] It was found that its racemization half-life was 14.5 min at 50 °C ($\Delta G^{\ddagger} = 23.5$ kcal/mol) (Scheme 1).[2] In 1971, Pincock et al. discovered that the racemic compound **1** underwent spontaneous resolution to generate the optically active *R*- or *S*-enantiomer when crystallized from the melt.[3] Pincock carried out 200 crystallization experiments of *rac*-**1** and found that the generation of the *R* or *S* enriched enantiomer was equally probable.

Scheme 1

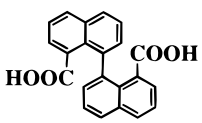


(*S*)-**1** (*R*)-**1**

When substituents are introduced into the 2,2′-positions of **1**, the chiral configuration of the 1,1′-binaphthyl compounds becomes very stable. For example, (*S*)-1,1′-binaphthyl-2,2′-dicarboxylic acid [(*S*)-(−)-**2**] could not be racemized at 175 °C in *N*,*N*-dimethylformamide.[4] However, the 8,8′-substituted compound **3** underwent racemization at a rate similar to that of **1**.[2] The half-life for racemization of the



(*S*)-**2**



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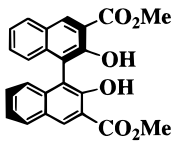
Lin Pu was born in 1965 in Xuyong, Sichuan Province, P. R. China. He received his B.S. degree in chemistry from Sichuan University in 1984. He then obtained the Doering Fellowship (the Chemistry Graduate Program of China) for graduate study in the United States and enrolled in the Department of Chemistry at University of California, San Diego, in 1985. Under the supervision of Professor Joseph M. O'Connor, he obtained his Ph.D. degree in 1990. From January 1991 to November 1992, he studied in Professor Henry Taube's laboratory at Stanford University as a postdoctoral fellow. From November 1992 to August 1994, he joined Professor Robert H. Grubbs' research group at California Institute of Technology to continue his postdoctoral training. In the fall of 1994, he became an Assistant Professor in the Department of Chemistry at North Dakota State University. In the fall of 1997, he moved to University of Virginia as an Associate Professor in the Department of Chemistry. The research projects in his laboratory focus on the design and synthesis of novel chiral polymers and the study of their applications in areas such as asymmetric catalysis, chiral separation, chiral sensors, and electrical and optical materials.

optically active **3** was 51.5 min at 50 °C ($\Delta G^{\ddagger} = 24.4$ kcal/mol). This may be due to steric repulsion of the 1,8-substituents on the naphthalene rings of **3** causing a rise in the ground-state energy and deformation of the molecule.

Absolute configurations of chiral binaphthyl compounds were originally proposed by Mislow on the basis of a study of optical properties, stereochemical mechanisms, and thermal analysis.[5] This was later confirmed by Yamada and co-workers from the X-ray analysis of (*R*)-(+)-**4** and its chemical correlation with other binaphthyl molecules.[6] In (*R*)-(+)-**4**, the dihedral angle between the two naphthalene rings is about 77°.



(*R*)-(+)-4

An optically pure 1,1′-binaphthyl molecule can exist in two conformations, either cisoid or transoid, as shown in Figure 1. In the (*S*)-cisoid conformation, the dihedral angle between the two naphthalene rings is less than 90°, whereas, in the (*S*)-transoid conformation, the dihedral angle is greater than 90°. The crystal structure of *rac*-**1** shows that it exists in the cisoid conformation with a dihedral angle of 68°.[7−9] However, its optically active crystals exist in the transoid conformation with a dihedral angle of 103°.[7−9] Gottarelli, Solladie, and co-workers studied the conformation of 1,1′-binaphthyls that contain either bridged or unbridged 2,2′-substituents in nematic liquid crystals.[10,11] Both their results and those

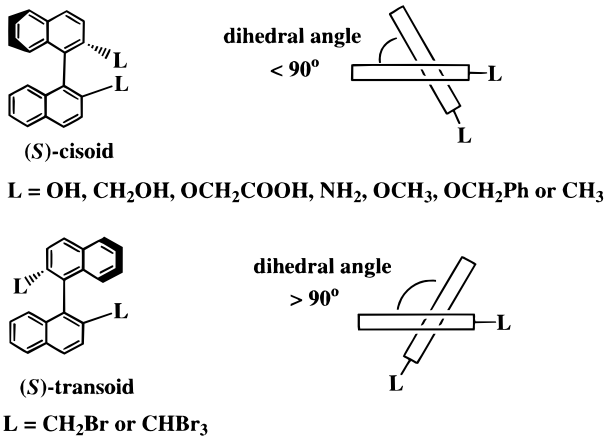


Figure 1.

of Mason's[12,13] have indicated that when the 2,2′-substituents L of the 1,1′-binaphthyl molecules are either small or capable of intramolecular hydrogen bonding, e.g., when L = OH, CH_2OH, OCH_2COOH, NH_2, OCH_3, CH_3, or OCH_2Ph, the cisoid conformation is preferred. When the 2,2′-substituents are large, e.g., when L = CH_2Br or $CHBr_2$, the transoid conformation is preferred. The CD spectra of compounds with the cisoid conformation are almost the mirror images of those with the transoid conformation even though their binaphthyl units have the same configuration, i.e., there is a dramatic inversion of the sign of the CD signals between the two conformations. The dynamics of the atropisomerization of **1** in liquid crystalline solvents was also studied by Weiss and co-workers.[14]

Because of their highly stable chiral configuration, the 2,2′-substituted 1,1′-binaphthyls have been extensively used to control many asymmetric processes and have demonstrated outstanding chiral discrimination properties.[15−17] Most 1,1′-binaphthyl molecules are C_2 symmetric with two identical naphthyl units. The rigid structure and the C_2 symmetry of the chiral binaphthyl molecules play important role in chiral induction. Binaphthyl-based C_1 symmetric catalysts or reagents have also been prepared and studied. Figure 2 lists a few examples of optically active monomeric binaphthyl molecules that have been used in asymmetric catalysis and chiral recognition. The rhodium and ruthenium complexes of (*S*)-**5** are used in catalytic asymmetric hydrogenations.[18−20] The Lewis acid complexes of (*R*)-**6** are used in an asymmetric hetero-Diels−Alder reaction[21] as well as an asymmetric Claisen rearrangement.[22] The titanium(IV) complexes of (*R*)-**7** are used in asymmetric aldol condensations.[23,24] Chiral metallocene complexes prepared from (*S*)-**8** have also been studied.[25,26] The enantioselective complexation of the binaphthyl-based crown ethers (*S*)-**9**,[27] (*S*)-**10**,[28,29] and (*S*)-**11**[30] with various chiral guest molecules has been investigated.

1,1′-Bi-2-naphthol (BINOL), **12**, often serves as the starting material for obtaining chiral binaphthyl compounds.[15−17] The 2,2′-hydroxyl groups of **12** can easily be converted into other functional groups. In addition, the 3,3′-, 4,4′-, and 6,6′-positions can be selectively functionalized, leading to a variety of binaphthyl derivatives. Because of the importance

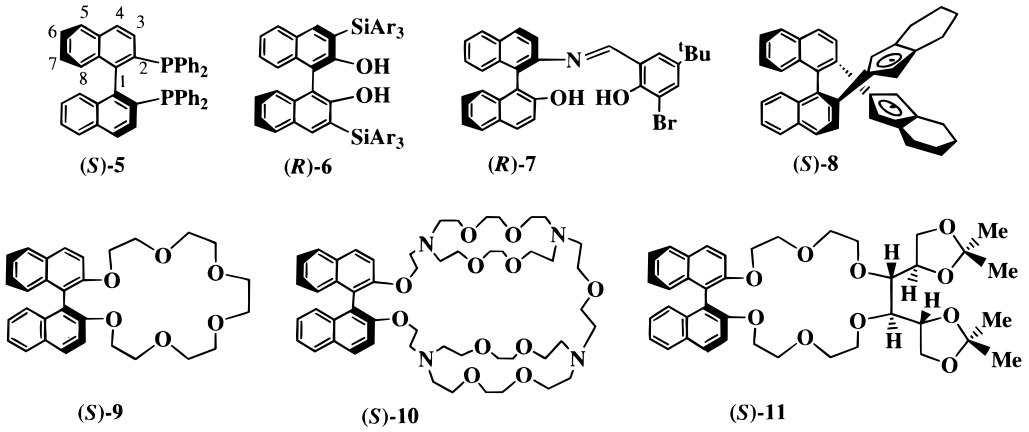
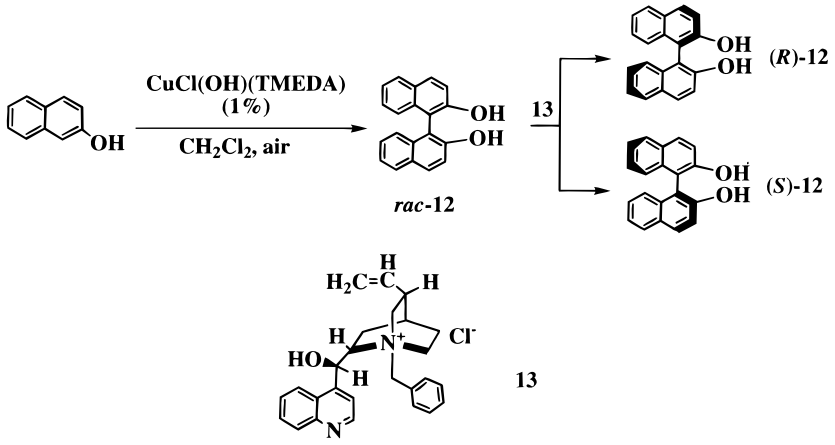


Figure 2.

Scheme 2



of this molecule, much effort has been devoted to preparing it in optically pure form.[31] Among the many methods reported, the use of (8*S*,9*R*)-(−)-*N*-benzylcinchonidinium chloride (**13**) to resolve racemic **12** into its optically pure *R*- and *S*-enantiomers is currently considered the simplest and also the most efficient laboratory procedure (Scheme 2).[32−35] This method was first developed by Toda et al.[32,33] and later improved by Pu[34] and Cai.[35] Both (*R*)-**12** and (*S*)-**12** can be obtained on a large scale with high optical purity using this method. The chiral resolving agent **13** is easily recovered after the resolution.[34] It is commercially available and can also be synthesized from the reaction of (−)-cinchonidine with benzyl chloride.[36] Racemic **12** is produced on a large scale from the oxidative coupling of 2-naphthol in air in the presence of a copper catalyst (Scheme 2).[34,37]

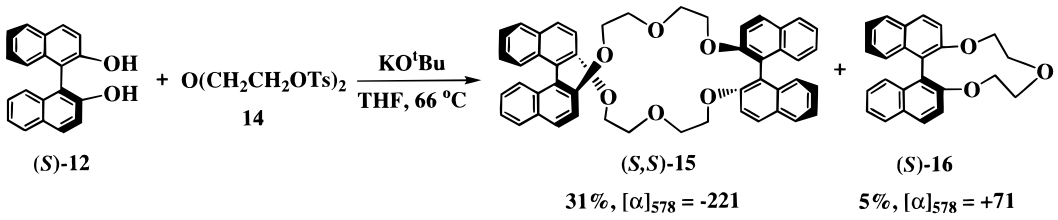
Although the study of monomeric chiral binaphthyl compounds continues to be of interest to many research groups, multiple binaphthyl units have been linked to extend the chiral differentiation power of the binaphthyl structure as well as giving rise to both molecules and polymers with unique structures and properties. This review will summarize recent studies of macrocycles, metal complexes, linear oligomers, and polymers containing two or more binaphthyl units. Materials made by anchoring monomeric binaphthyl compounds to organic polymers or inorganic solid supports are not included in this review.

For convenience, the discussion of binaphthyl-based materials in this article is divided into four parts. The first part describes the application of multibinaphthyl-based chiral hosts to molecular recognition. The second part covers the application of multibinaphthyls and polybinaphthyls to organic transformations, mainly asymmetric catalysis. The third part summarizes the use of binaphthyl polymers in the construction of new materials. The fourth part includes miscellaneous oligomeric binaphthyl molecules.

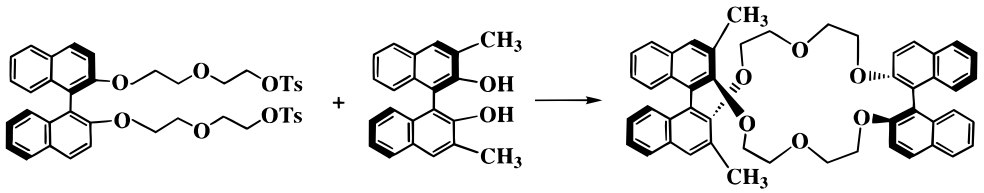
2. Multibinaphthyls in Chiral Recognition

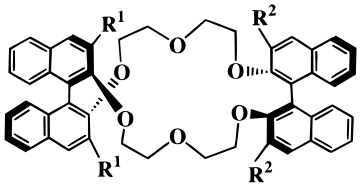
Research on the application of binaphthyls to molecular recognition was pioneered by Cram. All the multibinaphthyl hosts developed for molecular recognition purposes are macrocyclic compounds including crown ethers, cyclophanes, and cyclic amides. These macrocycles either undergo complexation-induced organization in the presence of the guest molecules or have preorganized cavities based on rigid structures. They interact with the functional groups of guest molecules through weak forces such as hydrogen bonding, $\pi-\pi$ stacking, and van der Waals forces. The chirality of the binaphthyl units in these hosts leads to their enantioselective complexation with chiral guest molecules. Chiral recognition of this kind has been applied to the resolution of racemic molecules such as amino acids, amino esters, amines, sugars, and other chiral alkyl or aryl compounds.

Scheme 3



Scheme 4





(*R*,*R*)-**20**

R^1 and R^2 are either the same or different groups including H, CH_3, CH_2OH, CH_2Cl, $C(CH_3)_2OH$, $CH(CH_3)_2$, $CH_2OCH_2CO_2CH_3$, CH_2OCH_2COOH, $CH_2N(CH_2CH_2)_2O$, etc.

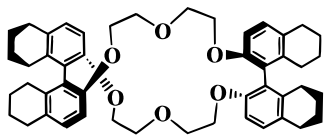
2.1. Cram's Multibinaphthyl Crown Ethers

Since the early 1970s, extensive studies on the use of chiral binaphthyl-based crown ethers as hosts for molecular recognition have been conducted in Cram's laboratory.[27,38−60] The first chiral bisbinaphthyl crown ether was reported in 1973.[27] As shown in Scheme 3, the reaction of (*S*)-**12** with diethylene glycol ditosylate (**14**) in the presence of potassium *tert*-butoxide in THF produced the bisbinaphthyl crown ether (*S*,*S*)-**15** in 31% yield. A small amount of a monobinaphthyl crown ether (*S*)-**16** was also obtained. The specific optical rotation of (*S*,*S*)-**15** was $[\alpha]_{578} = -221$. (*R*,*R*)-**15** was obtained from the reaction of (*R*)-**12** with **14**. These bisbinaphthyl crown ethers have a D_2 symmetry.

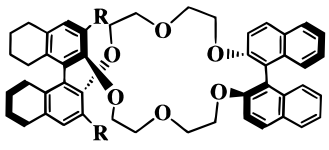
Methyl groups were introduced into the 3,3′-positions of one of the binaphthyl units in the bisbinaphthyl macrocycle to produce unsymmetric chiral crown ethers.[39] (*R*,*R*)-**19** was produced in 32% yield from the reaction of (*R*)-**17** with (*R*)-**18** (Scheme 4). The specific optical rotation of (*R*,*R*)-**19** was $[\alpha]_{578} = +152$. In a similar way, chiral bisbinaphthyl macrocycles (*R*,*R*)-**20** containing a variety of substituents in the 3,3′-positions were obtained.[40]

The 6,6′-positions of the bisbinaphthyl macrocycles were functionalized by either tetrabromination or tetraacylation of (*R*,*R*)-**15** directly to generate both (*R*,*R*)-**21** and (*R*,*R*)-**22** (Figure 3).[40] The chiral macrocycles **23**−**26** containing different functional groups in the 6,6′-positions were also prepared.[40] Because the 6,6′-positions are some distance from the crown ether cycle, substituents were introduced in order to adjust the solubility of the binaphthyl compounds, or in other cases to further incorporate these compounds into polymers or solid supports without significantly changing the binding properties of the chiral crown ether functions.

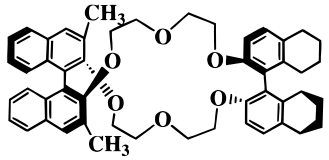
(*S*,*S*)-**15** was converted to (*S*,*S*)-**27** with each of the four naphthalene rings tetrahydrogenated under 3 atm of H_2 over PtO_2.[40] In this reaction, only the benzene rings with lower electron density were reduced. The crown ethers, (*R*,*R*)-**28** and (*S*,*S*)-**29**, containing both partially hydrogenated and nonhydrogenated binaphthyl units were made in multistep syntheses.[40]



(*S*,*S*)-**27**



(*R*,*R*)-**28**
R = H, CH_3, Br



(*S*,*S*)-**29**

Compounds **30**−**42** with different functional groups incorporated into the rim of the bisbinaphthyl crown ether macrocycles were prepared (Figure 4). For example, a pyridine-containing bisbinaphthyl macrocycle (*S*,*S*)-**30** was obtained in 26% yield from the

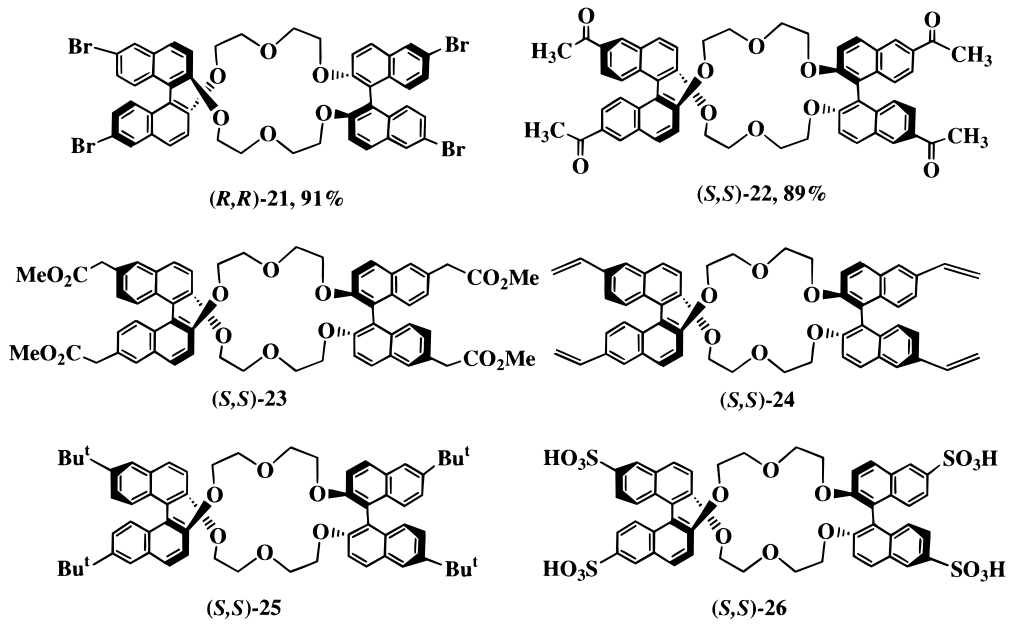


Figure 3.

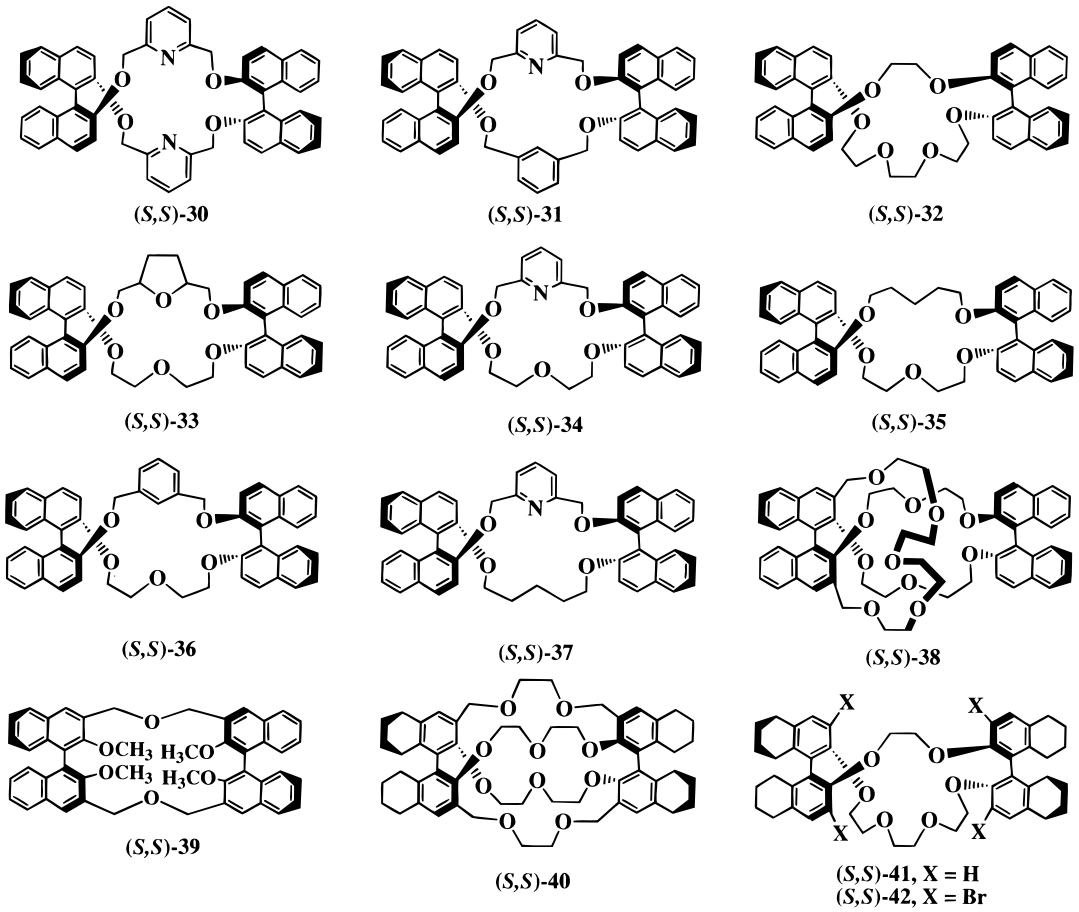
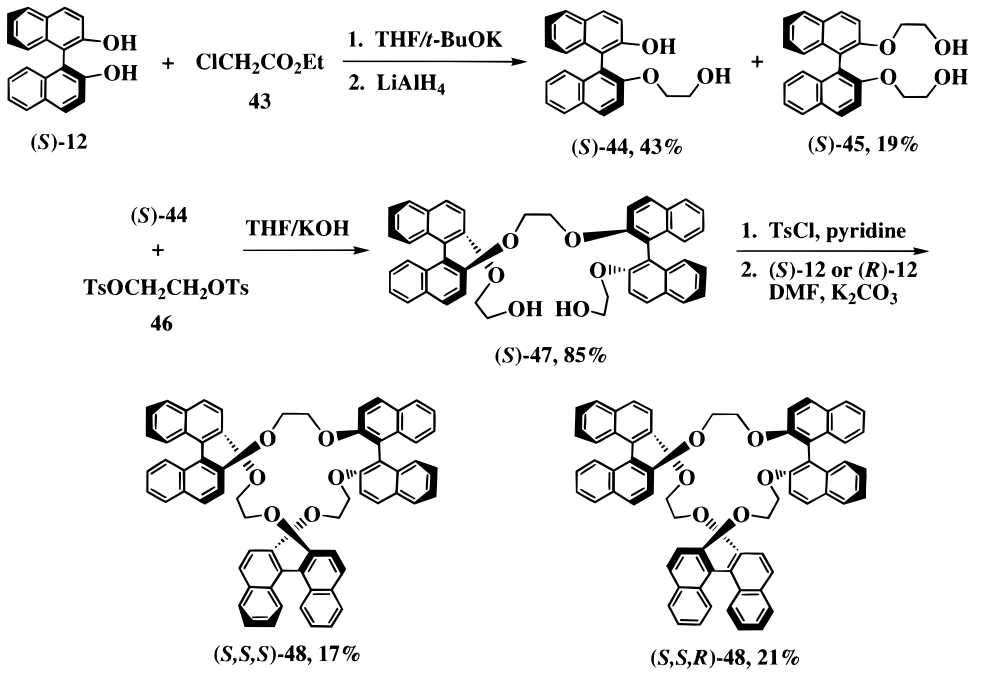


Figure 4.

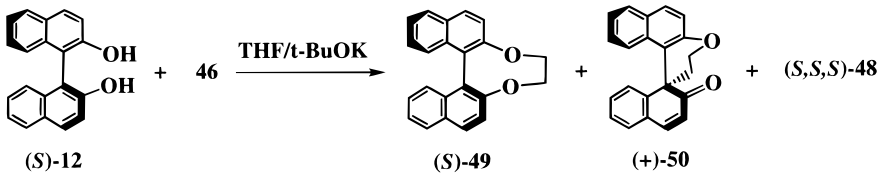
reaction of (*S*)-**12** with 2,6-bis(chloromethyl)pyridine in the presence of potassium *tert*-butoxide and THF.[38] Compounds **31**−**42** with unsymmetrical functional groups on the ring were made in a stepwise fashion.[38,41] (*S*,*S*)-**32** was partially hydrogenated to give (*S*,*S*)-**41** which was then converted to (*S*,*S*)-**42** on reaction with bromine.[40]

Three binaphthyl units were also joined together to make chiral macrocycles (Scheme 5).[38] From the reaction of (*S*)-**12** with ethyl chloroacetate (**43**) followed by reduction, (*S*)-**44** and (*S*)-**45** were obtained in 43% and 19% yields, respectively. The reaction of (*S*)-**44** with ethylene glycol ditosylate (**46**) generated (*S*)-**47** which reacted with (*S*)-**12** and (*R*)-**12**

Scheme 5

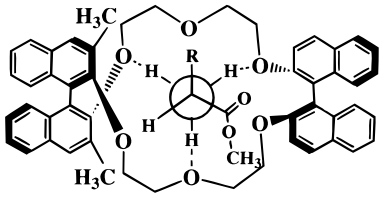


Scheme 6



respectively to give the trisbinaphthyl crown ethers (*S*,*S*,*S*)-**48** and (*S*,*S*,*R*)-**48**. The direct reaction of (*S*)-**12** with **46** in the presence of potassium *tert*-butoxide and THF generated (*S*)-**49** and (+)-**50** as the major products, and (*S*,*S*,*S*)-**48** as the minor product (Scheme 6).

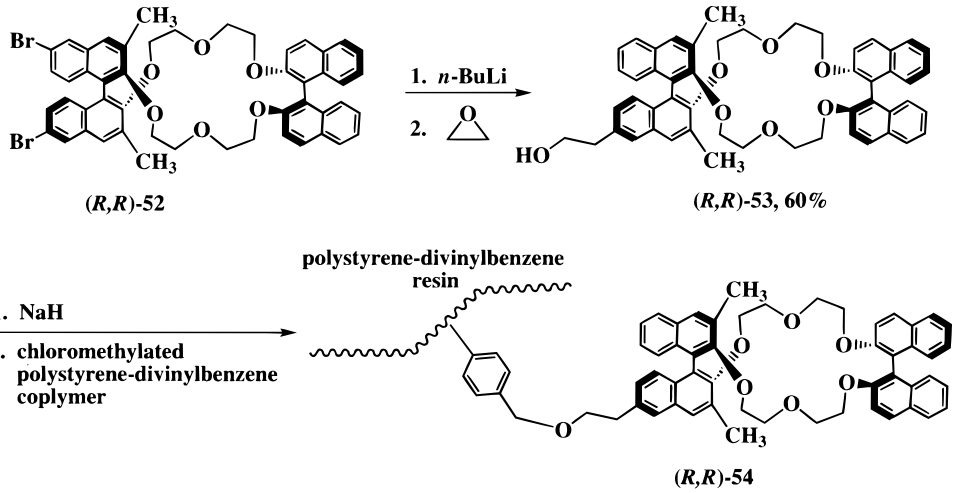
The chiral recognition abilities of all the binaphthyl macrocycles have been investigated.[27,38−50] The 3,3′-dimethylbisbinaphthyl macrocycle, (*R*,*R*)-**19** or (*S*,*S*)-**19,** was found to be the best chiral host in the differentiation of enantiomeric salts of chiral amines, chiral amino acids, and amino esters.[39,43,44] The chiral recognition factors, D_A/D_B (D_A being the distribution coefficient of the more complexed enantiomer; D_B that of the less complexed) as high as 52 for $PhCH(NH_3^+)CO_2HClO_4^-$, 48 for p-$HOC_6H_4CH(NH_3^+)CO_2HClO_4^-$, and 31 for $PhCH(CO_2CH_3)NH_3^+PF_6^-$ were observed when (*R*,*R*)-**19** or (*S*,*S*)-**19** was used to extract these ammonium salts from aqueous solution into the organic phase (chloroform or chloroform/acetonitrile solution). The D enantiomers of the amino acid or ester salts bind with the host (*R*,*R*)-**19** more favorably than the L enantiomers. Such high chiral recognition is due to a complementary complexation between host and guest. According to the Corey−Pauling−Koltun (CPK) model, the preferred complex between (*R*,*R*)-**19** and a *R* chiral amino ester has a structure such as shown in **51**. In this host−guest complex, the binding between the crown ether and the amino ester salt involves three O−H−N hydrogen bonds and a $\pi-\pi$ attractive interaction of the ester group with a naphthalene ring. This four-point binding is essential for the observed high chiral recognition. A single-crystal X-ray structure of (*S*,*S*)-**15** complexed with the hexafluorophosphate salt of (*R*)-phenylglycine methyl ester, the less stable diastereomeric complex, was obtained.[51] Structural analysis indicated that the introduction of substituents into the 3,3′-positions of (*S*,*S*)-**15** would increase the steric interaction between the two binaphthyl units in this unfavorable diastereomeric complex and further destablilize it. This led to the observed much higher chiral recognition capability of (*S*,*S*)-**19** over (*S*,*S*)-**15**. Crown ethers made of monobinaphthyl units generally showed lower enantioselectivity than the corresponding bisbinaphthyl hosts.[47] A liquid−liquid extraction device was designed to use (*S*,*S*)-**19** and (*R*,*R*)-**19** to catalytically resolve racemic amino ester salts. This technique could continuously extract enantiomers with up to 90% optical purity.[45]



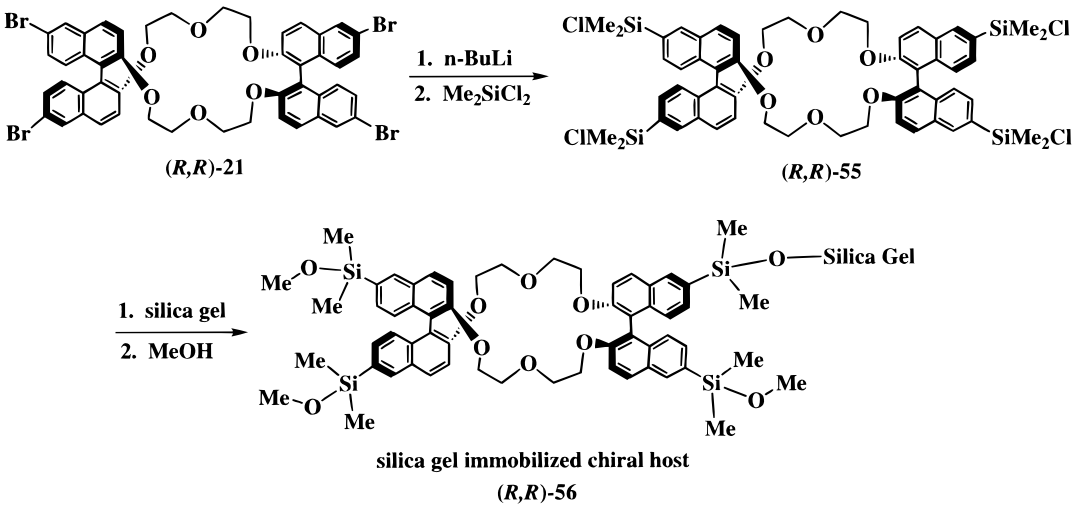
51, a (*R*,*R*)-19-(*R*)-amino ester complex

Apart from the use of these chiral crown ethers in liquid−liquid extractions, (*R*,*R*)-**19** was also covalently bound to polymer resins for the preparation of

Scheme 7



Scheme 8



chiral stationary phases for enantioselective chromatography.[52] When 6,6′-dibromobisbinaphthyl crown ether (*R*,*R*)-**52** was treated with *n*-butyllithium followed by reaction with ethylene oxide, (*R*,*R*)-**53** was obtained (Scheme 7). This molecule was then grafted onto a chloromethylated polystyrene-divinylbenzene polymer resin to yield a polymeric material (*R*,*R*)-**54**. Chromatography columns made using (*R*,*R*)-**54** gave baseline separation for the enantiomers of a number of amino acid and amino ester salts. The chiral recognition behavior of the immobilized host parallels that of the macrocycle itself.

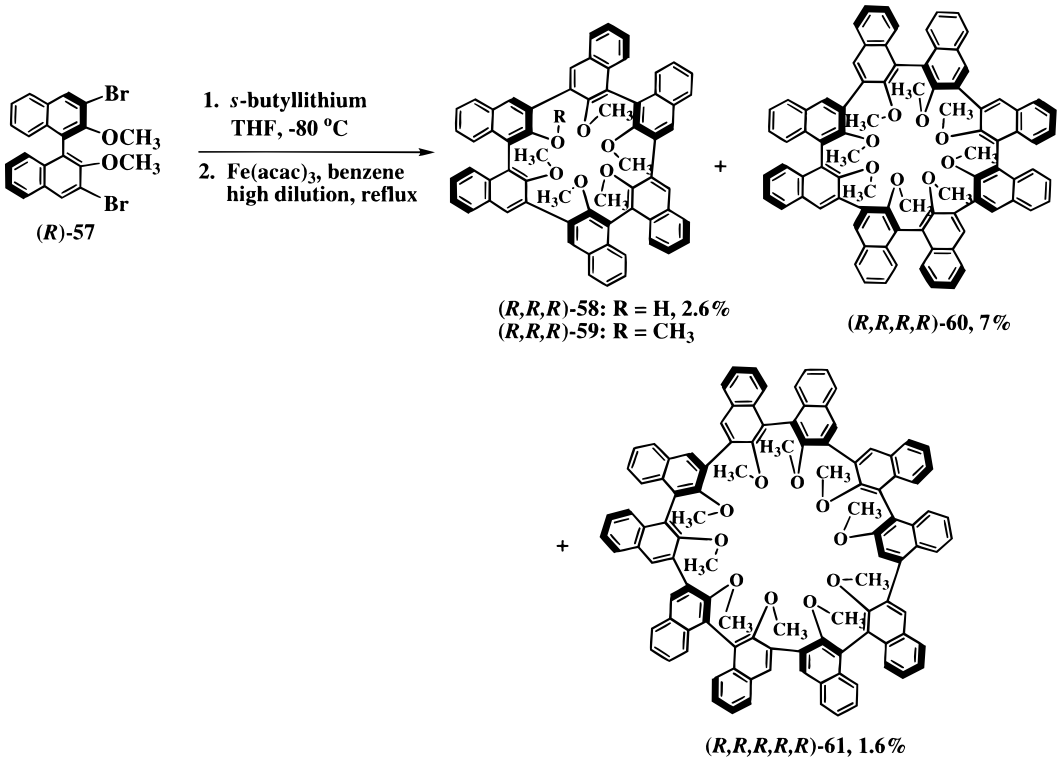
The tetrabromobisbinaphthyl molecule (*R*,*R*)-**21** was converted to (*R*,*R*)-**55** by reaction with *n*-butyllithium and then dichlorodimethylsilane (Scheme 8). Treatment of (*R*,*R*)-**55** with silica gel produced the immobilized material (*R*,*R*)-**56**. After pretreatment with trimethylsilyl chloride, (*R*,*R*)-**56** was used for the chromatographic separation of racemic amino ester salts. Baseline separation was observed for the enantiomeric methyl ester salts of *p*-hydroxyphenylglycine, phenylalanine, tyrosine, and tryptophan with chloroform as eluent.[54−56]

2.2. Structurally Rigid Multibinaphthyl Macrocycles

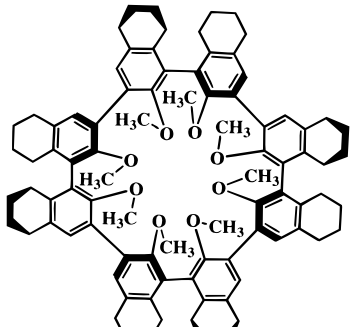
The recognition ability of chiral crown ethers toward amino acid salts as described above involves a reorganization of the polyether functions on complexation with the ammonium groups of the amino acids. Such complexation-induced reorganizations can produce chiral cavities for enantioselective discrimination. Binaphthyl compounds have also been used to build structurally rigid macrocycles that have preorganized rigid chiral cavities for molecular recognition.

In 1981, Cram and co-workers reported the self-coupling of (*R*)-3,3′-dibromo-2,2′-dimethoxy-1,1′-binaphthyl, (*R*)-**57**, which generated a mixture of chiral macrocycles (Scheme 9).[61] In this reaction, (*R*)-**57** was first treated with *sec*-butyllithium at −80 °C in THF, and the resulting solution was then added to a refluxing benzene solution of $Fe(acac)_3$ (acac = acetylacetonate) under very dilute conditions. After completion of the reaction, macrocycles (*R*,*R*,*R*)-**58**, (*R*,*R*,*R*,*R*)-**60**, and (*R*,*R*,*R*,*R*,*R*)-**61** were isolated in 2.6%, 7%, and 1.6% yields, respectively. In (*R*,*R*,*R*)-**58**, one of the methyl groups was removed during the isolation. This molecule was converted to (*R*,*R*,*R*)-**59** by reac-

Scheme 9



tion with potassium hydroxide and $(CH_3)_2SO_4$. A partially hydrogenated macrocycle (*R*,*R*,*R*,*R*)-**62** was prepared in a similar way starting from the corresponding partially hydrogenated binaphthyl monomer. These compounds are members of a class called

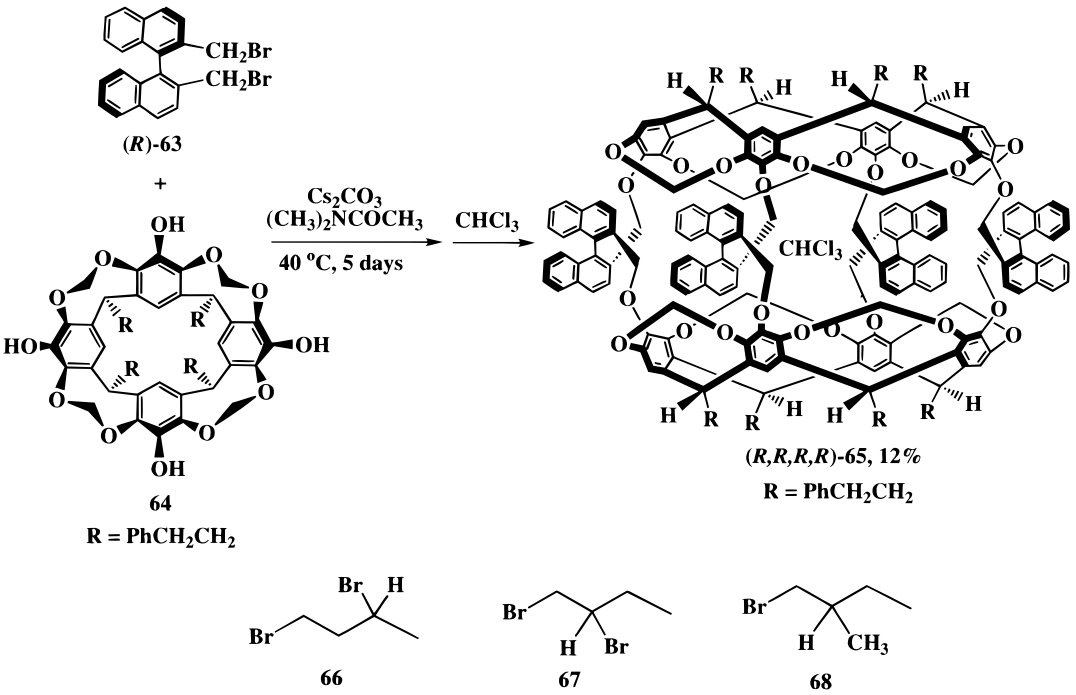


spherands—a family of molecules with completely preorganized ligand systems. They show selective binding with alkaline metal cations as well as ammonium salts. The cavity sizes of these molecules with the methyl groups facing outward and the oxygen facing inward are 1.5−2.0 Å for (*R*,*R*,*R*)-**59**, 3.4−5.2 Å for (*R*,*R*,*R*,*R*)-**60**, and 6−8.4 Å for (*R*,*R*,*R*,*R*,*R*)-**61**. The chiral recognition properties of these molecules was not reported. The poor yield of these interesting molecules might prove an obstacle to further study.

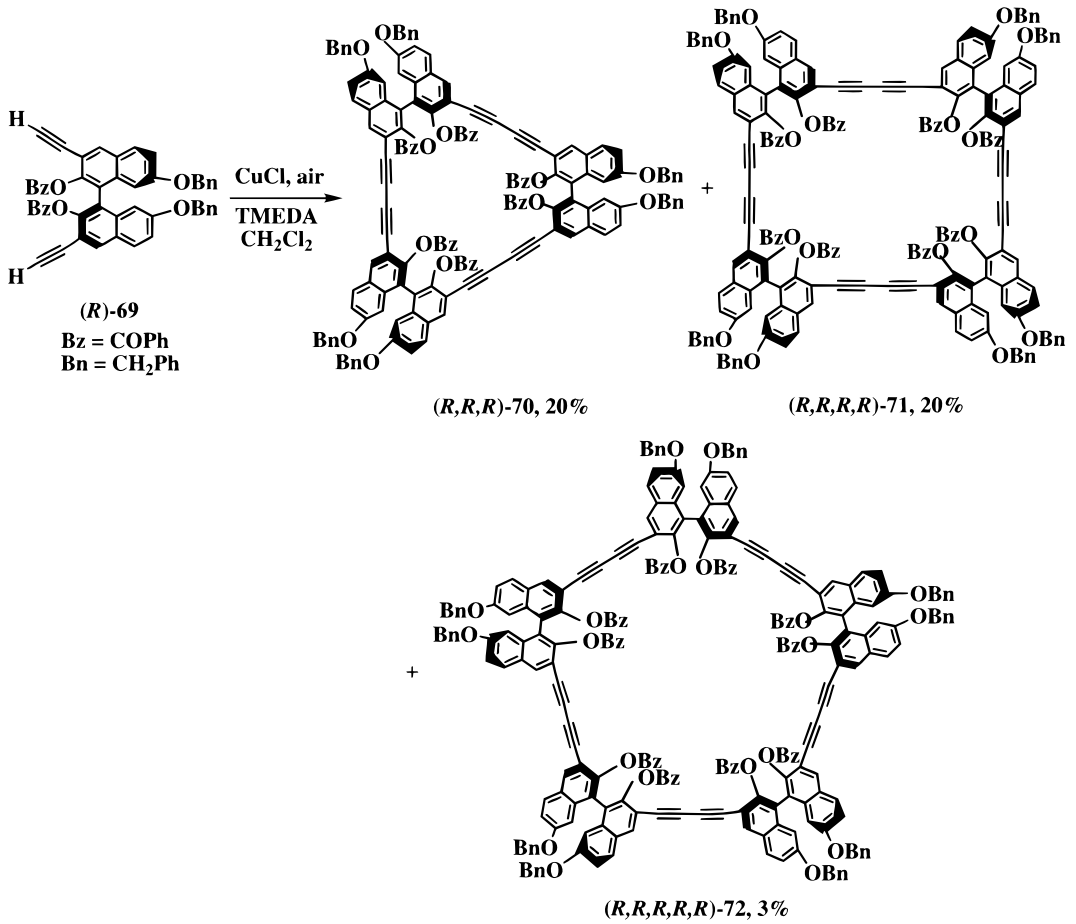
Cram and co-worker also used multiple binaphthyls to build chiral hemicarcerands capable of complexing molecules within their hollow interiors.[62] An optically pure hemicarcerand (*R*,*R*,*R*,*R*)-**65** was obtained as an 1:1 complex with $CHCl_3$ from the reaction of (*R*)-**63** with **64** (Scheme 10). This reaction was carried out at 40 °C in the presence of Cs_2CO_3 over 5 days and produced (*R*,*R*,*R*,*R*)-**65** in 12% yield. (*S*,*S*,*S*,*S*)-**65** was obtained from the reaction of (*S*)-**63** with **64**. (*S*,*S*,*S*,*S*)-**65** showed enantioselective binding when treated with a racemic mixture of chiral molecules such as **66**−**68**. After the displacement of the interior $CHCl_3$ molecule, the ratios of the two diastereomeric complexes between the host and enantiomers of the guest molecules **66**−**68** were about 2:1.

In 1995, Diederich and co-workers reported the self-coupling of a dilute methylene chloride solution of the optically pure binaphthyl alkyne molecule (*R*)-**69** (4×10^{-4} M) in the presence of CuCl in air.[63] A mixture of rigid chiral oligocyclophanes, (*R*,*R*,*R*)-**70** (20%), (*R*,*R*,*R*,*R*)-**71** (20%), and (*R*,*R*,*R*,*R*,*R*)-**72** (3%), were produced and isolated (Scheme 11). The specific optical rotations of these macrocycles in methylene chloride solution were $[\alpha]_D = -869.5$, −855.6, and −838.8, respectively. The specific optical rotation of the monomer (*R*)-**69** was $[\alpha]_D = +26.6$. Thus, on going from the monomer to the macrocycles, there was a large increase in the degree of the optical rotations as well as a change in sign. However, among the macrocycles, their specific optical rotations were very similar. (*R*,*R*,*R*)-**70** and (*R*,*R*,*R*,*R*)-**71** were hydrolyzed with potassium hydroxide in MeOH/THF to give (*R*,*R*,*R*)-**73** and (*R*,*R*,*R*,*R*)-**74** containing multiple hydroxyl groups inside the macrocycles (Figure 5). These molecules have been used as carbohydrate receptors. Computer modeling and CPK models showed that the size and shape of (*R*,*R*,*R*)-**73** was complementary to a hexopyranose molecule. Its interaction with the octyl glucopyranosides **75**−**78** was studied (Figure 5). As shown by ^{1}H NMR spectroscopy, (*R*,*R*,*R*)-**73** formed stable 1:1 complexes with these sugars in $CDCl_3$ with a modest enanti-

Scheme 10



Scheme 11



oselective binding. The ratio of the binding constants of (*R*,*R*,*R*)-**73** with the two enantiomers **75** and **77** was 2.2:1. The monomeric binaphthyl compound (*R*)-**79** did not show significant complexation with these sugars.

The tetrabinaphthyl macrocyclic alcohol (*R*,*R*,*R*,*R*)-**74** was converted into a tetraphosphate (*R*,*R*,*R*,*R*)-**80** by reaction with $POCl_3$ in the presence of triethylamine followed by hydrolysis and ion exchange. The interaction of this anionic host with the sugar **76**

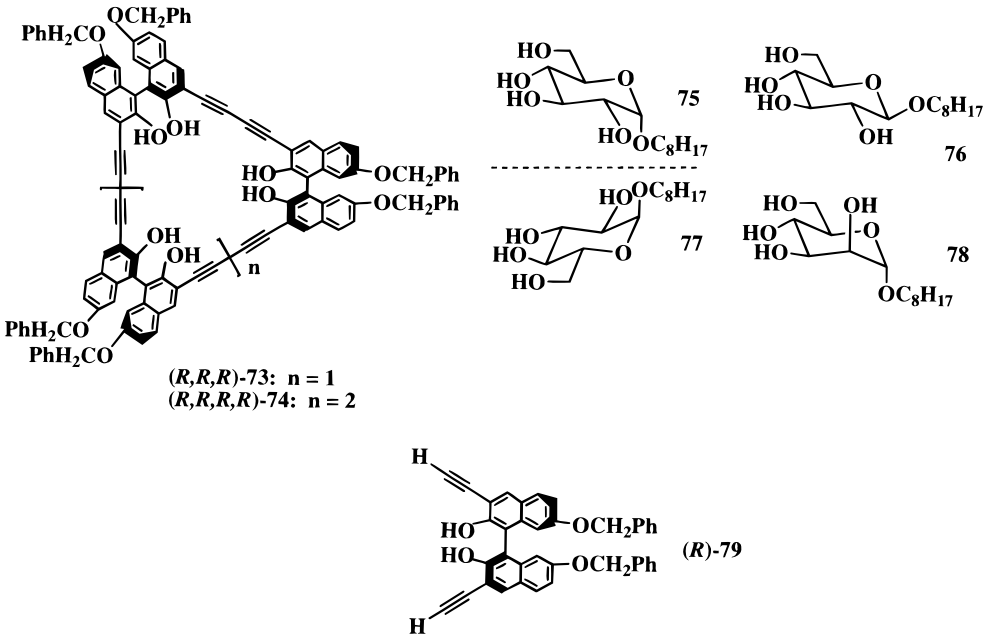
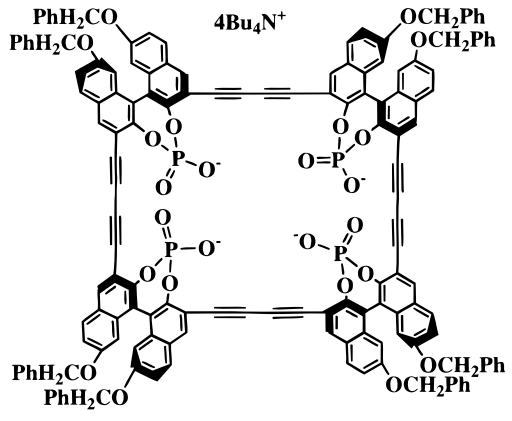
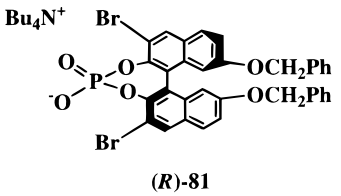


Figure 5.

demonstrated that (*R*,*R*,*R*,*R*)-**80** had a greatly enhanced binding ability over the neutral host due to the strong ionic hydrogen bonds between (*R*,*R*,*R*,*R*)-**80** and the sugar hydroxyl groups. Higher guest to host complexation, with probably formation of a 2:1 complex, was observed when excess **76** was used with (*R*,*R*,*R*,*R*)-**80**. The sugar molecule possibly approached the host molecule from opposite sides of the macrocycle to form the 2:1 complex. The host−guest complex of (*R*,*R*,*R*,*R*)-**80** with **76** was generated even in 20% methanol in acetonitrile. However, when the host was in excess, a 1:1 host−sugar complex dominated. No detectable binding between the monomeric binaphthyl compound (*R*)-**81** with the sugar **76** was observed when methanol was used as a cosolvent. In pure acetonitrile solution, there was formation of a weak 1:1 complex of (*R*)-**81** with **76**.





A larger tetrabinaphthyl anionic rigid macrocycle **84** was also synthesized (Scheme 12).[64] The palladium-catalyzed cross-coupling of a monoprotected 3,3′-diethynylbinaphthyl molecule (*R*)-**82** with 1,4-diiodobenzene gave (*R*,*R*)-**83** in 50% yield.[64] After removal of the trimethylsilyl protecting groups followed by oxidative coupling, hydrolysis, phosphonation, and ion exchange, the tetraanionic macrocycle (*R*,*R*,*R*,*R*)-**84** was obtained. The size of the preorganized cavity in this molecule is 11.6 × 7.2 Å, significantly larger than that found in (*R*,*R*,*R*,*R*)-**80** (7.2 × 7.2 Å). As shown by ^{1}H NMR titrations, (*R*,*R*,*R*,*R*)-**84** bound disaccharides **85**−**87** to form 1:1 complexes with very high association constants ($K_a \approx 10^4$ L/mol) in acetonitrile solution containing 12% methanol. However, no binding was observed between the host and the monosacharride **76** in the same solvent system. This is probably due to the fact that **76** could not form the necessary ionic hydrogen bonds with all four convergent phosphates within the large cavity of (*R*,*R*,*R*,*R*)-**84**. This host molecule, therefore, proved highly selective toward disaccharide guests over monosacharrides. (*R*,*R*,*R*,*R*)-**84** did not show selective binding toward a series of different disaccharides. In pure acetonitrile solution, (*R*,*R*,*R*,*R*)-**84** complexed the monosaccharide **76** presumably through the formation of a 2:1 host−guest complex.

In 1996, Stoddart and co-workers synthesized a bisbinaphthyl-based cationic chiral cyclophane capable of asymmetric recognition of aromatic compounds.[65] The self-assembly of (*R*)-**88**, 1,4-bis(2-(2-hydroxyethoxy)ethoxy)benzene (**89**), and (*R*)-**90** at room temperature led to the formation of (*R*,*R*)-**91** in which the electron-rich aromatic ring of **89** was included inside the electron deficient bipyridinum cyclophane to form a host−guest complex through $\pi-\pi$ interaction (Scheme 13).[65] The **89** moiety was removed from the cyclophane to give the chiral macrocycle (*R*,*R*)-**92**. During this process, **89** served

Scheme 12

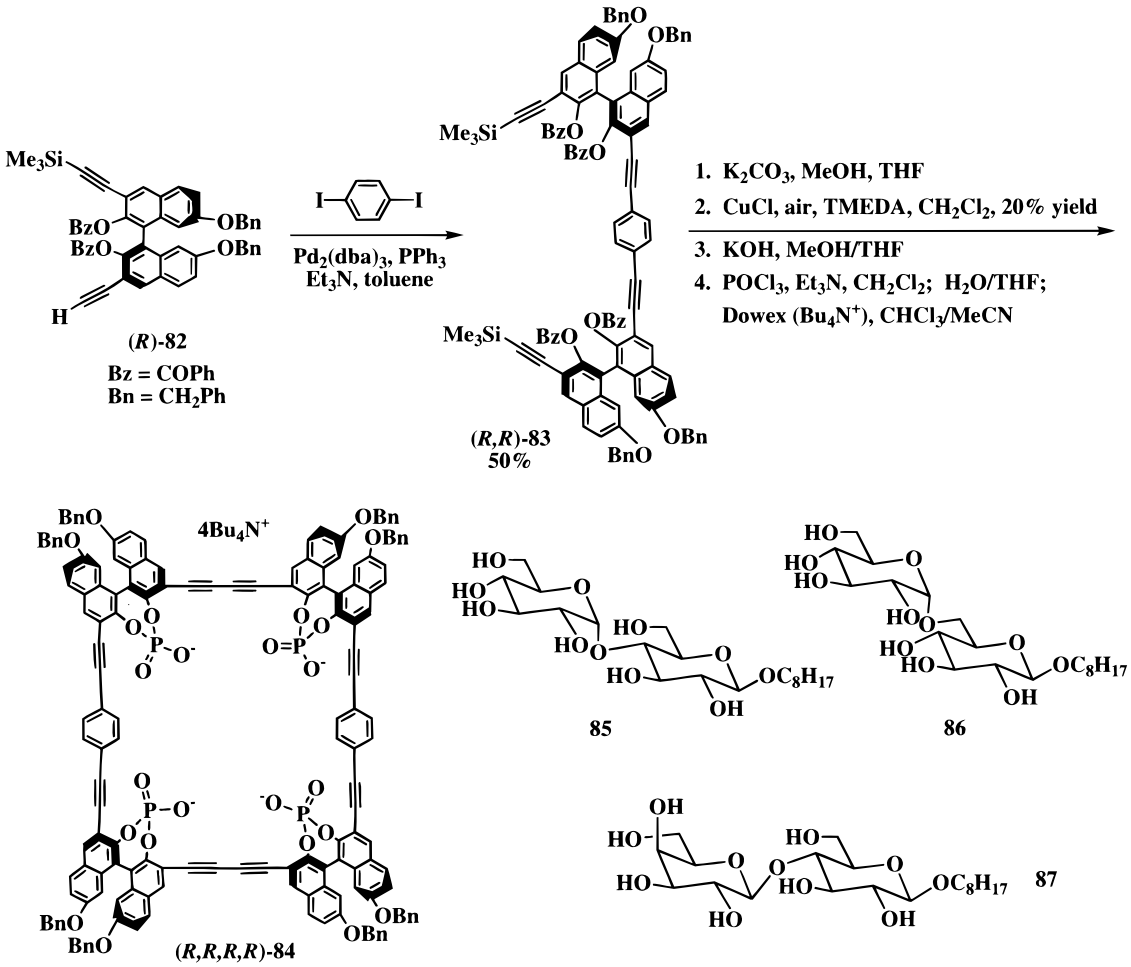
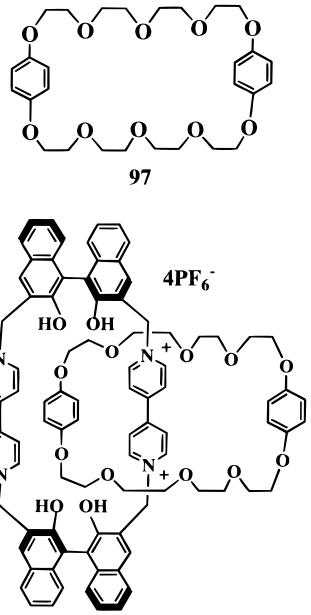


Table 1.

host	binding constants	**93**	**94**	**95**
(*R*,*R*)-**92**	Ka(L) (M^{-1})	219	2340	4280
	Ka(D) (M^{-1})	137	1047	1080
	Ka(L)/Ka(D)	1.60	2.23	3.96
(*R*)-**96**	Ka(L) (M^{-1})	1220	10060	20700
	Ka(D) (M^{-1})	2260	2125	2670
	Ka(L)/Ka(D)	0.54	4.73	7.75

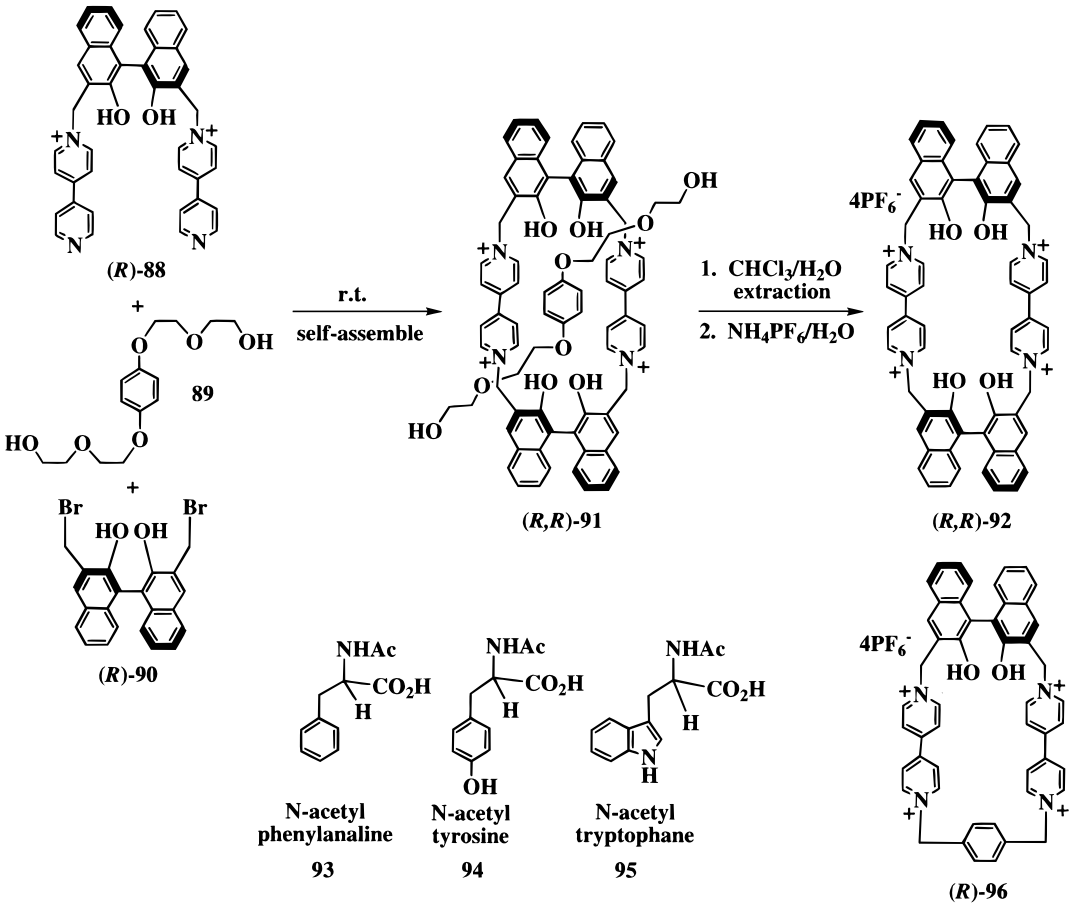
as a template for the induction of macrocycle formation. The cationic chiral cyclophane was used for the enantioselective recognition of amino acids containing aromatic substituents. The complexation of (*R*,*R*)-**92** with the L enantiomers of *N*-acetyl phenylanaline (**93**), *N*-acetyl tyrosine (**94**), and *N*-acetyl tryptophan (**95**) proved better than with the corresponding D enantiomers. Table 1 lists the relative binding constants of the L and D amino acid derivatives with the chiral host (*R*,*R*)-**92**. As shown in Table 1, the more electron rich the phenyl ring of the substrate, the larger the binding constant and the enantioselectivity. This is consistent with a primary host−guest binding mode to form complexes through electron-rich and electron-deficient $\pi-\pi$ interactions. The interaction of these amino acid derivatives with a monobinaphthyl ionic cyclophane (*R*)-**96** was also studied. (*R*)-**96** showed stronger complexation and better enantioselectivity toward the amino acid derivatives than (*R*,*R*)-**92**.

The self-assembly of (*R*)-**88**, (*R*)-**90**, and **97** in acetonitrile at room temperature was attempted,[66] but only trace amount of the chiral [2]catenane (*R*,*R*)-**98** was obtained. When **99**, a larger crown ether

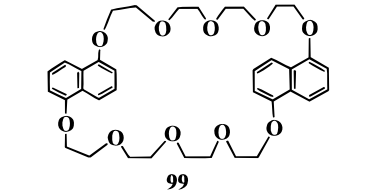


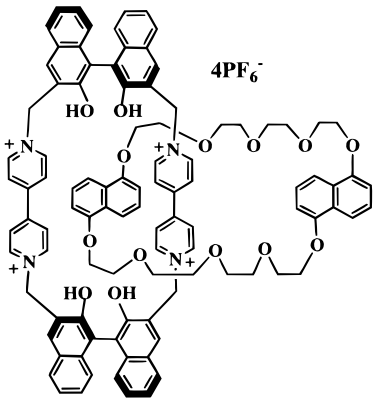
made from two 1,5-naphthylene units, was used in place of **97**, a chiral [2]catenane (*R*,*R*)-**100** was

Scheme 13

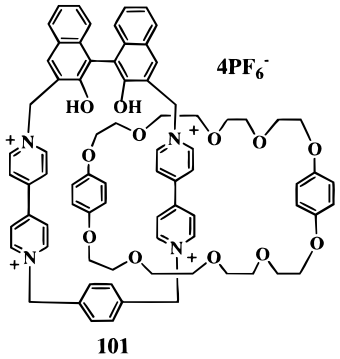


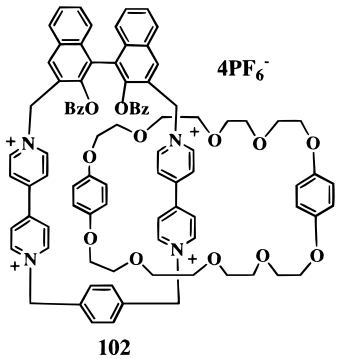
isolated after 14 days at room temperature in 47% yield. Since the association constant of (*R*,*R*)-**92** with 1,4-dioxyphenylenes was higher than with 1,5-dioxynaphthalenes, the inefficient formation of the bis-binaphthyl [2]catenane (*R*,*R*)-**98** is most likely due to the smaller cavity size of **97**.





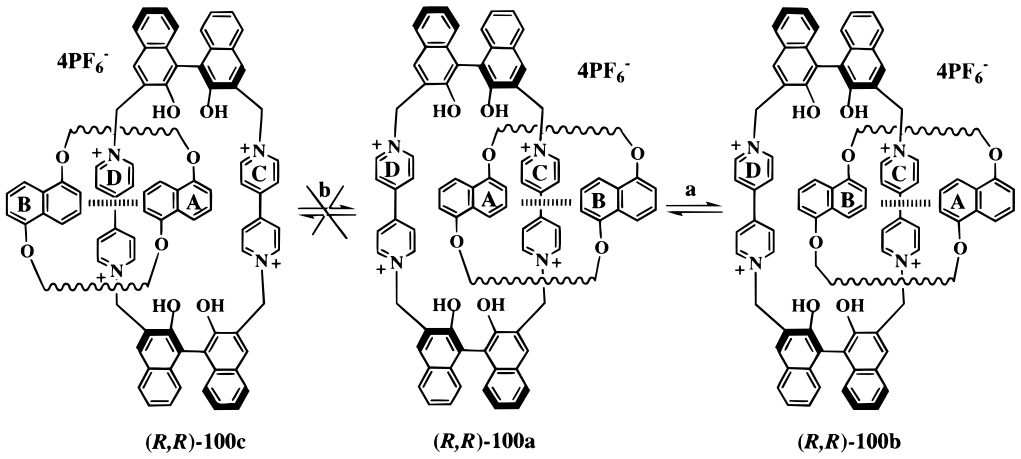
A racemic monobinaphthyl [2]catenane **101** was prepared in 54% yield in a similar self-assembly process.[66] (*R*)-**101** was also obtained from the optically active binaphthyl starting material. Benzoyl chloride was reacted with **101** in the presence of 2,6-lutidine to give **102** in quantitative yield. The



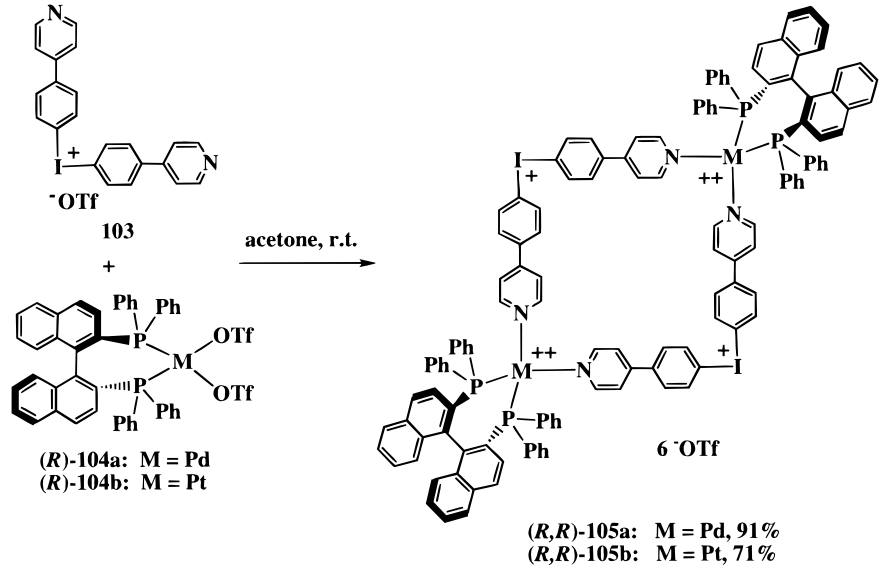


structure of racemic **101** was determined using X-ray

Scheme 14



Scheme 15



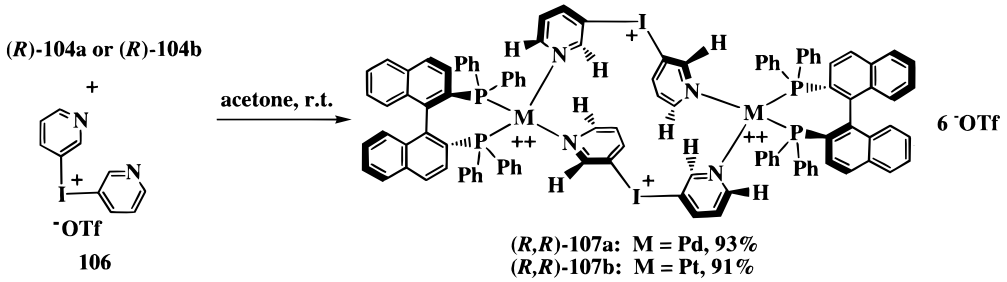
analysis. As expected, the bisphenylene crown ether was threaded through the center of the binaphthyl cyclophane with one of the hydroquinone rings included inside. The distance between the adjacent hydroquinone ring and pyridinium ring is about 3.5−3.6 Å. Hydrogen bonding between the binaphthyl hydroxyl protons and the second polyethyl oxygen was observed. The two naphthyl rings of the binaphthyl unit in **101** are 90° with respect to each other.

The dynamic processes of (*R*,*R*)-**100** as shown in Scheme 14 were studied by variable-temperature ^{1}H NMR spectroscopy. The $\Delta G^{\ddagger}$ of process **a** was found to be 12.5 kcal/mol in acetone-d_6. Because of the bulkiness of the binaphthyl units in the cyclophane, the energy barrier of process **b** was too high to be observed. However, because of the smaller phenylene linker in the cyclophane **101**, both these processes were observable.

A class of transition metal-based rigid chiral macrocycles was successfully synthesized by Stang and co-workers through self-assembly processes.[67] For example, by using the hypervalent iodine compound **103** and the 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) transition metal complexes (*R*)-**104a,b** as building blocks, the cationic molecular squares (*R*,*R*)-**105a,b** were obtained (Scheme 15). The C−I−C bond angle in **103** is approximately 90°. The self-assembly of **103** with (*R*)-**104a,b** to generate (*R*,*R*)-**105a,b** was completed at room temperature in acetone solution with high yields. Variable-temperature ^{1}H NMR spectroscopic studies of (*R*,*R*)-**105a,b** showed that the rotational barriers of the pyridine in these optically active molecular squares were about 12.9 kcal/mol for (*R*,*R*)-**105a** and 15.0 kcal/mol for (*R*,*R*)-**105b**. Thus, the pyridine rings in the two metal complexes had distinctly different rotational barriers. From 0 to 80 °C, the two peaks of the α-pyridyl protons of (*R*,*R*)-**105b** coalesced into one peak. The specific optical rotation of (*R*,*R*)-**105a** was $[\alpha]_D = +311$ ($c = 0.0205$, acetone) and that of (*R*,*R*)-**105b** $[\alpha]_D = +168$ ($c = 0.0055$, nitromethane).

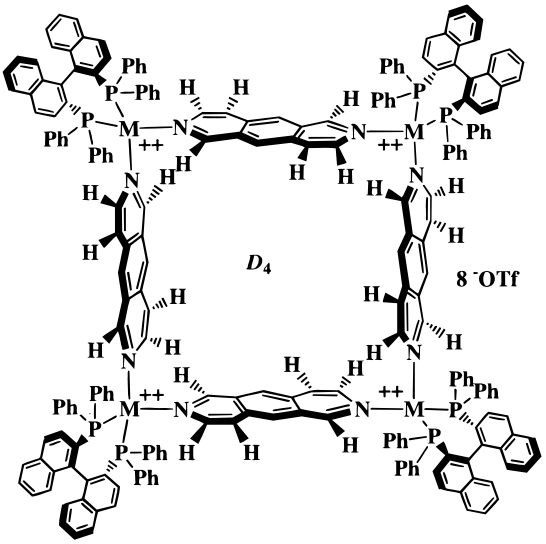
The self-assembly of bis(3-pyridyl)iodonium triflate (**106**) with (*R*)-**104a,b** was carried out giving the chiral macrocycles (*R*,*R*)-**107a,b** in high yields (Scheme 16). Unlike (*R*)-**105a,b**, the pyridine rings in the chiral macrocycle (*R*,*R*)-**107a,b** do not have rotational symmetry. The restricted rotation of the pyridine ring around the N−M bond should lead to 6 possible diastereomers. The ^{31}P NMR spectrum of (*R*,*R*)-**107a**, however, showed only one singlet and no

Scheme 16



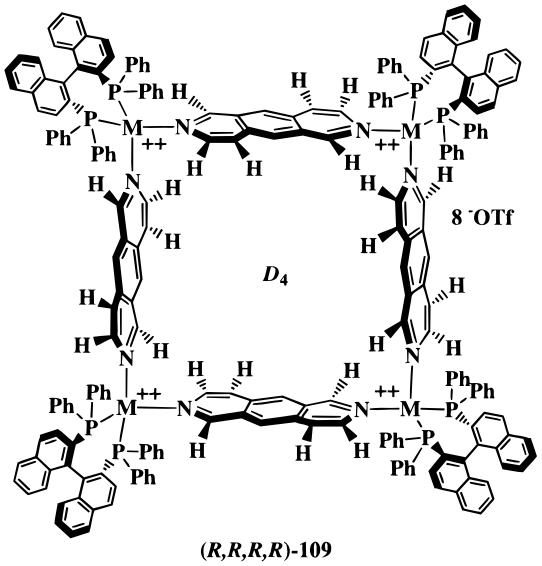
detectable line broadening or other changes were observed in the temperature range −30 to 40 °C. Therefore, only one diastereomer of (*R*,*R*)-**107a** was produced in the stereospecific self-assembly of **106** with (*R*)-**104a**. The pyridine ring in (*R*,*R*)-**107a** does not appear to have free rotation. The singlet ^{31}P NMR signal of (*R*,*R*)-**107a** also indicated that this macrocycle had a D_2 symmetry with all four phosphorus atoms equivalent. The ^{31}P NMR spectrum of (*R*,*R*)-**107b** displayed one major singlet corresponding to a D_2 symmetric macrocycle and several minor signals attributed to other diastereomers. The specific optical rotation of (*R*,*R*)-**107a** was $[\alpha]_D = +141$ ($c = 0.0152$, acetone) and that of (*R*,*R*)-**107b** was $[\alpha]_D = +99$ ($c = 0.0101$, acetone).

The self-assembly of 2,6-diazaanthracene with (*R*)-**104a,b** is also a highly stereospecific process. (*R*,*R*,*R*,*R*)-**108a,b** were generated each as a single diastereomer in high yields.[68] Both (*R*,*R*,*R*,*R*)-**108a** and



(*R*,*R*,*R*,*R*)-**108a**: M = Pd
(*R*,*R*,*R*,*R*)-**108b**: M = Pt

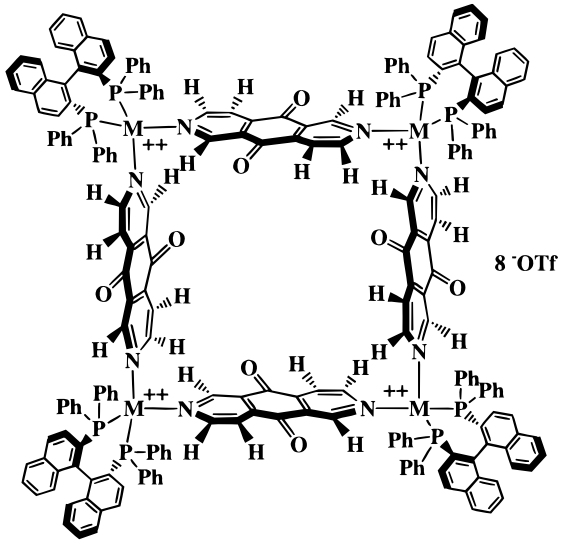
(*R*,*R*,*R*,*R*)-**108b** gave a singlet ^{31}P NMR signal, indicating a D_4 symmetry for the chiral macrocycles with all eight phosphorus atoms equivalent. No line broadening or splitting of the NMR signals between −80 and 80 °C was observed. According to MM2 calculations, the structure (*R*,*R*,*R*,*R*)-**108a,b** is preferred over the alternative D_4 symmetric structure (*R*,*R*,*R*,*R*)-**109**. This is due to a more favorable dipole interaction of the phenyl rings on the chiral binaphthyl ligands with the 2,6-diazaanthracene ligands in (*R*,*R*,*R*,*R*)-**108a,b**. The structures of the other four possible diastereomers were ruled out because their



(*R*,*R*,*R*,*R*)-**109**
the other D_4 diastereomeric structure

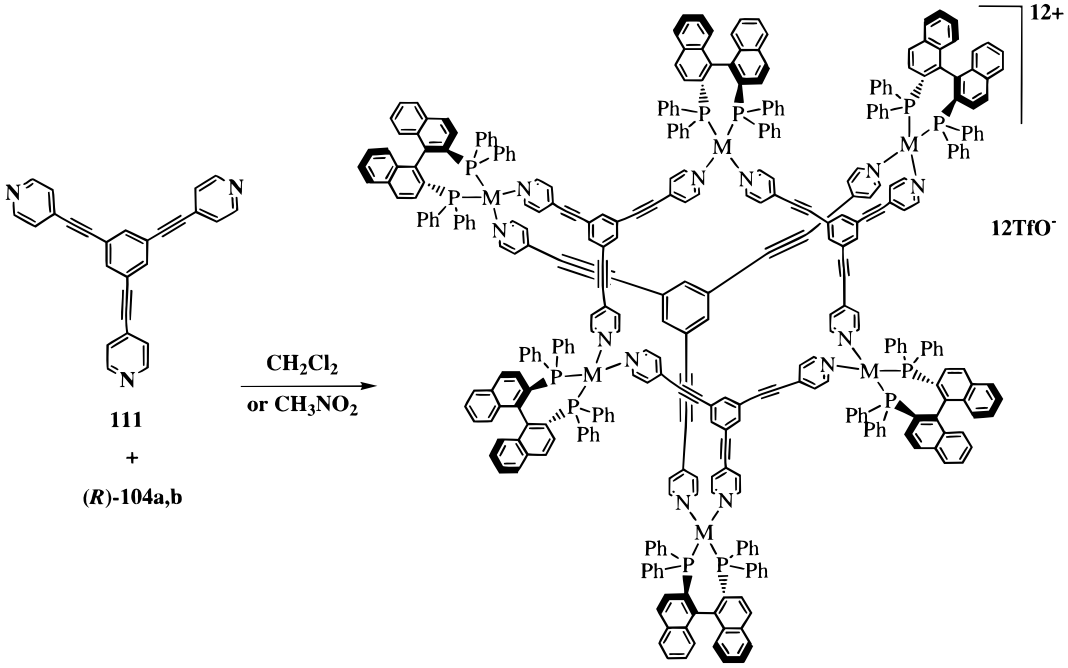
lower symmetry (D_2 or C_2) would be expected to lead to multiple ^{31}P NMR signals. The specific optical rotation of (*R*,*R*,*R*,*R*)-**108a** was $[\alpha]_D = +441$ ($c = 0.015$, acetone) and that of (*R*,*R*,*R*,*R*)-**108b** $[\alpha]_D = +237$ ($c = 0.0082$, acetone).

The self-assembly of 2,6-diazaanthracene-9,10-dione with (*R*)-**104a,b** gave the highly symmetrical macrocycles (*R*,*R*,*R*,*R*)-**110a,b** as the major products. Other minor diastereomers were also formed in the product mixture. The specific optical rotation of



(*R*,*R*,*R*,*R*)-**110a**: M = Pd
(*R*,*R*,*R*,*R*)-**110b**: M = Pt

Scheme 17



(*R*,*R*,*R*,*R*)-**110a** was found to be $[\alpha]_D = +395$ (*c* = 0.05, acetone) and that of (*R*,*R*,*R*,*R*)-**110b** $[\alpha]_D = +154$ (*c* = 0.011, nitromethane). The self-assembly of (*S*)-**104a,b** with 2,6-diazaanthracene-9,10-dione led to (*S*,*S*,*S*,*S*)-**110a,b**. The CD spectra of the compounds (*S*,*S*,*S*,*S*)-**110a** and (*S*,*S*,*S*,*S*)-**110b** were the exact mirror images of (*R*,*R*,*R*,*R*)-**110a** and (*S*,*S*,*S*,*S*)-**110b**, respectively. This is consistent with an enantiomeric relationship. The specific optical rotation of (*S*,*S*,*S*,*S*)-**110a** was $[\alpha]_D = +390$ (*c* = 0.0098, acetone) and that of (*S*,*S*,*S*,*S*)-**110b** $[\alpha]_D = -152$ (*c* = 0.0045, nitromethane).

Stang et al. also used the BINAP metal complexes as chiral auxiliaries to build three-dimensional molecular objects that are inherently chiral. Self-assembly of the tridentate ligand **111** with (*R*)-**104a,b** in methylene chloride or nitromethane solution produced compounds (*R*)-**112a,b** in high yields (Scheme 17).[69] These products were characterized using NMR spectroscopy, electrospray-ionization Fourier transform ion cyclotron resonance (ESI−FTICR) mass spectrometry, as well as molecular modeling. The specific optical rotation of (*R*)-**112a** was found to be $[\alpha]_D = +319$ (*c* = 0.022, methylene chloride) and that of (*R*)-**112b** $[\alpha]_D = +145$ (*c* = 0.025, nitromethane). These compounds have a unique chiral *T* symmetry.

All of these transition metal-based cationic chiral supramolecules are air stable microcrystalline solids with high decomposition points. They are very soluble in polar solvents such as methanol, acetone, and nitromethane and are potentially useful as hosts for chiral recognition.

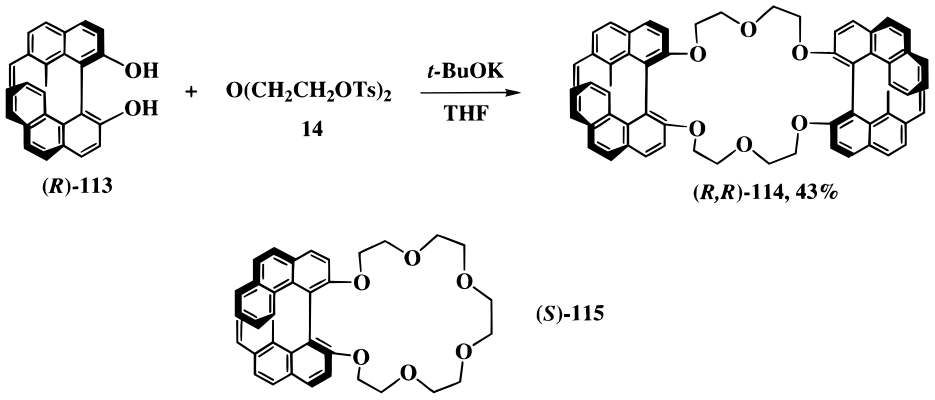
2.3. Other Multibinaphthyl Macrocycles

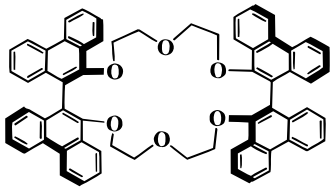
2.3.1. Macrocyclic Ethers

Biphenanthryl analogues of binaphthyl compounds are also possible. An optically active bis(4,4′-biphenanthryl) crown ether (*R*,*R*)-**114** was prepared by Yamamoto et al. from the reaction of (*R*)-3,3′-dihydroxy-4,4′-biphenanthryl [(*R*)-**113**] with diethylene glycol ditosylate (**14**) in the presence of potassium *tert*-butoxide and THF (Scheme 18).[70] The chloroform solutions of (*R*,*R*)-**114** and a monobiphenanthryl crown ether (*S*)-**115** were used as liquid membranes to carry out the enantioselective differential transport of racemic phenylglycinate hydrochloride, 1,2-diphenylethylamine hydrochloride, and 2-aminotetralin hydrochloride. In the resolution of 1,2-diphenylethylamine hydrochloride, (*R*,*R*)-**114** produced up to 42% ee of the *S* enantiomer, and (*S*)-**115** up to 74% ee of the *R* enantiomer. The monomeric biphenanthryl crown ether (*S*)-**115** showed better chiral recognition capability than the bisbiphenanthryl crown ether (*R*,*R*)-**114**. This is in contrast to what was observed for the chiral binaphthyl crown ethers where the bisbinaphthyl crown ethers showed better asymmetric recognition than the monobinaphthyl macrocycles.[47]

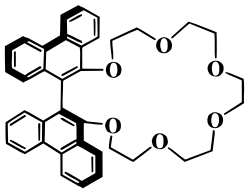
An optically active bis(9,9′-biphenanthryl) crown ether (*R*,*R*)-**116** was also prepared by Yamamoto et al.[71] The chiral recognition properties of (*R*,*R*)-**116** toward racemic amino esters or amines, such as methyl phenylglycinate hydrochloride, 1-phenylethylamine hydrochloride, and 1,2-diphenylethylamine hydrochloride, were studied and compared with the mono 9,9′-biphenanthryl crown ether (*S*)-**117**. (*R*,*R*)-**116** was found to have very low enantioselectivity. (*S*)-**117** proved to be a better chiral host. This is similar to what was observed for the 4,4′-biphenanthryl crown ethers (*R*,*R*)-**114** and (*S*)-**115**. The optical purities of the guests transported through a bulky liquid membrane apparatus containing a chloroform solution of (*R*,*R*)-**116** were in the range of 19−23%. When (*S*)-**117** was used, the optical purity of the guests transported reached 78%. (*S*)-**117** had the

Scheme 18





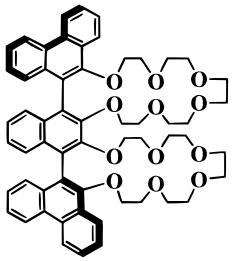
(*R*,*R*)-**116**



(*S*)-**117**

opposite enantiomer selectivity of (*R*,*R*)-**116** because of their opposite chirality in the 9,9′-biphenanthryl unit.

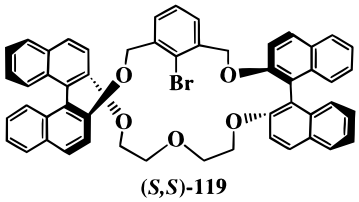
A bis-crown ether (*S*,*S*)-**118** was synthesized and used to carry out the differential transport of racemic amino esters and amines.[72] (*S*,*S*)-**118** selectively



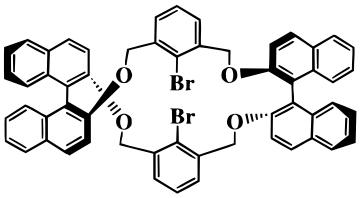
(*S*,*S*)-**118**

transported (*R*,*R*)-cystine dimethyl ester dihydrochloride with 66% optical purity, and (*S*,*S*)-1,6-diphenylhexamethylene-1,6-diamine dihydrochloride with 82% optical purity. When (*S*)-**117** was used, the optical purities for the two guests after transport were only 18% and 26%, respectively. It is possible that the two crown ether macrocycles of (*S*,*S*)-**118** are capable of complexation with the two ammonium groups in the guests, thus leading to the enhanced chiral recognition.

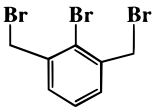
To introduce other functional groups into the rim of the binaphthyl macrocycles, Kiyooka et al. prepared two optically active bisbinaphthyl macrocycles **119** and **120** containing bromine atoms on the rings by reacting **121** with the optically active BINOL (**12**).[73] Both the *SS* and *RR* enantiomers of **119** and **120** were obtained. Further study of these macrocycles and their derivatives was not reported.



(*S*,*S*)-**119**



(*S*,*S*)-**120**



121

In the helical structure of a 1,1′-binaphthyl molecule, there exists a minor groove as well as a major groove divided by the 1,1′-bond. All the macrocyclic binaphthyl compounds described above were obtained through cyclization at the 2,2′- or 3,3′-positions of the binaphthyl monomers, i.e., at the minor groove of the binaphthyls. In 1991, Diederich and co-workers prepared the major groove bisbinaphthyl macrocycles (*R*,*R*)-**122**, (*R*,*R*)-**123**, and (*S*,*S*)-**124** through cyclization at the 7,7′-positions and/or 6,6′-positions (Figure 6).[74] The interaction of these hosts with naproxen derivatives **125** and **126** in a mixed water/methanol solvent was studied. It was found that (*R*,*R*)-**123** bound both the *R* and *S* enantiomers of **125** with a slight preference for the *S* enantiomer ($\Delta\Delta G \approx 0.09$ kcal/mol). (*S*,*S*)-**124** bound both **125** enantiomers equally well, and (*R*,*R*)-**122** did not show significant complexation with racemic **125**. This study showed that these major groove bisbinaphthyl macrocycles were not good candidates for chiral naproxen recog-

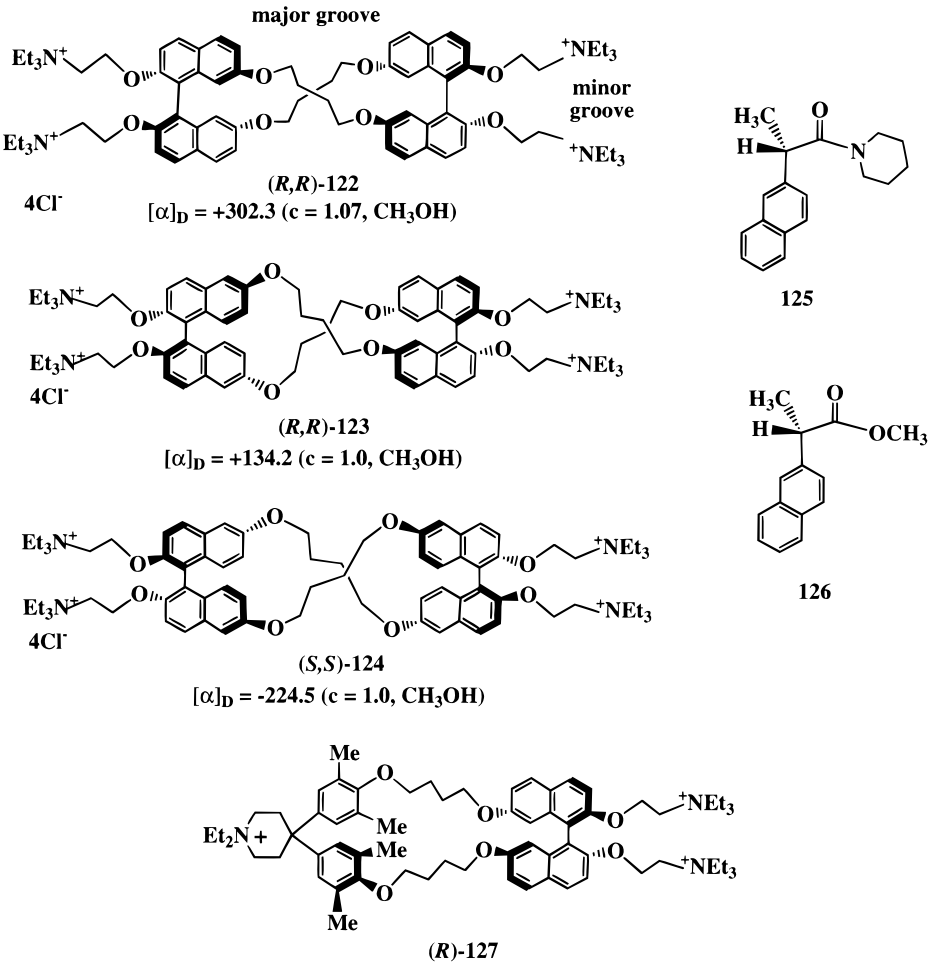


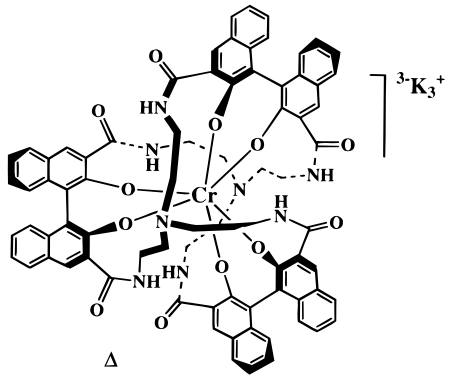
Figure 6.

nition. It was observed, however, that a monobinaphthyl macrocycle (*R*)-**127** was more promising. (*R*)-**127** showed a $\Delta\Delta G$ of 0.33 kcal/mol when complexed with the *R* and *S* enantiomers of **125**. Similar results were obtained for its complexation with **126**.

2.3.2. Macrocyclic Amides

The trisbinaphthyl chiral macrobicyclic amides (*R*,*R*,*R*)-**131** and (*S*,*S*,*S*)-**131** were prepared by Pierre and co-workers in 1997 (Scheme 19).[75] (*S*,*S*,*S*)-**130** was obtained from the reaction of (*S*)-**128** with tris-(2-aminoethyl)amine (**129**). This was then converted to (*S*,*S*,*S*)-**131** through a dilution reaction with **129** followed by removal of the methyl groups with BBr_3.

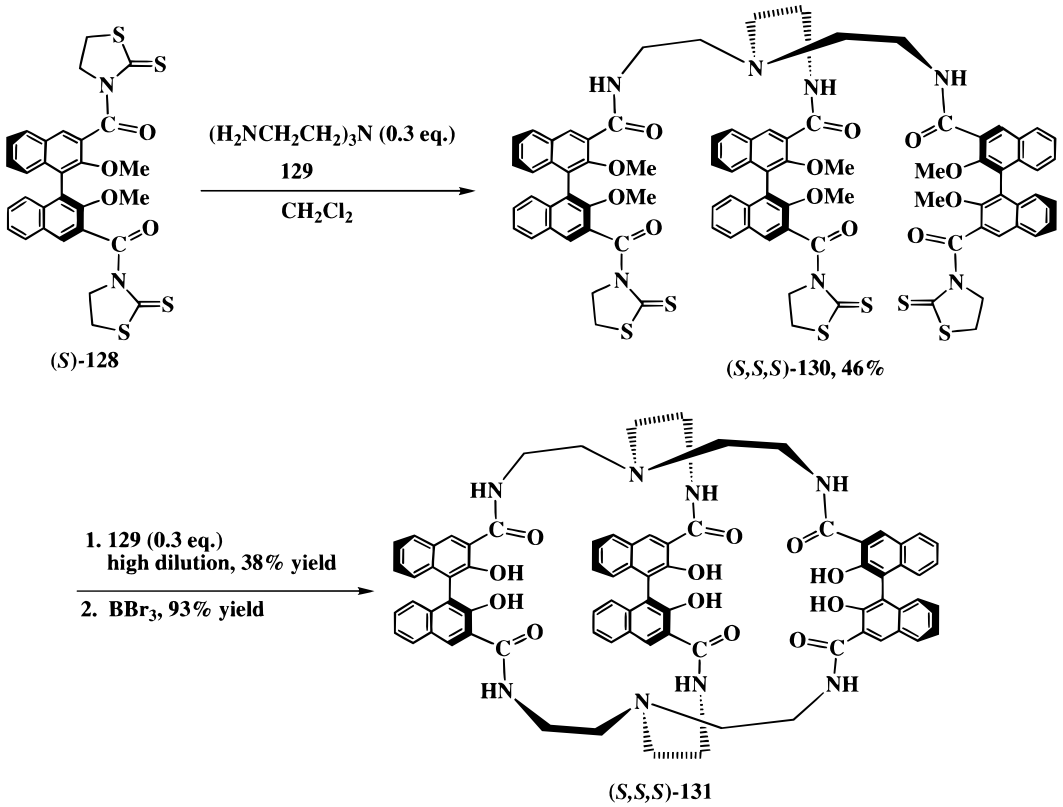
It was found that both these optically active tripodate ligands (*S*,*S*,*S*)-**131** and (*R*,*R*,*R*)-**131** formed 1:1 metal complexes with Ga(III), Cr(III), and Fe(III). Although both Δ and Λ isomers are possible for the chiral octahedral metal centers, only one isomer, e.g., (*S*,*S*,*S*)-**132** (the Δ isomer), was observed in each case. According to the CD spectrum of **132**, a Δ configuration was assigned to (*S*,*S*,*S*)-**132** and a Λ configuration to (*R*,*R*,*R*)-**132**. Molecular modeling studies support this assignment. The chirality of the ligands appears to have controlled the configuration of the metal centers. The CD spectra of both these complexes were found to be mirror images. Evidence also indicated that the chiral configuration of the Fe(III) complexes should be similar to that of the Cr(III)



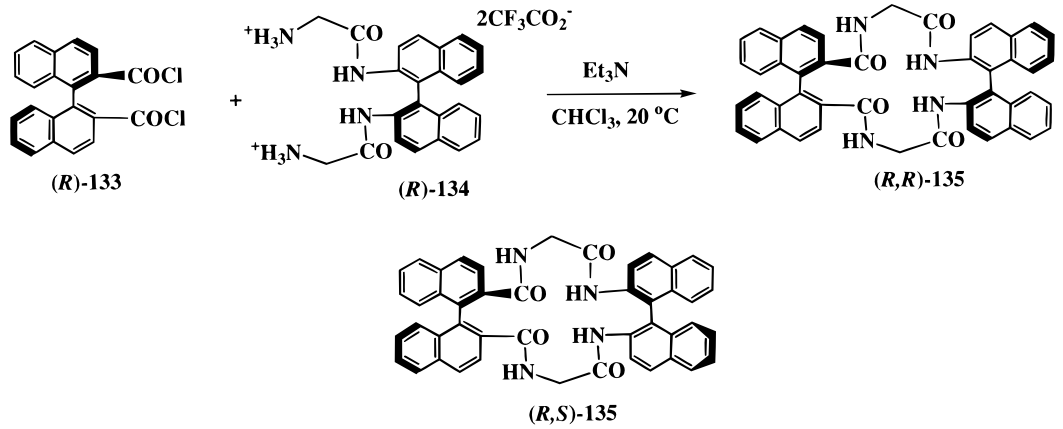
complexes. The binding of **131** with chiral molecules was not studied.

In 1997, Nozaki et al. reported the synthesis of the bisbinaphthyl macrocyclic amides (*R*,*R*)-**135** and (*R*,*S*)-**135** (Scheme 20).[76] The reaction of (*R*)-**133** with the binaphthyl glycine amide salt (*R*)-**134** gave (*R*,*R*)-**135**. (*R*,*S*)-**135** was made from the reaction of (*R*)-**133** with (*S*)-**134**. The crystal structures of both compounds were obtained. Both (*R*,*R*)-**135**·(DMSO) and (*R*,*S*)-**135**·$(DMF)_3$ were found to cause a split in the ^1H NMR signal of the methyl protons in the racemic mixture of methyl phenyl sulfoxide. An NMR study of these compounds also showed their binding with the peptide molecule $AcNHCH_2CONHCH_2CO_2Et$.

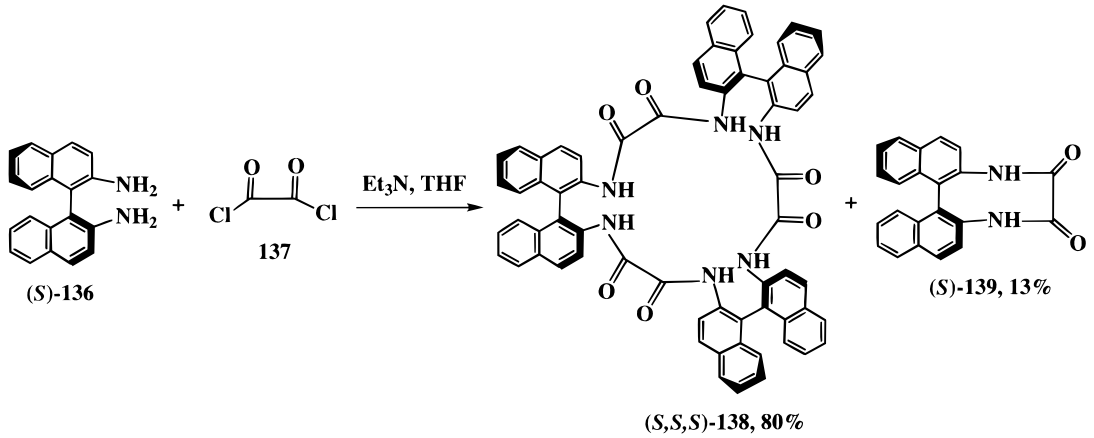
Scheme 19



Scheme 20



Scheme 21



A trisbinaphthyl oxamide chiral macrocycle (*S*,*S*,*S*)-**138** was obtained from the reaction of (*S*)-2,2′-diamino-1,1′-binaphthalene [(*S*)-**136**] with oxalyl chloride (**137**) by Lindauer et al. in 1995 (Scheme 21).[77]

(*S*)-**136** was converted to (*S*,*S*,*S*)-**138** in THF solution in the presence of triethylamine and **137** at room temperature giving an 80% yield after column chromatography and recrystallization. The structure of (*S*,*S*,*S*)-**138** was confirmed by single-crystal X-ray analysis. This chiral macrocycle is potentially useful in chiral recognition. A monobinaphthyl compound (*S*)-**139** was also isolated in 13% yield.

3. Multibinaphthyls in Asymmetric Reactions

Multibinaphthyl-based ligands have been used to prepare a variety of metal complexes which have proved useful in asymmetric organic transformations. Different functional groups are introduced into the binaphthyl structure which permit the coordination of different metal centers. Herein, multibinaphthyl metal complexes are classified mainly according to their principal coordination atoms. The following three sections will cover: the oxygen-based multibinaphthyl ligands; the nitrogen-based multibinaphthyl ligands; and the phosphorus-based multibinaphthyl ligands.

In general, the oxygen-based binaphthyl ligands are used to prepare complexes containing Lewis acid metal centers such as Ln, Ti, Zr, Al, Zn, etc. Most of the oxygen-based multibinaphthyl ligands are made from BINOL **12** or its substituted derivatives. The nitrogen-based binaphthyl ligands including porphyrins, salens, imines, and amines are used to prepare Fe, Rh, and Mn and other complexes. In the porphyrin complexes, the binaphthyl units are not directly involved in the coordination but serve as substituents on the porphyrin ring in order to generate a chiral environment around the porphyrin-bound metal center. The phosphorus-based multibinaphthyl ligands are used to prepare complexes of the late transition metals such as Ru, Rh, Pd, and Pt. Because of the diverse coordination capability of the binaphthyl ligands, they have found broad application in asymmetric catalysis. The multibinaphthyl complexes have been used to catalyze reactions such as nitro aldol reactions, Michael additions, ene reactions, Simmon−Smith reactions, alkyl additions to aldehydes, epoxidations, aziridinations, hydrogenations, hydroformylations, and the polymerization of methacrylates. As a result of such studies, some highly enantioselective catalysts have been discovered.

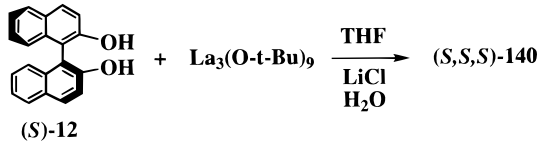
In the later sections of this part, the following topics will be discussed: the application of novel rigid and sterically regular polybinaphthyl catalysts in asymmetric catalysis; the use of chiral binaphthyls in intramolecular biaryl cyclization; the preparation of binaphthyl-based metallocence complexes for asymmetric epoxidations; and the study of binaphthyl selenium compounds.

3.1. Oxygen-Based Multibinaphthyl Ligands

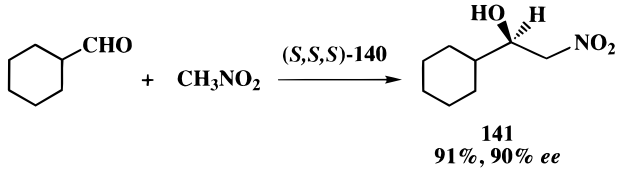
3.1.1. Shibasaki's Heterometallic BINOL Catalysts

Optically active BINOLs, (*R*)-**12** or (*S*)-**12**, are among the simplest members of the functionalized 1,1′-binaphthyl compounds. Many optically active binaphthyl compounds are derived from this molecule. Apart from their use as the chiral starting materials for building other binaphthyl structures, the deprotonated form of this molecule is also an excellent chelate diolate ligand for the coordination of a variety of Lewis acid metal centers. Highly enantioselective catalysts have been developed from complexes containing multiple BINOL-H ligands. Some of the most important of these complexes, the heterometallic BINOL catalysts, were discovered by Shibasaki and co-workers.

Scheme 22



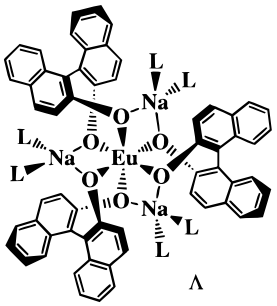
Scheme 23



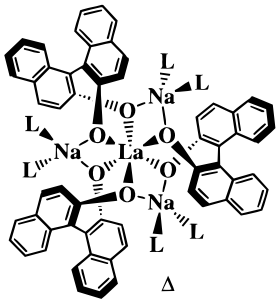
In 1992, they found that an optically active lanthanum(III) complex (*S*,*S*,*S*)-**140**, prepared from the reaction of (*S*)-**12** with La(O-t-Bu)$_3$, was able to catalyze nitro aldol reactions with a high enantioselectivity (Scheme 22).[78,79] For example, in the presence of (*S*,*S*,*S*)-**140**, the reaction of cyclohexanecarboxaldehyde with nitromethane produced a chiral alcohol **141** with 90% ee (Scheme 23).[78] They found that different rare earth metal−BINOL complexes such as those of Pr, Nd, Sm, Eu, Gd, Dy, Er, Yb, and Y also catalyzed the enantioselective nitro aldol reaction. In general, the lanthanum complex proved the most effective.[80,81] However, in the case of the nitro aldol reaction of α,α-difluoro aldehydes, the samarium−Li−BINOL complex was found to be better.[82]

A series of studies were carried out to determine the structure of the catalyst involved in this asymmetric process.[83] The laser desorption/ionization time-of-flight mass spectrum (LDI−TOF MS) of (*S*,*S*,*S*)-**140** indicated that this compound had a trisbinaphthyl structure with both La and Li metals. Single-crystal X-ray structures of the BINOL complexes of Eu, Nd, and Pr prepared from the reaction of $LnCl_3$ with disodium (*S*)-binaphthoxide were obtained. These confirmed the trisbinaphthoxy coordination. (*S*,*S*,*S*)-**142** is an example of such complexes. Although the metal centers in these BINOL complexes were chiral and could have two possible configurations, only the Λ configuration was observed for complexes made from (*S*)-BINOL. The Λ configuration may be thermodynamically more stable than the Δ configuration due to the *S* configuration of the BINOL ligands. Later, the X-ray structure of a La−Na−BINOL complex (*R*,*R*,*R*)-**143** was obtained. It was shown to be similar to that of (*S*,*S*,*S*)-**142** but it

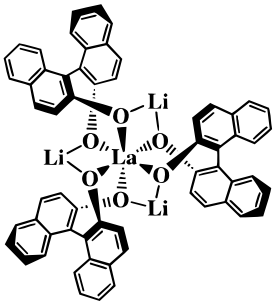
had the opposite configuration at the metal center as well as at the binaphthyl ligands.[84] The structure of the La−Li−BINOL complex (*S*,*S*,*S*)-**140** would be expected to be similar to that of (*R*,*R*,*R*)-**143**. However, while the BINOL−Ln−Li complexes catalyzed the nitro aldol reaction with a high enantioselectivity, the corresponding BINOL−Ln−Na complexes gave almost no optical yields for the same reaction.



(*S*,*S*,*S*)-**142**
L = THF



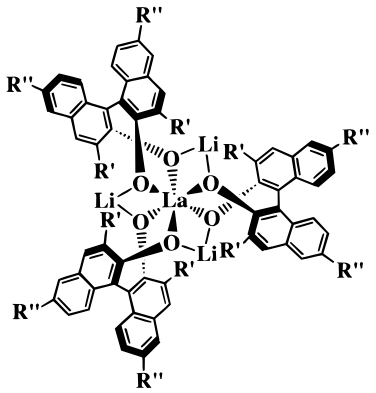
(*R*,*R*,*R*)-**143**
L = THF



(*S*,*S*,*S*)-**140**

When 1 equiv of H_2O and a 0.9 equiv of *n*-butyllithium were added to the complex (*R*,*R*,*R*)-**140**, its catalytic activity was greatly accelerated without any decrease in optical yield.[85] Scheme 24 shows a possible mechanism for the nitro aldol reaction catalyzed by (*R*,*R*,*R*)-**140** with or without the addition of H_2O and *n*-butyllithium. The H_2O/*n*-butyllithium accelerated reaction rate was explained by the formation of a tight LiOH−(*R*,*R*,*R*)-**140** complex **145** that could react with the nitroalkanes generating **146** faster than the direct conversion of (*R*,*R*,*R*)-**140** to **144**.

To generate lanthanum−BINOL complexes that not only have high enantioselectivity but also high diastereoselectivity for reactions such as that between hydrocinnamaldehyde (**147**) and 2-hydroxymethane (**148**) (Scheme 25), the structure of (*S*,*S*,*S*)-**140** has been modified. Different substituents were introduced into either the 3,3′- or 6,6′-positions of the BINOL ligands, giving the corresponding La−Li−BINOL complex (*R*,*R*,*R*)-**150**.[86] It was found that the 6,6′-substituted catalysts were much more efficacious than the 3,3′-substituted catalysts: overall, the best was (*R*,*R*,*R*)-**150a** (R′ = H, R″ = CCSiEt$_3$). When (*R*,*R*,*R*)-**150a** (3.3 mol %)

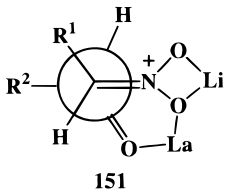


(*R*,*R*,*R*)-**150**

R′ = H, Me, SiMe$_3$
R″ = H, Br, Me, CN, CCH
C≡C−Ph
C≡C−SiMe$_3$
C≡C−SiEt$_3$
C≡C−SiBu$_3$
C≡C−SiMe$_2$Ph

(*R*,*R*,*R*)-**150a**: R′ = H, R″ = −C≡C−SiEt$_3$

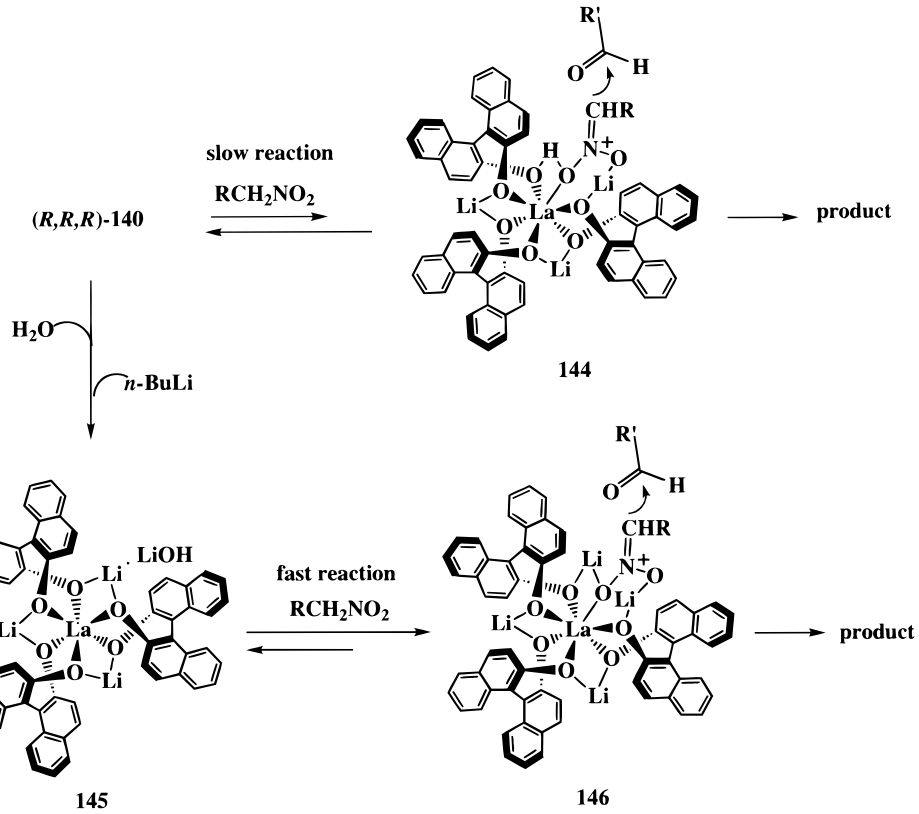
was used to catalyze the reaction of **147** with **148**, the syn and anti products **149** were obtained in a ratio of 92:8 with 97% ee of *syn*-**149**. When (*R*,*R*,*R*)-**140** (R′ = R″ = H) was used for this reaction, the observed syn/anti ratio was 84:16 and the ee of *syn*-**149** was only 66%. Although the mechanism for such greatly enhanced enantioselectivity as well as diastereoselectivity on the introduction of substituents into the 6,6′-positions of BINOL was unclear, a transition state **151** was proposed for the observed syn selectivity.



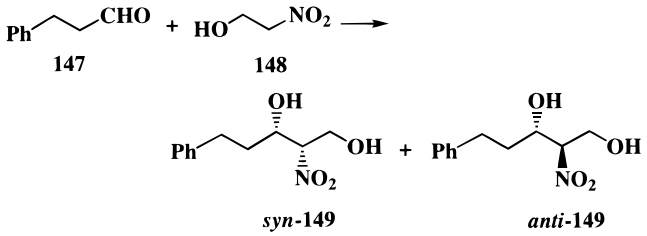
151

The lithium-containing BINOL−lanthanum complexes, although highly enantioselective for the nitro aldol reaction, showed very poor asymmetric induction in Michael additions. For example, the Michael addition of cyclopentenone with dibenzyl methylmalonate (**152**) (Scheme 26) catalyzed by (*S*,*S*,*S*)-**140** gave **153** with only 13% ee and 26% yields. However, when a lithium-free lanthanum complex, (*S*,*S*,*S*)-**154**,

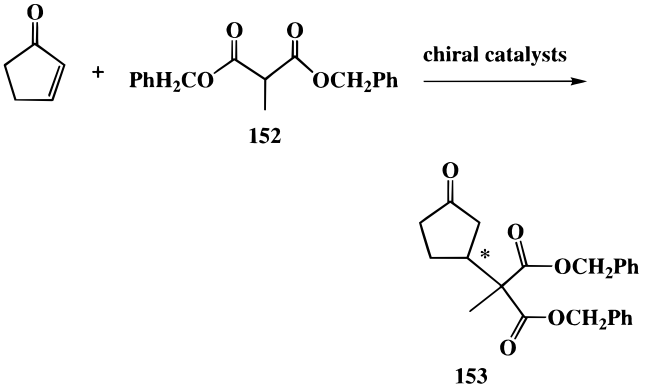
Scheme 24



Scheme 25



Scheme 26



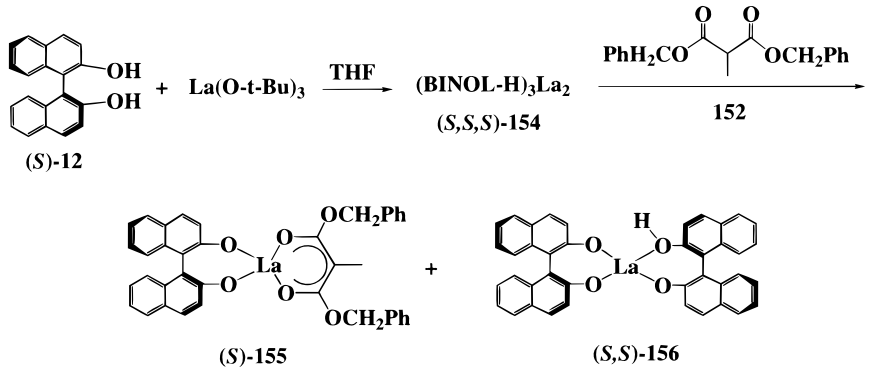
prepared from the reaction of La(O-*i*-Pr)$_3$ with BINOL (*S*)-**12** in THF (Scheme 27), was used for this reaction, up to 95% ee and a 97% yield of **153** was obtained.[87] Although the exact structure of (*S*,*S*,*S*)-**154** was unclear, the inductively coupled plasma spectroscopy (ICPS) analysis of (*S*,*S*,*S*)-**154** showed that the ratio of La/BINOL was 2:3. (*S*)-**155** has been proposed as the real catalyst in this asymmetric Michael addition. It was generated together with (*S*,*S*)-**156** from the reaction of (*S*,*S*,*S*)-**154** with **152**. The bisbinaphthyl complex (*S*,*S*)-**156** was expected to have low catalytic activity.

The La−Na−BINOL complex (*R*,*R*,*R*)-**143** was also found to be very effective for the asymmetric Michael addition.[84,88] For example, when (*S*,*S*,*S*)-**143** was used to catalyze the Michael reaction shown in Scheme 26, the product **153** was obtained in 96% yield with 90% ee at room temperature. (*R*,*R*,*R*)-**143** was believed to function not only as a base to generate the enone intermediate but also as a Lewis acid to control the direction of the carbonyl function for the asymmetric addition. The complex **157** was proposed as a possible intermediate in the Michael addition catalyzed by (*R*,*R*,*R*)-**143** (Scheme 28). The chiral center of the organic product is generated when **157** is converted to **158**. Unlike the lithium complex (*S*,*S*,*S*)-**140**, (*R*,*R*,*R*)-**143** was not effective in the asymmetric nitro aldol reaction.

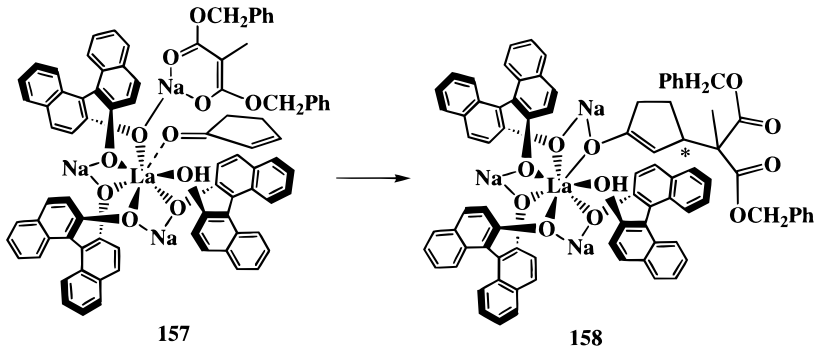
The La−K−BINOL complex (*R*,*R*,*R*)-**159** was prepared and was found to catalyze the asymmetric hydrophosphonylation of imines with good to excellent enantioselectivity (Scheme 29).[89] For example, the reaction of dimethyl phosphite with the imine **160** in the presence of 10 mol % of (*R*,*R*,*R*)-**159** gave **161** in 70% yield and 96% ee. Molecules such as **161** are precursors to the α-amino phosphonic acids which in turn are useful for enzyme inhibition.

The asymmetric hydrophosphonylation of cyclic imines has also been studied. It was found that when (*R*,*R*,*R*)-**162** was used to catalyze the reaction of **163** with dimethyl phosphite at 50 °C, **164** was obtained in 89% yield and 94% ee (Scheme 30).[90] The Yb(III) complexes (*R*,*R*,*R*)-**165** and (*R*,*R*,*R*)-**166** that contain 6,6′-bis(trimethylsilyl)ethynyl or 6,6′-bis(methoxy) BINOL ligands also catalyzed the reaction of cyclic

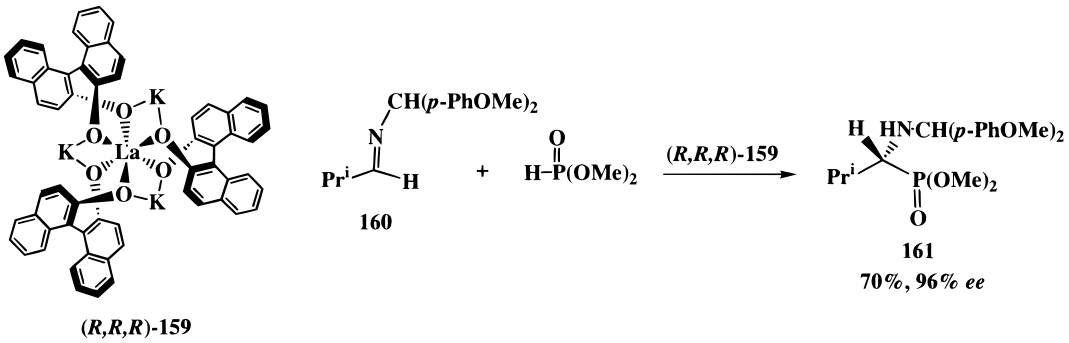
Scheme 27



Scheme 28

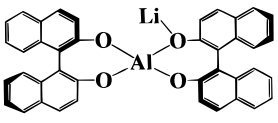


Scheme 29

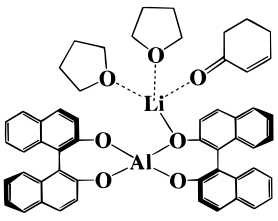


imines with dimethyl phosphite with high enantioselectivity. However, when the La(III) complex (*R*,*R*,*R*)-**159** was used in the cyclic imine reaction, much lower enantioselectivity was observed. Detailed studies on the catalytically active species in the hydrophosphonylation with (*R*,*R*,*R*)-**162** were carried out using spectroscopic methods such as NMR, FAB mass spectrometry and LDI−TOF mass spectrometry. In the postulated mechanism shown in Scheme 31, a tautomerization of the phosphite coordinated complex (*R*,*R*,*R*)-**167** to (*R*,*R*,*R*)-**168** generates a nucleophilic phosphorus atom which attacks the imine carbon of the cyclic imine substrate to give (*R*,*R*,*R*)-**169**. In (*R*,*R*,*R*)-**169**, a proton transfer from the oxygen to the nitrogen could form the chiral α-amino phosphonate product.

Shibasaki and co-workers extended their work of rare earth metal−alkaline metal−BINOL complexes to other heterobimetallic BINOL complexes.[91] For example, treatment of 2 equiv of (*R*)-**12** with $LiAlH_4$ led to the formation of a bisBINOL−Al−Li complex (*R*,*R*)-**170**. This complex was found to be an excellent catalyst for asymmetric Michael additions (91−98% ee). Although the structure of this complex was not completely established, a single-crystal X-ray structure of the cyclohexenone adduct (*R*,*R*)-**171** was obtained. Besides Li, other alkaline metals such as Na, K, and Ba were also incorporated into the

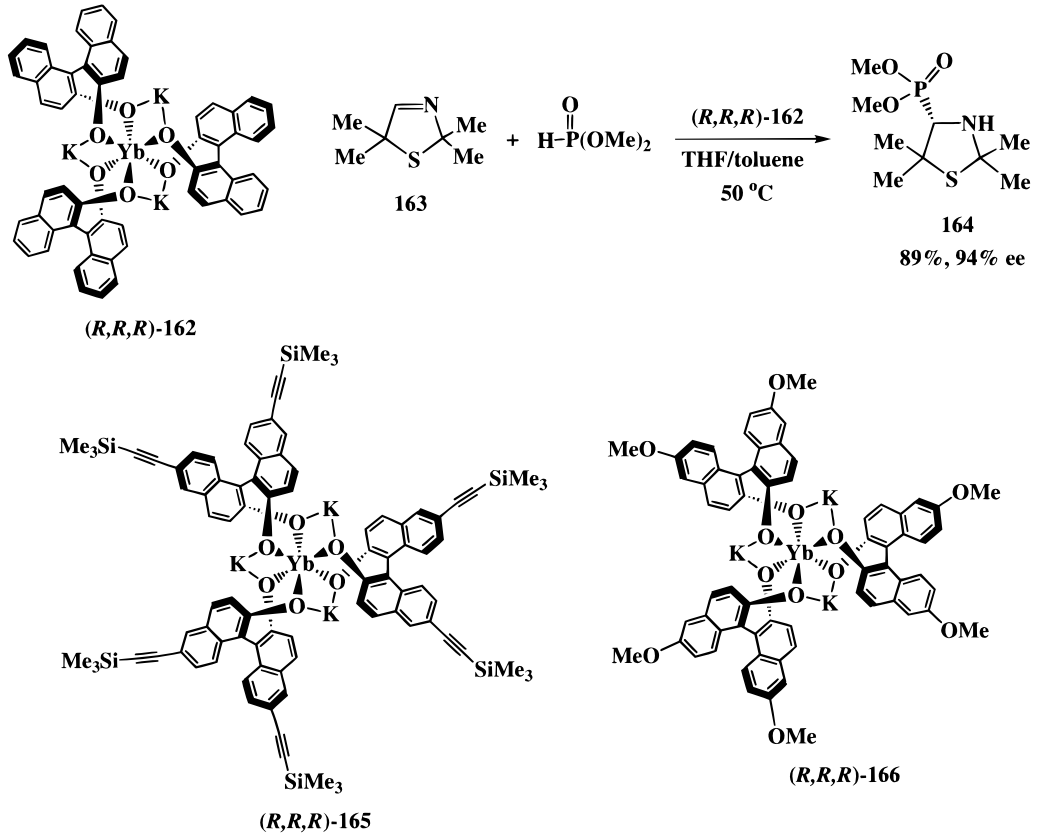


(*R*,*R*)-170

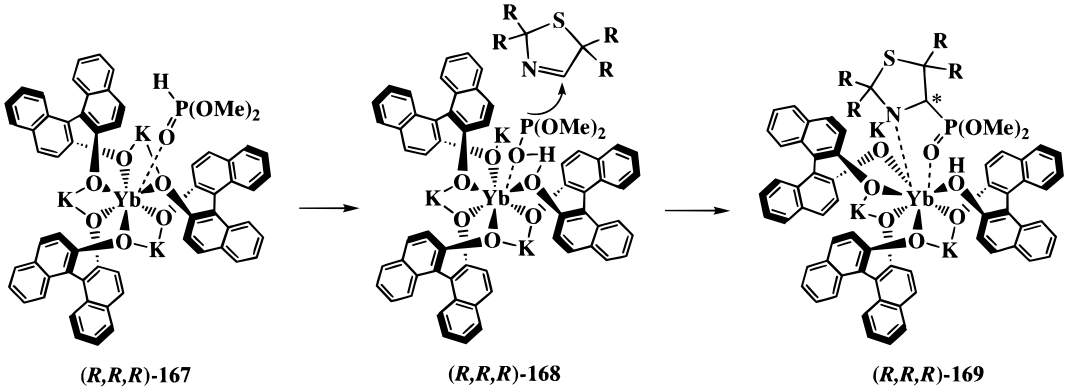


(*R*,*R*)-171

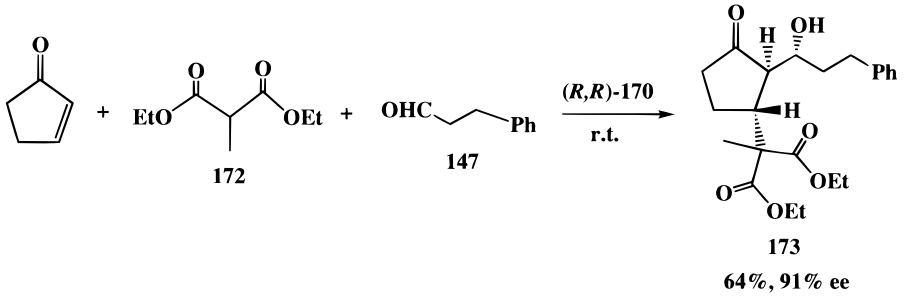
Scheme 30



Scheme 31



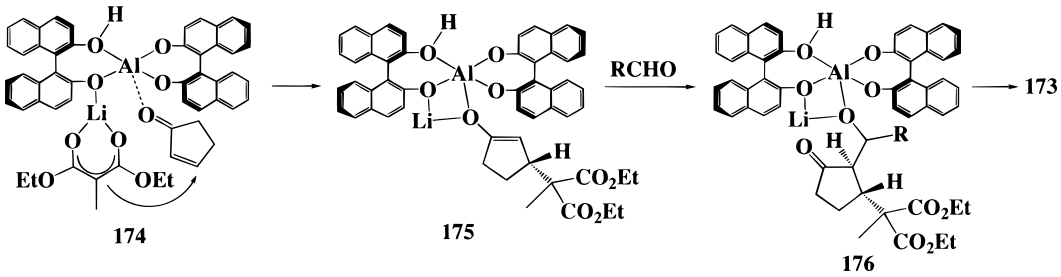
Scheme 32



BINOL−Al complex and the resulting heterobimetallic compounds also showed high enantioselectivity for the Michael reaction. This is in contrast to the La−alkaline metal−BINOL complexes where varying the alkaline metals produced very different catalytic properties.

Further study of (*R*,*R*)-**170** demonstrated that this complex was also highly enantioselective in a tandem Michael-aldol reaction.[91] As shown in Scheme 32, the three-component reaction of 2-cyclopentenone, diethyl methylmalonate (**172**), and dihydrocinnamaldehyde (**147**) in the presence of 10 mol % of (*R*,*R*)-

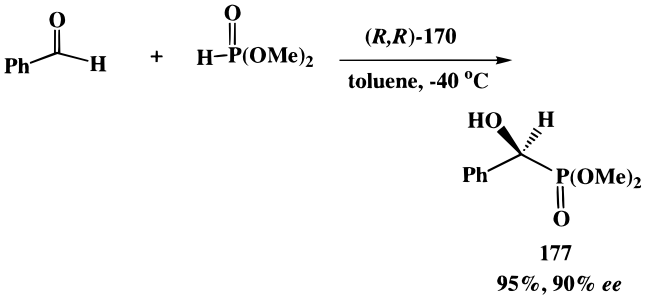
Scheme 33



170 produced **173** in 64% yield and 91% ee. Other heterobimetallic complexes such as La−Li−BINOL, La−Na−BINOL, and La−BINOL proved totally ineffective for this reaction. Scheme 33 shows a possible mechanism for the tandem Michael-aldol reaction catalyzed by (*R*,*R*)-**170**. One possibility is that after deprotonation of **172** by (*R*,*R*)-**170**, an intermediate **174** is produced. There is evidence for the formation of an aluminum enolate when (*R*,*R*)-**170** is treated with an enone. Since aluminum(III) has a larger electronegativity than lanthanum(III), the Al−enolate **175** generated from **174** will be less reactive toward acidic protons than the corresponding lanthanum enolate. Therefore, **175** can undergo further addition with the aldehyde to give **176** thus leading to the three-component addition product **173**.

The asymmetric hydrophosphonylation of aldehydes was found to be catalyzed by (*R*,*R*)-**170**.[92] Up to 90% ee was observed for the formation of an α-hydroxyl phosphonate, **177**, from the reaction of benzaldehyde with dimethyl phosphite in the presence of 10 mol % (*R*,*R*)-**170** (Scheme 34). The

Scheme 34

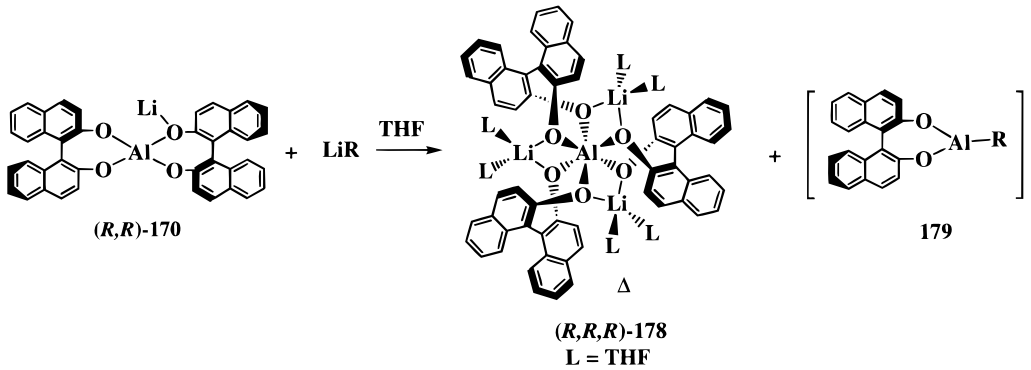


addition of dimethyl phosphite to aromatic aldehydes and α,β-unsaturated aldehydes in the presence of (*R*,*R*)-**170** showed good to excellent enantioselectivity, but the optical yields for the corresponding aliphatic aldehydes were very low (3−24% ee). The α-hydroxyl phosphonates and phosphonic acids produced from this reaction are well-known inhibitors for various enzymes including HIV protease, renin, and EPSP synthase.

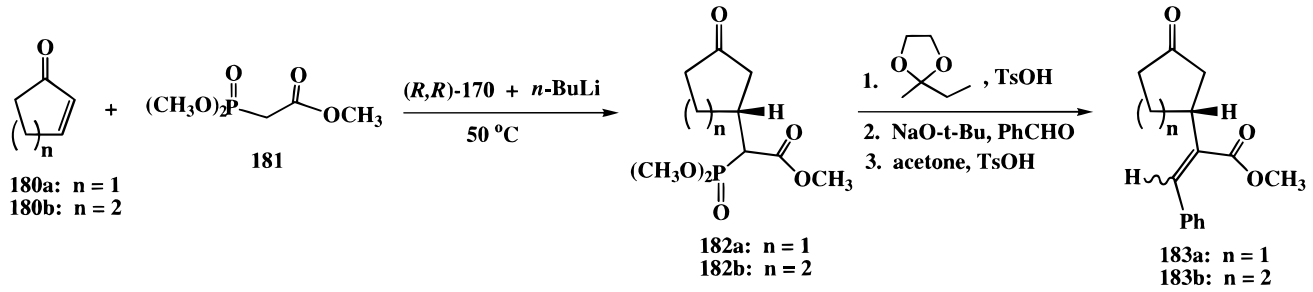
The asymmetric hydrophosphonylation of aldehydes was also catalyzed by (*R*,*R*,*R*)-**140** prepared by a newer synthetic procedure starting from $LaCl_3 \cdot 7H_2O$.[93] (*R*,*R*,*R*)-**140** gave better yields and ee's than the Al−Li−BINOL complex (*R*,*R*)-**170** for the hydrophosphonylation of aliphatic aldehydes and some aromatic aldehydes. These two catalysts play complementary roles in asymmetric hydrophosphonylations, leading to optically active α-hydroxyl phosphonates.

A trisbinaphthylaluminum complex (*R*,*R*,*R*)-**178** was obtained in 43% yield [based on (*R*,*R*)-**170**] from the reaction of (*R*,*R*)-**170** with an alkyllithium such as methyllithium and *n*-butyllithium (Scheme 35).[94] The structure of (*R*,*R*,*R*)-**178** was confirmed by X-ray analysis. Compound **179** is a possible side product in this reaction. Although the isolated complex (*R*,*R*,*R*)-**178** showed very low activity and low enantioselectivity for the reaction of **180b** with **181** to produce **182b** (Scheme 36), a mixture of (*R*,*R*)-**170** and *n*-butyllithium effectively catalyzed this reaction to give first **182b**, then **183b** in 98% ee. When *n*-butyllithium was replaced with sodium *tert*-butoxide, **180a** was converted to **182a** in 95% yield and 95% ee even at room temperature. (*R*,*R*)-**170** itself did not catalyze this reaction. To understand the nature of the complex **179** in Scheme 35, (*R*)-**12** was reacted with $AlMe_3$ which generated the dimeric complex (*R*,*R*)-**184** (Scheme 37). The structure of (*R*,*R*)-**184** was established by X-ray analysis. This complex failed completely to catalyze the reaction of **180b** with **181**. However, a mixture of (*R*,*R*)-**184** and (*R*,*R*,*R*)-**178** gave **182b** in 96% ee and 54% yield. This demonstrated that in solution the catalytically active species must be in equilibrium with (*R*,*R*)-**184** and (*R*,*R*,*R*)-**178**.

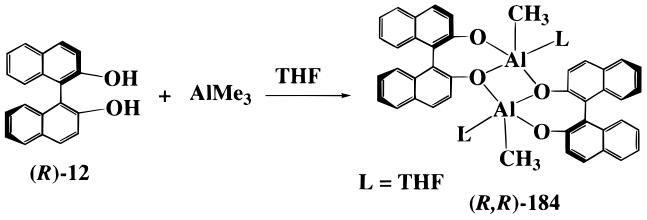
Scheme 35



Scheme 36

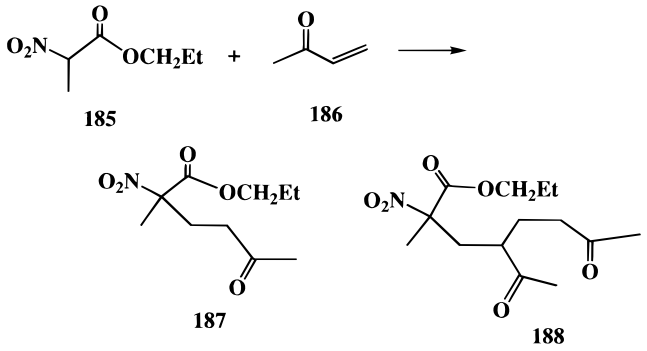


Scheme 37



At about the same time as Shibasaki, Feringa and co-workers also reported both the isolation and X-ray structure of the trisbinaphthyl complex (*R*,*R*,*R*)-**178** from the reaction of $LiAlH_4$ with 2.45 equiv of (*R*)-**12**.[95] The ^{27}Al NMR spectra of either a solution of $LiAlH_4$ (1 equiv)/(*R*)-**12** (2 equiv) or of $LiAlH_4$ (1 equiv)/(*R*)-**12** (2.45 equiv) were identical. They indicate the formation of at least three aluminum complexes with (*R*,*R*,*R*)-**178** as one of the major products. Thus, the in situ generated (*R*,*R*)-**170** is unlikely to be a single complex but rather a mixture containing (*R*,*R*,*R*)-**178**. Feringa and co-workers observed that the THF solution of $LiAlH_4$ (1 equiv)/(*R*)-**12** (2.45 equiv) had much better chemoselectivity than the THF solution of $LiAlH_4$ (1 equiv)/(*R*)-**12** (2 equiv) as a catalyst in the reaction of **185** with **186** to make **187** (Scheme 38). For example, in the

Scheme 38

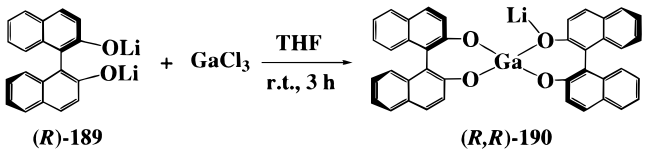


presence of 5 mol % of a THF solution of $LiAlH_4$ (1 equiv)/(*R*)-**12** (2.45 equiv), **185** reacted with **186** at −30 °C to give **187** in 81% yield and 80% ee. With less BINOL present, the side product **188** was produced in over 60% yield. The isolated complex (*R*,*R*,*R*)-**178** also catalyzed the formation of **187** in the same reaction with moderate enantioselectivity.

Besides Al, other group III elements such as B, Ga, and In were also used by Shibasaki and co-workers to prepare the bisBINOL heterobimetallic complexes.[96] Both the Ga−Na−BINOL complex and In−K−BINOL complex were found to be very effective in asymmetric Michael reactions. The addition of bases such as sodium *tert*-butoxide to the Ga−Na−BINOL complex greatly enhanced its catalytic activity in Michael reactions without decreasing the enantioselectivity. A similar phenomenon was observed for the Al−Li−BINOL complex (*R*,*R*)-**170**. When bases such as Li−hexamethyldisilazide and Na−malonate were added, the catalytic activity of (*R*,*R*)-**170** was increased with no reduction of its high enantioselectivity.

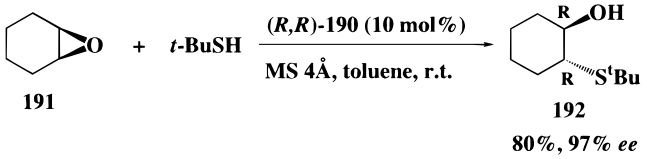
Deprotonation of (*R*)-**12** with *n*-butyllithium gave (*R*)-**189** which reacted with $GaCl_3$ to generate (*R*,*R*)-**190** (Scheme 39).[97] This complex was very efficient

Scheme 39



in the asymmetric ring opening of epoxides in the presence of thiols. For example, (*R*,*R*)-**190** catalyzed the reaction of *tert*-butyl thiol with cyclohexeneoxide (**191**) to give **192** with 97% ee (Scheme 40). The

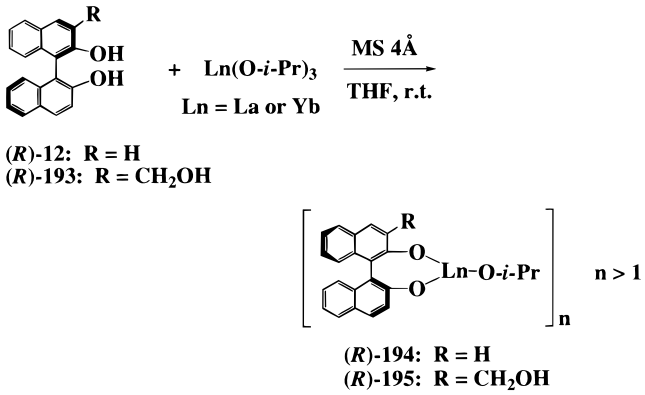
Scheme 40



reaction was carried out at room temperature in the presence of 10 mol % (*R*,*R*)-**190** and 4 Å molecular sieves. High ee's (82−98%) were observed for the asymmetric ring opening of different *meso*-epoxides using (*R*,*R*)-**190**.

Highly enantioselective La and Yb BINOL catalysts for the epoxidation of α,β-unsaturated ketones have also been discovered.[98] The complexes (*R*)-**194** and (*R*)-**195** prepared from the reaction of (*R*)-**12** or (*R*)-**193** with 1 equiv of $Ln(O\text{-}i\text{-}Pr)_3$ were shown to be oligomeric (Scheme 41). These complexes were used to catalyze the asymmetric epoxidation of α,β-unsaturated ketones. It was found that with one hydroxymethyl substituent in the 3-position of the BINOL ligand, the resulting catalysts (*R*)-**195,** especially the Yb complex, exhibited a higher chiral induction for the epoxidation. For example, in the presence of 5 mol % of (*R*)-**195a** (Ln = Yb), the α,β-unsaturated ketone **196** was oxidized to **197** by *tert*-butyl hydroperoxide in 83% yield and 94% ee (Scheme

Scheme 41



42). High ee's were observed for the epoxidation of both aromatic and aliphatic α,β-unsaturated ketones.

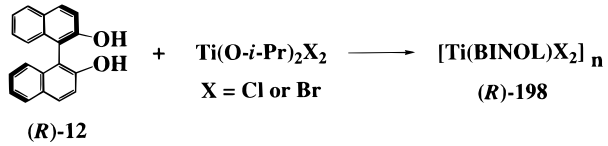
3.1.2. Other Lewis Acid Complexes (Ti, Zr, Al, B, Zn, and W) of BINOLs

Besides Shibasaki's heterometallic BINOL complexes, the catalytic properties of a number of other multi-BINOL-based complexes containing metal centers such as Ti, Zr, Al, B, Zn, and W have also been examined. These multi-BINOL catalysts exhibited high enantioselectivity in several reactions such as in Mikami's ene reaction, Kobayashi's Mannich-type reaction, Yamamoto's Claisen rearrangement, Katsuki's alkyl addition to aldehydes, and Kaufmann's Diels−Alder reaction described below.

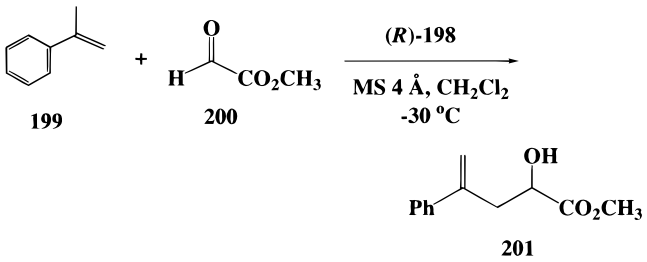
a. Titanium Complexes. In 1990, Mikami and co-workers found that titanium complexes prepared in situ from the reaction of diisopropoxytitanium dihalides with BINOL (Scheme 43) showed large positive nonlinear effects for ene reactions.[99,100] For example, when the optical purity of (*R*)-**12** was only 33.0%, the corresponding titanium complex (*R*)-**198** catalyzed the ene reaction of α-methyl styrene (**199**) with methyl glyoxylate (**200**) in the presence of molecular sieves, producing **201** with 91.4% ee and 92% yield (Scheme 44). It was proposed that the titanium−BINOL complex (*R*)-**198** forms dimeric structures in solution, and the meso form of heterochiral dimer is less reactive and more stable than the homochiral dimer, thus leading to the observed asymmetric amplification.

An attempt to prepare the (BINOL-H)$TiCl_2$ complex by azeotropic removal of 2-propanol from a toluene solution of (*R*)-**12** and (O-*i*-Pr)$_2TiCl_2$ in the presence of molecular sieves (4 Å) actually produced a bisBINOL μ-oxo titanium complex (*R*,*R*)-**202**.[101] The

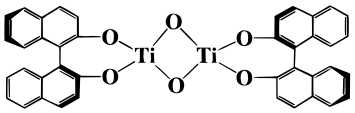
Scheme 43



Scheme 44



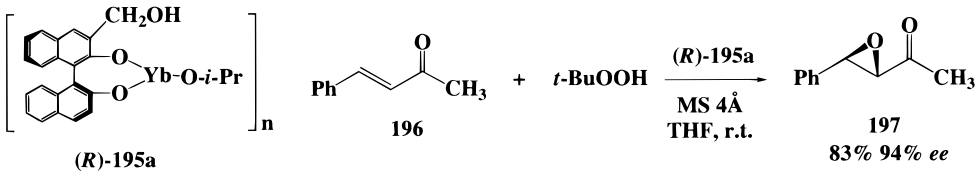
structure of (*R*,*R*)-**202** was established by vapor pressure osmometric (VPO) molecular mass measurement, IR, and elemental analysis. This complex



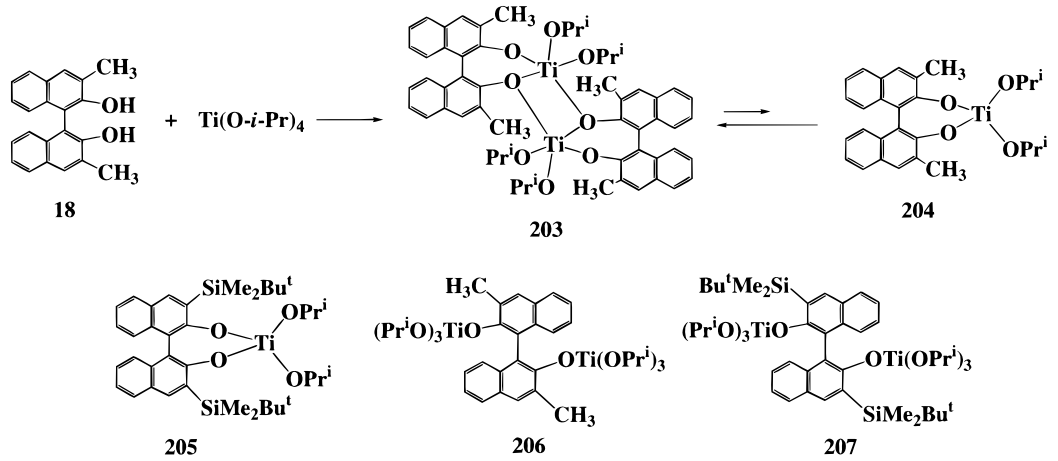
proved a very efficient catalyst for the asymmetric ene reaction of **199** with **200**. In the presence of 0.2 mol % of (*R*,*R*)-**202**, **201** was produced in 88% yield with 98.7% ee. The reaction was carried out at −30 °C in methylene chloride solution. A positive nonlinear effect between the optical purity of the BINOL ligands and the ee of the ene reaction product was observed. A VPO study of (*R*,*R*)-**202** and racemic **202** suggested that the heterochiral dimer should be more stable than the homochiral dimer. The authors concluded that the homochiral dimer would be a better catalyst than the heterochiral dimer, leading to the observed positive nonlinear effect. The rate of the ene reaction for the homochiral complex was estimated to be about 9 times faster than for the heterochiral complex. This explanation is similar to that proposed for the nonlinear effect of (*R*)-**198**.[99,100]

However, the study of the reaction of BINOL derivatives with titanium(IV) complexes carried out by Heppert and co-workers raised questions about the proposed mechanism for the nonlinear effect in the ene reaction. Heppert obtained **203** from the reaction of racemic **18** with 1 equiv of Ti(O-*i*-Pr)$_4$ (Scheme 45).[102] Variable-temperature NMR spectroscopic analysis and molecular weight measurements indicated that **203** was in equilibrium between the

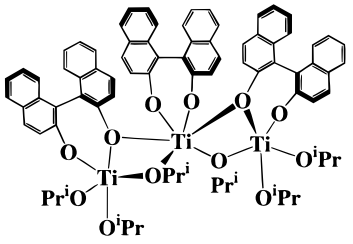
Scheme 42



Scheme 45



dimer form and the monomeric structure **204**. The NMR spectra of **203** were identical to those of (*R,R*)-**203** made from the optically active (*R*)-**18**. This suggests that the RR and SS diastereomers (the homodimers) should be thermodynamically more stable than the RS isomer (the heterodimer) in toluene solution, contrary to Mikaimi's proposal for (*R*)-**198** and (*R,R*)-**202**. A single-crystal X-ray analysis of **203** established the existence of the dimeric structure in the solid state. Because of the bulky silyl groups in **205**, this molecule only existed as a monomeric complex both in solution and in the solid state as shown by NMR and crystal structure analysis. The reaction of **18** with 2 equiv of Ti(O-*i*-Pr)$_4$ gave a binuclear complex **206**. The complex **203** was also reacted with Ti(O-*i*-Pr)$_4$ to give **206**. A similar compound **207** was obtained from the reaction of the corresponding binaphthol ligand with 2 equiv of Ti(O-*i*-Pr)$_4$. Its structure was also confirmed by X-ray analysis. Variable-temperature NMR studies demonstrated that **203** and **206** were in equilibrium in solution. When the temperature was increased to 340 K, **206** was almost completely converted to **203** and Ti(O-*i*-Pr)$_4$ in toluene solution. This study demonstrates that when there are bulky substituents in the 3,3′-positions of the BINOL ligand, the titanium complexes exist in the monomeric form. When the 3,3′-substituents are small like the methyl groups in **203**, the BINOL titanium complexes exist as dimers both in solution and in the solid state. The observation of Martin and Sharpless is consistent with this interpretation. They found that (*R,R,R*)-**208**, a BINOL complex without 3,3′-substituents, exists in a trimeric form as confirmed by X-ray analysis.[103]



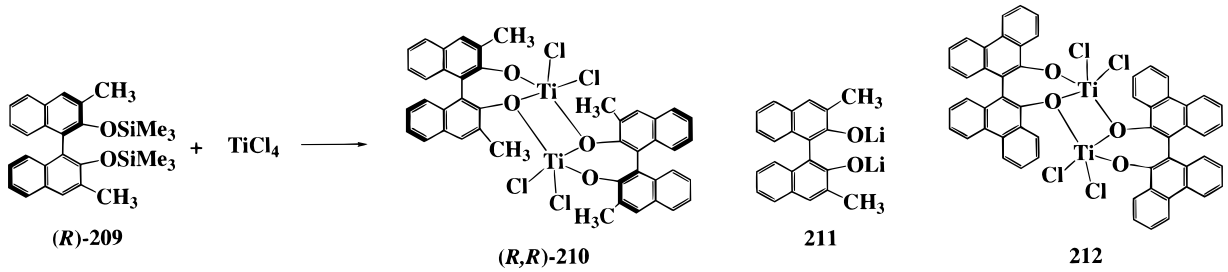
(*R,R,R*)-208

The reaction of the bistrimethylsilyl ether (*R*)-**209** with $TiCl_4$ gave the dimeric complex (*R,R*)-**210** (Scheme 46).[104] Racemic **210** was prepared from the reaction of **211** with $TiCl_4$. A dimeric biphenanthrolate complex **212** was also obtained. The NMR signals of racemic **210** were identical to those of (*R,R*)-**210**, indicating that the homochiral dimer was the preferred structure as is the case for **203**. A single-crystal X-ray analysis of **210** confirmed its structure.

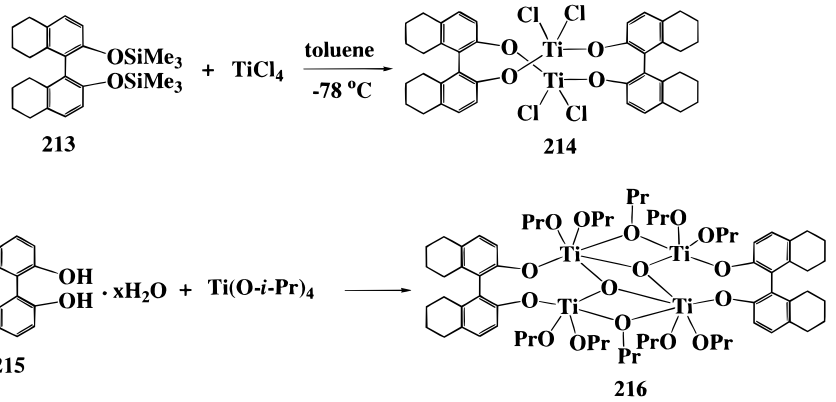
Heppert's results indicate there was no compelling evidence for the heterochiral dimer to be more stable than the homochiral dimer in the BINOL titanium complexes. This is contrary to Mikami's explanation of the chiral amplification of the ene reaction catalyzed by (*R*)-**198**.[99,100]

(*R,R*)-**210** was used to catalyze the Diels−Alder reaction of methyl acrylate with cyclopentadiene. It was found that a 2:1 titanium to methyl acrylate ratio gave the cycloaddition product with 26% ee.[104] At lower catalyst-to-substrate ratios, the ee's were sig-

Scheme 46



Scheme 47

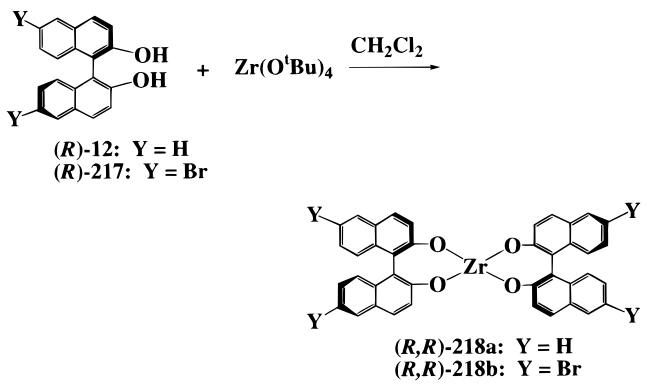


nificantly lower and a reversal in product configuration was observed. A kinetic study showed that the reaction was first order in titanium catalyst, the diene and the dienophile. Spectroscopic and kinetic studies showed that the probable catalytically active species in the asymmetric Diels−Alder reaction was dimeric rather than monomeric.

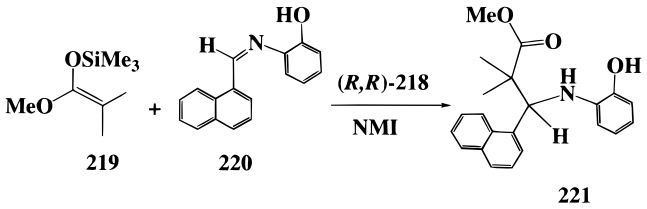
The complex **214** was obtained from the reaction of the partially hydrogenated racemic binaphthyl compound **213** with $TiCl_4$ in toluene solution at −78 °C (Scheme 47).[105] An X-ray analysis established a dimeric structure for this compound in the solid state. The dihedral angle of the two partially hydrogenated naphthyl rings in the binaphthyl ligand was found to be 93°. The dimeric form in solution was confirmed by a solution molecular weight measurement. A variable-temperature NMR study demonstrated that **214** existed as a single isomer in solution. Its NMR spectrum was identical to that of the complex made from the optically pure **213**. It appears, therefore, that **214** is a homochiral dimeric complex. When the partially hydrogenated BINOL **215** containing a small amount of water was reacted with Ti(O-*i*-Pr)$_4$, **216** was isolated and characterized by X-ray analysis. The two binaphthyl dihedral angles were found to be 80° and 88° respectively in this compound. Calculations were carried out to study how the binaphthyl dihedral angles influence the energies of both 2,2′-dimethoxy-1,1′-binaphthyl and 2,2′-dimethoxy-1,1′-bitetrahydronaphthyl. It was found that for 2,2′-dimethoxy-1,1′-binaphthyl, there was no significant energy difference over the range of 60−120°. However, for 2,2′-dimethoxy-1,1′-bitetrahydronaphthyl, when the dihedral angle deviated from 90°, the energy minimum, by ±10°, there were large increases in energy. Therefore, the titanium atoms in the complexes **214** and **216** preferred to form bridge bonds rather than the more strained chelating bonds as in (*R*,*R*)-**210** in order to maintain the dihedral angle of the 1,1′-bitetrahydronaphthyl ligands at about 90°.

b. Zirconium Complexes. In 1997, Kobayashi and co-workers found that bisBINOL−zirconium(IV) complexes (*R*,*R*)-**218a,b** were highly enantioselective in a catalytic Mannich-type reaction.[106] (*R*,*R*)-**218a,b** were prepared in situ from the reaction of Zr(O-*t*-Bu)$_4$ with 2 equiv of (*R*)-**12** and (*R*)-**217** respectively in methylene chloride solution (Scheme 48). These bisbinaphthyl complexes were used to catalyze the

Scheme 48



Scheme 49

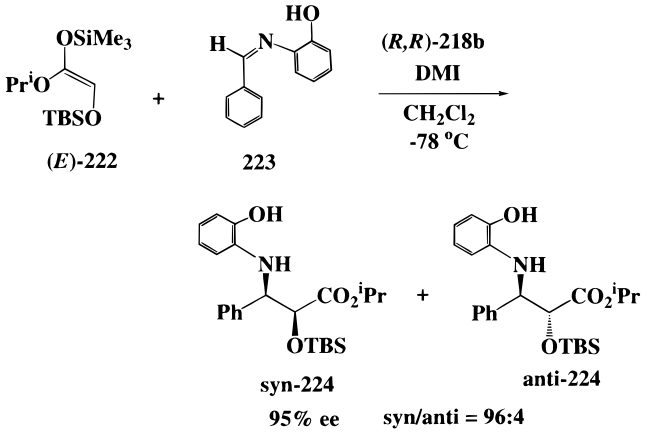


reaction of a silyl ketene **219** with an aldimine **220** to generate an *β*-amino ester **221** (Scheme 49). This reaction required the addition of *N*-methylimidazole (NMI) to achieve good enantioselectivity. (*R*,*R*)-**218b** exhibited much higher enantioselectivity than (*R*,*R*)-**218a**. For example, in the presence of 5 mol % of (*R*,*R*)-**218b** and 5 mol % of NMI at −45 °C, **221** was produced in 69% yield and 95% ee. Excellent ee's were observed for the reaction of various silylketenes with different aryl aldimines.

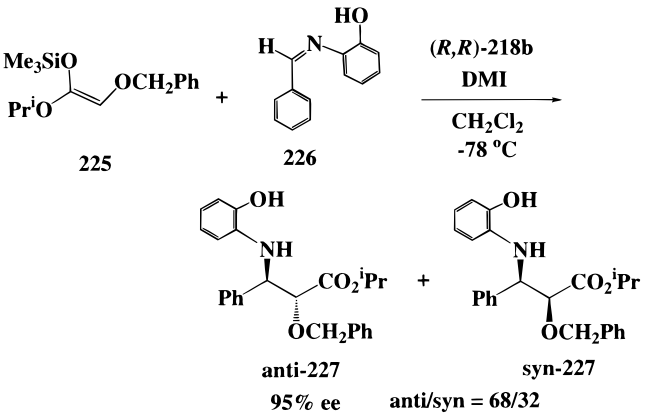
Both good enantioselectivity and diastereoselectivity were observed when (*R*,*R*)-**218b** was used to catalyze the asymmetric synthesis of *β*-amino alcohols in a Mannich type reaction using arylaldimines and various α-alkoxy enolates.[107] As shown in Scheme 50, in the presence of 10 mol % of (*R*,*R*)-**218b** as well as the base adduct 1,2-dimethylimidazole (DMI), at −78 °C in methylene chloride, (*E*)-**222** reacted with **223** to give **224** in a syn/anti ratio of 96:4 and 95% ee.

The reaction of (*Z*)-**222** with **223** under the same conditions also gave **224** with both high syn/anti ratio and ee. Changing the protecting groups of the α-alkoxy enolate gave the anti isomers with excellent ee's and as the major products. For example, under

Scheme 50

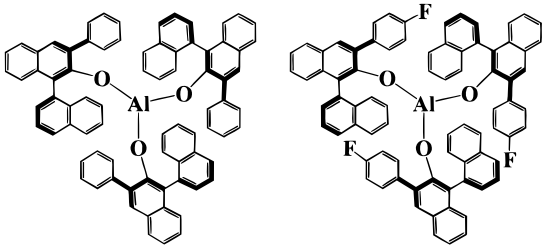


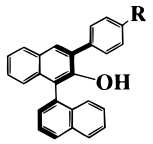
Scheme 51



the same conditions as the reaction of **222** with **223**, **225** reacted with **226** to produce **227** with an anti/syn ratio of 68/32 and 95% ee (Scheme 51).

c. Aluminum Complexes. In 1995, Yamamoto and co-workers synthesized the chiral aluminum complexes (*R*,*R*,*R*)-**228** and (*R*,*R*,*R*)-**229** from the reaction of trimethyl aluminum with (*R*)-**230** and (*R*)-**231** respectively.[108] Although both complexes were

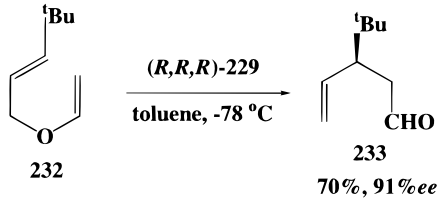




(*R*)-**230**: R = H
(*R*)-**231**: R = F

used to promote an asymmetric Claisen rearrangement, the fluorine-substituted binaphthyl aluminum complex (*R*,*R*,*R*)-**229** proved more efficacious than (*R*,*R*,*R*)-**228**. For example, in the presence of 1.1−2 equiv of (*R*,*R*,*R*)-**229** at −78 °C in toluene solution, the vinyl ether **232** was converted to **233** in 70% yield and 91% ee (Scheme 52). Under the same conditions, using (*R*,*R*,*R*)-**228**, **233** was obtained in 63% yield and 63% ee.

Scheme 52



Inoue and co-workers studied the polymerization of racemic **234** catalyzed by the optically active bisBINOL−aluminum complexes (*R*,*R*)-**235a**−**e** using **236** as the initiator (Figure 7).[109] They found that (*R*,*R*)-**235a** was the most enantioselective catalyst for this polymerization. In the presence of (*R*,*R*)-**235a**, when 75% of **234** was polymerized, the ee of the remaining monomer **234** was found to be 40%. Therefore, one enantiomer of **234** was selectively polymerized by the optically active catalyst.

d. Zinc Complexes. Katsuki and co-workers found that when (*R*)-**237a**, a BINOL with substituents in the 3,3′-positions, was treated with 1 equiv of $ZnEt_2$, 2 equiv of ethane were generated (Scheme 53).[110,111] The ^{1}H NMR spectrum of the product (*R*,*R*,*R*)-**238a** (R = Me) showed the hydroxyl proton signal of (*R*)-**237a** had disappeared. A single-crystal X-ray analysis of (*R*,*R*,*R*)-**238b** (R = Et) established a trimeric C_2 symmetric structure for this binaphthyl−zinc complex. In (*R*,*R*,*R*)-**238b**, each of the three zinc atoms is coordinated with six oxygen atoms. The central zinc atom has a triangular prismatic geometry with the coordination of the six phenoxide oxygens of the three binaphthyl ligands. The remaining two zinc atoms have a slightly distorted octahedral geometry with three phenoxide oxygens and three carbonyl oxygens coordinated to each zinc atom. These binaphthyl zinc complexes were used in an asymmetric Simmons−Smith reaction. Because the zinc centers in (*R*,*R*,*R*)-**238** were coordinatively saturated, they did not show catalytic activity. However, when the compounds (*R*)-**237** were treated with excess $ZnEt_2$, efficient catalysts resulted. Ideal conditions involved the use of 6 equiv of diethylzinc. For example, when (*R*)-**237b** was reacted with 6 equiv of diethylzinc, the resulting binaphthyl−Zn complex promoted the cyclopropanation of **239** with methylene diiodide to give the cyclopropane product (1*R*,2*R*)-**240** with an ee of up to 94% (Scheme 54). This process required the use of 1 equiv of (*R*)-**237** which was recovered after the reaction.

A ^{1}H NMR spectroscopic study for the reaction of (*R*,*R*,*R*)-**238a** (R = Me) with excess diethylzinc in CD_2Cl_2 at room temperature was carried out. Since four singlets for the methyl protons of the amide groups were observed rather than the two singlets in the C_2 symmetric trimer, it is possible that there is formation of a monomeric binaphthyl complex in the presence of excess diethylzinc. The structure of

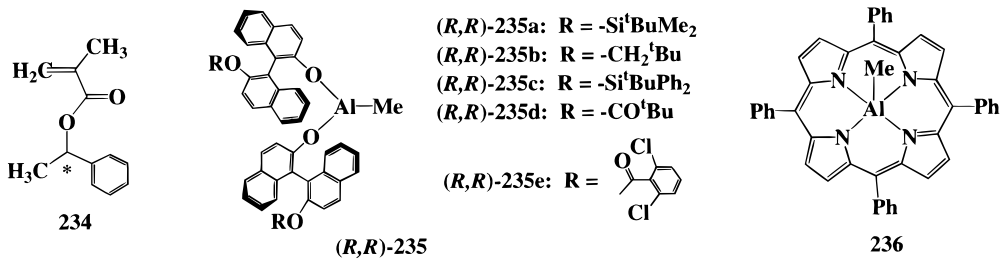
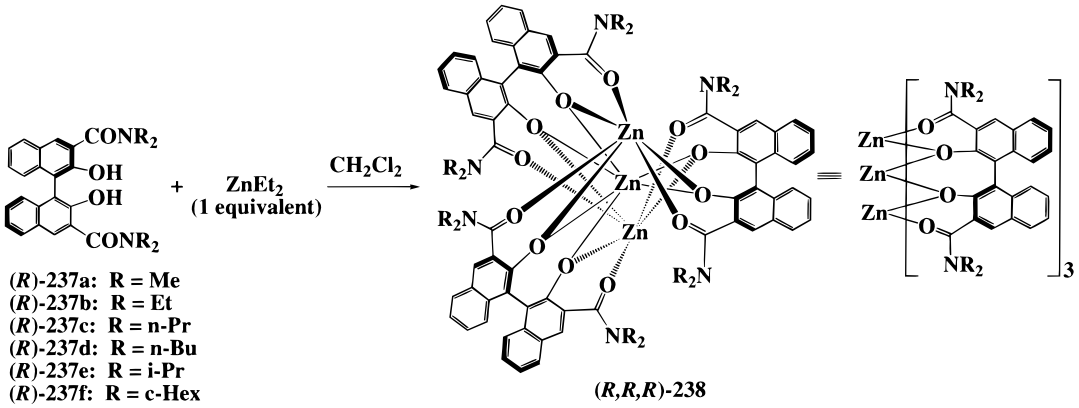
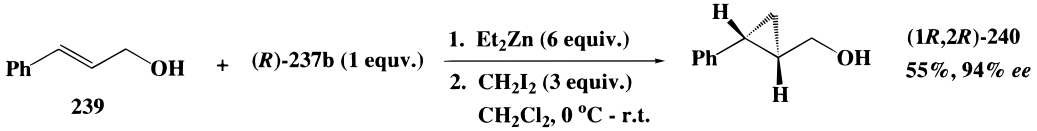


Figure 7.

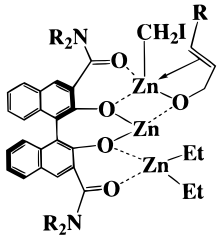
Scheme 53



Scheme 54



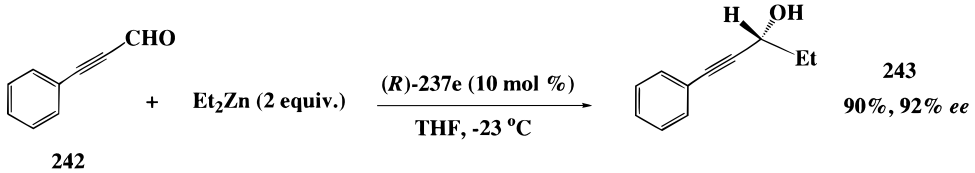
such monomeric complexes was unclear, but should contain multiple zinc centers. Other oligomeric binaphthyl−zinc complexes probably existed in equilibrium with the monomeric complex in solution. Complex **241** was proposed as a possible intermediate in the asymmetric Simmon−Smith reaction discussed above.



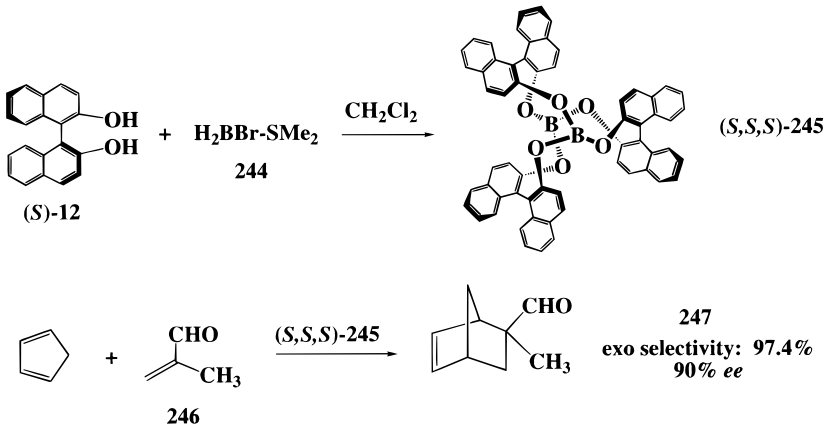
A catalytic amount of (*R*)-**237** brought about the asymmetric addition of diethylzinc to a series of aldehydes.[110,111] When 10 mol % of (*R*)-**237e** was used, in the presence of 2 equiv of diethylzinc, phenyl propargyl aldehyde (**242**) was converted to a chiral alcohol **243** in 90% yield and 92% ee at −23 °C (Scheme 55). Excellent enantioselectivity was also observed for the reaction of both para- and ortho-substituted aromatic aldehydes. Both the chemical yield and the enantioselectivity were better when the reaction was carried out in THF rather than in methylene chloride and toluene. Examination of the ^{1}H NMR spectrum of the trimer (*R*,*R*,*R*)-**238** showed that there were various species including monomers and trimers present in the THF solution. Since it appears that in the less polar methylene chloride only the trimer form was observed, the THF solution was more favorable for the generation of the catalytically active monomeric species.

e. Boron Compounds. In 1990, Kaufmann et al. found that the reaction of (*S*)-**12** with monobromoborane dimethyl sulfide (**244**) produced a C_3-symmetric trisBINOL−boron complex (*S*,*S*,*S*)-**245** (Scheme 56).[112] The structure of this propeller molecule was confirmed by single-crystal X-ray analysis of the corresponding complex made from racemic BINOL. (*S*,*S*,*S*)-**245** catalyzed the Diels−Alder reaction with both high diastereoselectivity and enantioselectivity. At

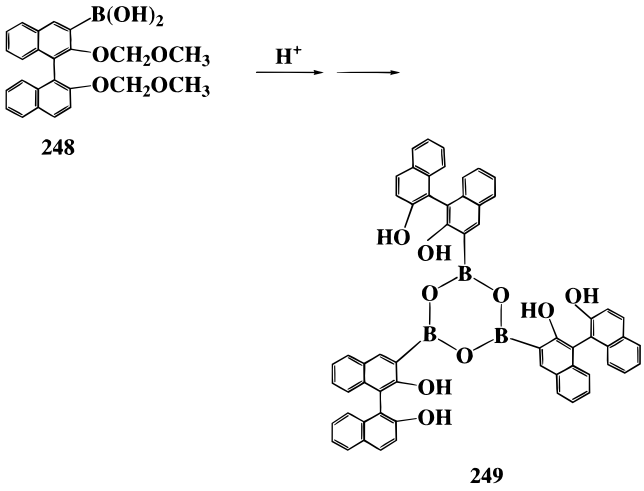
Scheme 55



Scheme 56



Scheme 57

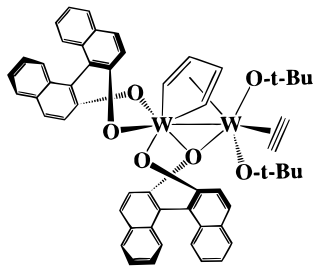


−78 °C in methylene chloride solution, in the presence of 3 mol % (*S*,*S*,*S*)-**245**, the reaction of cyclopentadiene with methacrolein (**246**) produced **247**: 97.4% of the exo isomer and 90% ee.

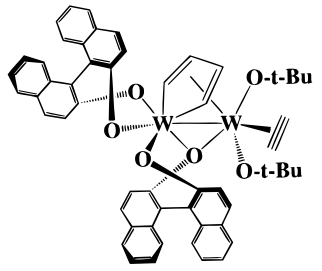
The novel Lewis acid trisbinaphthyl boroxin **249** was prepared by Kiyooka et al. by the hydrolysis of the racemic binaphthyl boronic acid **248** (Scheme 57).[113] This compound proved an effective catalyst for the reaction of a silylketene with α,*β*-unsaturated ketones in the presence of molecular sieves. The optically active form of **249** was not reported.

f. Tungsten Complexes. In 1992, Heppert and co-workers observed that the reaction of $W_2(O\text{-}t\text{-}Bu)_6$, **250**, with 2 equiv of (*R*)-**12** gave a bisBINOL complex (*R*,*R*)-**251** (Scheme 58).[114,115] (*R*,*R*)-**251** had three possible configurations, i.e., (*R*,*R*)-**251a** (Λ−Λ-gauche), (*R*,*R*)-**251b** (Δ−Δ-gauche), and (*R*,*R*)-**251c** (Λ−Δ-anti). ^{1}H NMR studies of this complex indicated that (*R*,*R*)-**251** was more likely to possess the gauche than the anti structure. The crystal structure of the monomeric BINOL complex (*R*)-**252**, made from **250** and 1 equiv of (*R*)-**12**, showed that the (*R*)-BINOL ligand on the tungsten adopted the Λ configuration. This leads to the conclusion that the bisBINOL tungsten complex most likely had the structure shown in (*R*,*R*)-**251a**. When racemic BINOL was reacted with **250**, out of six possible stereoisomers not including enantiomers, only a highly symmetric compound was obtained. On the basis of the NMR analysis, it was concluded that the anti-meso complex (*R*,*S*)-**253** was the most probable structure for the product. In (*R*,*S*)-**253**, the (*R*)-BINOL ligand adopted an Λ configuration and the (*S*)-BINOL ligand adopted a Δ configuration. The *t*-BuO groups in (*R*,*S*)-**253** were significantly shielded by the naphthalene rings to give a ^{1}H NMR signal at $\delta = 0.1$. The reaction of (*R*,*R*)-**251** with (*S*,*S*)-**251** in the presence of *tert*-butyl alcohol at 0 °C led to the formation of (*R*,*S*)-**253** as the major product. The reaction of **250** with 3 equiv of (*R*)-**12** gave the trisBINOL complex (*R*,*R*,*R*)-**254**.

(*R*,*S*)-**253** reacted with acetylene to give a product mixture of two isomers in a 2:1 ratio. The products had a number of possible structures. Their NMR spectra showed the presence of an μ^2,η^4-C_4H_4 unit as well as an η^2-C_2H_2 unit. The complexes **255a** and **255b** were proposed as the major and minor products, respectively.



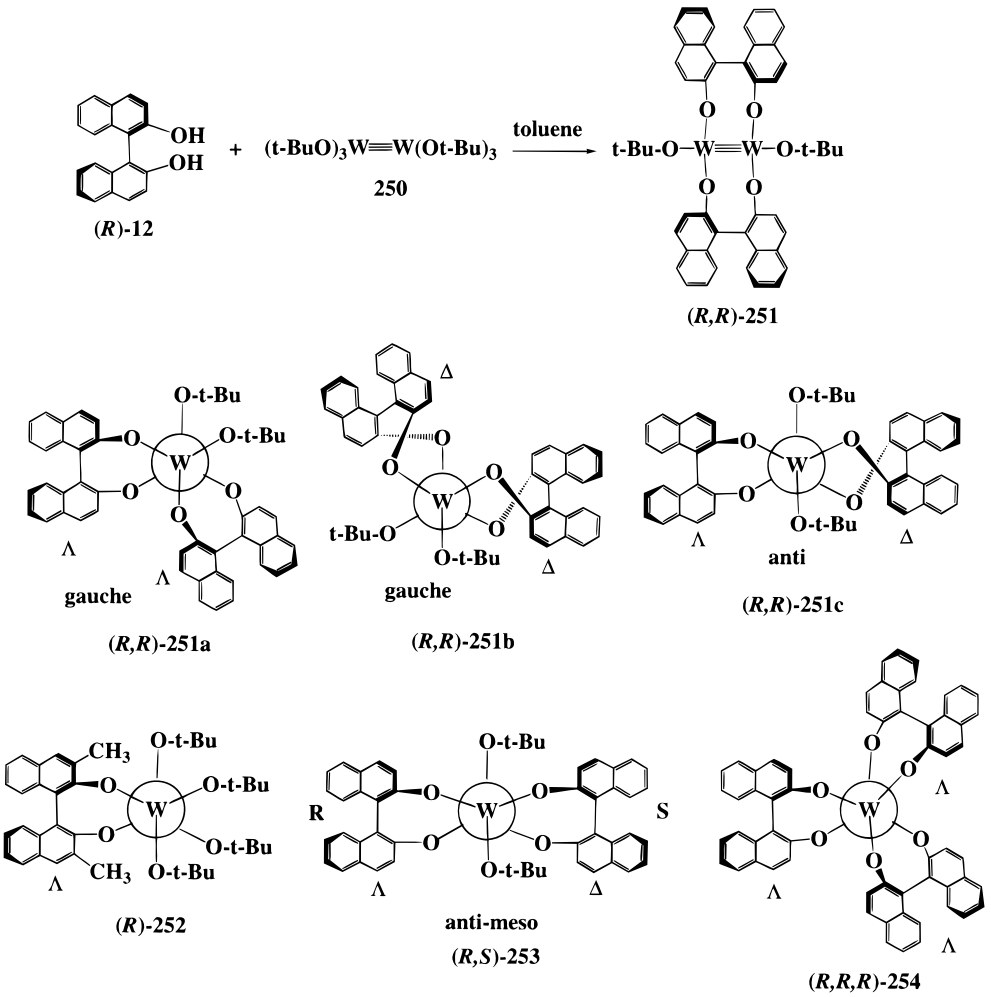
255a



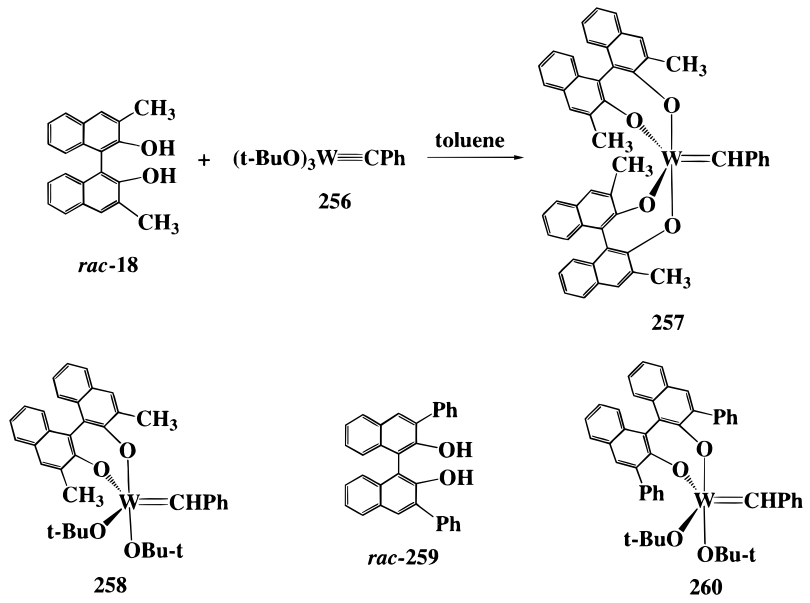
255b

BINOL-based tungsten(VI) alkylidene complexes were prepared by Heppert and co-workers.[116] The reaction of 2 equiv of *rac*-**18** with a tungsten carbyne complex **256** gave **257** after recrystallization (Scheme 59). The NMR study of **257** showed that this complex was generated as a single isomer identical to (*R*,*R*)-**257** made from (*R*)-**18**. Therefore, the stereospecific

Scheme 58



Scheme 59

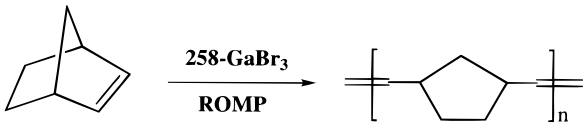


reaction of *rac*-**18** with **256** gave the thermodynamically more stable homochiral structure. One equivalent of *rac*-**18** reacted with **256** to give the monoBINOL complex **258**. The 3,3′-diphenyl BINOL **259** only produced a monoBINOL complex **260** because of steric hindrance. When either racemic **12** or optically pure **12** was reacted with **256**, no identifiable compounds were isolated from the very complicated product mixture.

The bisbinaphthyl tungsten carbene **257** was reacted with benzaldehyde to give a mixture of *cis*- and *trans*-stilbene in 2.3:1 ratio and 35% yield. When **257**

was used to catalyze the ring-opening metathesis polymerization (ROMP)[117] of norbornene, it showed very low activity with only 3−5% yield of the corresponding polymer being produced. Although **258** also had very low catalytic activity for the ROMP of norbornene, the addition of $GaBr_3$ as cocatalyst gave quantitative formation of the polymer at 0 °C (Scheme 60). However, **257** did not show much change in its

Scheme 60

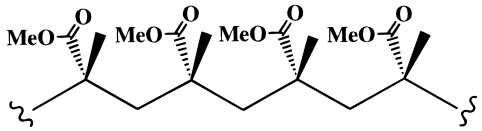


catalytic activity in the presence of $GaBr_3$. Compared to the *tert*-butoxy groups of **258**, the chelating BINOL ligands in **257** proved too difficult to remove in order to generate the open coordination site required for the ROMP of norbornene.

3.1.3. Binaphthyl-Crown Ethers in Asymmetric Catalysis

The bisbinaphthyl crown ether (*S*,*S*)-**19** is not only very useful as a host for chiral recognition, it can also act as a catalyst for asymmetric Michael additions.[57] When (*S*,*S*)-**19** was treated with alkaline bases such as potassium *tert*-butoxide, coordination of the oxygen atoms with the potassium cation produced a suitable chiral base catalyst. For example, in the presence of 5% of (*S*,*S*)-**19** and potassium *tert*-butoxide at −78 °C, the reaction of methyl vinyl ketone (**186**) with the *β*-ketone ester **261** generated (*R*)-**262** in 48% yield and about 99% ee (Scheme 61). (*S*,*S*)-**19** and potassium *tert*-butoxide also catalyzed the reaction of methyl acrylate with methyl phenylacetate (**263**) to give (*S*)-**264** in 80% yield and 65% ee.

The complex of (*S*,*S*)-**19** with potassium *tert*-butoxide was also used to carry out the anionic polymerization of methyl methacrylate.[58] The resulting poly(methyl methacrylate) was 88% isotactic with a transient specific optical rotation of $[\alpha]^{25}_{578} = -180$.

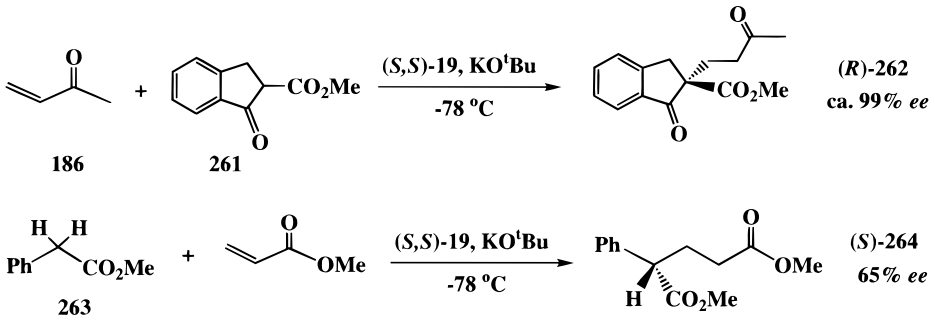


isotactic poly(methyl methacrylate)

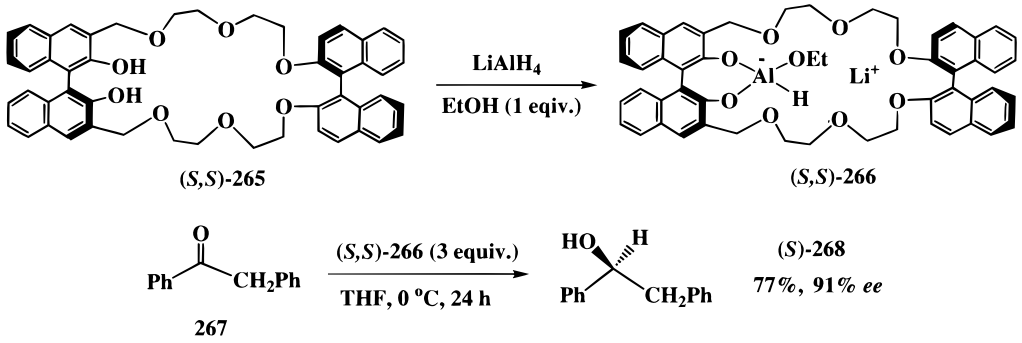
The optical rotation of the polymer was probably due to partial helicity of the polymer. Because isotactic poly(methyl methacrylate) is not inherently chiral, this polymer underwent conformation randomization at room temperature over several hours to lose its optical rotation.

In 1991, Yamamoto et al. prepared the bisbinaphthyl crown ether (*S*,*S*)-**265** and studied its use in the asymmetric reduction of ketones (Scheme 62).[118] When (*S*,*S*)-**265** was treated with 1 equiv of lithium aluminum hydride, a chiral aluminum hydride complex (*S*,*S*)-**266** was generated. This complex was highly enantioselective when used for the reduction of prochiral ketones. For example, at 0 °C in the presence of 3 equiv of (*S*,*S*)-**266**, phenylbenzyl ketone (**267**) was reduced to (*S*)-**268** in 77% yield and 91% ee. In this process, (*S*,*S*)-**266** probably acted as a bifunctional chiral host. The crown ether-bound lithium cation may coordinate with the carbonyl oxygen of **267**, followed by the chiral aluminum hydride delivering a hydride to one prochiral face of the carbonyl. In this bifunctional stereocontrol mode, the two binaphthyl units work cooperatively to generate the alcohol product with high enantioselectivity.

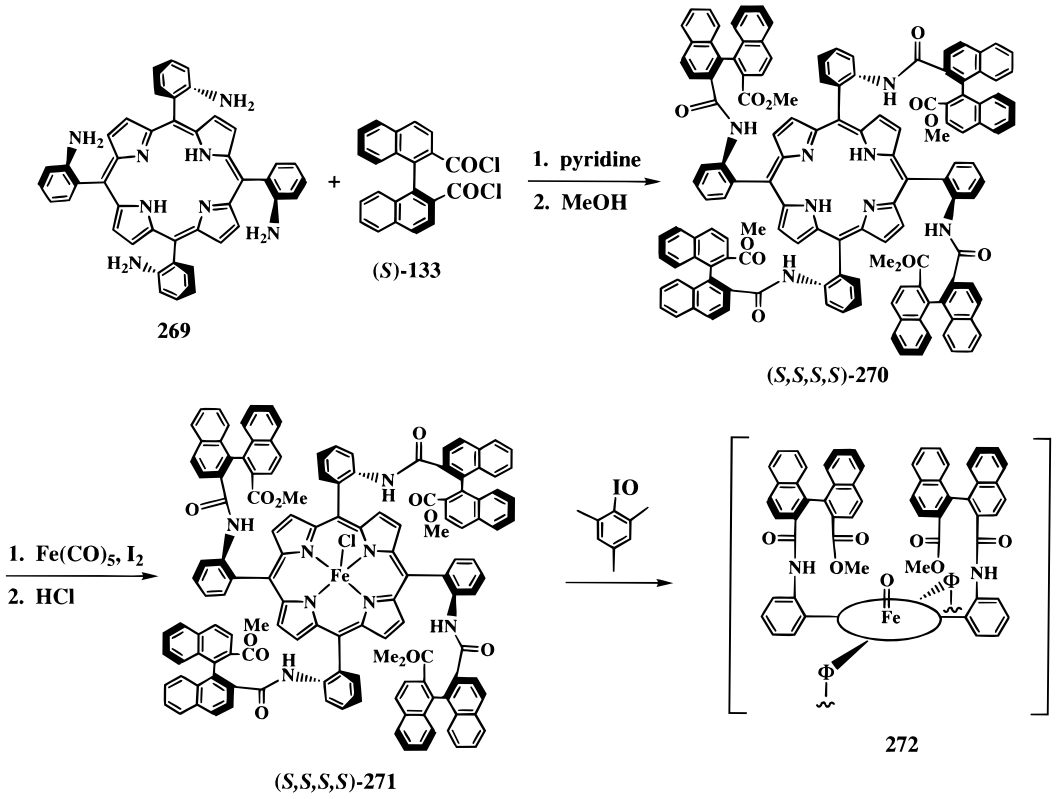
Scheme 61



Scheme 62

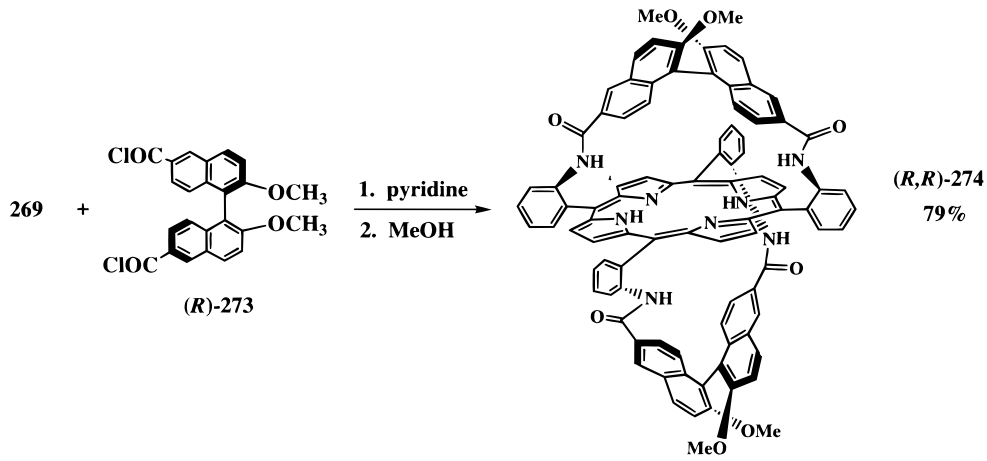


Scheme 63



269 (S)-133 (S,S,S,S)-270 (S,S,S,S)-271 272

Scheme 64



(R)-273

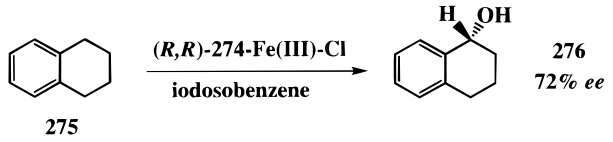
3.2. Nitrogen-Based Multibinaphthyl Ligands

3.2.1. Binaphthyl-Substituted Porphyrin Catalysts

Heme enzymes such as cytochrome P-450 can induce the highly selective oxidation of organic molecules. To mimic the functions of these enzymes as well as to develop useful enantioselective catalysts, extensive studies of synthetic chiral porphyrins have been carried out.[119] A number of multibinaphthyl-based chiral porphyrins were designed and synthesized to catalyze the asymmetric oxidations of alkanes, alkenes, and sulfides.

In 1983, Groves et al. prepared a tetrakisbinaphthyl-based chiral porphyrin (*S*,*S*,*S*,*S*)-**270**[120] from 5α,10*β*,15α,20*β*-tetrakis(o-aminophenyl)porphyrin (α,*β*,α,*β*-H_2TAPP) (**269**), a stable rotational atropisomer of H_2TAPP first synthesized by Collman et al.[121] (Scheme 63). The reaction of **269** with (*S*)-**133** followed by addition of methanol produced (*S*,*S*,*S*,*S*)-**270** in low yield. The ^{1}H NMR spectrum of this porphyrin displayed a sharp singlet at δ −0.72 for the methyl ester protons, indicating a D_2 symmetric structure with all the methyl groups lying either directly above or below the shielding porphyrin ring. (*S*,*S*,*S*,*S*)-**270** was metalated with $Fe(CO)_5$ and I_2 to give (*S*,*S*,*S*,*S*)-**271**. This metalloporphyrin was used to catalyze the epoxidation of various unfunctionalized olefins in the presence of iodosomesitylene. The highest enantioselectivity of this catalyst was observed when *p*-chlorostyrene was oxidized at −23 °C. The corresponding epoxide was produced in 63% yield and 51% ee. The complex **272** generated in the presence of iodosomesitylene was proposed as the catalytically active oxoiron intermediate.

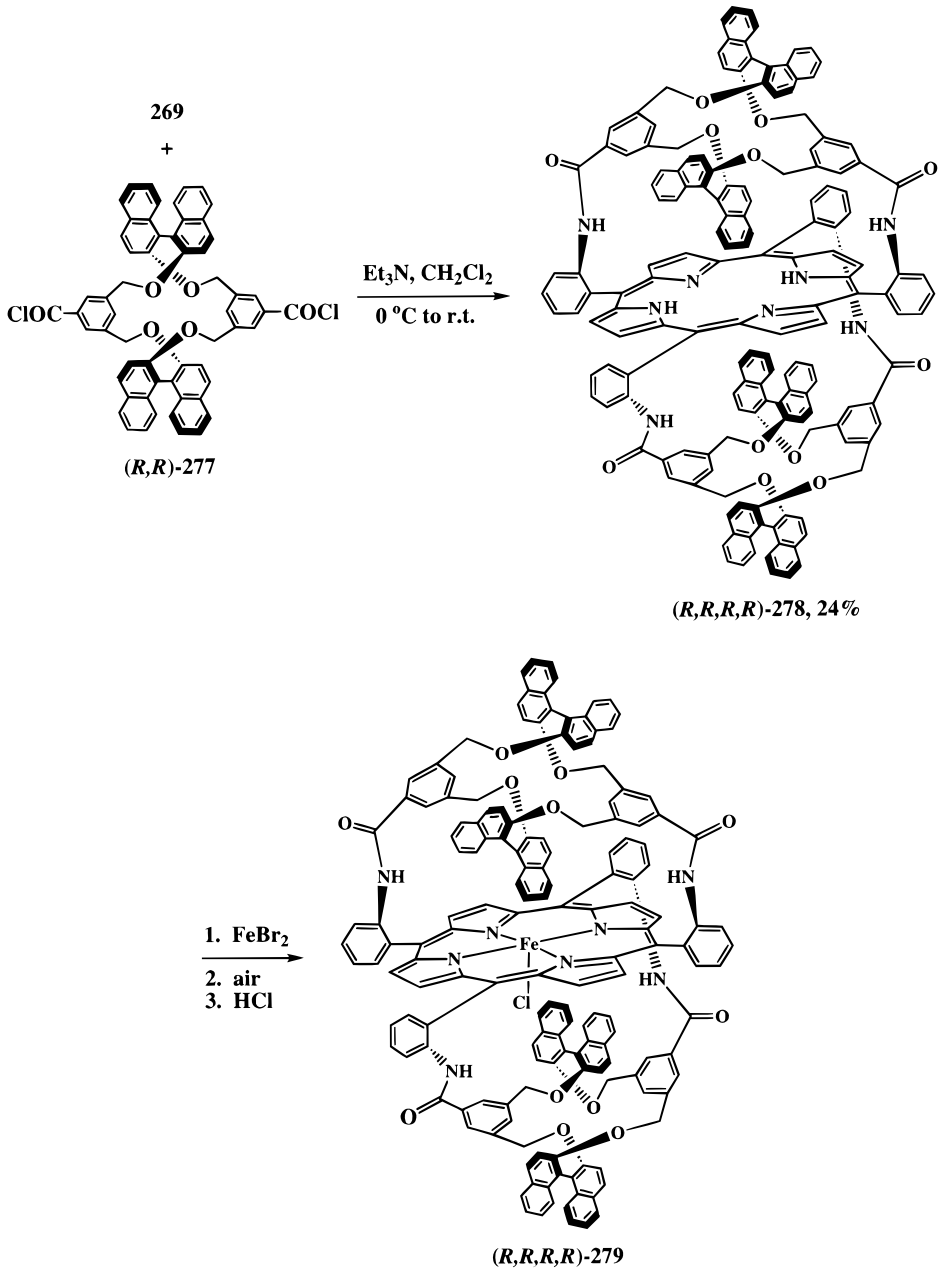
Scheme 65



Later, Grove et al. prepared a bisbinaphthyl-bridged chiral porphyrin (*R*,*R*)-**274** from the reaction of (*R*)-**273** with **269** with a remarkably high yield (79%) (Scheme 64).[122] Its $Mn^{III}Cl$ and $Fe^{III}Cl$ complexes were used to catalyze the asymmetric epoxidation of alkenes, the asymmetric hydroxylation of arylalkanes and the asymmetric oxidation of sulfides. Iodosobenzene was used as the stoichiometric oxidant in these reactions. The optimum optical yield for the epoxidation was found for *cis*-*β*-methylstyrene which gave the epoxide with an ee of 72% at −15 °C in the presence of (*R*,*R*)-**274**−$Fe^{III}Cl$. This metalloporphyrin complex also catalyzed the oxidation of arylalkanes such as ethyl benzene, 4-methoxyethylbenzene, tetrahydronaphthalene, and 1-ethylnaphthalene. The resulting chiral alcohols were obtained with ee's of 40−72%. Scheme 65 shows the example of tetrahydronaphthalene (**275**) which was oxidized to a chiral alcohol **276** with 72% ee in the presence of (*R*,*R*)-**274**−$Fe^{III}Cl$ and iodosobenzene. The complex (*R*,*R*)-**274**−$Mn^{III}Cl$ gave much lower ee's (12−26%) for the oxidation of arylalkanes. Whereas the oxidation of sulfides catalyzed by (*R*,*R*)-**274**−$Fe^{III}Cl$ gave the corresponding chiral sulfoxides with 14−48% ee.

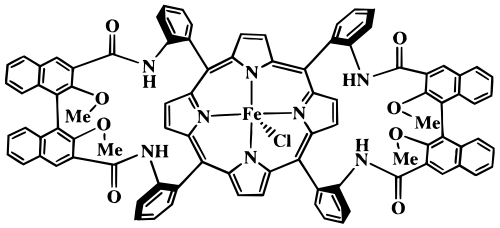
In 1992, Collman et al. reported a chiral porphyrin (*R*,*R*,*R*,*R*)-**278** that had two binaphthyl units capped onto each face of the porphyrin ring (Scheme 66).[123] It was made from the reaction of **269** with (*R*,*R*)-**277** in methylene chloride at 0 °C in the presence of triethylamine and gave a yield of 24%. (*R*,*R*,*R*,*R*)-**278** was converted to the iron(III) chloride complex

Scheme 66



(*R*,*R*,*R*,*R*)-**279** by reaction with $FeBr_2$, followed by air oxidation and aqueous HCl extraction which was subsequently used to catalyze the asymmetric epoxidation of several aryl substituted olefins in the presence of iodosobenzene. Although the best ee (63%) was for the epoxidation of 2-vinylnaphthalene, in general other alkenes gave ee's of 20−56%. A monobinaphthyl capped Mn^{III}−phorphyrin complex gave an ee of only 13% for the epoxidation of styrene.[124]

In 1987, Naruta et al. used **269** to prepare a bisbinaphthyl-based iron(III) porphyrin **280** catalyst for the oxidation of olefins.[125] Subsequently, they

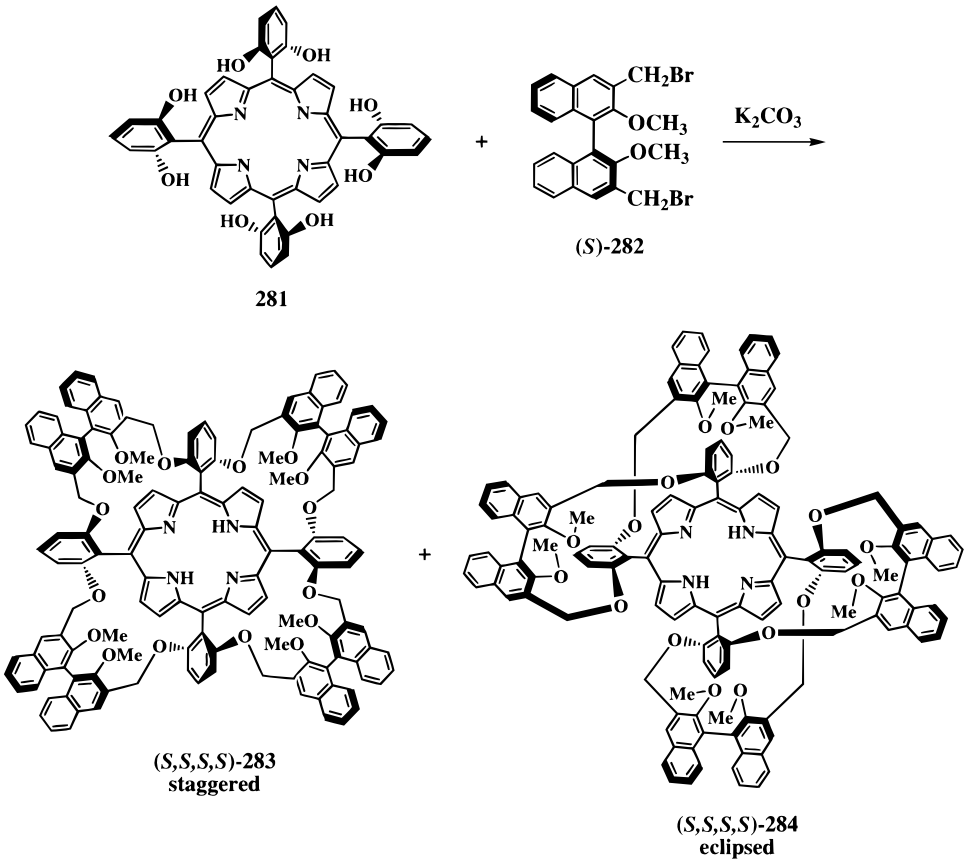


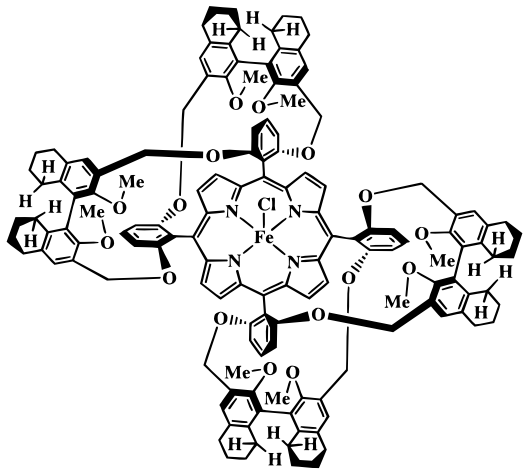
280

prepared tetrabinaphthyl-based chiral porphyrins containing etheral linkage rather than the amide linkages found in the binaphthyl porphyrins described above. Two chiral porphyrins (*S*,*S*,*S*,*S*)-**283** ("staggered") and (*S*,*S*,*S*,*S*)-**284** ("eclipsed") were obtained each in 4−5% yield from the reaction of 5,10,15,20-tetrakis(2,6-dihydroxyphenyl) porphine (**281**) with (*S*)-**282** in the presence of K_2CO_3 (Scheme 67).[126,127] Both compounds showed intense CD signals in the 400−700 nm range. Since the binaphthyl units themselves do not absorb above 400 nm, it appears that a chiral conformation for the porphyrin ring has been induced by the binaphthyl substituents. The CD spectra of (*R*,*R*,*R*,*R*)-**283** and (*R*,*R*,*R*,*R*)-**284** prepared from (*R*)-**282** were obtained which were the exact mirror images of those for (*S*,*S*,*S*,*S*)-**283** and (*S*,*S*,*S*,*S*)-**284**, respectively. (*S*,*S*,*S*,*S*)-**283** and (*S*,*S*,*S*,*S*)-**284** were then converted into the corresponding $Fe^{III}Cl$ complexes by reaction with $Fe(CO)_5/I_2$ followed by treatment with aqueous hydrogen chloride. These phorphyrin−$Fe^{III}Cl$ complexes were used to catalyze the epoxidation of styrene and its derivatives in the presence of iodosobenzene. Up to 80% ee of the *R* epoxide was obtained for the epoxidation of 2-nitrostyrene when (*S*,*S*,*S*,*S*)-**284**−$Fe^{III}Cl$ was used. However, only 54% ee was observed when the corresponding staggered (*S*,*S*,*S*,*S*)-**283** complex was used. In general, styrene derivatives containing electron-withdrawing groups on the benzene ring gave better optical yields than those containing electron-donating groups. A single electron-transfer mechanism between the ironoxo intermediate and the olefin was proposed to explain this catalytic epoxidation process. A $\pi-\pi$ interaction of the electron-deficient olefins with the electron-rich chiral auxiliaries was suggested as being responsible for the observed high asymmetric induction.

The partially hydrogenated (*R*)-binaphthyl-based chiral iron(III) porphyrin complex (*R*,*R*,*R*,*R*)-**285** has also been prepared.[128] This complex was shown to give higher optical yields in asymmetric epoxidations than (*S*,*S*,*S*,*S*)-**284**−$Fe^{III}Cl$. For example, (*R*,*R*,*R*,*R*)-**285** catalyzed the epoxidation of 2-nitrostyrene and 3,5-dinitrostyrene with 89% and 96% ee respectively.

Scheme 67





(*R,R,R,R*)-285

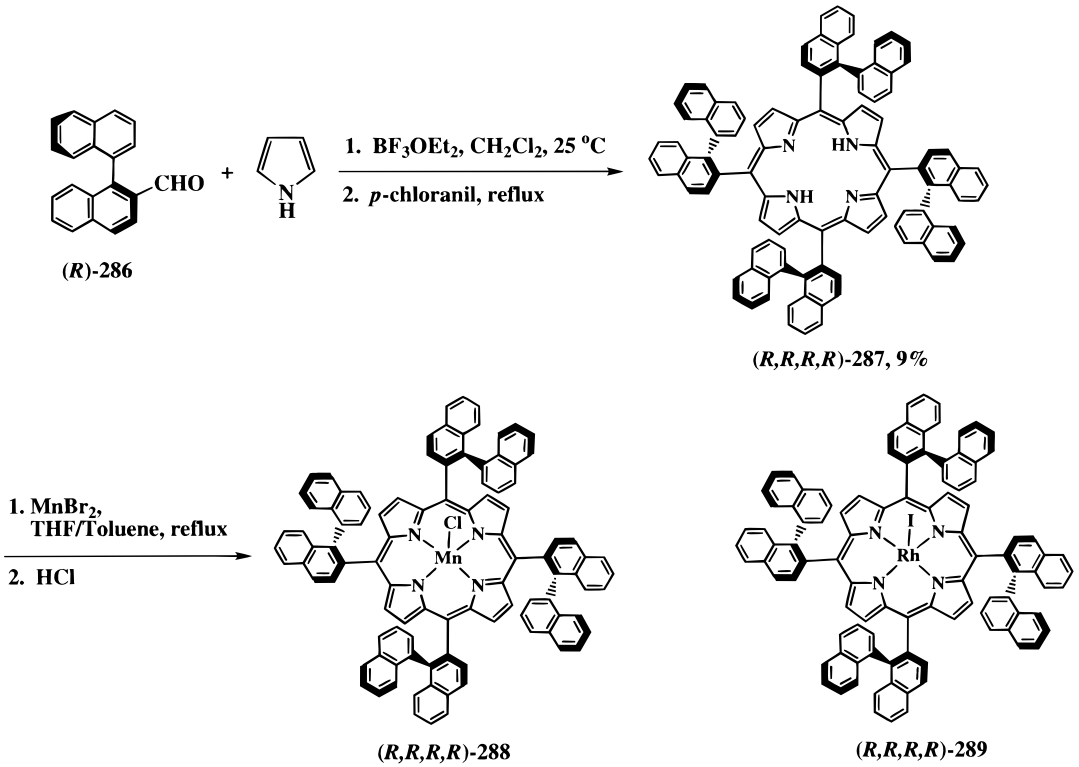
This increased enantioselectivity is probably due to the increased bulkiness of the partially hydrogenated binaphthyl ligands in the catalyst. The iron porphyrin complexes (*S,S,S,S*)-**283**−$Fe^{III}Cl$, (*S,S,S,S*)-**284**−$Fe^{III}Cl$, and (*R,R,R,R*)-**285** did not show catalyst degradation that is normally associated with porphyrin-based catalysts in oxidations. This is due to the advantage of the etheral linkage over the amide linkage in the previously prepared binaphthyl porphyrins. Although excellent ee's were observed for the epoxidation of 2-nitrostyrene and 3,5-dinitrostyrene by these porphyrin catalysts, other olefin substrates exhibited much lower ee's.

Both (*S,S,S,S*)-**283**−$Fe^{III}Cl$ and (*S,S,S,S*)-**284**−$Fe^{III}Cl$ were used to carry out the asymmetric epoxidation of sulfides to chiral sulfoxides in the presence of iodosobenzene.[129,130] An increment of 20−40% ee was observed with the addition of 1-methylimidazole as the axial ligand. It was proposed that the coordination of 1-methylimidazole to the metal center helped prevent the oxidative decomposition of the catalyst and probably also caused distortion of the iron porphyrin conformation, leading to favorable recognition of the substrates. The highest optical yield was for the oxidation of pentafluorophenyl methyl sulfide which gave the corresponding chiral sulfoxide with 73% ee in the presence of (*S,S,S,S*)-**284**−$Fe^{III}Cl$ at −15 °C. Other prochiral sulfides gave ee's all below 55%. (*S,S,S,S*)-**283**−$Fe^{III}Cl$ proved a less effective catalyst both chemically and optically.

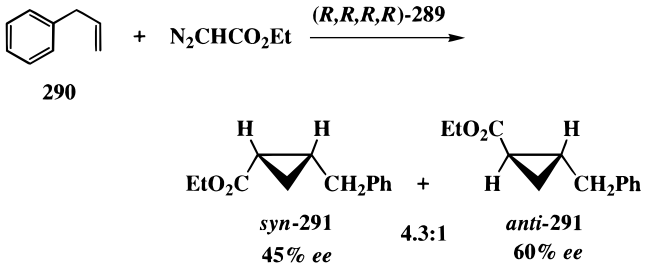
In 1989, Kodadek and co-workers reported a direct synthesis of a tetrabinaphthyl chiral porphyrin (*R,R,R,R*)-**287** from the condensation of (*R*)-1,1′-binaphthyl-2-carbaldehyde [(*R*)-**286**] with pyrrole (Scheme 68).[131] NMR spectroscopic studies of (*R,R,R,R*)-**287** indicated that this molecule was in fact an α,β,α,β atropisomer. (*R,R,R,R*)-**287** was converted to a manganese porphyrin (*R,R,R,R*)-**288** that was used to catalyze the epoxidation of several aryl olefins in the presence of hypochlorite. The highest ee obtained was 40% as a result of the epoxidation of *cis*-β-methylstyrene. The rhodium complex of (*R,R,R,R*)-**287** was synthesized from $[Rh(CO)_2Cl]_2$ and *N*-iodosuccinimide.[132] The resulting (*R,R,R,R*)-**289** was used to catalyze the cyclopropanation of alkenes with ethyl diazoacetate to give syn cyclopropanes as the major products. Scheme 69 shows an example of this cyclopropanation where 3-phenylpropene (**290**) was converted to the cyclopropane products *syn*-**291** and *anti*-**291** in a 4.3:1 ratio with moderate ee's in the presence of (*R,R,R,R*)-**289**.

An even bulkier chiral rhodium catalyst **292**, however, exhibited both lower catalytic activity and stereoselectivity than (*R,R,R,R*)-**289** in cyclopropa-

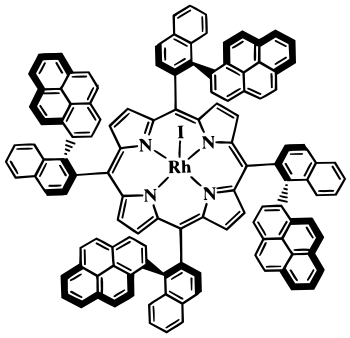
Scheme 68



Scheme 69



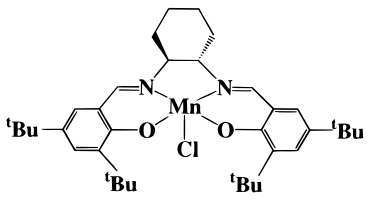
nations.[133] This is probably due to the generation of an over-crowded metal center by the pyrene rings.



292

3.2.2. Katsuki's Multibinaphthyl Salen Catalysts

Although efforts to develop chiral porphyrin catalysts for asymmetric epoxidations have not led to generally applicable enantioselective catalysts, major advances have been made by Jacobsen, Katsuki, and their groups using chiral salen catalysts.[134] Jacobsen's catalysts, such as (*S*,*S*)-**293**, are based on the chirality of the diamino unit alone, whereas Katsuki's catalysts are composed of both a chiral diamine unit as well as two chiral binaphthyl units.[135] The

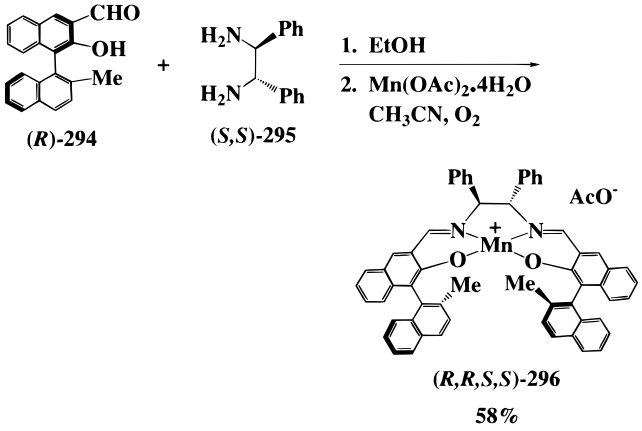


(*S*,*S*)-293

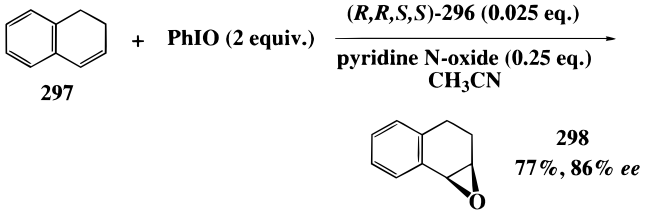
structures and functions of Katsuki's multibinaphthyl salen complexes are discussed below.

In 1993, Katsuki and co-workers prepared (*R*,*R*,*S*,*S*)-**296** from the reaction of (*R*)-**294** with (*S*,*S*)-**295** followed by treatment with $Mn(OAc)_2 \cdot 4H_2O$ in air (Scheme 70).[136] When (*R*,*R*,*S*,*S*)-**296** was used to carry out the epoxidation of dihydronaphthalene (**297**) in the presence of PhIO and pyridine *N*-oxide at room temperature, a chiral epoxide **298** was obtained with 71% yield and 86% ee (Scheme 71). Although under similar conditions, other cis olefins were also converted to chiral epoxides with 89−91% ee, very low ee's were observed for trans olefins. The

Scheme 70



Scheme 71



other diastereomeric (salen)manganese(III) complex (*R*,*R*,*R*,*R*)-**296** made from the reaction of (*R*)-**294** with (*R*,*R*)-**295** showed much lower enantioselectivity than (*R*,*R*,*S*,*S*)-**296**. It appears that matching the binaphthyl chirality with the chirality of the diamino unit is very important for effective asymmetric induction.

Structurally modified binaphthyl (salen)manganese(III) complexes such as (*R*,*R*,*S*,*S*)-**299**, (*R*,*R*,*S*,*S*)-**300**, and (*R*,*R*,*S*,*S*)-**301** were also prepared (Figure 8). (*R*,*R*,*S*,*S*)-**299** and (*R*,*R*,*S*,*S*)-**300** had bulkier and more electron-rich R and X substituents than (*R*,*R*,*S*,*S*)-**296**. They also showed enhanced enantioselectivity for the epoxidation of cis conjugated olefins (up to >99% ee) in most cases. However, (*R*,*R*,*S*,*S*)-**301** did not show the expected enhancement. This is probably because the X substituents in (*R*,*R*,*S*,*S*)-**301** are too bulky.[137,138] (*R*,*R*,*S*,*S*)-**300** was also found to catalyze the epoxidation of trisubstituted olefins[139] and enol ethers or esters[140] with high enantioselectivity (up to 99% ee). A Mn(III) complex (*S*,*S*,*S*,*S*)-**302** that contained electron-donating methoxy groups in the 6,6′-positions of the binaphthyl units was prepared. It showed a slightly lower enantioselectivity than (*R*,*R*,*S*,*S*)-**300** when used in asymmetric epoxidations.[141] (*S*,*S*,*R*,*R*)-**303** and (*S*,*S*,*R*,*R*)-**304** made from the *RR* diamines and the *S* binaphthyls were used to catalyze the asymmetric oxidation of sulfides to sulfoxides. Oxidation of *ortho*-nitrophenyl methyl sulfide (**305**) with iodosobenzene in the presence of (*S*,*S*,*R*,*R*)-**304** gave a chiral sulfoxide **306** in 94% yield and 94% ee (Scheme 72).[142] Good to excellent ee's were obtained for the oxidation of various substituted aryl alkyl sulfides. However, when the diastereomer (*S*,*S*,*S*,*S*)-**304** made from the *SS* diamine and the *S* binaphthyl was used, only low enantioselectivity was observed.

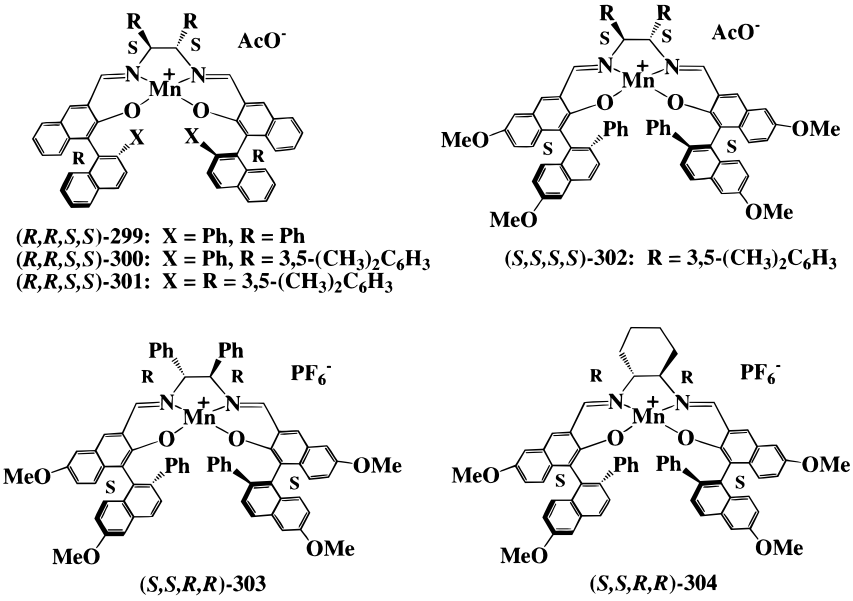


Figure 8.

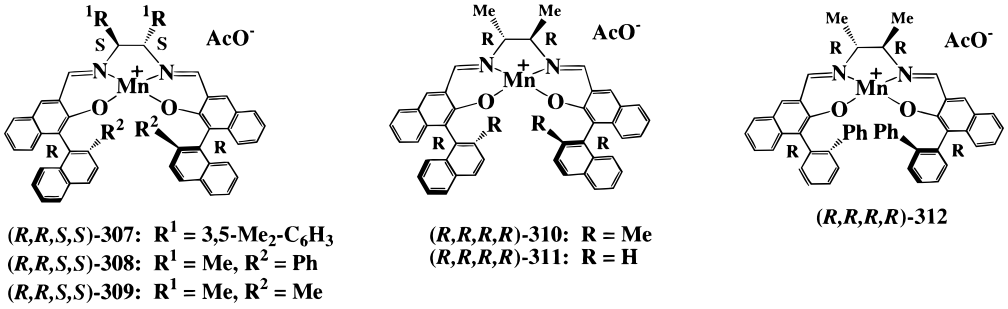
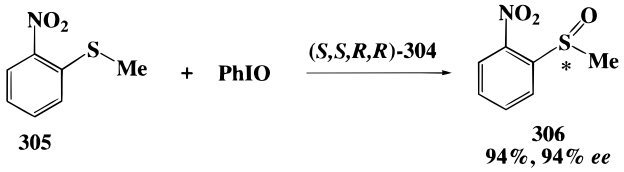


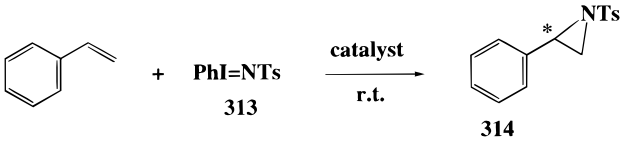
Figure 9.

Scheme 72



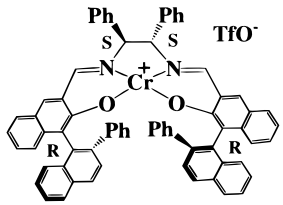
The (salen)Mn(III) complexes (*R*,*R*,*S*,*S*)-**307** to (*R*,*R*,*R*,*R*)-**312** were used in asymmetric aziridination (Figure 9).[143] (*R*,*R*,*S*,*S*)-**307** to (*R*,*R*,*R*,*R*)-**311** catalyzed the reaction of styrene with [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane (**313**) to give chiral aziridine **314** in low enantioselectivity with ee's in the 7−47% range (Scheme 73). However, the Mn(III)

Scheme 73

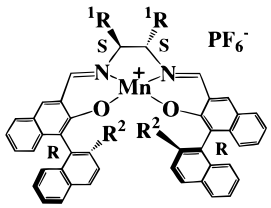


complex (*R*,*R*,*R*,*R*)-**312**, where the binaphthyl units were replaced with naphthyl−phenyl units, showed a greatly enhanced enantioselectivity and good chemical yields. In the presence of (*R*,*R*,*R*,*R*)-**312**, up to 94% ee of **314** was obtained in the aziridination of styrene.

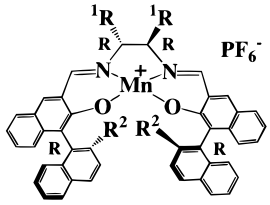
The (salen)Cr(III) complex (*R*,*R*,*S*,*S*)-**315** was synthesized and its use in asymmetric epoxidation was studied.[144] Its enantioselectivity and the stereochemistry of the resulting epoxides were found to be very sensitive to the nature of the solvent. This would seem to indicate an ionic mechanism for the epoxidation process. (*R*,*R*,*S*,*S*)-**315** exhibited both lower catalytic activity and stereoselectivity than the corresponding (salen)Mn^{III} catalyst.



Katsuki and co-workers also studied the use of the Mn^{III}−bisbinaphthylsalen complexes (*R*,*R*,*S*,*S*)-**316** to (*R*,*R*,*R*,*R*)-**321** in asymmetric C−H oxidations.[145] They found that when these complexes were used in the oxidation of **322** to **323** in the presence of iodosobenzene (Scheme 74), (*R*,*R*,*R*,*R*)-**319** showed the highest enantioselectivity. In the presence of (*R*,*R*,*R*,*R*)-**319**, ee's of up to 82% and a yield of 59% for **323** was obtained at −30 °C. Other complexes gave significantly lower ee's. The chirality matching of the binaphthyl units and the diamine unit in the



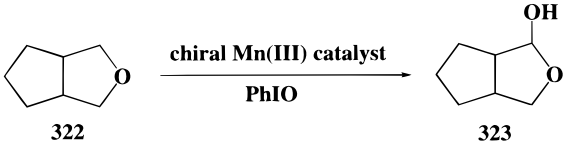
(*R,R,S,S*)-316: $R^1 = -(CH_2)_4-$, R^2 = Ph
(*R,R,S,S*)-317: $R^1 = -(CH_2)_4-$, R^2 = 4-TBDPSPh
(*R,R,S,S*)-318: R^1 = Ph, R^2 = 4-TBDPSPh



(*R,R,R,R*)-319: $R^1 = -(CH_2)_4-$, R^2 = Ph
(*R,R,R,R*)-320: $R^1 = -(CH_2)_4-$, R^2 = 4-TBDPSPh
(*R,R,R,R*)-321: R^1 = Ph, R^2 = 4-TBDPSPh

manganese salen complexes for catalytic asymmetric C−H oxidations appears very different from that required for catalytic asymmetric epoxidations. In the C−H oxidation of **322**, the *RRRR* configuration of the chiral salen complex was much more effective than the *RRSS* configuration. Whereas in the epoxidation of **297**, the *RRSS* configuration was much more favorable than the *RRRR* configuration.

Scheme 74

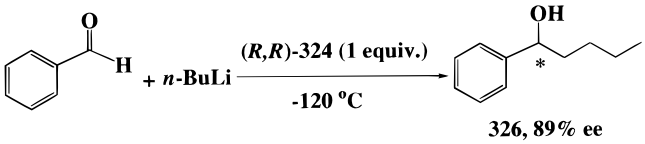


322 323

3.2.3. Other Multibinaphthyl Imine and Amine Compounds in Asymmetric Catalysis

In 1981, Cram and co-workers prepared a bisbinaphthyl diamine catalyst for the addition of alkyllithiums to aldehydes.[146] A bisbinaphthyldiamine (*R,R*)-**324** was obtained from the reaction of racemic *rac*-**63** with ethylenediamine followed by optical resolution with (−)-dibenzoyltartaric acid (Scheme 75). This compound was used to catalyze the reaction of alkyl lithium compounds with benzaldehyde to make chiral secondary alcohols. The alcohol product **326** from the reaction of *n*-butyllithium with benzaldehyde in the presence of (*R,R*)-**324** at −120 °C was obtained with an ee of up to 89% (Scheme 76). A stoichiometric amount of (*R,R*)-**324** was used in this

Scheme 76



326, 89% ee

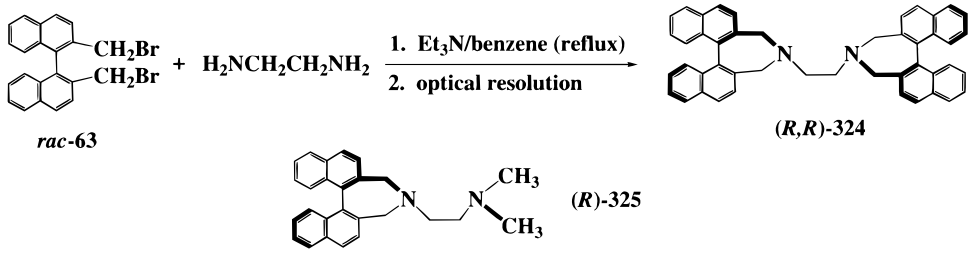
reaction. The enantioselectivity of this bisbinaphthyl molecule was much higher than the corresponding monobinaphthyl diamine (*R*)-**325**. The monobinaphthyl compound gave only 55% ee for the reaction of *n*-butyllithium with benzaldehyde.

The *n*-butyllithium complex of (*S,S*)-**324** was used to initiate the asymmetric anionic polymerization of methyl methacrylate.[58] It generated a highly isotactic polymer (90%) that had a transient specific optical rotation of $[\alpha]_D = +70$. The polymer lost most of its optical rotation over 24 h due to randomized conformations. This observation was similar to the polymerization of methyl methacrylate carried out by the potassium *tert*-butoxide complex of (*S,S*)-**19** (section 3.1.3).

In 1994, Brunner et al. found that the reaction of (*R,R*)-**295** with (*S*)-**327** gave a bisbinaphthyl macrocycle (*S,S*)-**328** (Scheme 77).[147] However, when (*R*)-**327** was reacted with (*R,R*)-**295**, no macrocycle was produced. A polymer was probably generated but not characterized. This variance in reactivity of (*R*)- and (*S*)-**327** with (*R,R*)-**295** was used by the authors to resolve the racemic binaphthyl molecule. The racemic **327** reacted with (*R,R*)-**295**, and the macrocycle **328** generated from (*S*)-**327** was easily separated from the polymer formed from (*R*)-**327**. Treatment of (*S,S*)-**328** and the polymer with aqueous hydrochloric acid separately, gave optically pure (*S*)-**327** and *R*-enriched **327**. The macrocyclic imine (*S,S*)-**328** was reduced to (*S,S*)-**329** when treated with $NaBH_4$. (*S,S*)-**328** was used as the ligand in a Cu(II)-catalyzed cyclopropanation of styrene with ethyl diazoacetate. From this reaction, a 36.6% ee of (1*R*,2*S*)-2-phenylcyclopropancarboxylic acid ethyl ester (**330**) was obtained (Scheme 78).[148]

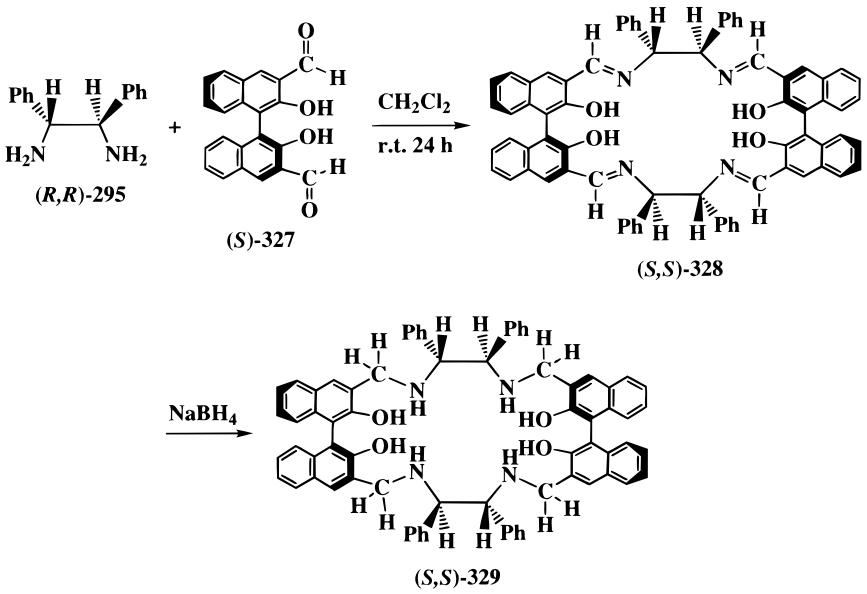
The reaction of prochiral dienes such as **331** with pentacarbonyl iron generated chiral tricarbonyl(η^4-1,3-diene)iron complexes such as (*R*)-**332** and (*S*)-**332** which were proved useful synthetic building blocks (Scheme 79).[149] Knölker et al. found that 1-aza-1,3-butadienes could serve as catalysts for the complexation of 1,3-dienes with pentacarbonyliron.[149] When they used the optically active bisbinaphthyl-based imine (*S,R*)-**333** to catalyze the reaction of **331** with $Fe(CO)_5$, (*S*)-**332** was obtained in 20% yield and 16% ee. The monobinaphthyl imine (*S*)-**334** catalyzed the

Scheme 75

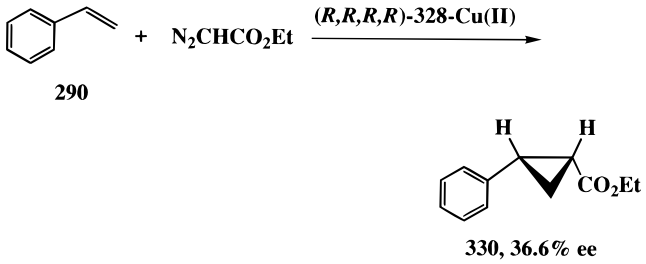


rac-63 (*R,R*)-324 (*R*)-325

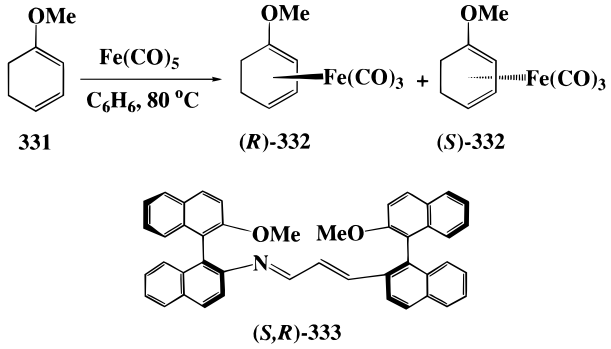
Scheme 77



Scheme 78



Scheme 79



formation of (*R*)-**332** in 87% yield and 25% ee. (*R*)-**335** gave the highest ee (62%) for this reaction but with very low yield (9%).

A racemic rigid bisbinaphthyl macrocycle containing phenanthroline units was synthesized by Cram and co-workers in 1993.[150] The compound **337** was isolated in 41% yield from the Ullmann coupling of **336** in refluxing biphenyl−copper bronze at 255 °C (Scheme 80). Since the corresponding meso compound **338** was not formed, it is probable that the coupling process to give racemic **337** was templated by Cu^+. The four nitrogen atoms in **337** were capable of achieving a tetrahedral arrangement in order to bind the Cu^+ ion, whereas the nitrogen atoms in **338** could not. After removal of the coordinated Cu^+, the D_2 symmetric ligand **339** was obtained. This molecule had a preorganized ligand environment and showed greatly enhanced binding ability over the corresponding monobinaphthyl compound **340** toward alkaline cations. Optically active **339** is a potential chiral ligand for applications in asymmetric catalysis.

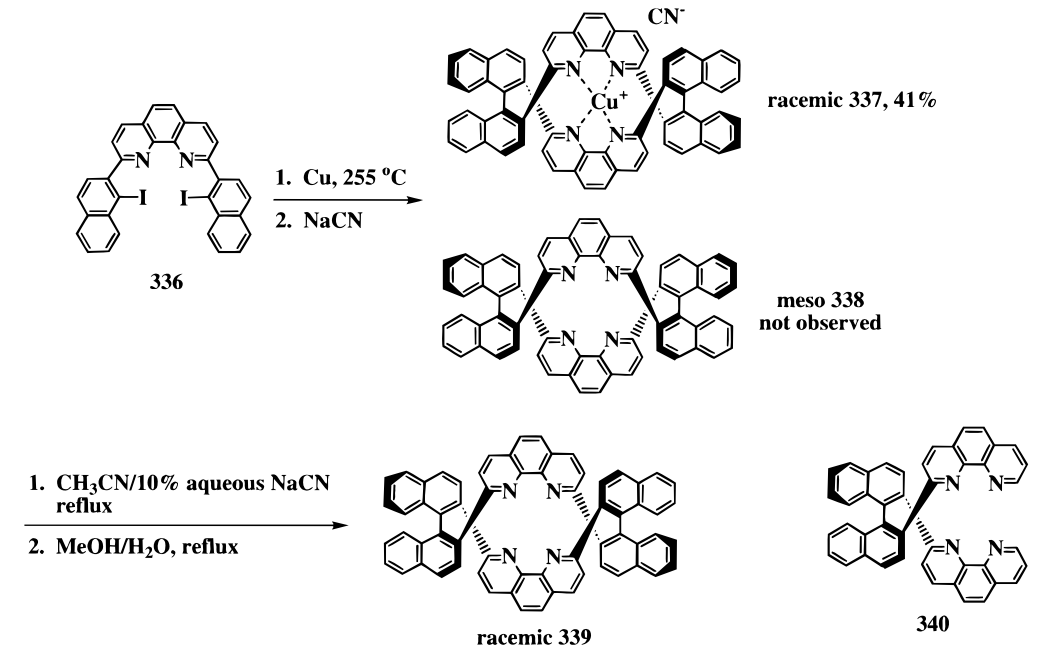
3.3. Phosphorus-Based Multibinaphthyl Ligands

3.3.1. Multi-BINAP Coordinated Metal Complexes

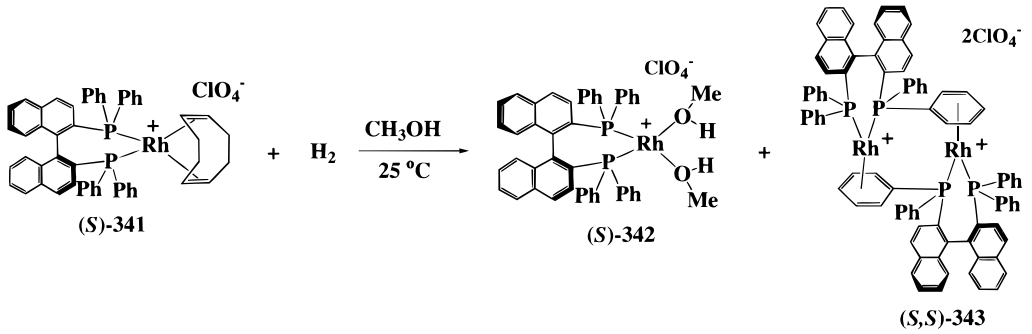
Rh and Ru complexes of BINAP [BINAP = 2,2′-bis(diphenylphosphine)-1,1′-binaphthyl, **5**] ligands have been extensively used for the asymmetric hydrogenation of olefins and carbonyl compounds.[18,19] In addition to these BINAP-based catalysts, the catalytic properties of several multi-BINAP metal complexes have been studied.

In 1980, Takaya and Noyori discovered that [Rh(BINAP)(MeOH)$_2$]ClO_4 [(*S*)-**342**] was a highly enantioselective catalyst for the asymmetric hydrogenation of various α-(acylamino)acrylic acids to generate optically active amino acids.[151,152] During the hydrogenation of (*S*)-**341** to prepare this complex, a dimeric complex (*S*,*S*)-**343** was also isolated and characterized (Scheme 81). The ratio of (*S*)-**342**/(*S*,*S*)-**343** was 9:1. Unlike (*S*)-**342**, (*S*,*S*)-**343** was a poor catalyst

Scheme 80

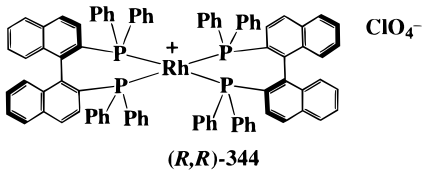


Scheme 81



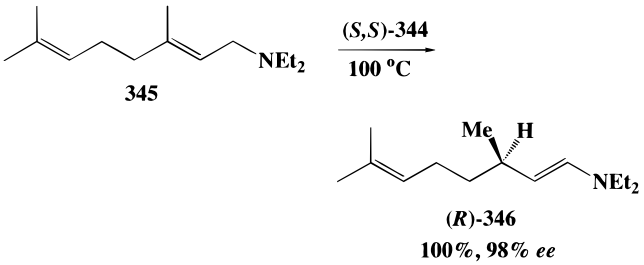
for the asymmetric hydrogenation of α-(acylamino)-acrylic acids and gave less than 30% ee.

In 1985, Tani et al. prepared a bisBINAP−rhodium complex (*R*,*R*)-**344** in 70% yield from the reaction of (*R*)-**341** with 1 equiv of (*R*)-**5** in acetone at room temperature.[153] Both (*R*,*R*)-**344** and (*S*,*S*)-**344** cata-



lyzed the isomerization of allylic amines to enamines with high enantioselectivity. For example, at 100 °C for 15 h when 0.0125 mol % of (*S*,*S*)-**344** was used, **345** was converted to (*R*)-**346** in 100% yield and with 98% ee (Scheme 82). The monomeric BINAP rhodium complex (*S*)-**342** catalyzed this isomerization to give (*R*)-**346** in high optical yield (93−99% ee) at lower temperatures (40−60 °C).[154,155] Although (*S*,*S*)-**344** required much higher temperatures than (*S*)-**342**, it showed more stable catalytic activity after repeated use than the monomeric catalyst. The mechanism for this catalytic isomerization may involve the dissociation of one of the BINAP ligands

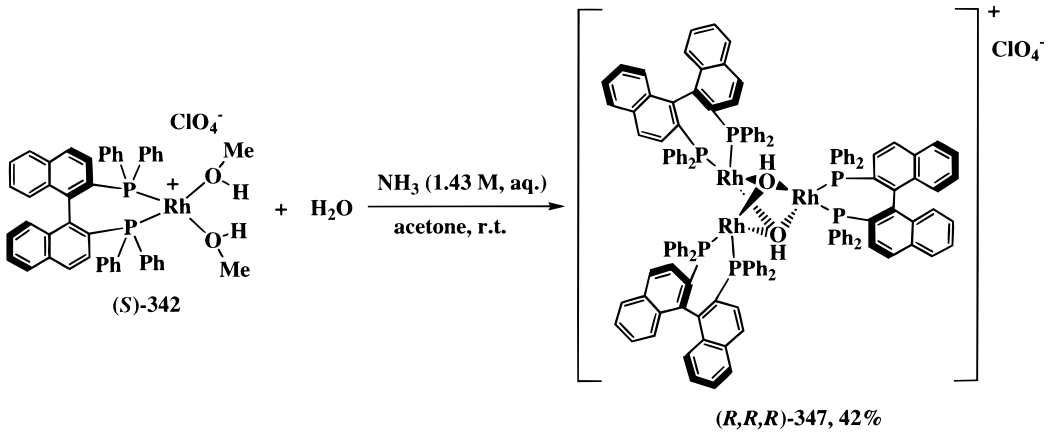
Scheme 82



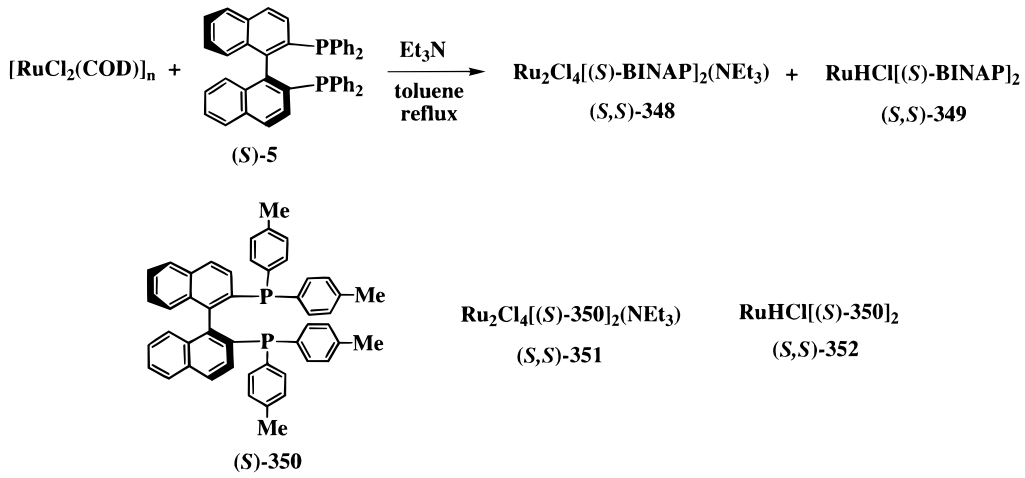
and the formation a π-allylhydridorhodium(III) intermediate.

The highly enantioselective [Rh(BINAP)L_n]ClO_4 (L = solvent or diene) complexes used in the 1,3-hydrogen migration of allylic amines proved sensitive to impurities such as water and oxygen. For example, if (*R*)-**342** was not carefully dried, red-brown crystals were produced and the catalytic isomerization of allylic amines would eventually stop. The same red-brown crystals were obtained by Yamagata et al. when (*R*)-**342** was reacted with aqueous triethylamine or ammonia (Scheme 83).[156] A single-crystal X-ray analysis of the product (*R*,*R*,*R*)-**347** revealed a trimeric structure. The two central hydroxyl groups in (*R*,*R*,*R*)-**347** were blocked by three bulky BINAP ligands so that no H−D exchange was

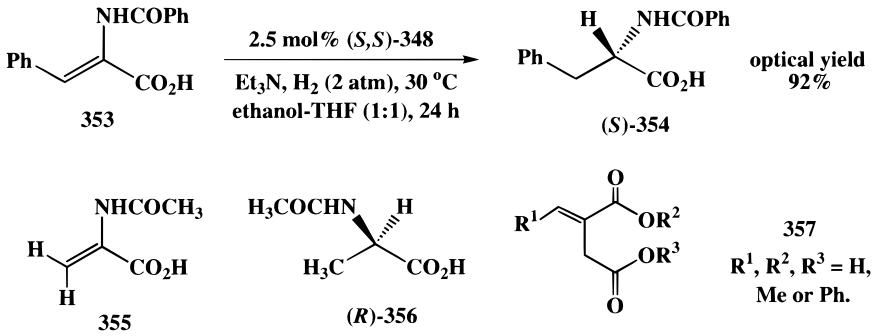
Scheme 83



Scheme 84



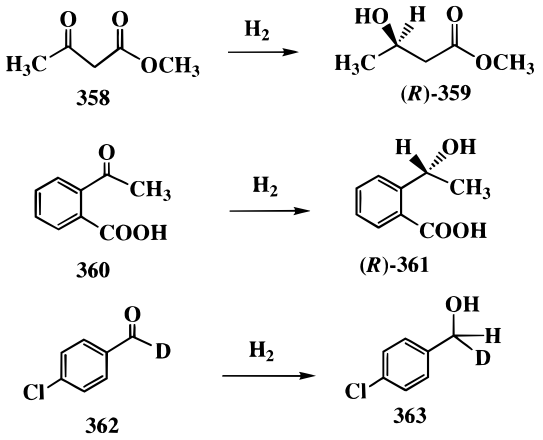
Scheme 85



observed when (*R*,*R*,*R*)-**347** was treated with D_2O even in the presence of DCl and NaOD. (*R*,*R*,*R*)-**347** was incapable of catalyzing the 1,3-hydrogen migration of allylic amines and is believed to be responsible for the deactivation of (*R*)-**342**.

Ikariya et al. reported the synthesis of ruthenium bisBINAP complexes in 1985.[157] They found that in the presence of triethylamine, the reaction of $[RuCl_2(COD)]_n$ (COD = cyclooctadiene) with (*S*)-**5** in refluxing toluene solution gave (*S*,*S*)-**348** in 85% yield as well as a small amount of (*S*,*S*)-**349** (Scheme 84). The formulation of (*S*,*S*)-**348** as $Ru_2Cl_4[(S)\text{-BINAP}]_2(NEt_3)$ by the authors was later found to be incorrect (vide infra).[163] (*S*,*S*)-**349** was obtained quantitatively from the reaction of $[RuCl_2(COD)]_n$ with (*S*)-**5** (2 equiv) in the presence of triethylamine in refluxing ethanol solution. Similarly, (*S*,*S*)-**351** and (*S*,*S*)-**352** were prepared from (*S*)-**350**. (*S*,*S*)-**348** was used to catalyze the asymmetric hydrogenation of acylaminoacrylic acids. The highest optical yield was observed for the hydrogenation of **353** in the presence of triethylamine under 2 atm of H_2 (Scheme 85). (*S*)-**354** was obtained almost quantitatively with an optical yield of 92%. For other substrates, the optical yields were in the 65−86% range. (*S*,*S*)-**349** and (*R*,*R*)-**349** were found to also catalyze asymmetric hydrogenations. In the presence of (*R*,*R*)-**349** and without the addition of triethylamine, **355** was hydrogenated to (*R*)-**356** in up to 95% optical yield. If triethylamine was added, the optical yield dropped to 79%. In the case of the bulkier substrate **353**, the addition of triethylamine, however, increased the optical yield of (*R*)-

Scheme 86



354 from 49% to 79%. In this case, (*R*,*R*)-**349** was also the catalyst. Both (*R*,*R*)-**348** and (*R*,*R*)-**349** catalyzed the asymmetric hydrogenation of various derivatives of methylenesuccinic acid, **357**, in 48−90% optical yields.[158,159]

BisBINAP ruthenium complexes also catalyzed asymmetric carbonyl hydrogenations as shown in Scheme 86. In the presence of (*R*,*R*)-**348** under 100 atm of H_2, **358** was hydrogenated to give (*R*)-**359** in 95% yield and >99% ee.[160] Under 43 atm of H_2, (*R*,*R*)-**348** catalyzed the conversion of **360** to (*R*)-**361** with 100% yield and 92% ee.[161] With the addition of H_2O in THF solution, (*S*,*S*)-**348** catalyzed the hydrogenation of **362** to the isotope labeled chiral primary alcohol **363** in 70% ee under 11 atm of H_2.[162]

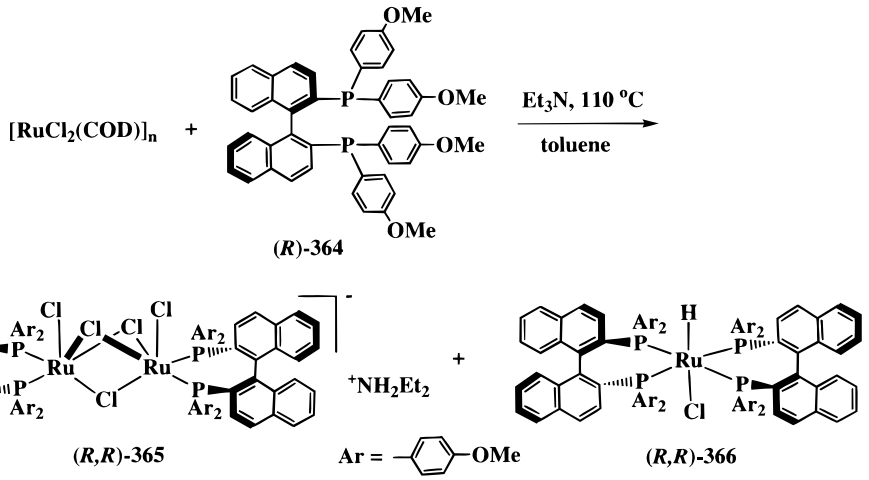
In 1995, King et al.[163] pointed out that the actual composition of (*S*,*S*)-**348** was not $Ru_2Cl_4[(S)\text{-BINAP}]_2(NEt_3)$ as originally formulated.[157] Through a careful NMR analysis, they concluded that the correct structure is $\{Ru_2Cl_5[(S)\text{-BINAP}]_2\}^-Et_2NH_2^+$, an anionic complex with a closely bound diethylammonium ion. The diethylammonium ion was apparently generated from triethylamine during the preparation. However, the use of either diethylamine or diethylammonium chloride failed to produce (*S*,*S*)-**348**.

Further evidence for the structure of (*S*,*S*)-**348** was obtained by X-ray analysis. In 1996, Takaya and coworkers used $[RuCl_2(COD)]_n$ with 1 equiv of (*R*)-**364** to give the complexes (*R*,*R*)-**365** (37% yield) and (*R*,*R*)-**366** (Scheme 87).[164] However, with 2 equiv of (*R*)-**364**, (*R*,*R*)-**366** was obtained in almost quantitative yield. The structure of the binuclear anionic complex (*R*,*R*)-**365** was established by single-crystal X-ray analysis which confirmed King's result for the structural determination of (*S*,*S*)-**348**. This compound contained three bridging chlorine atoms and a diethylammonium counterion. The dihedral angle between the two naphthyl planes in one of the binaphthyl ligands of (*R*,*R*)-**365** was 70.4°. (*R*,*R*)-**365** catalyzed the asymmetric hydrogenation of methyl 3-oxobutanoate (H_2 100 kg/cm^2, methanol−dichloromethane, 27 h, substrate/catalyst = 4000) to give methyl (*R*)-3-hydroxybutanoate with over 99% ee. It also catalyzed the hydrogenation of tiglic acid to give (*R*)-2-methylbutanoic acid with 73% ee.

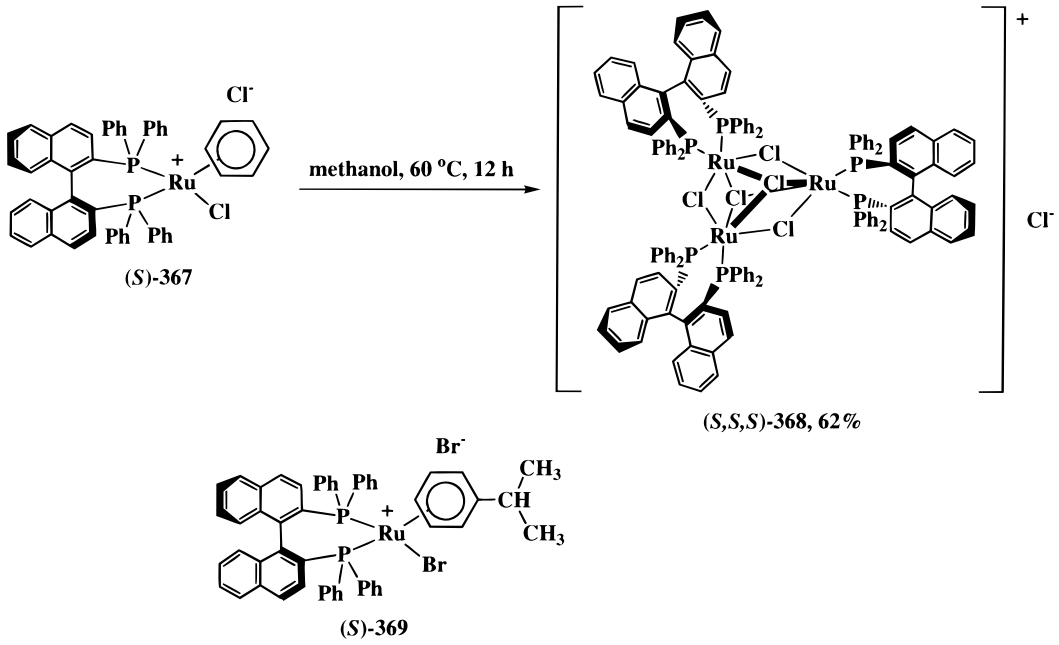
Takaya and co-workers obtained a trinuclear BINP−Ru^{II} complex (*S*,*S*,*S*)-**368** when heating a methanol solution of (*S*)-**367** at 60 °C for 12 h (Scheme 88).[165] Single-crystal X-ray analysis of the tetrafluoro borate salt of (*S*,*S*,*S*)-**368** established its trimeric structure. The corresponding bromide analogue of (*S*,*S*,*S*)-**368** was obtained by UV irradiation of (*S*)-**369** in methanol at room temperature. Although the monomeric BINAP ruthenium complexes catalyzed the asymmetric hydrogenation of methyl 3-oxobutanoate with ee's of up to 98%,[166] the trinuclear BINAP−Ru^{II} complexes proved inert under similar conditions. When (*S*,*S*,*S*)-**368** was treated with a small amount of acid and/or water followed by removal of solvent under reduced pressure, it collapsed to give a mixture of compounds which turn out to be an excellent catalyst for the asymmetric hydrogenation of various ketones. An NMR spectroscopic study showed that the catalytically active mixture gradually reconverged to give (*S*,*S*,*S*)-**368** in the mixed solvent $CDCl_3/CD_3OD$ (1:1) at room temperature.

In 1997, Togni and co-workers found that a bisBINAP iridium complex (*S*,*S*)-**370** showed high enantioselectivity in a hydroamination reaction.[167] (*S*,*S*)-**370** was prepared from the reaction of either $IrCl(C_2H_4)_4$ or $[IrCl(COD)_2]_2$ with (*S*)-**5**. This complex (1 mol %) catalyzed the reaction of norbornene with aniline to produce (*R*)-**371** in 95% ee and 22% yield at 75 °C (Scheme 89). The addition of fluoride anions was necessary for the reaction to proceed.

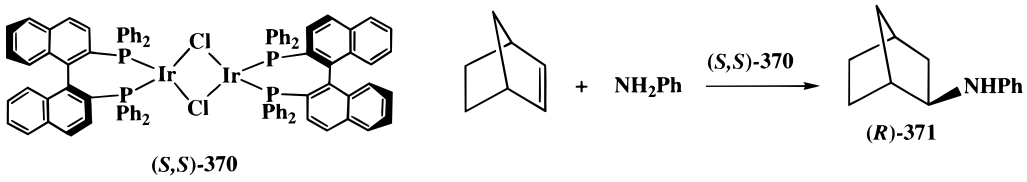
Scheme 87



Scheme 88

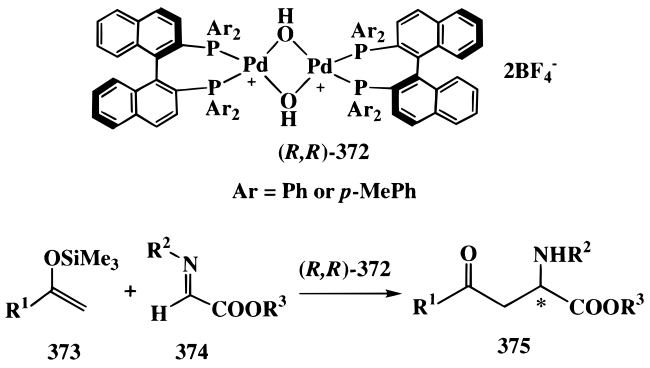


Scheme 89



In 1998, Sodeoka and co-workers reported that bisBINAP palladium complexes (*R*,*R*)-**372** catalyzed the reaction of enol silyl ethers **373** with imines **374** to generate the acylalanine derivatives **375** with ee's of up to 90% (Scheme 90).[168] The best result was

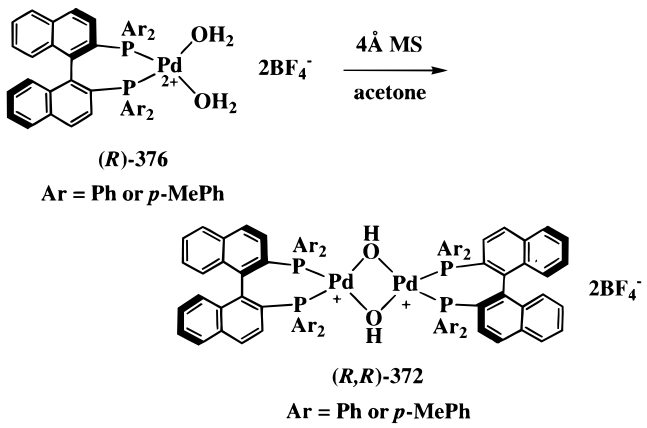
Scheme 90



obtained when the aryl groups of (*R*,*R*)-**372** were *p*-tolyl groups and the substituents of the substrates were R^1 = phenyl, R^2 = *p*-methoxylphenyl and R^3 = isopropyl. When the monoBINAP complexes (*R*)-**376** were used to catalyze this reaction, much lower ee's were observed. It was proposed that the diaquo complexes (*R*)-**376** may release HBF_4 which catalyzes the formation of racemic **375**.

However, because the protons in (*R*,*R*)-**372** were much less acidic, HBF_4 could not be generated during the catalytic process, making them better enantioselective catalysts. The complexes (*R*,*R*)-**372** were synthesized by treating (*R*)-**376** with 4 Å molecular sieves in acetone (Scheme 91).

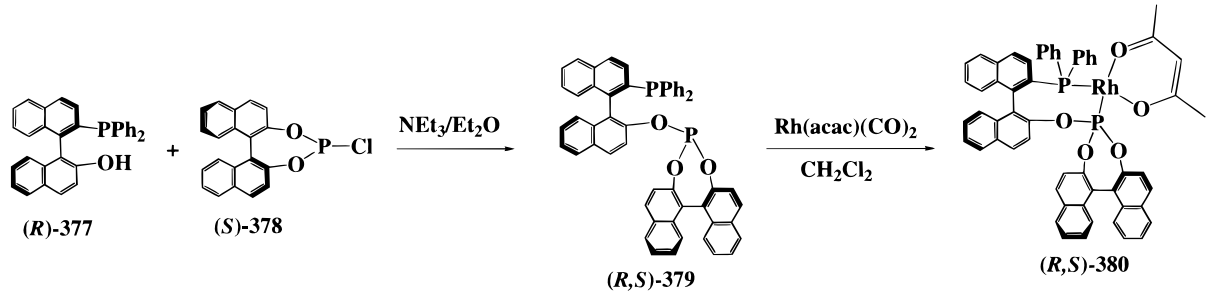
Scheme 91



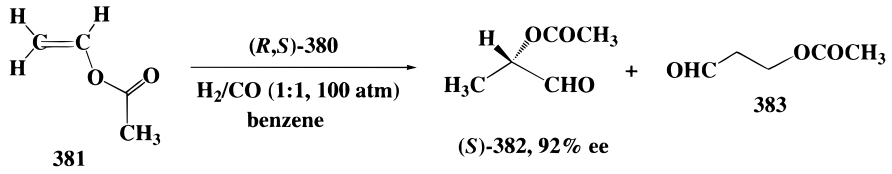
3.3.2. Takaya's Bisbinaphthyl Phosphinephosphite Metal Complexes

In 1993, Takaya and co-workers designed and synthesized a novel bisbinaphthyl phosphinephosphite rhodium complex to catalyze the asymmetric hydroformylation of various alkenes.[169] Hydroformylation of alkenes is a very useful process for the synthesis of various functionalized organic mol-

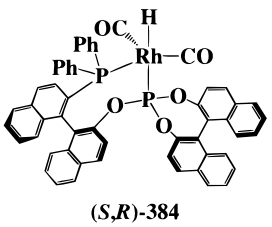
Scheme 92



Scheme 93



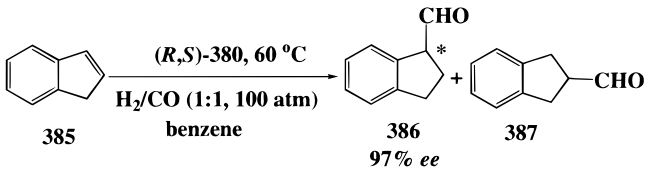
ecules.[170] It converts an alkene molecule to an aldehyde through catalytic reaction with H_2 and CO. From the reaction of (*R*)-**377** with (*S*)-**378** in diethyl ether and triethylamine, (*R*,*S*)-**379** was obtained in nearly quantitative yield (Scheme 92).[169] Treatment of (*R*,*S*)-**379** with Rh(acac)$(CO)_2$ generated (*R*,*S*)-**380**. In the presence of 1−3 equiv of (*R*,*S*)-**379**, (*R*,*S*)-**380** was found to be highly effective for such asymmetric hydroformylations. (*R*,*S*)-**380** can also be prepared in situ. For example, a benzene solution of Rh(acac)-$(CO)_2$ with 2.2 equiv of (*R*,*S*)-**379** catalyzed the conversion of vinyl acetate **381** to (*S*)-**382** with 92% ee under H_2 and CO pressure (1:1, total 100 atm) at 60 °C (Scheme 93). The ratio of branched aldehyde **382** to linear aldehyde **383** was 86:14 with a conversion of **381** of over 99%. In this reaction, 0.25 mol % of the rhodium complex versus **381** was used. Very good branch-to-linear ratios as well as good to excellent ee's were also observed for various monoaryl substituted ethenes, sulfur-containing olefins,[171] and 1,3-dienes.[172] However, for simple terminal olefins such as 1-hexene, the branched hydroformylation product was isolated only as the minor product with 75% ee.[169,173] (*R*,*R*)-**380**, a diastereomer of (*R*,*S*)-**380**, proved to be a mis-matched complex because when it was used, much lower enantioselectivity was observed. Under H_2 and CO, (*S*,*R*)-**380** was converted to a carbonyl hydrido complex with the possible structure (*S*,*R*)-**384**.[169] This compound was



catalytically active and might be an intermediate involved in the catalytic cycle of the (*S*,*R*)-**380**-mediated asymmetric hydroformylations.

(*R*,*S*)-**380** was also found to be very efficient for the hydroformylation of internal olefins.[174] For example, in the presence of the in situ generated (*R*,*S*)-**380**, indene (**385**) underwent hydroformylation to give **386** and **387** in a 95:5 ratio. (−)-**386** was obtained with 97% ee (Scheme 94). In this reaction, the ligand

Scheme 94



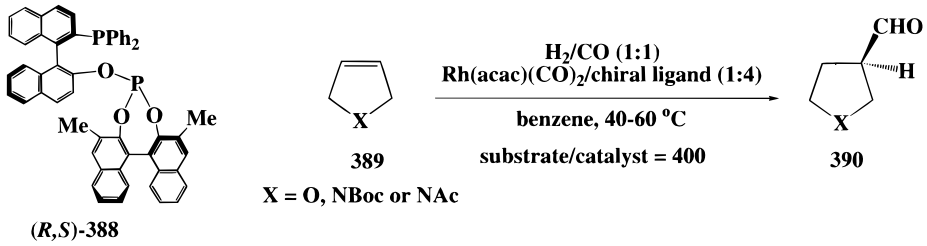
(*R*,*S*)-**379** to Rh(acac)$(CO)_2$ ratio was 4:1 and the rhodium complex-to-substrate ratio was 1:100. High stereoselectivity was observed for the hydroformylation of several other internal olefins.

The activity of a catalyst prepared from mixing Rh-(acac)$(CO)_2$ with (*R*,*S*)-**379** or its derivative (*R*,*S*)-**388** in the asymmetric hydroformylation of heterocyclic olefins was studied.[175] For example, up to 73% ee and 99% yield were observed in the conversion of **389** to **390** (Scheme 95). (*R*,*S*)-**388** had higher catalytic activity, as well as higher enantioselectivity, than (*R*,*S*)-**379** in this reaction due to the 3,3′-methyl substituents on one of the binaphthyl units.

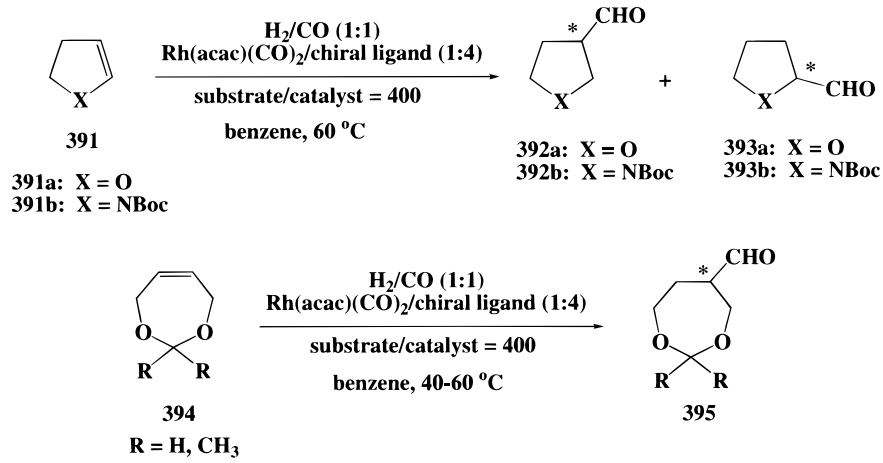
Using the catalyst system of (*R*,*S*)-**379** and (*R*,*S*)-**388**, the hydroformylation of **391** gave a mixture of **392** and **393** (Scheme 96). For example, the hydroformylation of **391b** in the presence of the chiral ligand (*R*,*S*)-**379** produced **392b** and **393b** in 33% and 67% yield, and 71% and 97% ee, respectively. In the presence of the chiral ligand (*R*,*S*)-**388**, the yields and ee's were 37%, 63% and 22%, 88%, respectively. The hydroformylation of **394** to **395** gave up to 76% ee and 99% conversion. In this reaction, (*R*,*S*)-**379** exhibited higher enantioselectivity than (*R*,*S*)-**388**. In general, (*R*,*S*)-**388** was not only better for sterically less demanding substrates such as **389**, it also had a higher catalytic activity than (*R*,*S*)-**379** for most substrates.

The reaction of (*R*,*S*)-**388** with Rh(acac)$(CO)_2$ under a 1:1 mixture of H_2 and CO at atmospheric pressure in benzene-d_6 solution gave (*R*,*S*)-**396**. This was

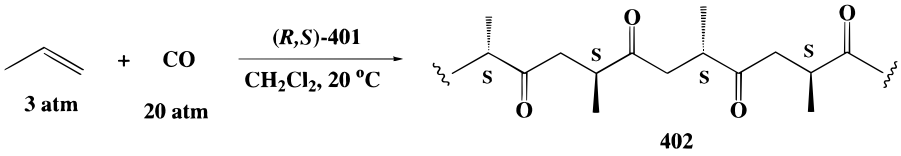
Scheme 95



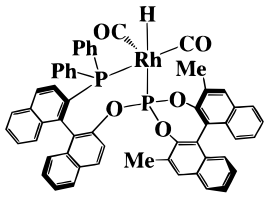
Scheme 96



Scheme 97



shown to be structurally similar to (*S*,*R*)-**384** by NMR spectroscopy.



Ligands analogous to (*R*,*S*)-**379** including (*R*,*S*)-**397** to (*R*)-**400** were also prepared (Figure 10).[176] The rhodium complex of (*R*,*S*)-**397** demonstrated a slightly lower enantioselectivity than (*R*,*S*)-**379** when used to catalyze the hydroformylation of styrene and vinyl acetate. The enantioselectivity of (*S*,*R*)-**399** was almost equal to that of (*R*,*S*)-**379**. It was found that (*R*)-**398** and (*R*)-**400** existed as an equilibrium mixture of two diastereomers probably because of the rotation around the biphenyl axis. Their rhodium complexes exhibited lower enantioselectivity than (*R*,*S*)-**380**.

The palladium(II) complex (*R*,*S*)-**401** containing the bisbinaphthyl ligand (*R*,*S*)-**379** catalyzed a highly enantioselective alternating copolymerization of propylene with carbon monoxide.[177] The relative positions of the methyl group and the acetonitrile ligand in (*R*,*S*)-**401** were not determined. In the presence of (*R*,*S*)-**401**, the copolymerization of propylene and CO gave the polymer **402** with molecular weights of up to $M_w = 104\,400$ and a molar optical rotation of $[\Phi]_D = +40$ (Scheme 97). The polymer **402** gave

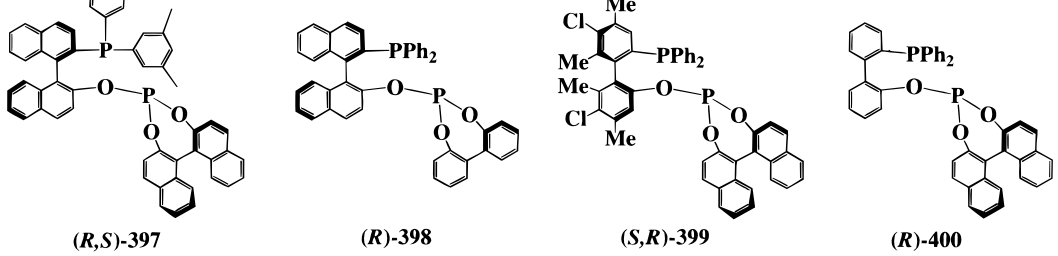
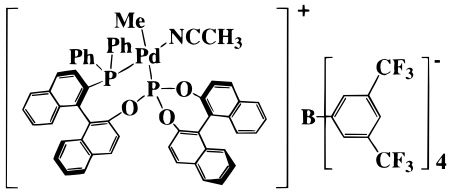


Figure 10.



(*R*,*S*)-401

simple, sharp ^{13}C NMR signals, indicating a complete stereoregularity of the polymer chain without the presence of any other isomeric structures.

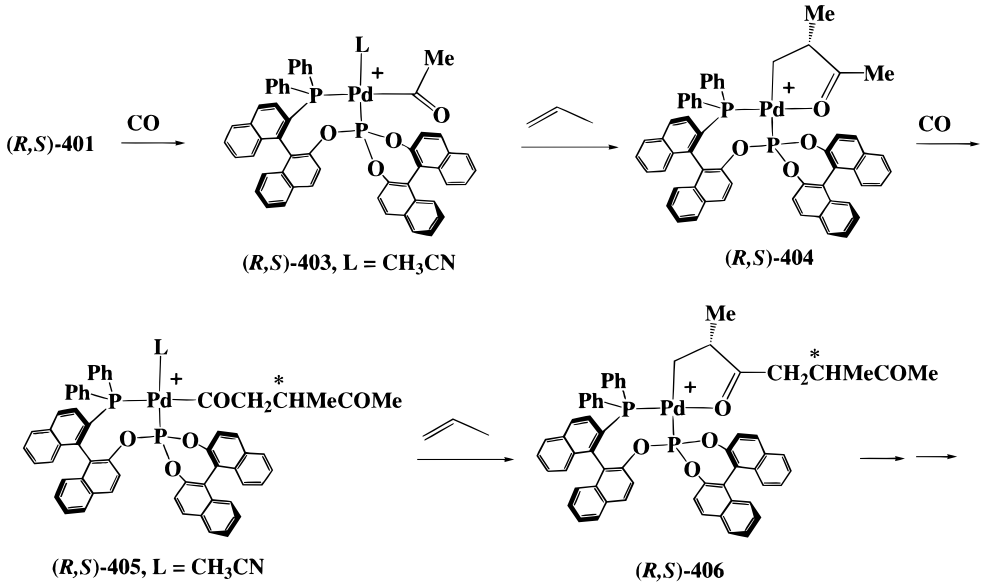
Scheme 98 shows a plausible mechanism for the copolymerization of propylene with carbon monoxide in the presence of (*R*,*S*)-**401**. All the proposed intermediates (*R*,*S*)-**403** to (*R*,*S*)-**406** were characterized by NMR analyses.[177] The study of these intermediates showed that the two nonequivalent coordination sites in (*R*,*S*)-**401**, i.e., either cis or trans to the phosphine or phosphite ligand, were important requirements for the high stereoselectivity of the copolymerization. The *S* configuration of the chiral centers in **402** was determined by the reaction of (*R*,*S*)-**404** with carbon monoxide and methanol to produce a chiral γ-ketone ester.

(*R*,*S*)-**401** was also used for the cyclopolymerization of α,ω-dienes with carbon monoxide.[178] The cyclocopolymerization of 1,4-pentadiene with carbon monoxide (20 atm) in the presence of (*R*,*S*)-**401** generated the polymer **407** (Scheme 99) whose structure was established by NMR. It was shown that the two diastereomeric centers in each of the cyclopentanone units in **407** were produced in a 56:44 ratio. Almost no enantioselectivity was observed for this polymerization since the optical rotation of the polymer was nearly zero. The molecular weight of **407** was quite low with $M_w < 2500$. Cyclopolymerization of 1,5-hexadiene with carbon monoxide in the presence of (*R*,*S*)-**401** gave a higher molecular weight polymer ($M_w = 15\,600$) at a higher concentration of the diene. However, a significant vinylic content in this polymer was observed by NMR spectroscopy, indicating a noncyclized structure of the polymer chain. This is probably due to the entropically less favorable six-membered-ring formation compared to five-membered-ring formation. The 1,5-hexadiene-CO copolymer had a molar optical rotation of $[\Phi]_D = 13.8$ ($c = 0.50$, CH_2Cl_2).

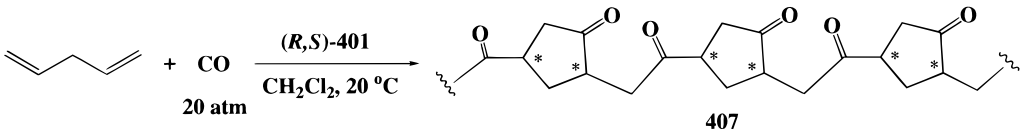
The Ni(0) and Pd(0) complexes of (*R*,*S*)-**379** were prepared and used in asymmetric hydrocyanations.[179] Treatment of $Ni(COD)_2$ (COD = 1,5-cyclooctadiene) with 2 equiv of (*R*,*S*)-**379** led to the formation of a chiral nickel complex (*R*,*S*,*R*,*S*)-**408** (Scheme 100). Although (*R*,*S*,*R*,*S*)-**408** can exist as two diastereomers, its ^{31}P NMR spectrum indicated the formation of only one diastereomer. When (*R*,*S*)-**379** was treated with excess $Ni(COD)_2$, both the formation of (*R*,*S*,*R*,*S*)-**408** and nickel metal was observed. This is probably due to the dispropotionation of Ni(COD)-[(*R*,*S*)-**379**].

Mixing $Pd_2(dba)_3$ (dba = dibenzylideneacetone) with 1 equiv (relative to Pd) of (*R*,*S*)-**379** gave a mixture of what are probably two monochelated complexes. When either $Pd_2(dba)_3$ or Pd(η-C_3H_5)(η-C_5H_5) was treated with excess (*R*,*S*)-**379**, a diastereomeric mixture of (*R*,*S*,*R*,*S*)-**409** was produced. Variable-temperature ^{31}P NMR studies of (*R*,*S*,*R*,*S*)-

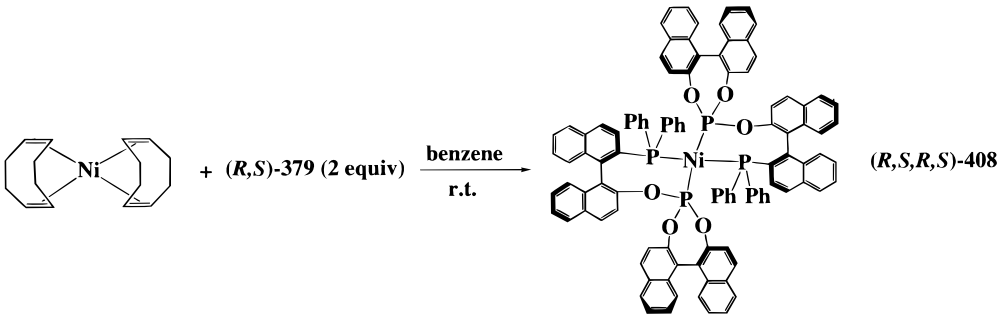
Scheme 98



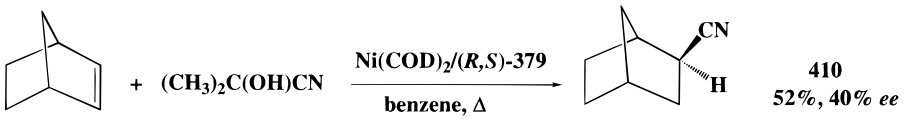
Scheme 99



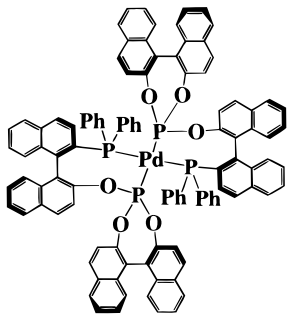
Scheme 100



Scheme 101



409 showed a possible nondissociative interconversion between the two diastereomers.



(*R,S,R,S*)-**409**

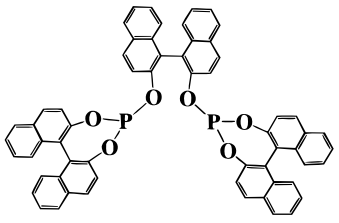
These chiral Ni(0) and Pd(0) species were used to catalyze the asymmetric hydrocyanation of norbornene. When (*R,S,R,S*)-**408** was generated in situ by mixing $Ni(COD)_2$ with 2 equiv of (*R,S*)-**379**, it catalyzed the reaction of acetone cyanohydrin with norbornene to give *exo*-2-cyanonorbornane (**410**) was obtained as the only product (40% ee) (Scheme 101). The same result was obtained when the isolated (*R,S,R,S*)-**408** was added. If only 1 equiv of (*R,S*)-**379** was mixed with $Ni(COD)_2$, the ee was lower. However, when 2 equiv (relative to Pd) of (*R,S*)-**379** were mixed with $Pd_2(dba)_3$, the resulting solution had almost no catalytic activity. It was found that the benzene solution of one equiv of (*R,S*)-**379** with $Pd_2(dba)_3$ catalyzed the formation of **410** in 52% yield and 48% ee.

3.3.3. Other Phosphorus-Containing Multibinaphthyl Catalysts

As well as the BINAP and phosphinephosphite ligands described above, other multibinaphthyl phosphine, phosphite, phospholes, phosphate, or phsophinoyl compounds have been prepared as chiral ligands for asymmetric catalysis.

a. Phosphite Ligands. A chiral bisbinaphthyl phosphite ligand (*S,S,S,S,*)-**412** was prepared by Bakos and co-workers for use in asymmetric hydroformylations.[180] From the reaction of (*S*)-**378** with (*S,S*)-**411**, (*S,S,S,S*)-**412** was obtained which was then converted into a platinum complex (*S,S,S,S*)-**413** (Scheme 102). With the addition of $SnCl_2$ as cocatalyst, (*S,S,S,S*)-**413** catalyzed the hydroformylation of styrene. Under 100 atm of initial total pressure of H_2 and CO (1:1) at 17 °C in methylene chloride solution, the (*R*)-branched aldehyde was produced with 91% ee. The branch/normal ratio was 60/40. In this reaction, ethylbenzene was also obtained as a side product in 54% yield. When the mismatched chiral complex (*S,S,R,R*)-**413** made from (*R,R*)-**411** and (*S*)-**378** was used for this hydroformylation, the (*S*)-branched aldehyde was produced with only 14% ee. Both of rhodium complexes made from the reaction of (*S,S,R,R*)-**412** and (*S,S,S,S*)-**412** with $Rh(CO)_2(acac)$ catalyzed this hydroformylation with the same enantioselectivity (16% ee of the *R* enantiomer) and the same regioselectivity (branch/normal, 81/19). These rhodium complexes exhibited complete chemoselectivity.

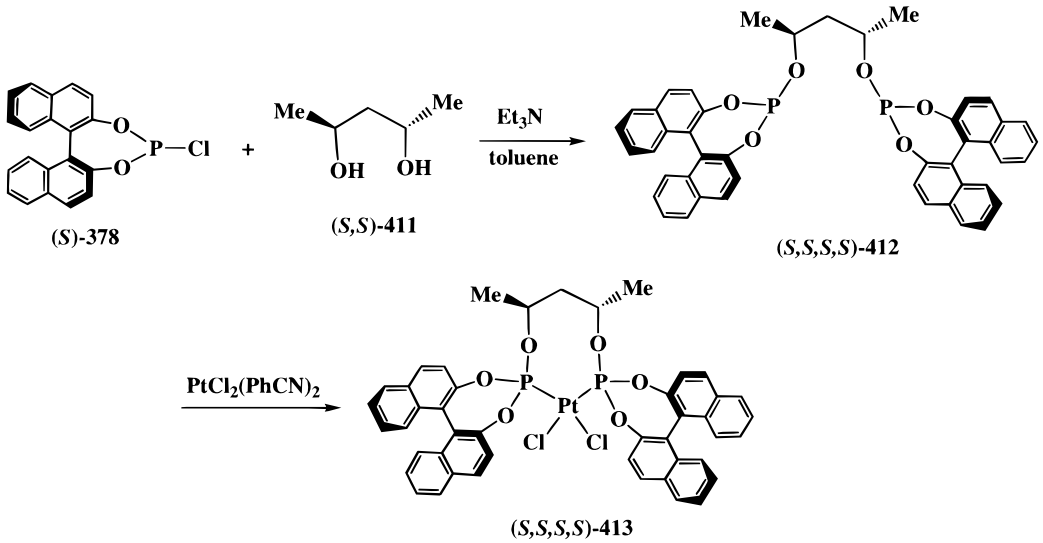
Trisbinaphthyl phosphites were prepared from the reaction of BINOL with **378**.[181] When racemic **12** was reacted with racemic **378**, a mixture of diastereomers of **414** was produced. (*R*)-**12** and (*R*)-**378** were reacted to give (*R,R,R*)-**414**, the catalytic property of which was not reported.



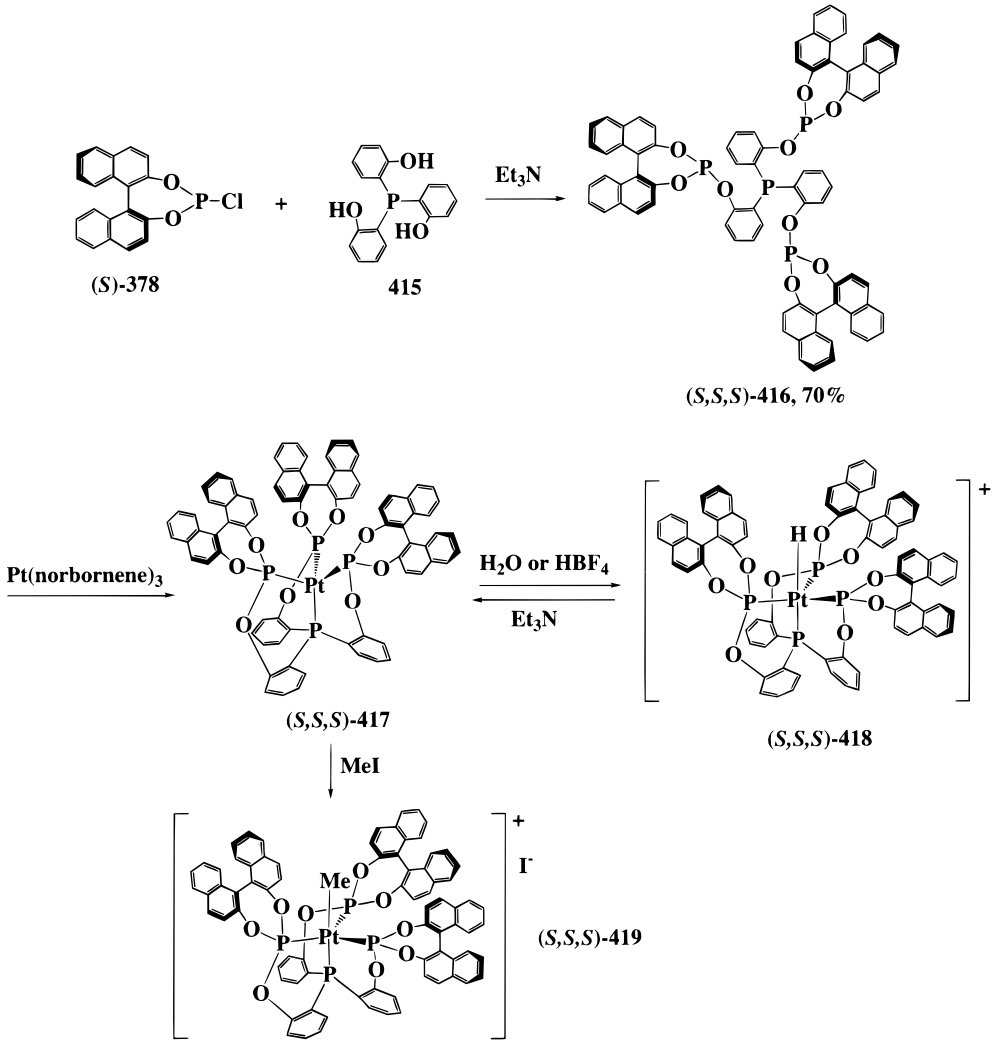
414

In 1993, Pringle and co-workers prepared a C_3 symmetric tetraphos ligand based on a chiral binaphthyl structure.[182] The reaction of **415** with 3 equiv of (*S*)-**378** in the presence of triethylamine gave the trisbinaphthyl-based chiral ligand (*S,S,S*)-**416** in 70% yield (Scheme 103). This compound reacted readily with $Pt(norbornene)_3$ to give (*S,S,S*)-**417**. The ^{31}P NMR spectrum of (*S,S,S*)-**417** showed a doublet and a quartet, while its ^{195}Pt NMR spectrum showed a quartet of doublets. These data are consistent with

Scheme 102



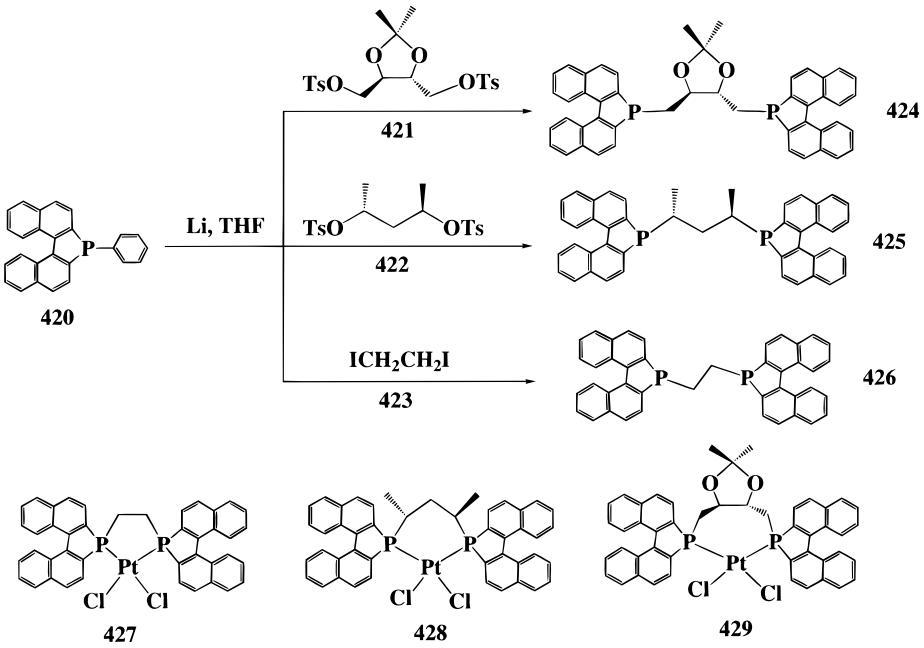
Scheme 103



a C_3 symmetry of this tetraphosphorus-coordinated compound. (*S*,*S*,*S*)-**417** was protonated by water or HBF_4 to give a cationic platinum hydride (*S*,*S*,*S*)-**418**. (*S*,*S*,*S*)-**418** was deprotonated by treatment with triethylamine. (*S*,*S*,*S*)-**417** reacted with methyl iodide to give a platinum(II) methyl complex (*S*,*S*,*S*)-**419**. The use of these chiral complexes in asymmetric reactions has not been reported.

b. Phosphole and Phosphine Ligands. Bisbinaphthophosphole ligands were synthesized by Gladiali et al. in 1995.[183] Treatment of the binaphthophosphole **420** with Li in THF resulted in selective

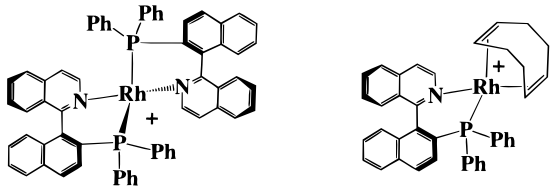
Scheme 104



cleavage of the phenyl group (Scheme 104). Reaction of the resulting phospholyl anion with substrates **421**−**423** produced bisbinaphthophosphole compounds **424**−**426** in yields of 50−60%. The binaphthophospholes were found to undergo fast atropisomerization in solution at room temperature both in metal coordinated and uncoordinated states. When **426** was reacted with $[(PhCN)_2PtCl_2]$, a mixture of three compounds was obtained. On the basis of the NMR analyses, one of the compounds is believed to be a mononuclear complex **427**, whereas the remaining species were proposed to be polynuclear complexes. When the mixture was heated at 90 °C in the presence of $SnCl_2$, the polynuclear complexes were converted to **427**. Compounds **425** and **424** reacted with $[(PhCN)_2PtCl_2]$ to give the expected mononuclear complexes **428** and **429** without the formation of polynuclear compounds. Variable-temperature NMR experiments of **428** and **429** in $CDCl_3$ solution showed that these complexes were fluxional because of atropisomerization of the binaphthyl groups in the bisbinaphthophosphole ligands. This atropisomerization was much slower than in the free ligand.

Complexes **427**−**429** were used to catalyze the hydroformylation of styrene in toluene with 2 equiv of $SnCl_2$ as the promoter. Complex **427** was a very poor catalyst for this reaction, but both **428** and **429** showed good catalytic activity. When either **428** or **429** was used, of the normal and branched aldehyde products, the later was formed in yields of 63−85%, with **429** showing better enantioselectivity. The ee of the resulting 2-phenyl propionaldehyde varied from 17 to 44% depending on reaction conditions.

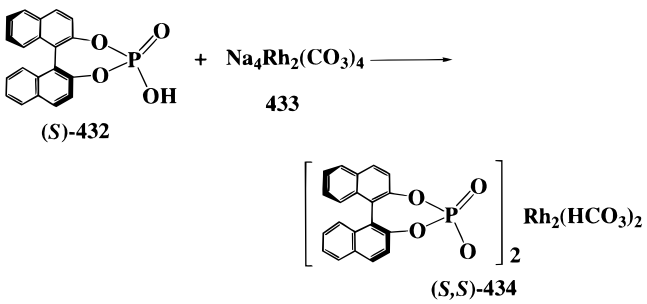
A rhodium complex (*S*,*S*)-**430**, containing (*S*)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline ligands, was synthesized by Brown et al.[184] In (*S*,*S*)-**430**, the chiral ligand is an analogue of 1,1′-binaphthyl with one of the carbon atoms in a naphthalene ring replaced by a nitrogen atom. The absolute configuration of the rhodium center of (*S*,*S*)-**430** is unknown. Although the complex (*S*)-**431**, containing only one chiral ligand, catalyzed the asymmetric hydroboration of arylalkenes with high enantioselectivity,[184,185] the catalytic property of (*S*,*S*)-**430** was not reported.



c. Phosphate and Phosphinoyl Ligands. Unlike phosphite and phosphine ligands, the coordination of phosphate and phosphinoyl ligands to transition metal centers is not through their phosphorus atoms but rather through the oxygen atoms. This is because the phosphorus atoms in the phosphate and phosphinoyl ligands no longer have lone pairs of electrons that can form the dative bonds with transition metals.

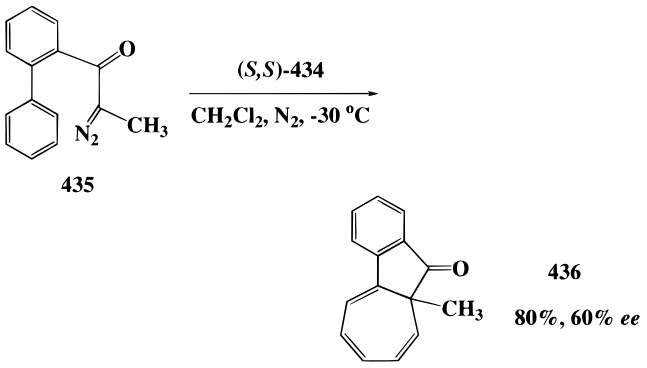
McCarthy et al. prepared a rhodium complex (*S*,*S*)-**434** containing two binaphthyl phosphate ligands from the reaction of (*S*)-**432** with **433**, (Scheme 105),[186] and studied its role in asymmetric catalysis. (*S*,*S*)-**434** was found to catalyze a 2,3-sigmatropic

Scheme 105



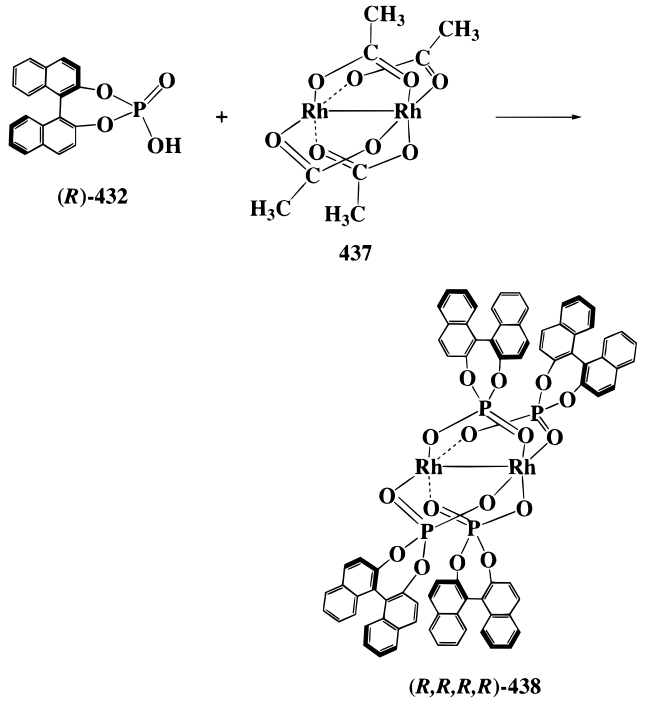
rearrangement as well as a intramolecular C−H insertion of diazocompound with ee's in the 9−30% range. An intramolecular cycloaddition of the diazo compound **435** was catalyzed by (*S,S*)-**434** to give **436** with 60% ee and 80% yield (Scheme 106).

Scheme 106

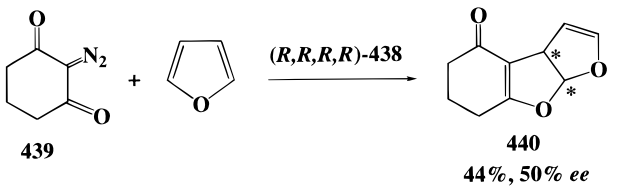


Pirrung et al. prepared a tetrakisbinaphthyl phosphate rhodium(II) complex with the possible structure (*R,R,R,R*)-**438** from the reaction of (*R*)-**432** with $Rh_2(OAc)_4$ (**437**) (Scheme 107).[187] This complex catalyzed the cycloaddition of diazo compounds with furan or dihydrofuran at room temperature. In the presence of (*R,R,R,R*)-**438**, the reaction of **439** with furan gave a tricyclic product **440** in 44% yield and 50% ee (Scheme 108).

Scheme 107

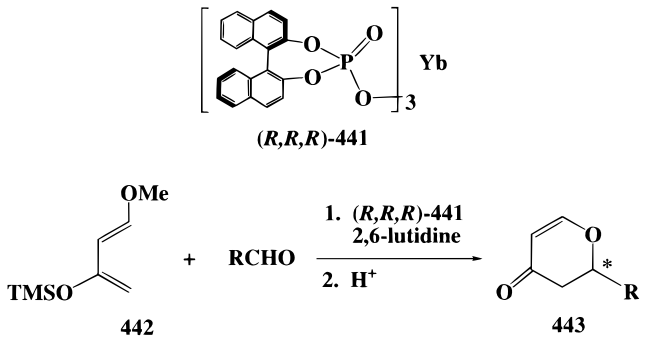


Scheme 108



In 1997, Inanaga and co-workers reported the use of a ytterbium(III) trisbinaphthyl phosphate complex (*R,R,R*)-**441** in an asymmetric hetero-Diels−Alder reaction.[188] (*R,R,R*)-**441** was prepared from the reaction of (*R*)-**432** with $YbCl_3 \cdot 6H_2O$ in the presence of NaOH in 89% yield. When (*R,R,R*)-**441** was used to catalyze the Diels−Alder reaction of the Danishefsky's diene **442** with aldehydes in the presence of 2,6-lutidine, high enantioselectivity was observed for certain aromatic aldehyde substrates. For example, the reaction of *p*-methoxybenzaldehyde with **442** at room temperature in the presence of (*R,R,R*)-**441** gave the corresponding cycloaddition product **443** with 93% ee (Scheme 109). However, the ee for reaction with an aliphatic aldehyde was very low (11%). Although the addition of 2,6-lutidine was necessary for the observed high enantioselectivity, more than 1 equiv of 2,6-lutidine to (*R,R,R*)-**441** led to a reduction in ee. Besides the ytterbium(III) complex, the authors also prepared similar lanthanum(III) and scandium(III) trisbinaphthyl phosphate complexes and studied their application in asymmetric hetero-Diels−Alder reactions.[189] Of the complexes studied, (*R,R,R*)-**441** proved the best catalyst.

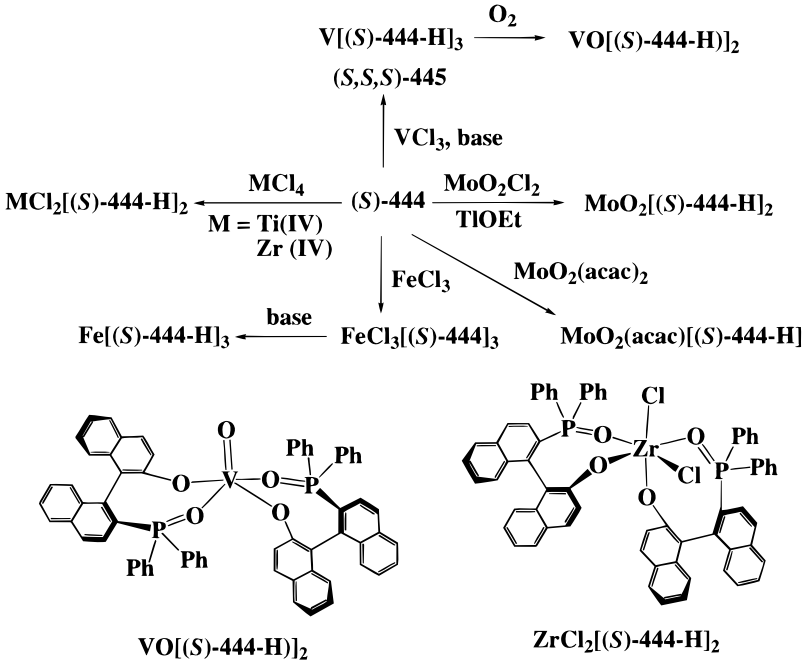
Scheme 109



Metal complexes containing 2-(diphenylphosphinoyl)-2′-hydroxy-1,1′-binaphthalene (**444**) as a ligand were studied by Cross et al. in 1996.[190] Treatment of (*R*)- or (*S*)-**444** with potassium *tert*-butoxide followed by reaction with VCl_3 generated a trisbinaphthyl complex (*S,S,S*)- or (*R,R,R*)-**445**. The structure of (*S,S,S*)-**445** was established by X-ray analysis. Of the two possible geometric isomers, the *facial* and *meridional*, only the former was found. In addition, (*S*)-**444** generated only the Λ and (*R*)-**444** only the Δ complex. Therefore, the formation of the trisbinaphthylmetal complex is a stereospecific process controlled by the chiral binaphthyl ligand.

The reaction of (*S*)-**444** with $FeCl_3$ in the presence of potassium *tert*-butoxide also gave a similar trisbinaphthyl complex, Fe[(*S*)-**444**-H]$_3$. When (*S*)-**444** was reacted with $FeCl_3$ in the absence of base, the complex [$FeCl_3$[(*S*)-**444**]$_3$] was produced. In this complex, probably only the phosphoryl oxygen of the neutral ligand (*S*)-**444** was coordinated to the metal center, while the hydroxyl group of (*S*)-**444** remained uncoordinated. Treatment of this compound with 3 equiv of base gave Fe[(*S*)-**444**-H]$_3$. Other metal complexes of (*S*)-**444** including Mo, Zr, and Ti complexes were also prepared. Their syntheses are summarized in Scheme 110. The electronic and CD

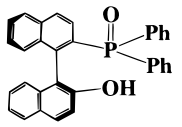
Scheme 110



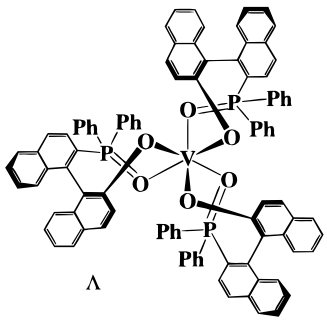
VO[(*S*)-444-H)]$_2$

ZrCl$_2$[(*S*)-444-H]$_2$

spectra of these complexes were studied. The crystal structures of VO[(*S*)-**444**-H]$_2$ and ZrCl$_2$[(*S*)-**444**-H]$_2$ were also obtained. VO[(*S*)-**444**-H]$_2$ had a distorted square-pyramidal structure with an apical vanadyl oxygen and ZrCl$_2$[(*S*)-**444**-H]$_2$ had a distorted octahedral structure with the two chlorine atoms cis to each other. A few of these complexes were used to carry out the oxidation of *p*-tolylmethyl sulfide, but very low enantioselectivity (*ee* = 0−12%) was observed.



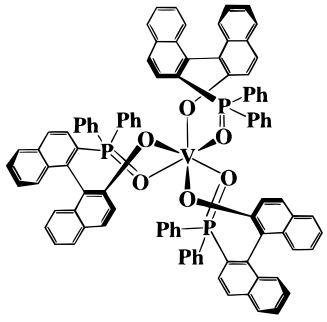
(*S*)-444



Λ

facial

(*S,S,S*)-445



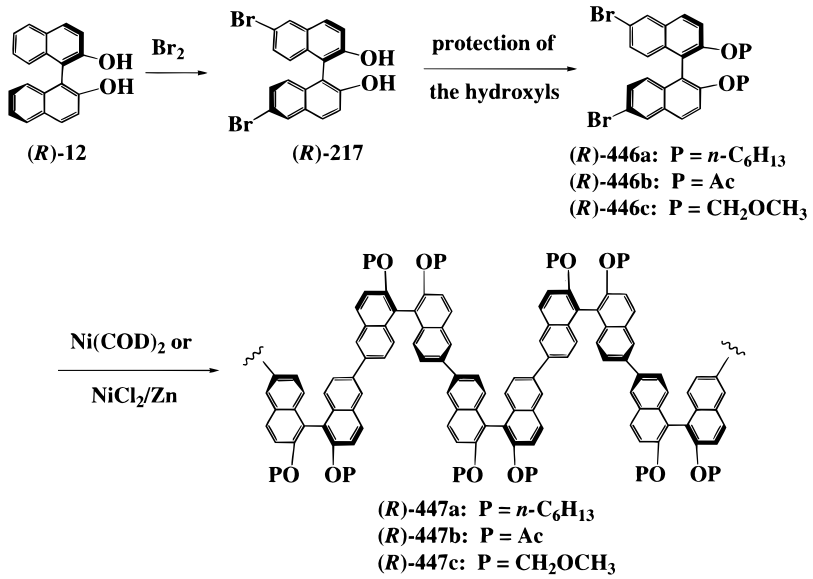
meridional

3.4. Binaphthyl Polymers in Asymmetric Catalysis

Although the application of binaphthyl-based chiral polymers in asymmetric catalysis is discussed in this section, the majority of research on binaphthyl polymers will be presented in section 4.

Recently, Pu and co-workers used chiral binaphthyls to build novel rigid and sterically regular polymer catalysts for asymmetric catalysis. The polymerization of 6,6′-dibromobinaphthyl monomers in the presence of Ni(0) or Ni(II)/Zn catalysts has been reported (Scheme 111).[191−193] Treatment of (*R*)-**12** with bromine gave (*R*)-**217** in high yields. After protection of the hydroxyl groups of (*R*)-**217**, the resulting monomers (*R*)-**446a**−**c** were polymerized with Ni(0) or Ni(II)/Zn catalysts to give the optically active polybinaphthyls (*R*)-**447a**−**c**.[191−193] (*R*)-**446a** was also converted to a 6,6′-dibronic acid binaphthyl (*R*)-**448** by reaction with magnesium and triethyl borate (Scheme 112). The Suzuki coupling of (*R*)-**446a** with (*R*)-**448** in the presence of Pd(PPh$_3$)$_4$ catalyst was used to prepare (*R*)-**447a**. The racemic monomers *rac*-**446a** and *rac*-**448** were used to prepare *rac*-**447a**. To determine whether the polymer *rac*-**447a** was a stereoregular polymer or in fact made of randomly distributed *R* and *S* binaphthyl units, the Suzuki coupling of 2 equivs of *rac*-**446a** with 1 equiv of (*R*)-**448** was carried out. An oligomer was isolated that had a specific optical rotation of $[\alpha]_D = -97.7$ ($c = 1.0$, THF). The recovered *rac*-**446a** had a specific optical rotation of $[\alpha]_D = -0.7$. This demonstrated that there was no enrichment of either the *R* or *S* enantiomer after the reaction and the coupling of *rac*-**448** with *rac*-**446a** was not stereoselective. The polymer *rac*-**447a** was, therefore, made of randomly distributed *R* and *S* binaphthyl units.

Scheme 111

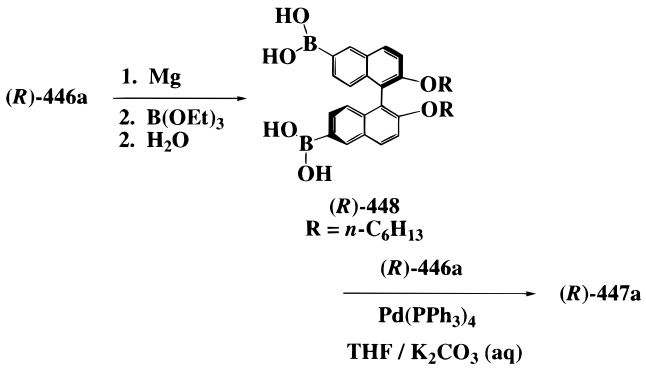


(*R*)-12 (*R*)-217

(*R*)-446a: P = *n*-C_6H_{13}
(*R*)-446b: P = Ac
(*R*)-446c: P = CH_2OCH_3

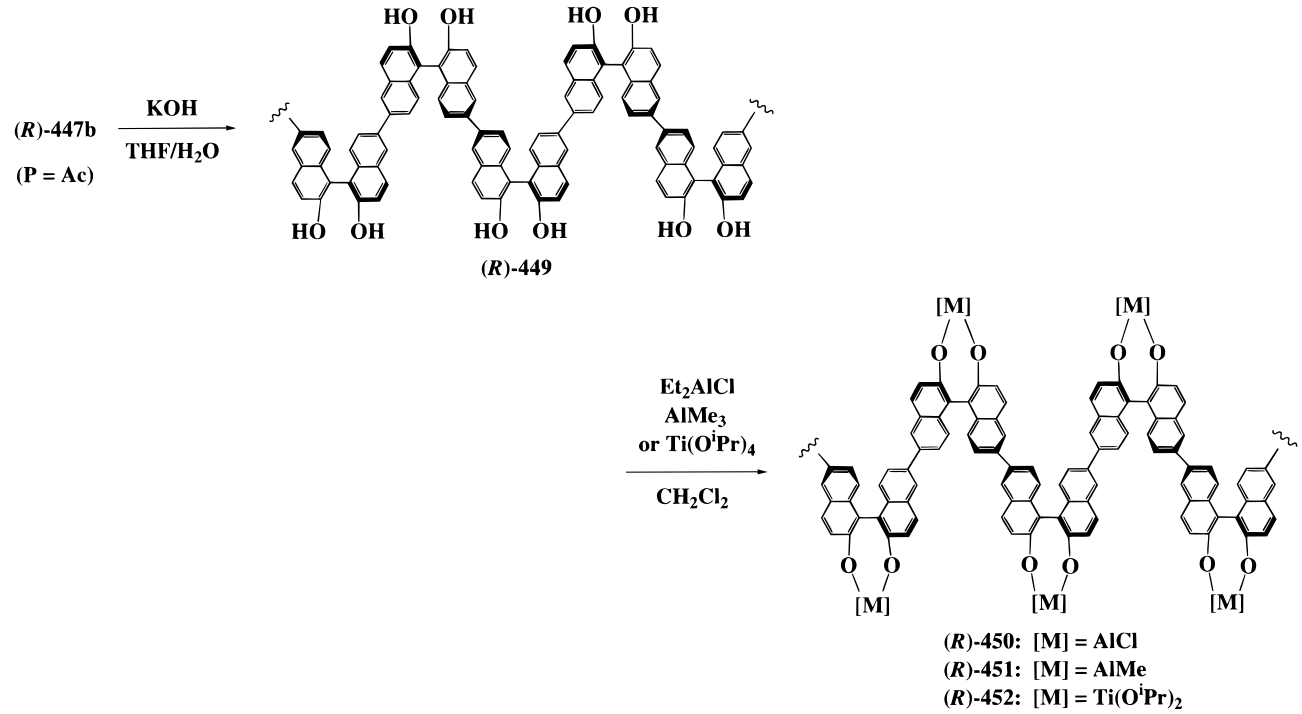
(*R*)-447a: P = *n*-C_6H_{13}
(*R*)-447b: P = Ac
(*R*)-447c: P = CH_2OCH_3

Scheme 112



Hydrolysis of (*R*)-**447b** in the presence of potassium hydroxide generated the first optically active and sterically regular BINOL polymer (*R*)-**449** (Scheme 113). This polymer was soluble in DMSO and basic water solution and insoluble in common organic solvents such as THF and chloroform. Its specific optical rotation was $[\alpha]_D = -139.8$ ($c = 0.5$, 0.5 M aqueous KOH). The molecular weight of (*R*)-**449** was $M_w = 7590$ as determined by laser light scattering study in a NaOH (1 M) solution. This is about 20% higher than the molecular weight of the precursor polymer (*R*)-**447b** measured by gel permeation chromatography (GPC) relative to polystyrene standards ($M_w = 6400$). When treated with diethyl aluminum chloride, trimethyl aluminum or tetraisopropyltitanium, (*R*)-**449** gave polymeric Lewis acid complexes with the possible structures (*R*)-**450** to (*R*)-**452**. In the Mukaiyama condensation of 1-phenyl-1-[(trim-

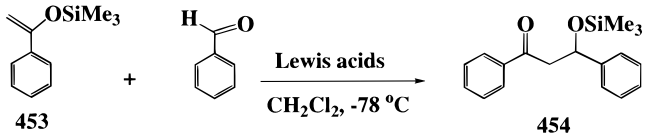
Scheme 113



(*R*)-450: [M] = AlCl
(*R*)-451: [M] = AlMe
(*R*)-452: [M] = $Ti(O^iPr)_2$

ethylsilyl)oxy]-ethylene (**453**) with benzaldehyde to form **454** (Scheme 114), (*R*)-**450** showed greatly

Scheme 114



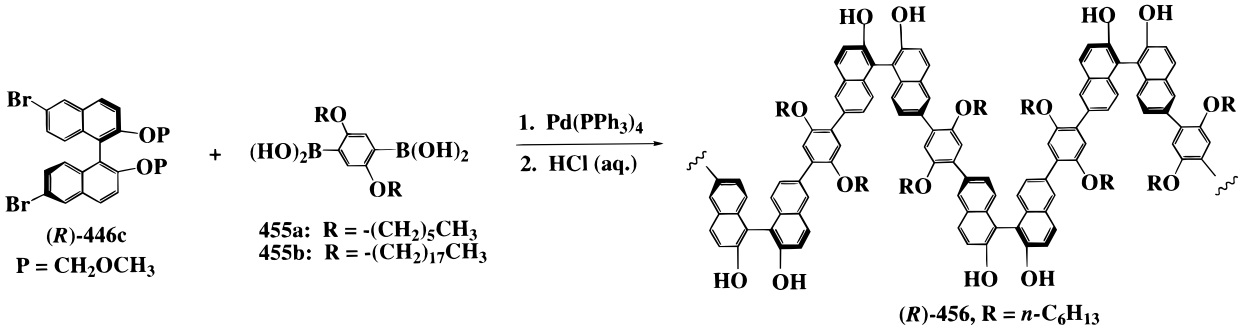
enhanced catalytic activity over the corresponding aluminum complex made from the reaction of BINOL with diethyl aluminum chloride. However, no enantioselectivity was observed for this reaction when either the polymer or monomer catalyst was used. While (*R*)-**451** was less active than (*R*)-**450** in this reaction, (*R*)-**452** was completely inactive even though the corresponding monomeric BINOL−titanium(IV) complex was catalytically active. This observation supports the assumption that the catalytically active species are binuclear or polynuclear rather than mononuclear when binaphthyl titanium complexes are used. In (*R*)-**452**, each binaphthyl titanium(IV) center was restricted in a rigid polymer chain so that catalytically active multititanium sites could not be generated. The situation was opposite in the case of aluminum. The monomeric binaphthyl aluminum complex possibly undergoes oligomerization through the formation of Al−O−Al bonds to fill the empty P orbital of the Al centers, leading to reduced Lewis acidity. In (*R*)-**450**, however, such Al−O−Al bonds could not be formed leading to greatly enhanced catalytic activity.

Another poly(BINOL) (*R*)-**456** was prepared via the Suzuki coupling of (*R*)-**446c** with a *p*-phenylenediboronic acid **455a** followed by hydrolysis (Scheme 115).[194,195] Unlike (*R*)-**449**, (*R*)-**456** was soluble in common organic solvents such as toluene, methylene chloride, chloroform, and THF. The specific optical rotation of (*R*)-**456** was $[\alpha]_D = -398.6$ ($c = 1.0$, CH_2Cl_2). GPC analysis showed that the molecular weight was $M_w = 18\,500$ (PDI = 2.1). When (*R*)-**456** was treated with diethyl aluminum chloride, it produced an insoluble polymeric aluminum complex which although catalytically active for the Mukayama reaction remained nonenantioselective.

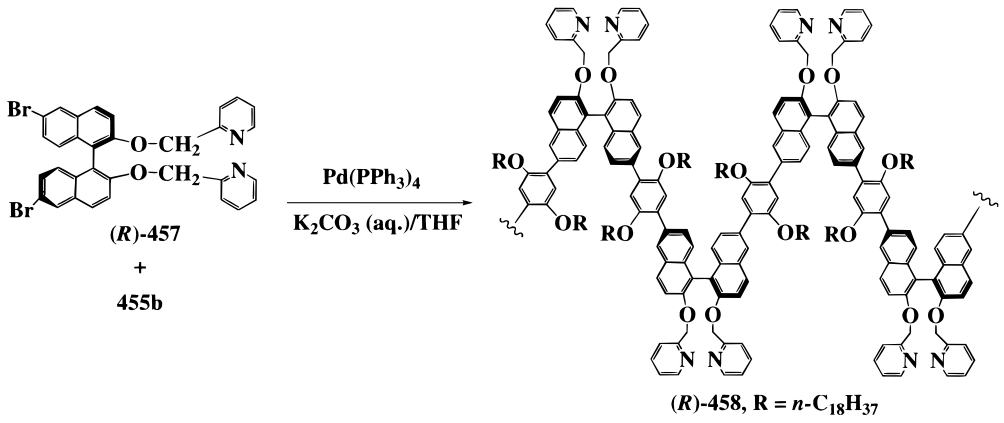
(*R*)-**458**, an optically active binaphthyl polymer containing pyridine functional groups and soluble in common organic solvents, was synthesized by the Suzuki coupling of (*R*)-**457** with **455b** (Scheme 116).[195] Its molecular weight was $M_w = 9900$ (PDI = 1.2) as measured by GPC, with a specific optical rotation of $[\alpha]_D = -73.1$ ($c = 0.204$, CH_2Cl_2). The solubility of this polymer was very low or even completely insoluble with shorter alkyl chains (e.g., $R = n\text{-}C_6H_{13}$) or without the phenylene spacers.

The catalytic properties of (*R*)-**449**, (*R*)-**456**, and (*R*)-**458** in the reaction of benzaldehyde with diethylzinc were also studied.[194,195] When (*R*)-**449** was used at room temperature, a mixture of compounds including the desired chiral alcohol **459** as well as the side product benzyl alcohol were obtained (Scheme 117). The ratio of **459** versus benzyl alcohol was 53:47 and the ee of **459** was 13%. Since (*R*)-**449** was not soluble in common organic solvents, the soluble polymer (*R*)-**456** was used, resulting in improved enantioselectivity. After 20 h at room temperature, about 33% conversion of benzaldehyde was observed. A mixture of **459** and benzyl alcohol was generated

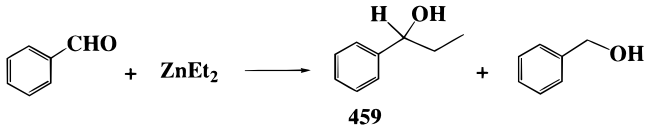
Scheme 115



Scheme 116



Scheme 117



in a 71:29 ratio with an ee for **459** of 40%. Polymer (*R*)-**458** showed no catalytic activity for this reaction.

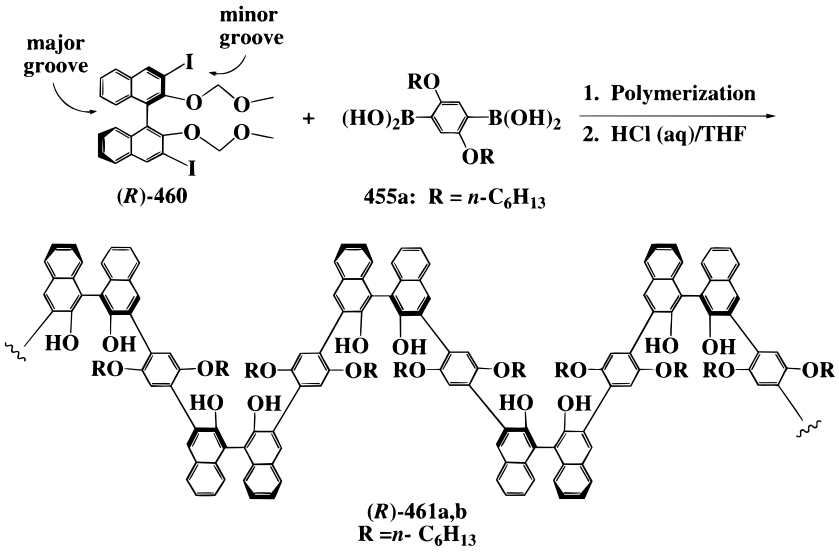
To improve the catalytic properties of such binaphthyl polymers, polymerization at the 3,3′-positions of the chiral binaphthyl monomers leading to polybinaphthyl catalysts with inherently better steric control at the catalytic sites was carried out. The Suzuki coupling of (*R*)-**460** with the diboronic acid **455a**, followed by hydrolysis, generated (*R*)-**461** (Scheme 118).

Since the polymerization occurred at the minor groove of the binaphthyl monomer, this polymer was designated as a minor-groove polybinaphthyl. The corresponding polymers (*R*)-**449**, (*R*)-**456**, and (*R*)-**458** were named the major-groove polybinaphthyls. In the presence of $Pd(OAc)_2$ and P(*o*-MePh)$_3$, (*R*)-**461a** was obtained. It had a molecular weight of M_w = 5900 (PDI = 1.53) as determined by GPC relative to polystyrene standards. Its specific optical rotation was $[\alpha]_D = -63.4$ (c = 0.50, THF). A higher molecular weight polymer (*R*)-**461b** was obtained when $Pd(PPh_3)_4$ was used as the catalyst. GPC showed that the molecular weight of (*R*)-**461b** was M_w = 20 200 (PDI = 1.53) while its specific optical rotation was $[\alpha]_D = -90.1$ (c = 0.5, THF). The minor-groove polymer (*R*)-**461** differs from the major-groove polybinaphthyls when used in asymmetric catalysis in two ways: (1) In (*R*)-**461**, both the phenylene linkers and the two adjacent naphthalene units can provide steric control for each binaphthyl catalytic site. (2) The alkoxy groups on the phenylene linkers not only make this polymer soluble in organic solvents, but also act as ligands to bind the catalytic metal centers.

The UV spectra of (*R*)-**456** and (*R*)-**461** showed an ~14-nm blue-shift going from the major-groove to the minor-groove polymer. The longest wavelength absorption for (*R*)-**456** was at λ_{max} = 336 nm and that of (*R*)-**461** at λ_{max} = 322 nm. (*R*)-**461** has reduced conjugation probably due to steric interaction between the alkoxy groups on the phenylene spacer and the hydroxyl groups on the binaphthyl unit resulting in disrupted planarity. Such interaction is absent in the repeating unit of (*R*)-**456**. Although both the minor-groove polymer (*R*)-**461** and the major-groove polymer (*R*)-**456** were made of optically pure *R* binaphthyl monomer, their CD signals were almost mirror images of each other except that the signals of (*R*)-**456** were red-shifted because of better conjugation. According to Gottarelli[10,11] and Mason,[13] the observed inverted CD effects between (*R*)-**456** and (*R*)-**461** indicate that the major-groove polymer may prefer the cisoid conformation, while the minor-groove polymer prefers the transoid conformation due to larger steric interaction in the cisoid form. Figure 11 is a schematic representation of the possible chain structures for the minor-groove and major-groove (*R*)-polybinaphthyls.

(*R*)-**461a** showed excellent enantioselectivity in the reaction of benzaldehyde with diethylzinc. In the presence of 5 mol % (based on the repeating unit) of (*R*)-**461a**, benzaldehyde was converted to (*R*)-**459** with 92% ee and 90% isolated yield.[194,195] In the presence of this polymer, the reaction of other aldehydes including para-substituted benzaldehydes and cinnamaldehyde gave over 90% ee. Good enantioselectivities were also observed for the reaction of aliphatic aldehydes with diethylzinc. For example, in the presence of (*R*)-**461a**, cyclohexanecarboxaldehyde reacted with diethylzinc to give 83% ee of the corresponding chiral alcohol. (*R*)-**461a** was easily recovered from the reaction solution by precipitation with methanol and the recovered polymer showed the same enantioselectivity as the original polymer. The high molecular weight polymer (*R*)-**461b** exhibited very similar catalytic activity and enantioselectivity to the lower molecular weight polymer (*R*)-**461a**. This demonstrated that the catalytic properties of the polymer catalysts in this process are independent of the molecular weights, the molecular weight distributions as well as preparative methods. This makes the use of these polymers in asymmetric catalysis very practical.

Scheme 118



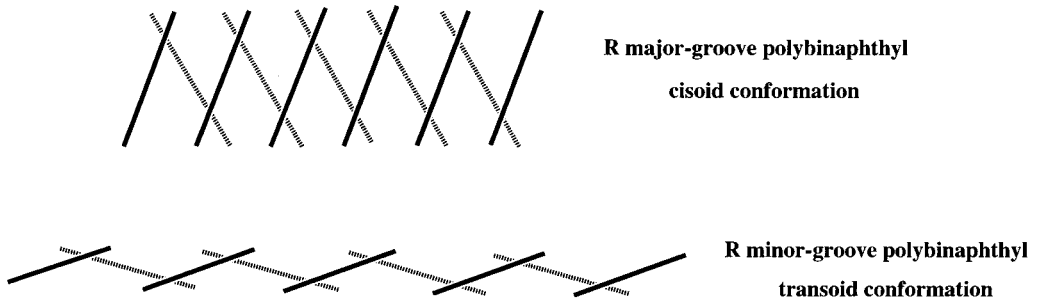
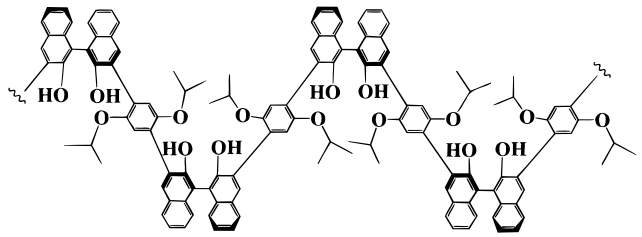


Figure 11.

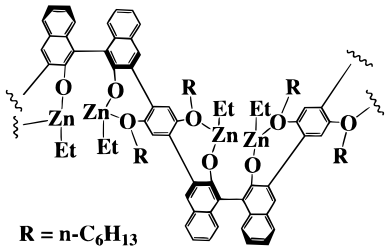
The influence of the size of the R groups in (*R*)-**461** on the catalytic asymmetric reaction of aldehydes with diethylzinc was studied. It was found that when the hexyl groups in (*R*)-**461** were replaced with bulkier isopropyl groups, the resulting polymer (*R*)-**462** showed slight decreases in both enantioselectivity and catalytic activity for the reaction of diethylzinc with benzaldehyde or cyclohexanecarboxaldehyde.[196]



(*R*)-**462**

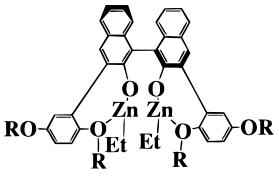
To further improve the catalytic properties of (*R*)-**461**, Pu and co-workers synthesized a monomeric model compound (*R*)-**464** by the Suzuki coupling of (*R*)-**460** with **463** followed by hydrolysis (Scheme 119).[197] When (*R*)-**464** was used to catalyze the asymmetric reaction of aldehydes with diethylzinc, it showed excellent enantioselectivity with broad range of aldehydes and proved the most general enantioselective catalyst for this reaction. Ee's of 91 to >99% were observed for para-, ortho-, or meta-substituted benzaldehydes, linear or branched aliphatic aldehydes, and aryl- or alkyl-substituted α,β-unsaturated aldehydes.

Compared to this monomeric binaphthyl catalyst, the polymer (*R*)-**461** exhibited much lower enantioselectivity for the reaction of ortho-substituted benzaldehyde and aliphatic aldehydes with diethylzinc. (*R*)-**464** also showed higher catalytic activity than the polymer. The difference in the catalytic properties of the monomer versus the polymer has been attributed to differences in the structures of the catalytically active species. When (*R*)-**461** and (*R*)-**464** are treated with diethylzinc, it is possible that the complexes (*R*)-**465** and (*R*)-**466** are respectively produced. In (*R*)-**465**, the two alkoxy oxygens on the



$R = n\text{-}C_6H_{13}$

(*R*)-**465**

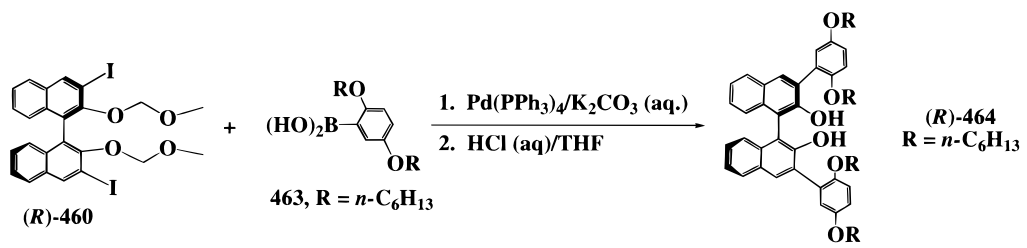


(*R*)-**466**

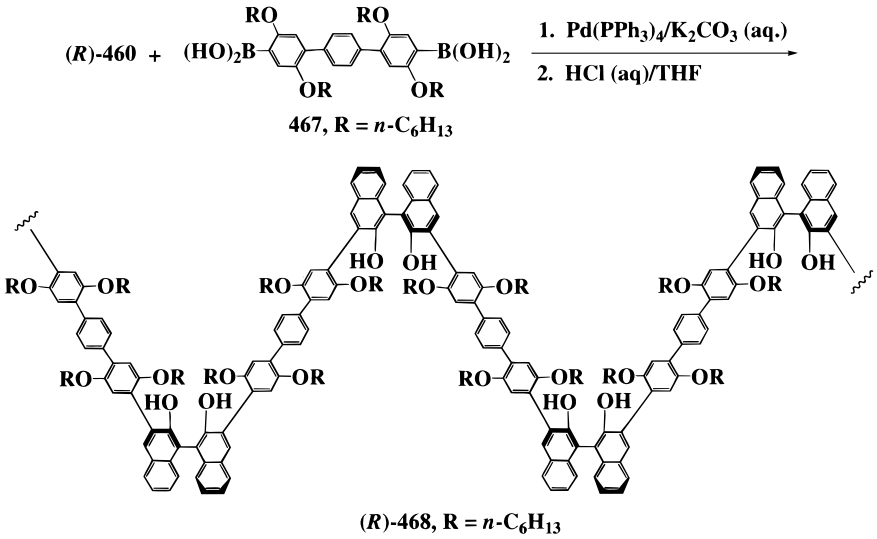
phenylene spacer serve as a dual ligand for coordination to the zinc atoms for both of the adjacent binaphthyl units. However, in (*R*)-**466**, the alkoxy groups on the 3,3′-phenyl substituents are only coordinated to the zinc centers of one binaphthyl unit. The result is that the electronic and steric environments of the catalytic sites in the polymer are very different from that in the monomer leading to the observed differences in enantioselectivity and catalytic activity.

On the basis of this analysis, Pu and co-workers synthesized a structurally modified polymer (*R*)-**468** via the Suzuki coupling of (*R*)-**460** with **467** followed by hydrolysis (Scheme 120).[198] GPC analysis of (*R*)-**468** showed its molecular weight was $M_w = 25\,800$ (PDI = 1.8). Its specific optical rotation was $[\alpha]_D = -92.9$ ($c = 1.01$, CH_2Cl_2). Phenylene spacers were introduced to increase the distance of the two adja-

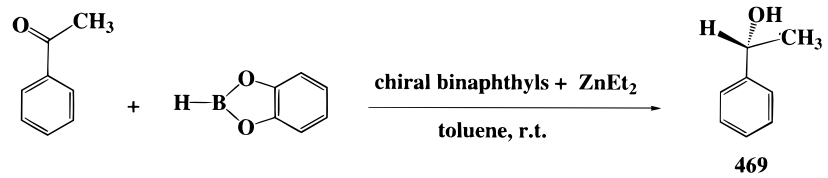
Scheme 119



Scheme 120



Scheme 121



interference between each of the binaphthyl catalytic sites.

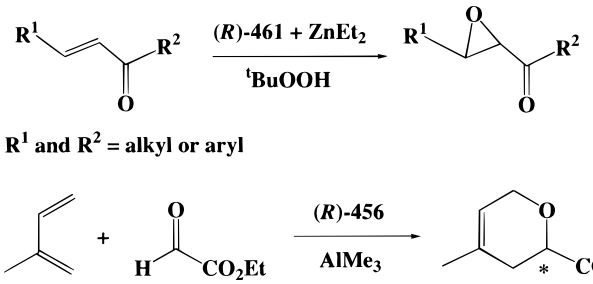
It was found that the zinc complex (*R*)-**466**, generated from the reaction of (*R*)-**464** with diethylzinc, exists in the monomeric rather than the dimeric or oligomeric forms found for the reaction of amino alcohols with alkylzincs.[199−201] This is attributed to the steric bulkiness of the ligand. When (*R*)-**464** of varying enantiomeric purity (20% ee to 99% ee) was used to catalyze the reaction of diethylzinc with benzaldehyde, a linear relationship between the optical purity of the catalyst and that of the product was observed.[199] This further demonstrates that the catalytically active species formed from the reaction of (*R*)-**464** with diethylzinc contains only one binaphthyl unit. Therefore, the catalytic properties of the new polymer (*R*)-**468** should closely resemble those of (*R*)-**464** because the microenvironment of the monomer (*R*)-**464** was generally preserved in the rigid and sterically regular polymer (*R*)-**468**. As expected, (*R*)-**468** exhibited an extremely general enantioselectivity for the reaction of various types of aldehydes with diethylzinc. (*R*)-**468** is the best polymeric catalyst with ee's of 90−98% observed for the reaction of diethylzinc with para-, ortho-, or meta-substituted benzaldehydes, linear or branched aliphatic aldehydes, and α,β-unsaturated aldehydes.

The binaphthyl polymers (*R*)-**461** and (*R*)-**468** represent a new generation of enantioselective polymeric catalysts that are made of sterically regular and rigid chiral polymer main chains. The study of polymers such as (*R*)-**449**, (*R*)-**456**, (*R*)-**461**, and (*R*)-**468** demonstrates that systematic modification of the catalytic activity and stereoselectivity of these novel polymeric chiral catalysts can be carried out to develop highly enantioselective polymer catalysts because the catalytic sites of these rigid, sterically regular polymers have much better defined microenvironments. This is in contrast to the traditional polymeric chiral catalysts prepared by attaching chiral catalysts to a flexible and sterically irregular polymer backbone, since it is not possible to systematically modify the microenvironment of the catalytic sites in the traditional polymeric chiral catalysts if they do not perform as well as their monomeric version.

The zinc complexes of polymers (*R*)-**461** and (*R*)-**468** as well as the monomer (*R*)-**464** were also used to catalyze the asymmetric reduction of ketones.[202a] In the presence of (*R*)-**465**, a possible complex generated from the reaction of (*R*)-**461** with diethylzinc, acetophenone was reduced to 1-phenylethanol (**469**) with catecholborane in 67% ee (Scheme 121). The reaction was carried out at −30 °C in toluene solution. Under the same conditions, the zinc complex of the monomer (*R*)-**464** showed a much better ee (81%). The zinc complex of the polymer (*R*)-**468** was also used to catalyze the reduction and gave an ee of 80%, as good as for (*R*)-**464**. Other aryl methyl ketones were also reduced using catecholborane in the presence of the polymer (*R*)-**468** and diethylzinc and ee's were in the 70−80% range.

In both catalytic reactions of diethylzinc with aldehydes and acetophenone with catecholborane, the polymer (*R*)-**468** exhibited a very similar enantioselectivity to the monomer (*R*)-**464**. This indicates that a monomeric catalyst can be converted into a polymeric catalyst with similar catalytic properties by incorporating it into a rigid and sterically regular polymer backbone. This technique is viable as long as the catalytically active species is monomeric rather than a monomer aggregate. Using this strategy, the

Scheme 122

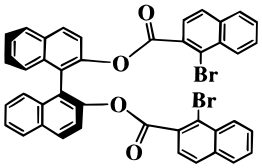


catalytic properties of the monomeric catalyst are generally preserved due to the rigidity and stereoregularity of the polymer structure. This methodology may yet find general application in converting existing highly enantioselective monomeric catalysts to highly enantioselective polymeric catalysts.

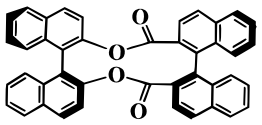
Scheme 122 shows two additional examples of the asymmetric reactions catalyzed by Lewis acid complexes of the chiral polybinaphthyls. Pu and coworkers discovered that the zinc complex of (*R*)-**461** catalyzed the asymmetric epoxidation of α,β-unsaturated ketones with up to 81% ee.[202b] Using the aluminum complex of (*R*)-**456**, Jørgesen, Pu, and coworkers found that a hetero-Diels−Alder reaction was catalyzed with up to 95% ee (Scheme 122).[202c] These results demonstrate that the chiral binaphthyl polymers have great potential in asymmetric catalysis.

3.5. Binaphthyls in Stereocontrolled Cyclization

Binaphthyls have been used to control the stereochemistry of intramolecular cyclizations of aryl halides for the preparation of other functionalized chiral biaryl compounds. In 1980, Miyano et al. discovered a highly stereoselective intramolecular Ullmann coupling reaction for generating a bisbinaphthyl cyclic ester.[203,204] (*S*,*S*)-**471** was produced stereospecifically in 36% yield from the 5 h reaction of (*S*)-**470** with copper powder under N_2 in refluxing DMF. The

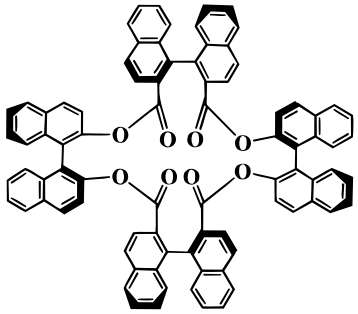


(*S*)-**470**

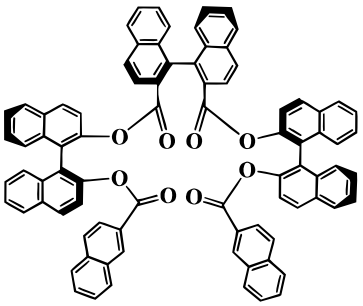


(*S*,*S*)-**471**

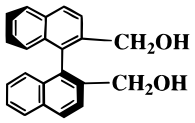
SR diastereomer was not observed. The side products included the debrominated compounds as well as a few oligomers. At higher concentrations of (*S*)-**470**, a tetrabinaphthyl macrocycle (*S*,*S*,*S*,*S*)-**472** was isolated in 11.2% yield from the coupling reaction.[205] A diastereomeric mixture of the open chain dimer **473** was formed in 3.6% yield. The ratio of the two diastereomers, (*S*,*S*,*S*)-**473** and (*S*,*R*,*S*)-**473**, was about 0.85:1. (*S*,*S*,*S*,*S*)-**472** was found to be optically pure because its reaction with lithium aluminum hydride gave the optically pure BINOL (*S*)-**12** and (*S*)-**474**. Formation of the optically pure (*S*,*S*,*S*,*S*)-



(*S*,*S*,*S*,*S*)-**472**



(*S*,*S*,*S*)-**473**



(*S*)-**474**

472 demonstrated that ring closure of other diastereomeric structures was very unfavorable. Molecular models of the tetrabinaphthyl cyclic esters suggested that of the four possible diastereomers (*S*,*S*,*S*,*S*)-**472** should have the least steric strain. According to models, the chiral cavity of (*S*,*S*,*S*,*S*)-**472** was about the size of a benzene molecule.

The intramolecular coupling of optically pure **475** followed by base-catalyzed hydrolysis was used to prepare the chiral biaryls **476**−**479** with over 99% optical purity (Figure 12).[206,207]

When the monobrominated compound (*R*)-**480** was subjected to Ullmann coupling conditions, a trisbinaphthyl compound (*R*,*R*,*R*)-**481** as well as a debrominated compound (*R*)-**482** were obtained in an 85:15 ratio and almost quantitative yield (Scheme 123).[204] However, the optical yield of (*R*,*R*,*R*)-**481** was very low. Reduction of (*R*,*R*,*R*)-**481** with lithium aluminum hydride or hydrolysis with base produced (*R*)-**474** or (*R*)-**2** with an optical purity of only 3−6%. Therefore, the intermolecular Ullmann coupling of (*R*)-**480** was nonstereoselective. It appears that the cyclic transition state in the coupling of (*S*)-**470** played an important role in the observed stereospecificity.

The intramolecular Ullmann coupling of (*S*)-**483**, prepared from the binaphthyl dicarboxylic acid (*S*)-

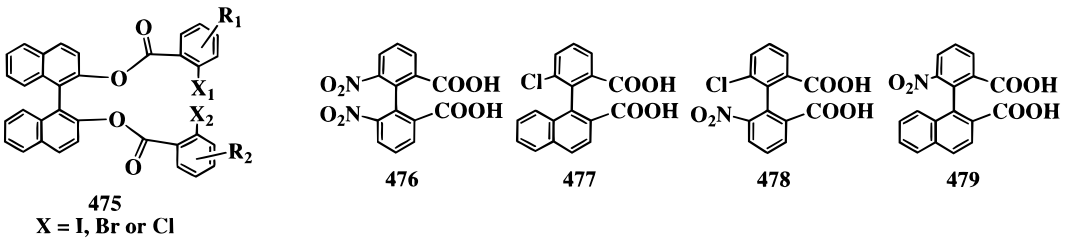
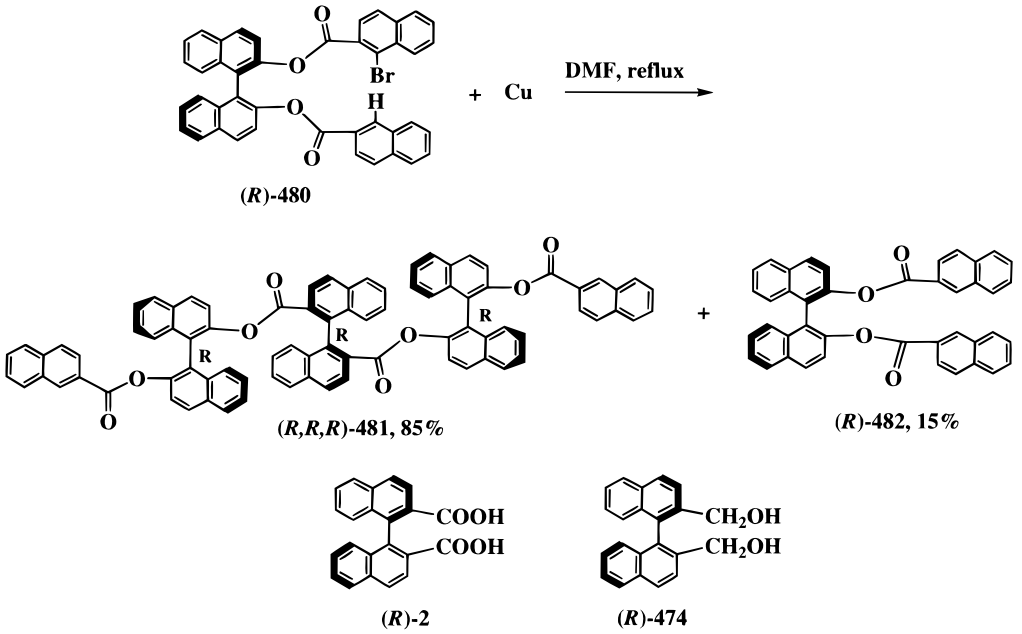
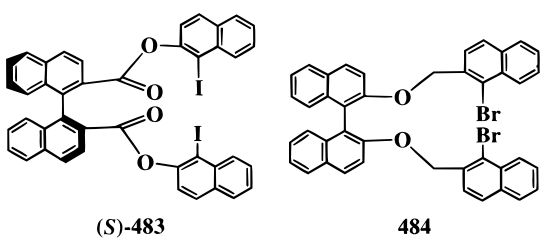


Figure 12.

Scheme 123



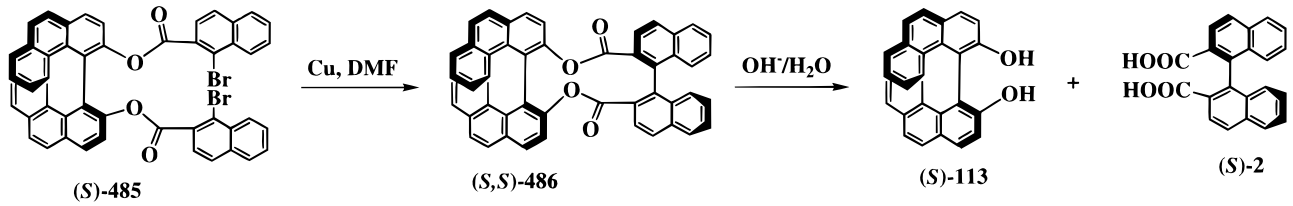
2, was also examined.[208] Even though iodide was used in place of bromide, the coupling of (*S*)-**483** was still much slower than (*S*)-**470** because the aryl iodide moieties in (*S*)-**483** were more electron-rich than the aryl bromide moieties in (*S*)-**470**. A more complex product mixture was obtained from the coupling of (*S*)-**483**, and the dehalogenated compound was the major product. (*S,S*)-**471** was obtained in 11% yield and its ee was estimated to be about 90% by reduction to (*S*)-**474**. Since this optical purity was almost the same as that of the starting material (*S*)-**2** used to make (*S*)-**483**, the intramolecular Ullmann coupling of (*S*)-**483** must have proceeded stereospecifically just like that of (*S*)-**470**. The binaphthyl diether **484** did not undergo Ullmann coupling or debromination even when heated with activated copper powder in refluxing DMF over a long period of time.[207]



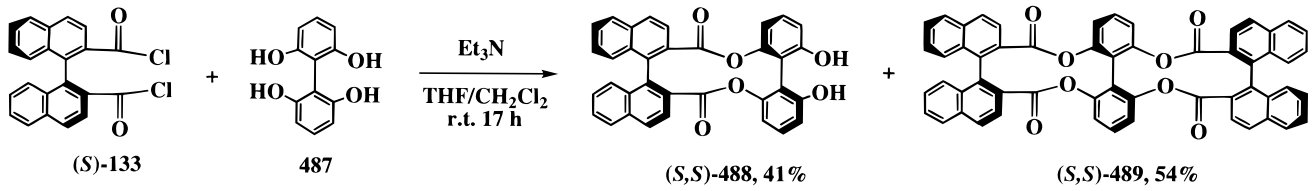
Determination of the absolute configuration of the optically active 3,3′-dihydroxy-4,4′-biphenanthryl (*R*)-**113** and (*S*)-**113** (section 2.3.1) was attempted by carrying out an intramolecular Ullmann coupling of (*S*)-**485** to generate **486** (Scheme 124).[70] According to Miyano's study as shown in the conversion of (*S*)-**470** to (*S,S*)-**471**,[204−208] the *R* binaphthyl should produce the *R* enantiomer and the *S* binaphthyl the *S* enantiomer in an intramolecular Ullmann coupling. After hydrolysis of **486** with base, the configuration of the resulting binaphthyl molecule **2** should, therefore, correspond to that of **113**. The original report by Yamamoto et al.[70] used this method to assign (−)-**113** the *S* enantiomer. However, on the basis of the CD spectrum of the optically active **113** and an X-ray analysis of a related compound published by Yamamura et al.,[209] Hayashi et al. found this to be incorrect.[210] Later, Miyano et al. reacted racemic **113** with (*R*)-1,1′-bi-2-naphthylcarbonyl chloride [(*R*)-**133**] and generated (*R,R*)-**486** as the only diastereomer.[211] Reduction of (*R,R*)-**486** with lithium aluminum hydride gave both (*R*)-**113** and (*R*)-**474**. These results supported Hayashi's assignment for the configuration of (*R*)-(−)-**113** and (*S*)-(+)-**113**.

In 1998, Nozaki et al. reported the use of chiral binaphthyls for building double-helical oligo esters.[212] From the reaction of (*S*)-**133** with biphenyl-2,2′,6,6′-tetrol (**481**), the two compounds (*S,S*)-**488** and (*S,S*)-**489** were obtained in 41% and 54% yield, respectively (Scheme 125). This cyclization was highly stereospecific, and the other diastereomer of **488** with a (*R*)-biphenyl unit was not formed. Methylation of (*S,S*)-

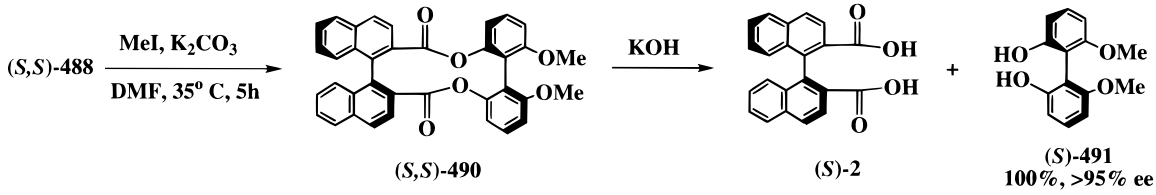
Scheme 124



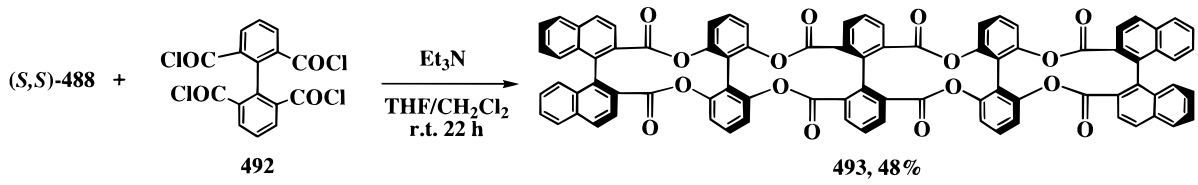
Scheme 125



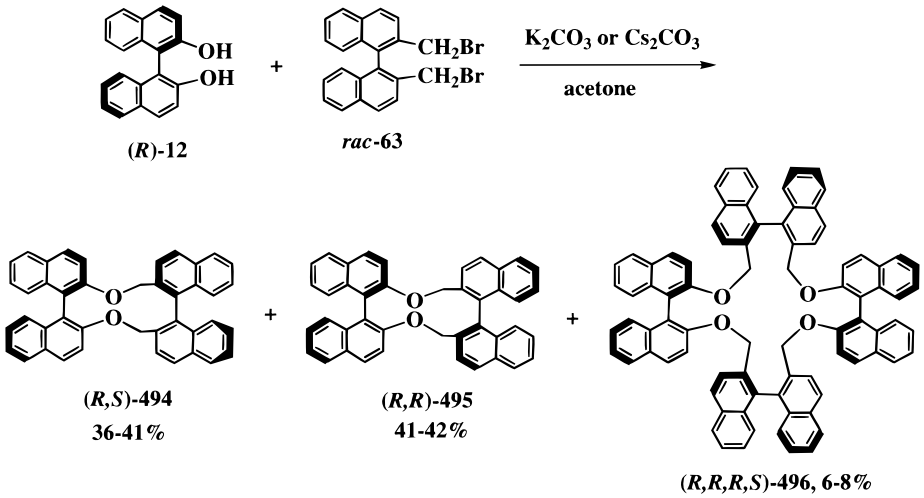
Scheme 126



Scheme 127



Scheme 128

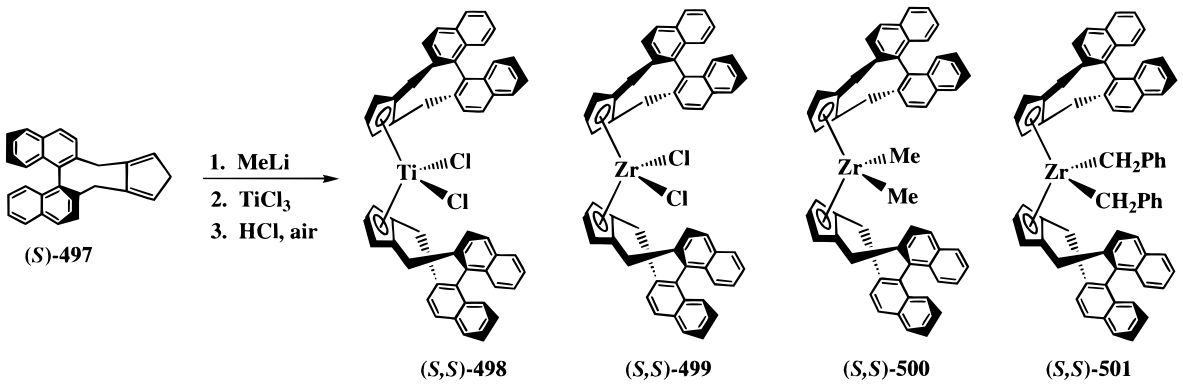


488 gave (*S*,*S*)-**490** which was then hydrolyzed to produce (*S*)-**491** with over 95% ee (Scheme 126).

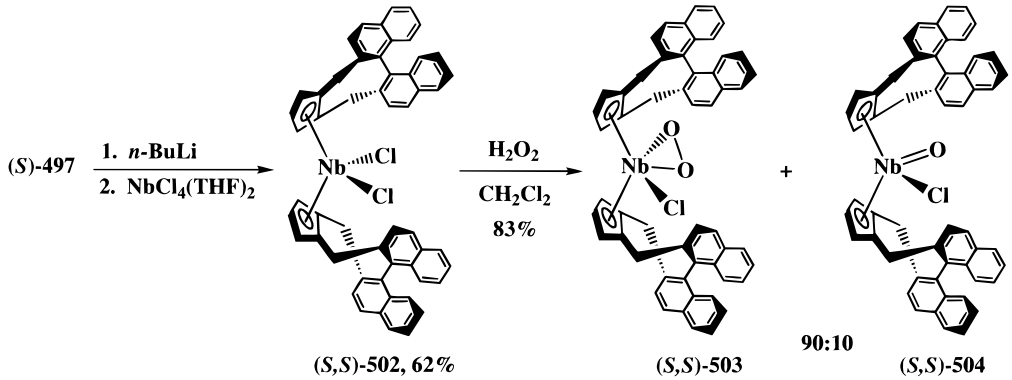
A space-filling model of (*S*,*S*)-**489** showed that it adopts a double helical configuration. The reaction of (*S*,*S*)-**488** with biphenyl-2,2′,6,6′-tetracarbonyl chloride (**492**) led to the formation of a longer biphenyl ester **493** (Scheme 127). The oligomer **493** possibly has a double helical configuration similar to (*S*,*S*)-**489**. From (*S*,*S*)-**489** ($[\alpha]_D = -589$, $c = 1.00$, $CHCl_3$) to **493** ($[\alpha]_D = -821$, $c = 1.00$, CH_2Cl_2), the large increase in optical rotation was attributed to a double helical structure.

Mazaleyrat et al. studied the Williamson reaction of (*R*)-**12** with *rac*-**63** in an effort to resolve this molecule.[213] A mixture of diastereomeric macrocycles (*R*,*S*)-**494** (36−41%), (*R*,*R*)-**495** (41−42%), and (*R*,*R*,*R*,*S*)-**496** (6−8%) were obtained (Scheme 128). After separation, they were treated with BBr_3 in methylene chloride to give optically pure (*R*)-**63** and (*S*)-**63** in 65−67% yield.

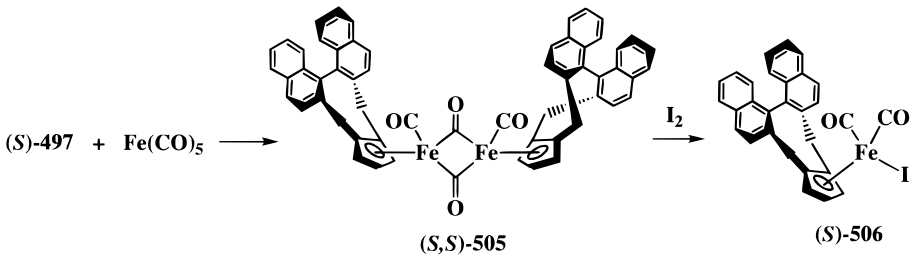
Scheme 129



Scheme 130



Scheme 131



3.6. Other Multibinaphthyl Compounds in Asymmetric Reactions

3.6.1. Binaphthyl Metallocene Complexes

Bisbinaphthyl metallocene complexes were prepared by Halterman and co-workers in 1991.[214,215] After treatment of (*S*)-**497** with methyllithium followed by reaction with $TiCl_3$ and then with HCl in air, (*S,S*)-**498** was obtained (Scheme 129).[215] The structure of (*S,S*)-**498** was established using X-ray analysis. The bisbinaphthyl zirconocene complex (*S,S*)-**499** was made from $ZrCl_4$. (*S,S*)-**499** was converted to (*S,S*)-**500** and (*S,S*)-**501** by reaction with methyllithium or benzylpotassium. The reaction of (*S*)-**497** with *n*-butyllithium then with $NbCl_4(THF)_2$ gave (*S,S*)-**502** (Scheme 130). Oxidation of (*S,S*)-**502** with hydrogen peroxide generated a mixture of (*S,S*)-**503** and (*S,S*)-**504** in a 90:10 ratio.[26] (*S,S*)-**503** was converted to (*S,S*)-**504** by treatment with PPh_3.

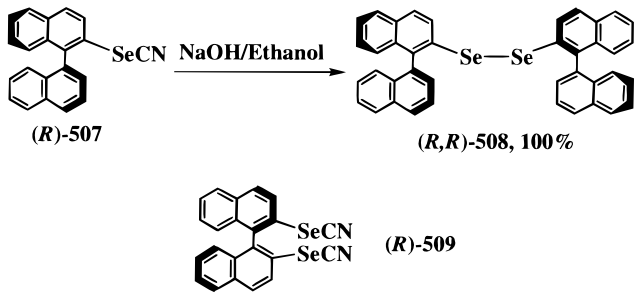
The reaction of (*S*)-**497** with ironpentacarbonyl gave the bisbinaphthyl complex (*S,S*)-**505** which was then converted to a mononuclear binaphthyl complex (*S*)-**506** after reaction with iodine (Scheme 131).

The bisbinaphthyl titanocene (*S,S*)-**498** as well as the bisbinaphthyl niobocene (*S,S*)-**503** were used to catalyze the asymmetric epoxidation of unfunctionalized olefins in the presence of aqueous H_2O_2. However, both the yields and the ee's of the resulting epoxides were very low. The highest enantioselectivity was observed for the epoxidation of *trans*-3-hexene in the presence of (*S,S*)-**498** giving a chiral epoxide with 20% ee.[26]

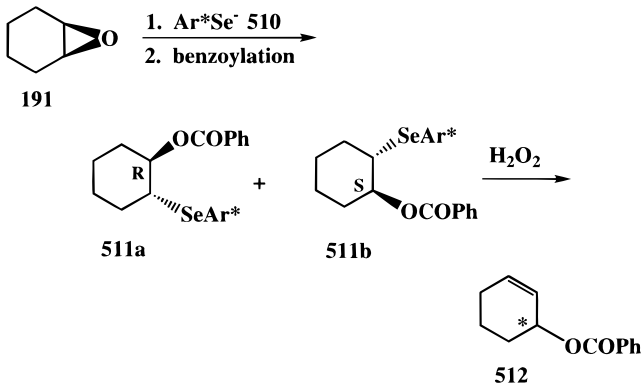
3.6.2. Binaphthyl Selenium Compounds

The synthesis of a bisbinaphthyl diselenide compound (*R,R*)-**508** from the reaction of (*R*)-**507** with sodium hydroxide in ethanol has been reported (Scheme 132).[216] (*R*)-**507**, (*R,R*)-**508**, as well as the monobinaphthyl diselenide (*R*)-**509** were used to carry out the asymmetric ring opening of cyclohexene oxide (**191**) (Scheme 133). When these binaphthyl selenides were treated with excess sodium borohydride or lithium borohydride, the corresponding selenoate anions **510** were generated. These compounds underwent nucleophilic attack of **191** to give the ring-opening products **511a,b** after benzoylation.

Scheme 132



Scheme 133



Oxidative elimination of **511a,b** gave a chiral allylic ester **512**. Of the three chiral selenides used, the bisbinaphthyl compound (*R,R*)-**508** showed the best enantioselectivity. (*S*)-**512** was produced with 50% ee when (*R,R*)-**508** was used as the chiral nucleophile precursor.

4. Binaphthyl Polymers

In this section, the syntheses and studies of binaphthyl polymers with various structures and properties will be discussed. The application of polybinaphthyls to asymmetric catalysis has already been described in section 3.5. A variety of methods including the condensation of functionalized binaphthyl monomers, the cyclopolymerization of binaphthyls containing olefin groups or oxazoline groups, the ring-opening polymerization of binaphthyl carbonates, as well as transition metal-catalyzed cross couplings have all been used to prepare these polymers. All the optically active binaphthyl polymers are obtained by polymerization of the optically active binaphthyl monomers. To date, no enantioselective process has been developed to couple naphthalene groups to make chiral polybinaphthyls. In some cases, polymers are produced only in the optically inactive forms being made either from the racemic binaphthyl monomers or through nonstereocontrolled coupling of the naphthyl monomers. The use of binaphthyl polymers as chiral stationary phases for enantioselective separation has been demonstrated. Other potential applications of binaphthyl polymers are in fields such as liquid crystallines, optical nonlinearity, soluble high-temperature materials, electrochemical sensors, and polarized light emissions.

4.1. Optically Active Binaphthyl Polymers

Optically active binaphthyl polymers will be classified according to the polymerization positions of the binaphthyl units. The optically active BINOL (*R*)- or (*S*)-**12** is the main starting material used to prepare various functionalized binaphthyl monomers. Other chiral binaphthyl starting materials include 1,1′-binaphthyl-2,2′-diamine (**136**) and 1,1′-binaphthyl-2,2′-dicarboxylic acid (**2**). Polymerization at the different positions of the binaphthyl monomers leads to polymers of diverse chain structures.

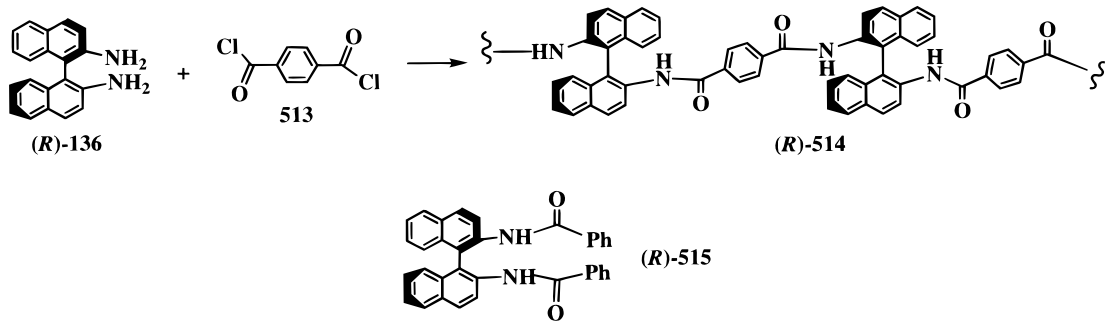
4.1.1. Polymerization at the 2,2′-Positions

a. Condensation Polymerization To Produce Polyamides and Polyimides. In 1968, Schulz et al. synthesized an optically active polyamide, (*R*)-**514**, from the condensation of (*R*)-**136** with terephthaloyl chloride (**513**) (Scheme 134).[217] The molecular weight of this polymer was found to be $M_w = 7000$ as measured by vapor pressure osmometry (VPO). A monomeric binaphthyl amide (*R*)-**515** was synthesized as a model compound for (*R*)-**514** and their UV, ORD, and CD spectra were compared. No significant difference between the polymer and this monomeric compound was observed except that the CD signals of the polymer showed a slight red-shift.

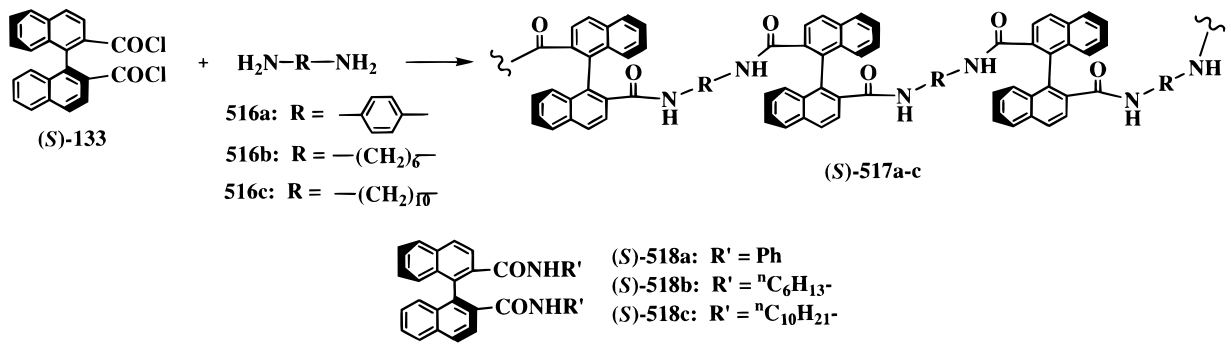
The binaphthyl-based polyamides (*S*)-**517a**−**c** were prepared from the condensation of (*S*)-**133** with diamines **516a**−**c** by Miyano and co-workers in 1991 (Scheme 135).[218] These polymers were soluble in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), *N*,*N*-dimethylformamide, *N*,*N*-dimethylacetamide (DMAc), and DMSO, but insoluble in THF, chloroform, and other normal nonpolar solvents. The molecular weights of (*S*)-**517a**−**c** were in the range of $M_n =$ 20000−27000 as measured by GPC relative to polystyrene standards. Cyclic oligomers were also observed in the polymerization of **516b,c**. The monomeric amides (*S*)-**518a**−**c** have been prepared. There was a significant red shift for the CD signals of (*S*)-**517a** at wavelengths above 260 nm in DMAc when compared to those of (*S*)-**518a**. However, the CD spectra of (*S*)-**517a** and (*S*)-**518a** in HFIP were found to be very similar. In DMAc, the mean residue rotation of (*S*)-**517a** was very small ($[m]_D = -2.1$) compared to the molar rotation of (*S*)-**518a** ($[\phi]_D = -70.5$). The polymers (*S*)-**517b,c** showed similar CD effects and optical rotations as the corresponding monomers (*S*)-**518b,c**. The rigidity and conjugation of the phenylene linker in (*S*)-**517a** was responsible for the change in chiroptical properties of this polymer from its corresponding monomer. Materials made by coating spherical macroporous silica gel with DMAc solutions of these chiral polymers have been used as chiral stationary phases for HPLC. It was shown that racemic mixtures of some aryl amides and aryl carbamates could be separated using these chiral columns. Hydrogen bonding interactions between polymers and substrates was found to play an important role in the chiral resolution of these compounds.

In 1996, Ding and co-workers reported the condensation polymerization of a binaphthyl anhydride (*R*)-**519** with 4,4′-oxydianiline (**520**) (Scheme 136).[219] The

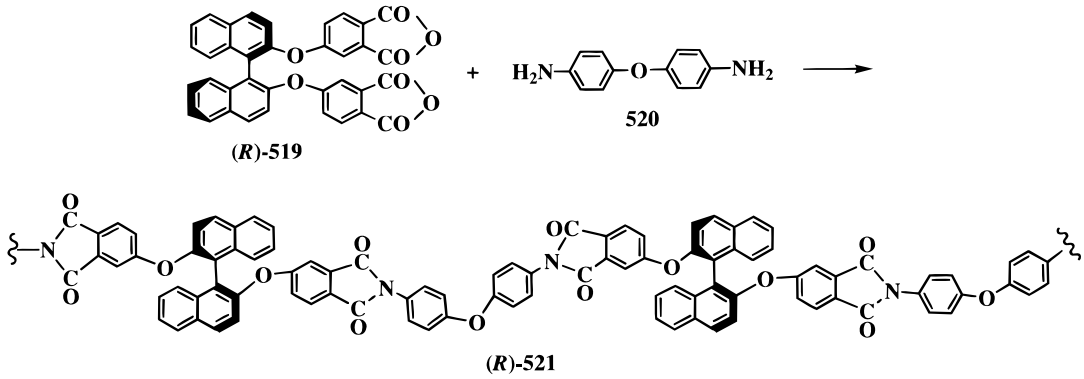
Scheme 134



Scheme 135



Scheme 136

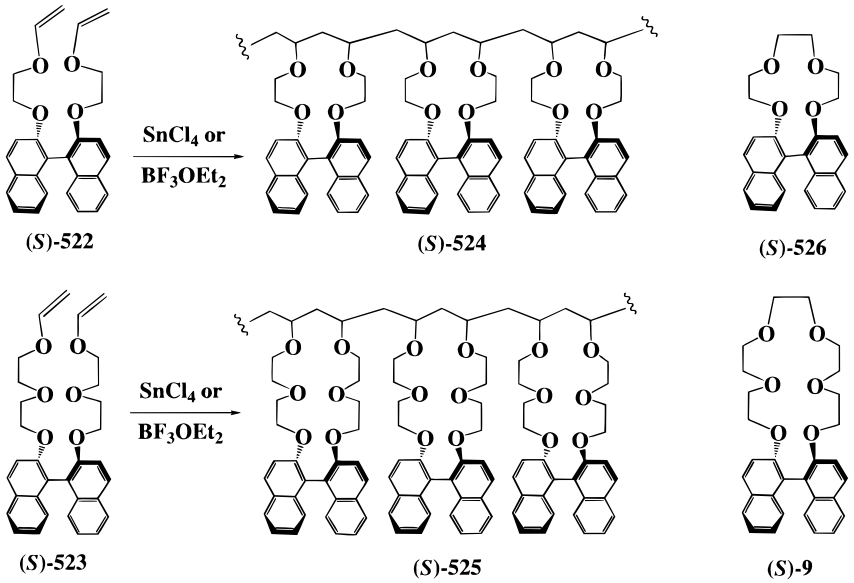


resulting polyimide (*R*)-**521** had a molecular weight of $M_w = 22\ 100$ (PDI = 1.51) as determined by GPC relative to polystyrene standards. (*S*)-**521** was obtained from the polymerization of (*S*)-**519** with **520**. These polymers were soluble in many common organic solvents such as methylene chloride, chloroform, THF, and pyridine. The glass transition temperatures (T_g) of (*R*)-**521**, (*S*)-**521,** and the polymer made from the racemic monomer were all at 274 °C, indicating no stereocomplex formation in these materials. (*R*)-**521** and (*S*)-**521** showed very intense CD signals and their CD spectra were exact mirror images of each other. The longest wavelength CD maximum was at 348 nm. The chiral configurations of both (*R*)-**521** and (*S*)-**521** were shown to be extremely thermally stable. When these polymers were heated at 250 °C in air for 96 h, no change in optical rotation was observed. After heat treatment, the polymers became insoluble in chloroform, methylene chloride, THF, and DMSO, but were still soluble in DMAc and NMP.

b. Cyclopolymerization. Cyclopolymerization of alkene or oxazoline substituents at the 2,2′-positions of binaphthyl monomers have been used to synthesize chiral polymers containing macrocyclic ethers, esters, and amides.

In 1985, Yokota and co-workers carried out a cationic cyclopolymerization of the binaphthyl-based divinyl ethers (*S*)-**522** and (*S*)-**523** to synthesize the chiral polymers (*S*)-**524** and (*S*)-**525** (Scheme 137).[220] This polymerization was catalyzed by Lewis acids including $SnCl_4$ and $BF_3{\cdot}OEt_2$ in methylene chloride or nitromethane solution. NMR and IR spectroscopies showed the disappearance of vinyl signals in most cases. This supports the existence of a cyclopolymerization process. The molecular weights of these polymers were in the range of $M_n = 9000-15000$ as determined by VPO. Their optical rotations were compared to those of the monomeric model compounds (*S*)-**526** and (*S*)-**9**. The specific optical rotation of (*S*)-**524** was $[\alpha]_D = -130$ and that of (*S*)-**525** $[\alpha]_D = -95$. These values were close to the specific

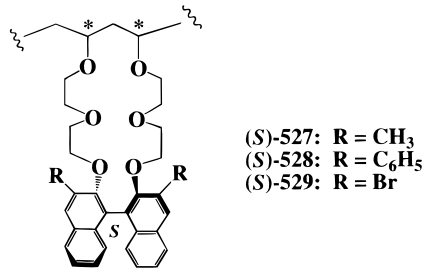
Scheme 137

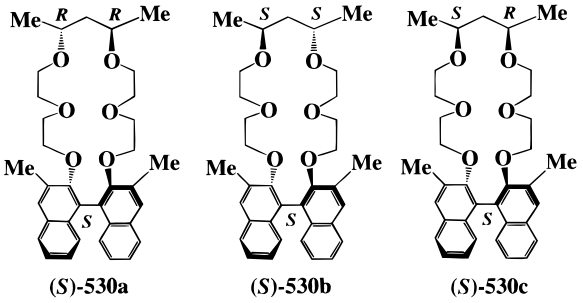


optical rotations of the corresponding monomeric models (*S*)-**526** ([α]$_D$ = −127) and (*S*)-**9** ([α]$_D$ = −70.5), respectively. It was also observed that polymers containing uncyclized structural units had lower optical rotations. These polymers were used to extract ammonium and alkali metal picrates from the aqueous solution. (*S*)-**524** could not extract any of the picrates and (*S*)-**525** showed selective binding to K^+ and NH_4^+ salts. The binding constants of (*S*)-**525** with K^+ and NH_4^+ were about 6−9 times smaller than those of (*S*)-**9**.

When the polymerization of (*R*)-**523** was carried out in methylene chloride solution in the presence of a $SnCl_4$ catalyst at 0 °C, (*R*)-**525** was obtained with M_n = 14 000 and [α]$_D$ = +106.8 (*c* = 1.0 g/dL, CH_2Cl_2). The chiral recognition ability of this polymer was studied by using it to extract various racemic alkylammonium and amino ester salts from their aqueous solutions into methylene chloride.[221] (*R*)-**525** showed a chiral recognition factor of 1.5 for the enantiomers of phenylglycine methyl ester. This is very similar to the monomer (*R*)-**9**.

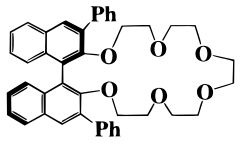
The binaphthyl crown ether polymers (*S*)-**527** to (*S*)-**529** containing substituents in the 3,3′-positions of the binaphthyl units were synthesized.[222a−c] These compounds, unlike the polymers (*S*)-**524** and (*S*)-**525** which did not show much changes in optical rotation with respect to polymerization conditions, exhibited a wide range of optical rotations when prepared under different conditions. This optical rotation variation was attributed to the different stereochemistry of the polymer main chain induced by the steric barrier of the binaphthyl units extended by the 3,3′-substituents. Three monobinaphthyl compounds (*S*)-**530a**−**c** were prepared as model compounds for (*S*)-**527**. All were made from (*S*)-binaphthyl and had different chiral configurations at the two macrocycle chiral carbon centers. The specific optical rotation of (*S*)-**530a** was found to be [α]$_D$ = −61.6 and that of (*S*)-**530b** [α]$_D$ = −2.8. A comparison of their NMR spectra with that of (*S*)-**527** provided information for





the main-chain configuration of the polymer. It was found that the different optical rotations of the polymer (varying from −42.8 to +20.9) were due to the relative contents of the structure (*S*)-**530a** versus (*S*)-**530b** in the main chain. As the optical rotations of the polymer changed toward a positive direction, the NMR spectra indicated an increase in the (*S*)-**530b** components in the polymer chain. In addition, the chiral induction of the substituted binaphthyl units was found to be very sensitive to both monomer concentration and solvent polarity. On the basis of these observations, a mechanism involving intramolecular solvation was proposed for the cyclopolymerization. These crown ether polymers were used to recognize the enantiomers of the methyl ester salts of phenylglycine, phenylalanine, valine, and methionine.[222c] Chiral recognition factors in the range 1.1−1.7 were observed. Polymer (*R*)-**528** with bulkier phenyl substituents exhibited higher enantioselectivity. However, the enantioselectivity of this polymer was about 5 times lower than that of its

monomeric model compound (*R*)-**531**. Therefore, in this case it appears that the main-chain configuration of the polymer contributed unfavorably to chiral recognition.

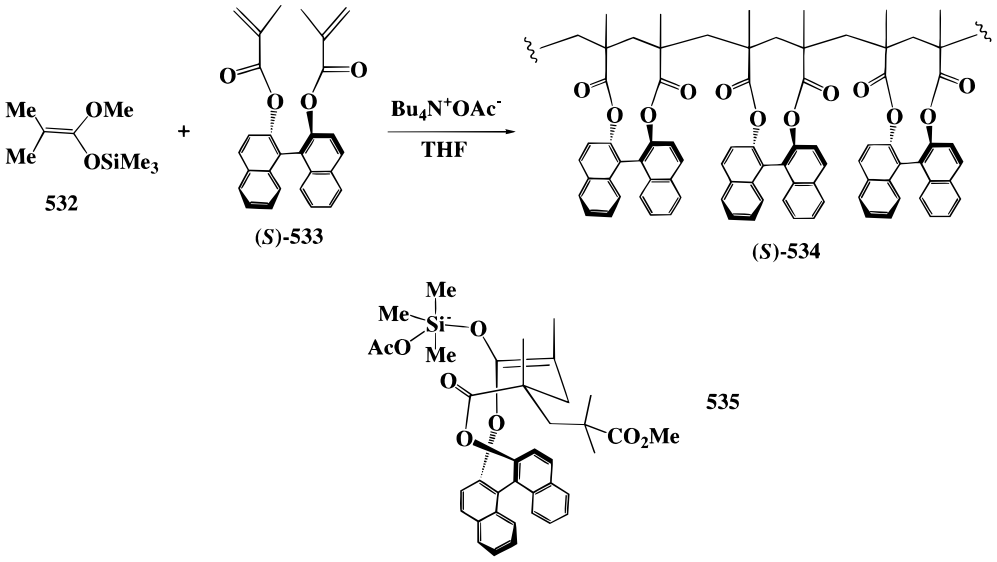


(*R*)-531

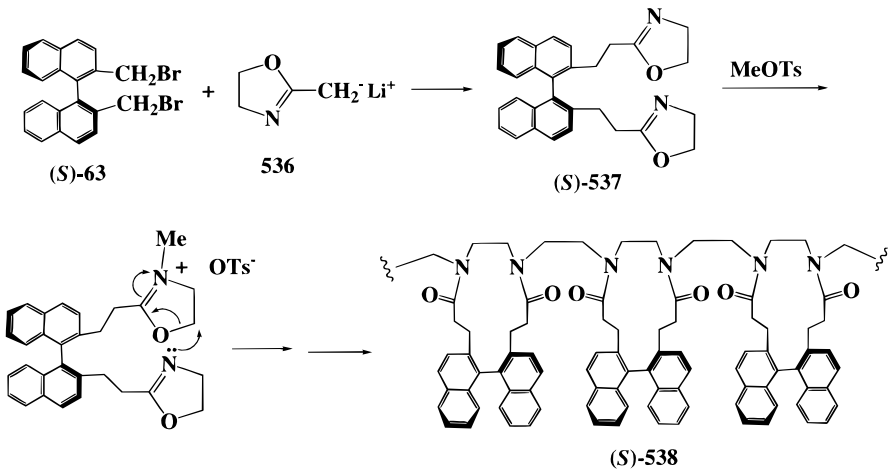
In 1995, Sogah and Nakano reported on the use of chiral binaphthyls in controlling the stereochemistry of the group-transfer polymerization (GTP) of methacrylates.[223] In the presence of the silylketene initiator **532** and an anionic catalyst, tetrabutylammonium acetate, the binaphthyl dimethacrylate (*S*)-**533** underwent GTP to give (*S*)-**534** at 25 °C (Scheme 138). (*S*)-**534** was soluble in THF and chloroform, and its molecular weight was M_n = 13 600 (PDI = 2.30) as determined by universal calibration. Its ^{1}H NMR spectrum displayed no vinyl protons, indicating that it was generated exclusively through a cyclopolymerization process. Racemic **533** was polymerized to give polymers of similar molecular weights. At higher monomer concentration (0.3 M), the resulting polymer was found to be insoluble in common organic solvents. (*S*)-**534** was converted to poly(methylmethacryclate) (PMMA) by hydrolysis in the presence of potassium *tert*-butoxide followed by reaction with diazomethane. NMR spectroscopy showed a large increase in isotacticity of this PMMA compared to the PMMA obtained directly from the GTP of methyl methacrylate. It can be concluded, therefore, that the optically active binaphthyl unit provided the steric control to favor a cis geometry for both the monomer addition as well as ring closure during the GTP of (*S*)-**533** as shown in the proposed transition state **535**. The polymer generated from the free radical polymerization of (*S*)-**533** using azobis(isobutyronitrile) (AIBN) as the initiator, however, exhibited a much lower isotacticity. The transferring silyl group must play an important role in the stereocontrol of the GTP of (*S*)-**533**.

The cyclopolymerization of a binaphthyl oxazoline has also been studied by Sogah and co-worker.[224] Treatment of 2-methyl-2-oxazoline with lithium diisopropylamide at −78 °C generated **536** which on reaction with (*S*)-**63** gave (*S*)-**537** (Scheme 139). A

Scheme 138

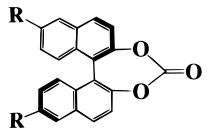


Scheme 139

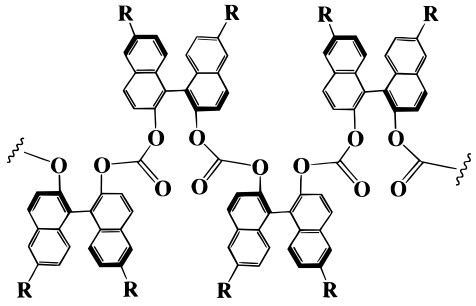


polymer (*S*)-**538** with a molecular weight of M_n = 17 800 (PDI = 1.5) as measured by GPC relative to polystyrene standards was synthesized from (*S*)-**537**. Initially (*S*)-**537** was methylated with methyl tosylate which then underwent an intramolecular nucleophilic ring opening−closing followed by an intermolecular nucleophilic ring-opening to give the product. The mean residue molar optical rotation of (*S*)-**538** was found to be $[\phi]_D = -1157$ ($c = 0.9$, THF). This was in sharp contrast with the monomer (*S*)-**537** that had a very low molar optical rotation ($[\phi]_D = +4$). (*S*)-**538** also showed a higher glass transition temperature (T_g) and a higher decomposition onset temperature than the corresponding polymer made of the racemic monomer.

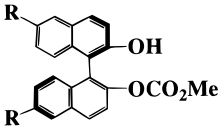
c. Ring-Opening Polymerization. Recently, Takata et al. reported a nucleophilic ring-opening polymerization of optically active binaphthyl carbonates (*R*)-**539a,b** in the presence of KOBu^t to generate polycarbonates poly[(*R*)-**539a,b**].[225] Poly[(*R*)-**539a**] (R = H) was not soluble in common organic solvents although the polymer made from the racemic **539a** was found to be soluble in THF, chloroform, and benzene.[226] With the introduction of the flexible octyl groups, poly[(*R*)-**539b**] became a soluble polymer. The model compound (*R*)-**540** was synthesized from the treatment of (*R*)-**539b** with methanol. The specific



(*R*)-539a: R = H
(*R*)-539b: R = *n*-C_8H_{17}



poly[(*R*)-539a]: R = H
poly[(*R*)-539b]: R = *n*-C_8H_{17}



(*R*)-540

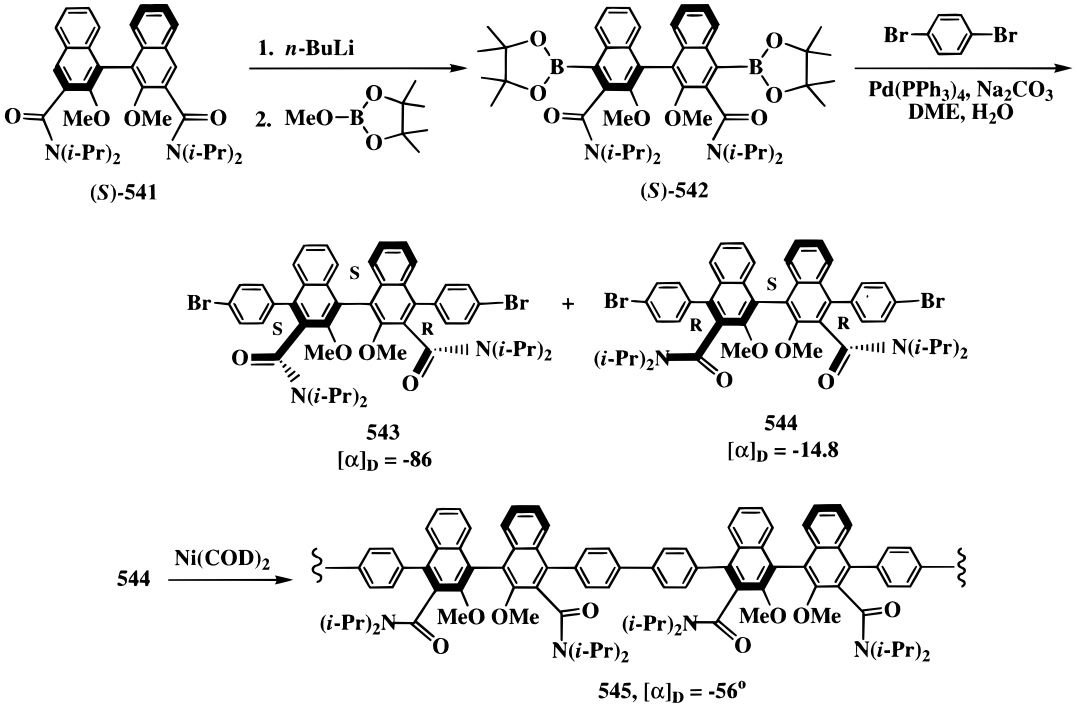
optical rotation of poly[(*R*)-**539b**] was +530 ($[\alpha]_D$, c = 0.15, THF). This optical rotation is significantly larger than that of the model compound (*R*)-**540** ($[\alpha]_D$ = −21) and also has the opposite sign. A CD spectroscopic study showed that the bisignate Cotton effects of the model compound (*R*)-**540** were inverted in the polymer. The oligomeric models of poly[(*R*)-**539a**] containing 2−8 (*S*)-binaphthyl units were prepared. Through theoretical calculation and spectroscopic study of these oligomers, it was concluded that the optically active poly[(*R*)-**539b**] had a stable helical conformation in solution.

4.1.2. Polymerization at the 4,4′-Positions

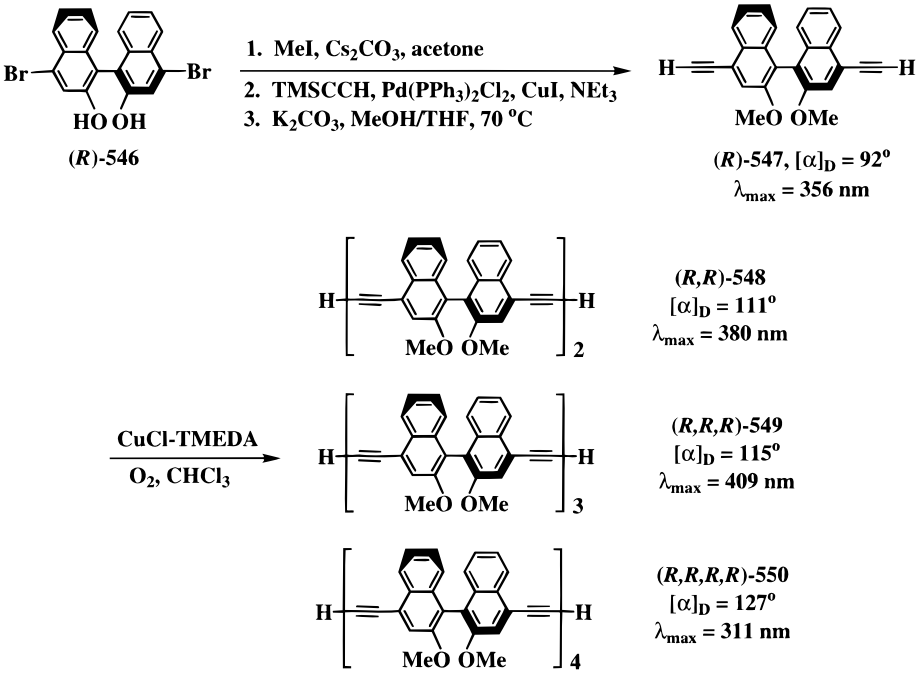
The polymerization of a 1,1′-binaphthyl molecule at the 4,4′-positions was studied by Tour and Bedworth.[227] Since the direct electrophilic aromatic substitution at the 4,4′-position of 2,2′-dimethoxy-1,1′-binaphthyl was not successful, a 3,3′-biamide molecule (*S*)-**541** was prepared as a precursor for introduction of the 4,4′-substituents (Scheme 140). Treatment of (*S*)-**541** with *n*-butyllithium followed by reaction with a pinacolboronic acid ester gave (*S*)-**542**. The Suzuki coupling of (*S*)-**542** with 1,4-dibromobenzene did not generate a polymer but rather gave a mixture of diastereomers. This was attributed to the steric hindrance around the naphthyl boronic ester sites. The NMR spectra of the two isolated major products **543** and **544** indicated that **544** had C_2 symmetry and **543** C_1 symmetry. They are diastereomers of three axes of atropisomerism. The *SSR* and *RSR* configurations were assigned to **543** and **544** respectively because these structures had smaller steric interaction than the other possible configurations and might therefore be produced preferentially. Nickel(0)-promoted coupling of **544** at 70−80 °C led to the formation of **545** with a molecular weight of M_n = 7000 and M_w = 14 700 as determined by GPC relative to polystyrene standards. The specific optical rotation of **545** was $[\alpha]_D$ = −63 (c = 0.16, THF). It was found that both **543** and **544** underwent isomerization at 100 °C in solution to give the same equilibrium mixture with **543** the most stable isomer. Therefore, under the conditions of the nickel(0)-promoted coupling reaction, it is unlikely that the asymmetry of the amide functions was retained, although the 1,1′-binaphthyl stereochemistry was preserved. Thus, both compounds gave **545** after the nickel(0)-promoted coupling. Because the chiral binaphthyl segments in **545** were at regular intervals along the rigid linear backbone, its optical rotation was very similar to the monomer unit with a value intermediate between those of **543** and **544**. This is quite different from most optically active polymers where significant optical rotation enhancements from monomers to polymers are usually observed.

Starting from the optically resolved 4,4-dibromo-1,1′-bi-2-naphthol, (*R*)-**546**, Chow et al. prepared several oligobinaphthyl molecules.[228,229] (*R*)-**547** was obtained from (*R*)-**546** by methylation, cross-coupling, and deprotection (Scheme 141). Oxidative Hay's coupling of (*R*)-**547** gave a mixture of oligomers rather than a polymer. The oligomers were isolated using chromatography: the binaphthyl dimer (*R*,*R*)-**548**, 30% yield, the trimer (*R*,*R*,*R*)-**549**, 10% yield, and the tetramer (*R*,*R*,*R*,*R*)-**550**, 4% yield. The solubility of these oligomers in THF or chlorinated solvents decreased with an increasing number of binaphthyl units. On going from the monomer to the tetramer, there were also small increases in specific optical rotations. Compounds (*R*)-**547** to (*R*,*R*,*R*,*R*)-**550** all had very strong CD effects with a negative

Scheme 140



Scheme 141

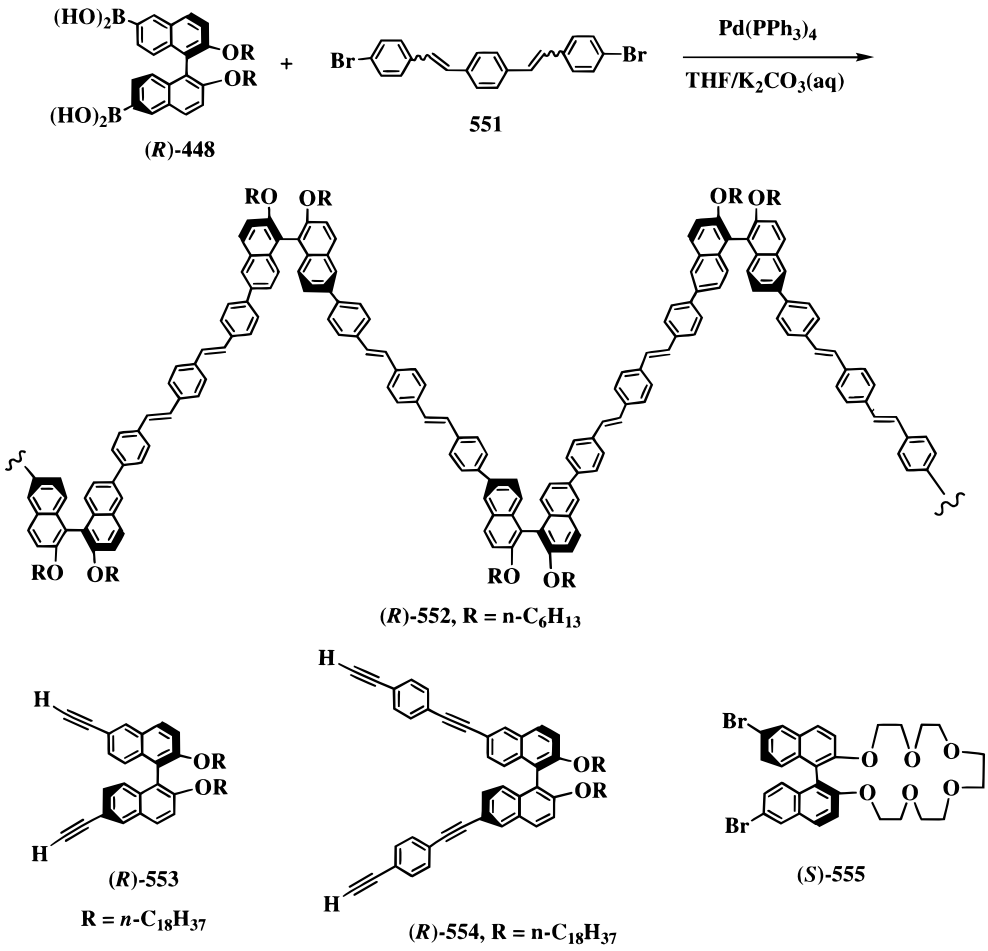


signal at $\lambda = 240$ nm and a positive signal at $\lambda = 226$ nm. An additional positive CD signal was observed at $\lambda = 340$ nm. The molar ellipticity of the CD signals and the UV absorption wavelengths steadily increased going from the monomer to the dimer and the trimer. However, the trimer (*R*,*R*,*R*)-**549** and tetramer (*R*,*R*,*R*,*R*)-**550** had almost identical CD spectra as well as UV absorption maxima, indicating that the latter has reached a plateau of increasing optical activity as well as increasing conjugation. The initial modest optical rotation changes were due to the fact that the isolated binaphthyl units could not have cooperative effect to give a significantly enhanced optical activity. This is a similar situation to that observed for **545** by Tour. Cyclic voltammetry studies of these compounds were also carried out. In THF solution, the oligomers (*R*,*R*)-**548** to (*R*,*R*,*R*,*R*)-**550** had almost identical first reduction potentials at ca. −1.9 V. This indicates little conjugation increase as a result of the orthogonal naphthalene rings in the binaphthyl unit.

4.1.3. Polymerization at the 6,6′-Positions

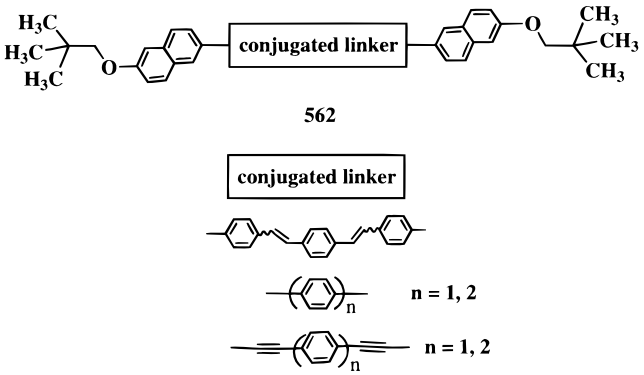
Since 1996, Pu and co-workers have reported a series of binaphthyl-based main chain chiral conjugated polymers synthesized by polymerization at the 6,6′-positions of optically active binaphthyl mono-

Scheme 142



mers.[191−196,230−240] The application of polybinaphthyls (*R*)-**449**, (*R*)-**456**, and (*R*)-**458** to asymmetric catalysis has been described in section 3.4. In this section, the main chain chiral conjugated binaphthyl polymers with potential materials applications are discussed.

The Suzuki coupling of the optically active binaphthyl diboronic acid monomer (*R*)-**448** with the dibromo-terminated phenylenevinylene molecule **551** gave an optically active poly(arylenevinylene) (*R*)-**552** (Scheme 142).[232,233] Other binaphthyl monomers such as (*R*)-**553**,[234] (*R*)-**554**,[235] and (*S*)-**555**[236] were synthesized from the optically active 6,6′-dibromo-1,1′-bi-2-naphthols (**217**, Scheme 111). These monomers were used to prepare various types of main-chain chiral conjugated polymers as shown in Figure 13. The Suzuki coupling of (*R*)-**448** with 1,4-dibromobenzene and 4,4′-dibromobiphenyl gave optically active polyarylenes (*R*)-**556** and (*R*)-**557** respectively.[237] The palladium-catalyzed cross-coupling of (*R*)-**553** with either 1,4-diiodobenzene or 4,4′-diiodobiphenyl produced the optically active poly(aryleneethynylenes) (*R*)-**558** and (*R*)-**559**, respectively.[234] The cross-coupling of (*R*)-**554** with 1,4-diiodobenzene generated (*R*)-**560**.[235] (*S*)-**561**, a conjugated polymer with chiral molecular receptors, was obtained from the chiral crown ether monomer (*S*)-**555**.[236] To study the structures and conjugation of these polymers, repeating units **562** containing the corresponding conjugated linkers of these chiral conjugated polymers were prepared.[233,234,237] Polymers made from racemic binaphthyl monomers were also obtained.



All these polymers were soluble in common organic solvents such as THF, chloroform, and methylene chloride and their structures were characterized by NMR, IR, and other spectroscopic methods. The molecular weights were in the range of $M_w = 10000-70000$ as determined GPC relative to polystyrene standards. A laser light scattering study of (*R*)-**559** and its corresponding optically inactive polymer indicated that the GPC molecular weights of these polymers were ca. 1.4−2.5 times smaller than their absolute molecular weights. The longest wavelength absorptions were between 320 and 400 nm (λ_{max}), and

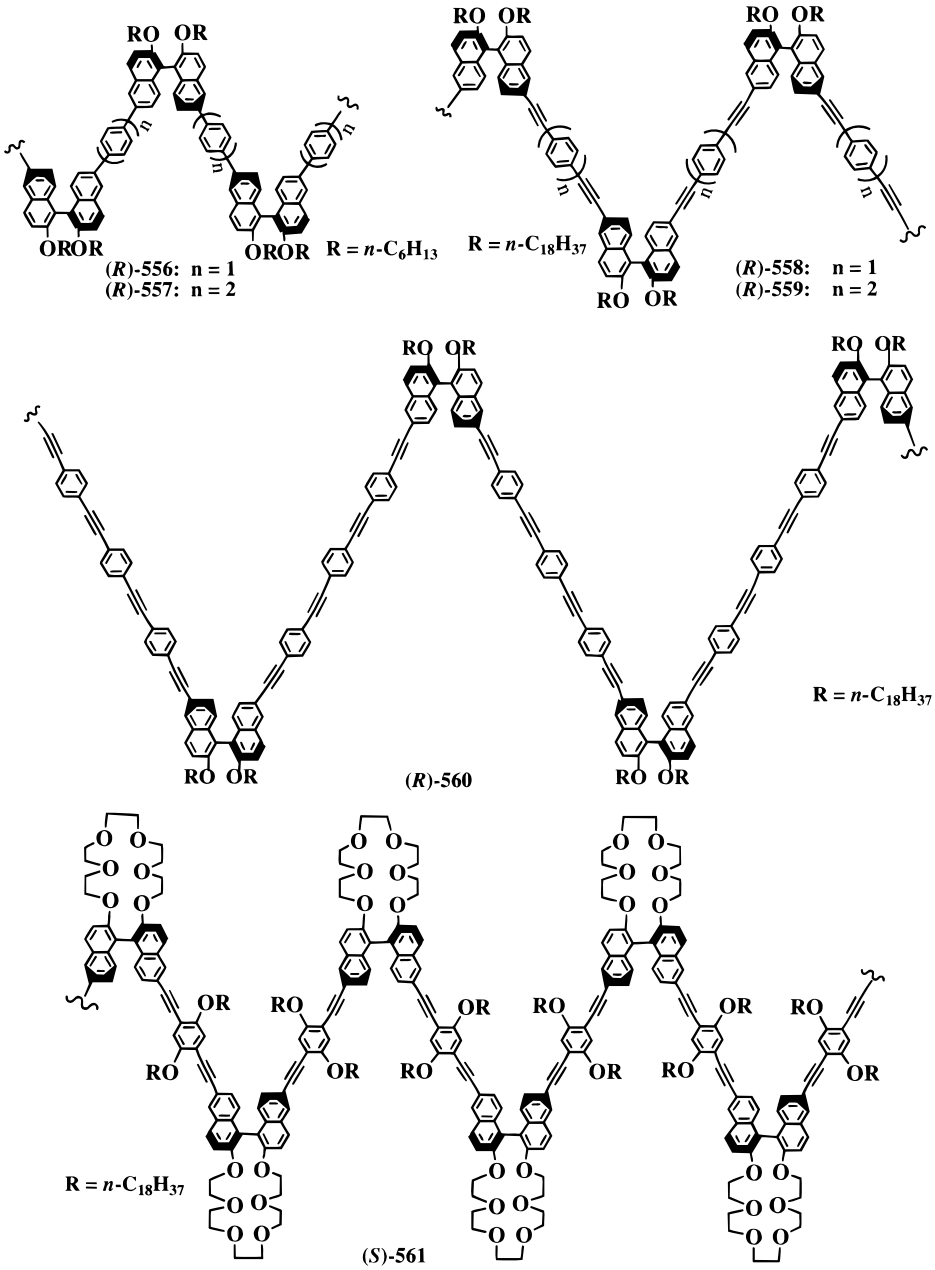


Figure 13.

they were all blue light emitting materials with strong fluorescence in the range of $\lambda_{emi} = 400-500$ nm. The quantum yield for the fluorescence of (*R*)-**552** was estimated to be 80%, significantly higher than that of its corresponding optically inactive *rac*-**552** (ca. 50%). By comparing the UV absorption wavelengths of the polymers with those of their repeating units, it was concluded that there is almost no extended conjugation across the 1,1′-bond of the binaphthyl units in the backbone of these polymers. Rather, the conjugation of these binaphthyl based polymers is determined by the conjugation of their repeating units.

The specific optical rotations ($[\alpha]_D$) of most of these main chain chiral conjugated polymers were about + or −300, much larger than those of the monomers (ca. + or −30). Strong CD effects were also observed in the 200−400 nm range, very similar to those of (*R*)-**456**. All of these major-groove (*R*)-polybinaphthyls are therefore expected to have a cisoid conformation in their binaphthyl units.

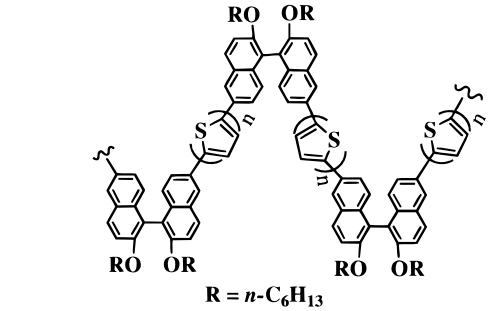
After doping (*R*)-**552** with $NOBF_4$, a conductivity of 4×10^{-5} to 7×10^{-5} S cm^{-1} was found. This is much lower than that of the fully planar poly(*p*-phenylene)vinylene. The conductivity of the corresponding optically inactive polymer was very similar to this optically active (*R*)-**522**. Thermal gravimetric analysis (TGA) showed that these materials had a very high thermal stability with most of these binaphthyl-based polymers not starting to lose mass until above 390 °C. After the fragmentation of their alkyl groups, polymers (*R*)-**556**, (*R*)-**557**, (*R*)-**558**, and (*R*)-**559** became very stable toward weight loss even at temperatures up to 800 °C. The chiral configuration of these materials were also very stable. For example, when a toluene solution of (*R*)-**556** was heated at reflux for 40 h, only ca. 5% decrease in optical rotation was observed. These materials are

Table 2.

polymer	no. of thiophenes per repeat unit	M_w (PDI)	UV: λ_{max} (nm)	fluorescence: λ_{emi} (nm)	color of the polymer
563	1	35,500 (2.6)	236, 298, 368	421, 446, 475 (sh)	yellow-green
564	2	30,300 (1.7)	246, 406	463, 498	yellow
565	4	5,500 (1.1)	232, 270 (sh), 440	515, 549 (sh)	orange
566	5	28,000 (1.6)	236, 348 (sh), 434	530, 568 (sh)	bright red
567	7	6 100 (2.6)	234, 264 (sh), 454	545, 583, 631 (sh)	dark red

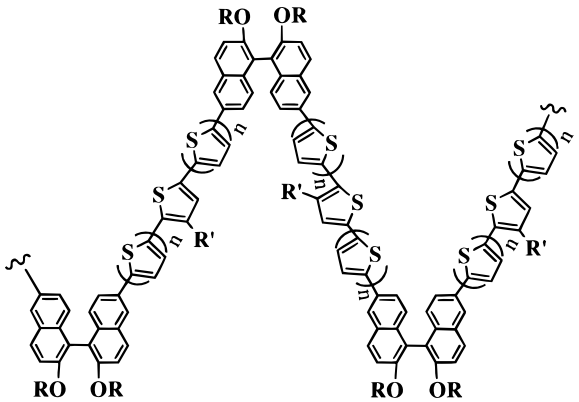
potentially useful for asymmetric electrosynthesis as well as polarized light emission. Polymers such as (*S*)-**561** containing molecular receptors may be useful as chiral sensors for the enantioselective detection of chiral molecules.

Since the conjugation of binaphthyl-based polymers is defined by their repeating units, it should be possible to tune the absorption and emission wavelengths of these materials by systematically changing the conjugation length of the repeating units. To obtain a broad range of emissions, oligothiophene units, because of their lower band gaps than arenes, alkenes, and alkynes, were incorporated into the binaphthyl polymers. Polymers **563**−**567** containing one to seven thiophene rings in their repeating units were prepared by the Suzuki coupling of racemic **448** with α,α′-dibromooligothiophenes.[238] In **566** and **567**,



R = *n*-C_6H_{13}

563: n = 1
564: n = 2
565: n = 4



566: n = 2, R = R' = *n*-C_6H_{13}
567: n = 3, R = *n*-C_6H_{13}, R' = *n*-$C_{18}H_{37}$

R′ groups were attached to the thiophene units in order to make the oligothiophene dibromide monomers soluble before the polymerization. Although these polymers are made up of racemic binaphthyls rather than optically active ones, they are included here because of their close relationship with other polymers described in this section. Their physical data are summarized in Table 2. An increase in the number of thiophene rings in the repeating unit leads to a systematic red-shift for both the absorption and the emission wavelengths of the polymers. Thus, polymers capable of emitting lights of different colors were obtained. The absorptions of polymer **566** did not show the expected red-shift from **565** probably because the R′ group partially disrupted the conjugation in the repeating unit of **566**.

(*R*)-**569** was obtained from the cross-coupling of (*R*)-**553** with 4,5-dibromo-1,2-dinitrobenzene (**568**) in the presence of $Pd(PPh_3)_4$ and CuI (Scheme 143).[239,240] If all the aromatic rings in the dipole unit of (*R*)-**569** are assumed to be coplanar, this polymer should have a helical structure with the dipole units revolving along the polymer axis like the blades of a propeller. An infinite polymer chain of this structure should lead to a cancellation of the dipole moment. The structural similarity of (*R*)-**569** with the propeller molecule **570**,[241] an octopolar molecule that showed a large second-order nonlinear optical (NLO) property, may lead to interesting electrooptical properties.

Other chiral polymers (*R*)-**571** to (*R*)-**575** containing different electron acceptors and conjugated dipole units were also prepared (Figure 14).[239,240] (*R*)-**571** was made from the cross-coupling of (*R*)-**553** with 3,4-dibromonitrobenzene. In (*R*)-**571**, the nitro groups are randomly distributed in either position 1 or 2 of the phenylene rings. (*R*)-**572** was prepared from the coupling of (*R*)-**554** with **568**. (*R*)-**573** contained fluorine atoms as the electron acceptors. (*R*)-**574** was synthesized by the Suzuki coupling of (*R*)-**448** with 3,4-dibromonitrobenzene. (*R*)-**575** was made using *m*-phenylene linkers rather than *o*-phenylene linkers. Compounds **576** and **577** were the repeating units of (*R*)-**569** and (*R*)-**575**, respectively.

Table 3 lists the physical data for all of these propeller-like chiral polymers and the repeating units. They all showed similar strong positive and negative CD signals in the wavelength range 230−280 nm due to the chiral binaphthyl units. Due to their varying conjugations, the main differences were found at wavelengths above 300 nm. Similar to the *p*-phenylene linked polymers such as (*R*)-**552** and (*R*)-**556** to (*R*)-**559**, these *o*- and *m*-phenylene-linked polybinaphthyls had little conjugation across the binaphthyl units as confirmed by comparing the UV spectra of the repeating units **576** and **577** with the polymers (*R*)-**569** and (*R*)-**575**.

Chiral propeller-like polymers containing amino groups rather than alkoxy groups as the electron donors were also prepared (Scheme 144).[242a] Starting from the optically active 1,1′-binaphthyl-2,2′-diamine (*R*)-**136**, the monomer (*R*)-**578** was obtained. The cross coupling of (*R*)-**578** with **568** led to the formation of (*R*)-**579**. The molecular weight of this polymer was M_w = 23 500 and M_n = 12 330 (PDI = 1.9) as determined by GPC. An optically active arylenevinylene oligomer (*R*)-**582** was prepared by the Heck

Scheme 143

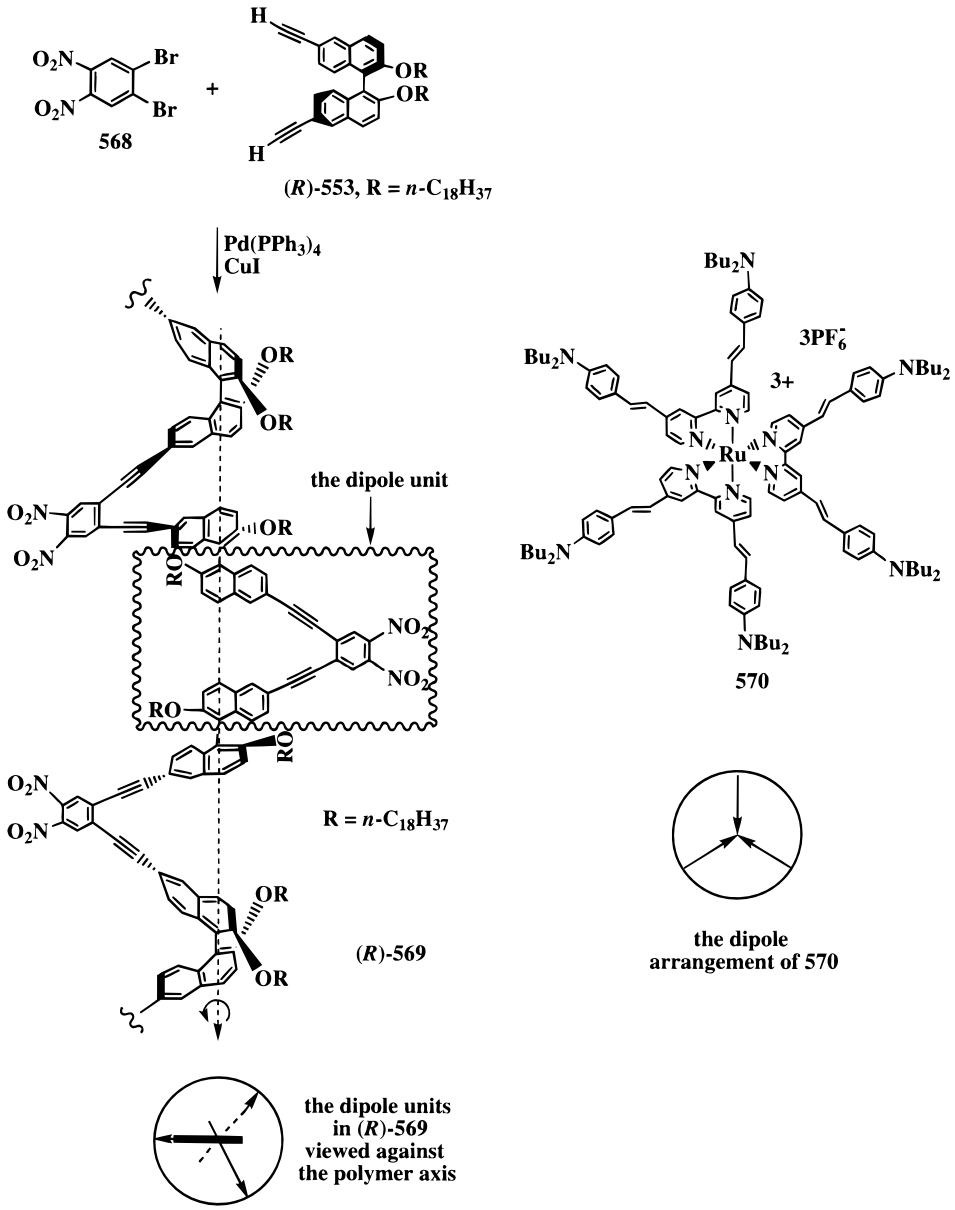


Table 3.

sample	M_w (PDI)	$[\alpha]_D$	UV: λ_{max} (nm)	CD: $[\theta]_\lambda$ (nm)
(*R*)-**569**	18 000 (1.5)	−163.9 (c = 0.16, CH_2Cl_2)	238, 277 (sh), 309 (sh), 358, 418	2.68×10^5 (234), -1.40×10^5 (277), 9.14×10^3 (356), -9.71×10^3 (419)
576			236, 300, 354,406	
(*R*)-**571**	7 200 (1.4)	−160.0 (c = 0.15, CH_2Cl_2)	234, 295 (sh), 346, 380	2.19×10^5 (235), -5.42×10^4 (264), 4.82×10^3 (351), -5.05×10^3 (396)
(*R*)-**572**	10 700 (1.8)	−227.0 (c = 0.13, CH_2Cl_2)	234, 296, 346	2.29×10^5 (234), -4.63×10^4 (264), -6.56×10^4 (296), -2.78×10^4 (383)
(*R*)-**573**	7 200 (1.4)	−103.0 (c = 0.29, CH_2Cl_2)	262, 278, 344	2.38×10^5 (237), -2.14×10^5 (284), -2.38×10^4 (381)
(*R*)-**574**	10 100 (2.1)	−170.9 (c = 0.5, CH_2Cl_2)	246, 350	3.34×10^5 (240), -1.80×10^5 (275), -6.18×10^4 (306 sh), 2.12×10^4 (348)
(*R*)-**575**	30 500 (1.9)		256, 284 (sh), 359 (sh), 442	2.53×10^5 (238), -1.16×10^5 (270), -3.11×10^4 (470)
577			244, 282, 354, 430	

coupling of (*R*)-**580** with **581** (Scheme 145). The molecular weight of (*R*)-**582** was found to be M_w = 2820 (PDI = 1.45) as determined by GPC. The compound **583** was prepared as a model for the repeating unit of (*R*)-**582**.

The UV absorption spectra of (*R*)-**579** showed that there was a large red-shift ($\Delta\lambda_{max}$; 50 nm) on going from (*R*)-**569** to (*R*)-**579** due to the more electron-donating alkylamino groups in the latter. The longest wavelength absorption of (*R*)-**579** was observed at λ_{max} = 470 nm and the longest wavelength absorption of (*R*)-**582** at λ_{max} = 486 nm. There was a further red-shift going from (*R*)-**579** to (*R*)-**582** because the triple bonds were replaced by more polarizable double bonds. The UV absorptions of the model compound **583** were similar to those of (*R*)-**582** with a small red-

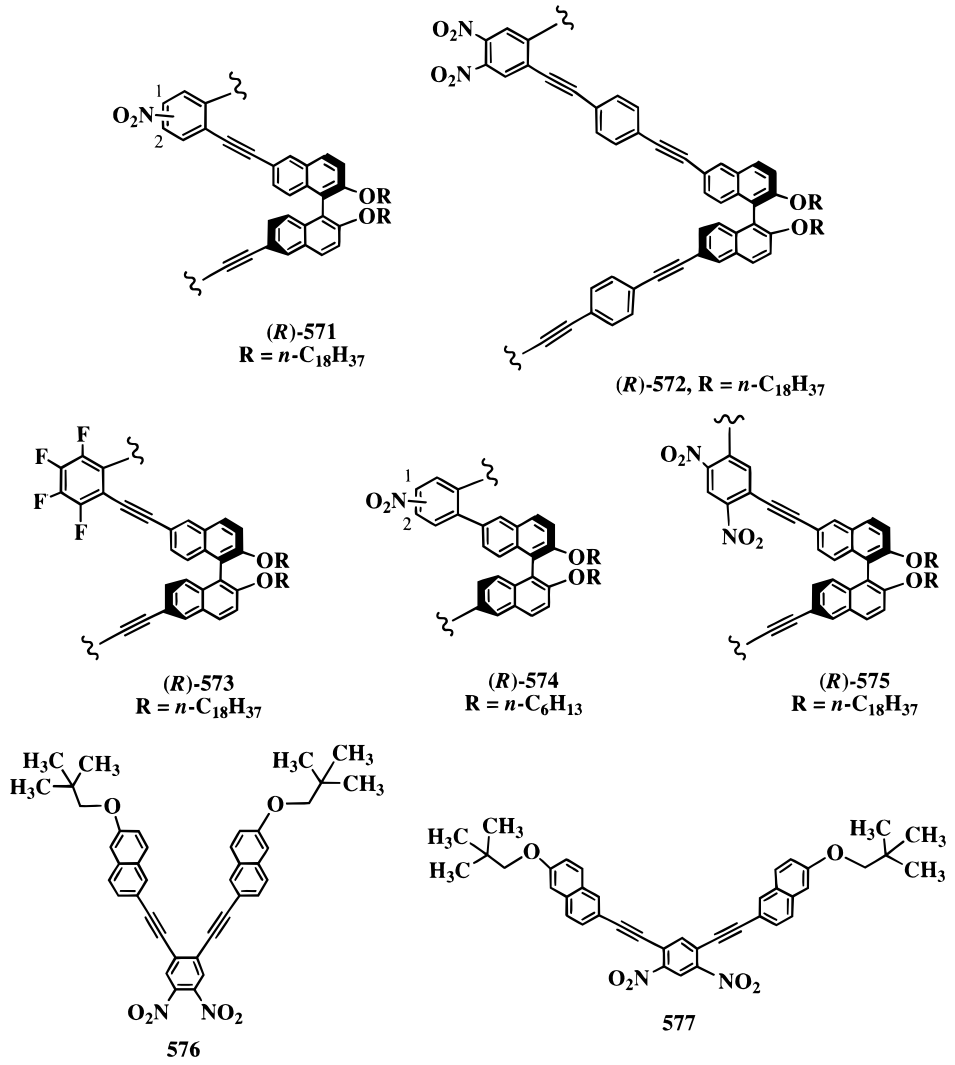
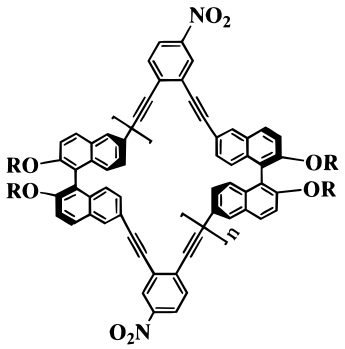


Figure 14.

shift. Both (*R*)-**579** and (*R*)-**582** exhibited very intense CD signals with both positive and negative Cotton effects. The preliminary study has shown that (*R*)-**582** exhibits the strongest second-order NLO signals among these propeller-like polymers.[242b] This indicates that the better electron-donating amino groups and the more polarizable double bonds in the polymer make a good combination for the NLO effects.

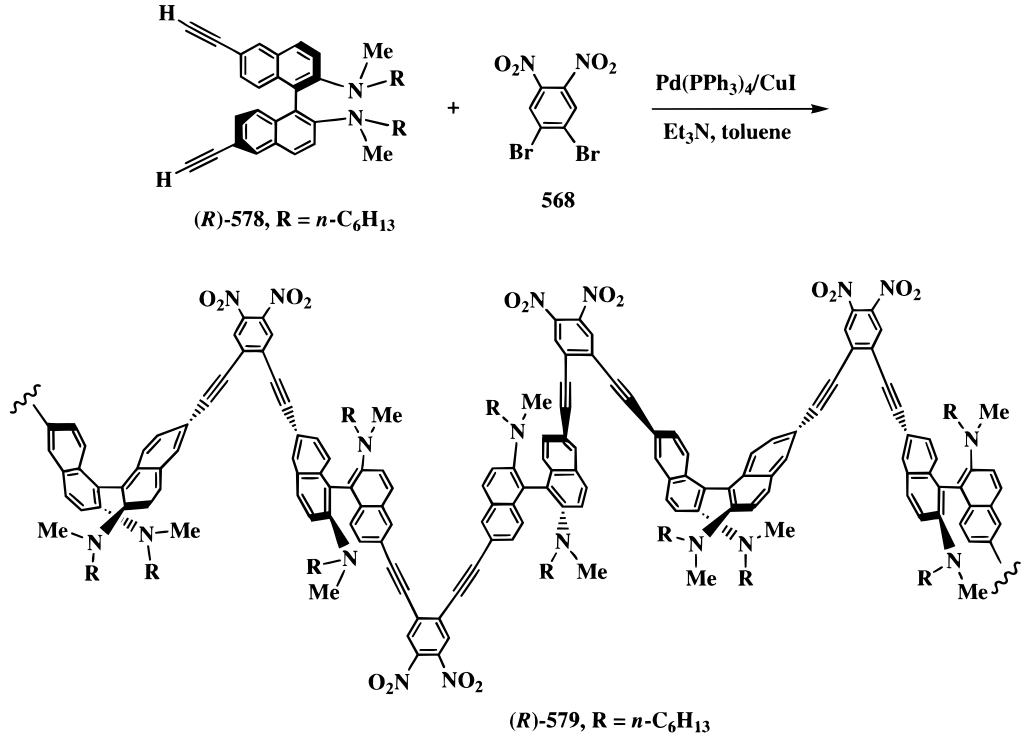
Pu and co-workers prepared a chiral binaphthyl-based AB monomer (*R*)-**586** for the synthesis of dipole-oriented polymers (Scheme 146).[243] (*R*)-**584** containing two different acetylene protecting groups was prepared from (*R*)-**446a**. After selective hydrolysis of the trimethylsilyl group of (*R*)-**584**, it was coupled with **585** followed by removal of the triisopropylsilyl group to produce (*R*)-**586**. At a concentration of 0.24 M, this compound underwent polymerization in the presence of palladium(0)/CuI catalysts to generate the polymer (*R*)-**587**. Its molecular weight was $M_w = 34\,000$ (PDI = 2.0) and its specific optical rotation $[\alpha]_D = -197.6$ ($c = 0.16$, CH_2Cl_2). This polymer showed UV absorptions at $\lambda_{max} = 236$, 284, 346, and 380 nm and strong CD signals with $[\theta]_{\lambda(nm)} = 2.7 \times 10^5$ (232), -1.6×10^5 (271), -1.80×10^5 (282), 1.90×10^4 (350), and -1.80×10^4 (387). Unlike (*R*)-**569** expected to be nonpolar at infinite chain length, (*R*)-**587** could have a large dipole moment since the dipole units are tilted in one direction along the polymer axis. Polymers of such organized geometry are very interesting since orientation correlated NLO chromophores on a helical polymer have been observed to generate an enhanced second-order NLO response.[244]

The homocoupling of (*R*)-**586** in the presence of palladium(0)/CuI catalysts at a concentration of 0.064 M led to the formation of the chiral multipolar macrocycles (*R,R*)-**588**, (*R,R,R*)-**589**, and (*R,R,R,R*)-**590** with yields of 34%, 18%, and 12%, respectively.[243]

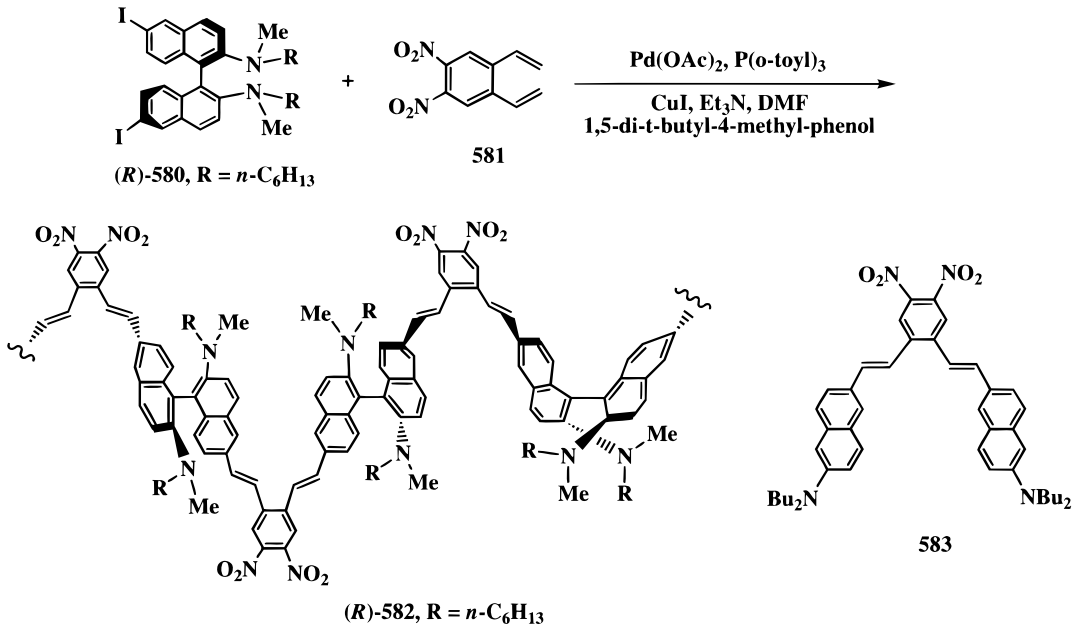


(*R,R*)-**588**: n = 1, 34%
(*R,R,R*)-**589**: n = 2, 18%
(*R,R,R,R*)-**590**: n = 3, 12%

Scheme 144



Scheme 145



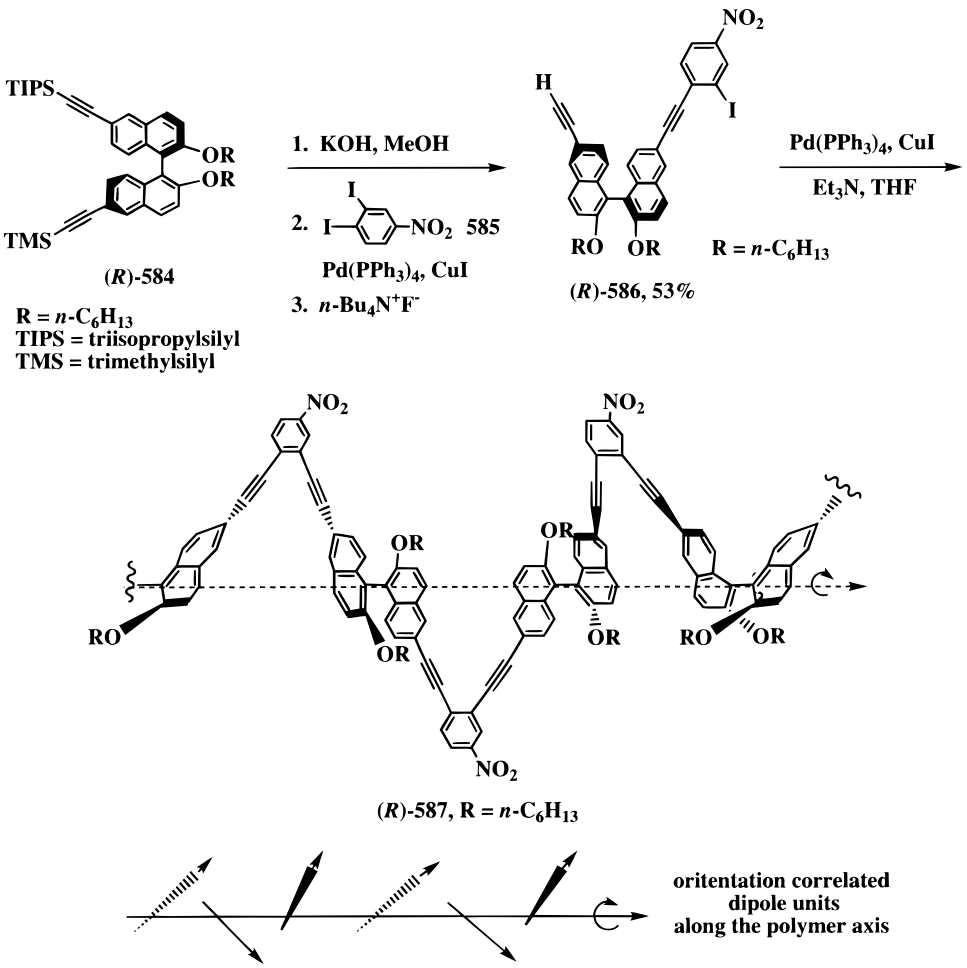
Such a high total yield (64% total) of macrocycle formation under a relatively high monomer concentration is quite remarkable. The specific optical rotations were found to be $[\alpha]_D = -301.3$, -282.3, and -297.0 for (*R*,*R*)-**588**, (*R*,*R*,*R*)-**589**, and (*R*,*R*,*R*,*R*)-**590** respectively. The UV spectra were very similar with the longest wavelength absorptions at $\lambda_{max} = 384$ to 390 nm. In solution, a C_2 symmetry for (*R*,*R*)-**588**, a C_3 symmetry for (*R*,*R*,*R*)-**589**, and a C_4 symmetry for (*R*,*R*,*R*,*R*)-**590** is expected. These chiral macrocycles constitute a series of dipolar, quadrupolar and octupolar structures all within the same chemical system.

Binaphthyl-based chiral polymers containing transition metals were synthesized by Takahashi and coworkers in 1998.[245] Reaction of (*R*)-**553** (R = Me, Et, or ^{i}Pr) with metal complexes **591a,b** gave chiral organometallic polymers (*R*)-**592a,b** in the presence of copper iodide and diethylamine (Scheme 147). The molecular weights of these polymers were in the M_w = 6100−100000 range. Their specific optical rotations were in the −180 to −370 ($[\alpha]_D$, $CHCl_3$) range. Monomeric binaphthylmetal complexes (*R*)-**593a,b** which showed much lower optical rotations than the corresponding polymers were also prepared.

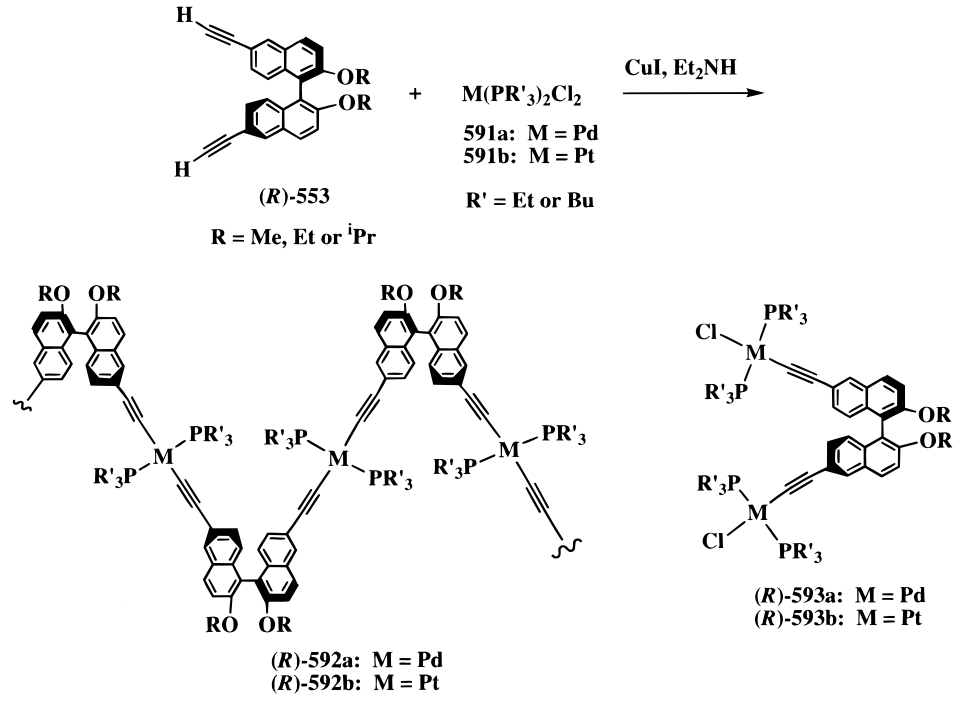
4.1.4. Polymerization at the 3,3′-Positions

Polymerization of optically active binaphthyl monomers at the 3,3′-positions has been carried out. The application of these polymers to asymmetric catalysis

Scheme 146



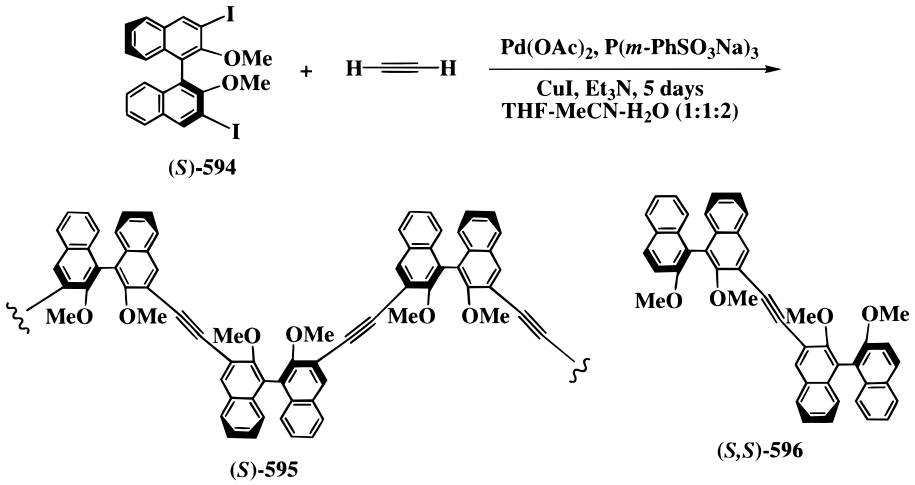
Scheme 147



was discussed in section 3.4. As shown by Pu and co-workers, the Lewis acids complexes of the polybinaphthyls (*R*)-**461** and (*R*)-**468** are highly enantioselective catalysts in the reaction of aldehydes with organo zincs, the reduction of aryl methyl ketones and the epoxidation of α,β-unsaturated ketones.

In 1997, Li et al. reported the coupling of (*S*)-**594** with acetylene gas in the presence of $Pd(OAc)_2$, P(*m*-

Scheme 148



$PhSO_3Na)_3$, Et_3N, and CuI in the mixed solvent THF−MeCN−H_2O (1:1:2) (Scheme 148).[246] The resulting minor-groove binaphthyl oligomer (*S*)-**595** had a molecular weight of $M_w = 3200$ (PDI = 2.5) as shown by GPC measurement. Strong fluorescence was observed at 435 nm when (*S*)-**596** was excited at 324 nm. In the CD spectrum of (*S*)-**596**, a negative Cotton effect was observed at $\lambda = 245$ nm and a positive effect was observed at $\lambda = 277$ nm. A dimeric compound (*S,S*)-**596** was prepared using the Stille coupling of a monoiodobinaphthyl compound with bis-(tributylstannyl)acetylene.[247]

4.2. Optically Inactive Polybinaphthyls

A number of optically inactive polybinaphthyls have been made from either the racemic binaphthyl monomers or by the coupling of naphthalene monomers in a nonstereoselective fashion.

4.2.1. Polymerization of Racemic Binaphthyl Monomers

In 1969, Jedlinski et al. studied the polycondensation of *rac*-**12** and 2,2-bis(4-hydroxyphenyl)propane (**597**) with **513** to make the copolyester **598** (Scheme 149).[248] The polymerization was conducted in ethylene chloride in the presence of triethylamine. The molecular weight of the resulting polymer was low ($M_n = 1625$) and had a melting point of 260 °C.

A series of polymers derived from racemic 1,1′-binaphthyl-4,4′-diol (**599**) were also reported by Jedlinski et al.[249] Since the solubility of the polyester made from **599** and **513** was very low, they were copolymerized with **597**, **600,** or **601** in ethylene chloride solution in the presence of triethylamine.

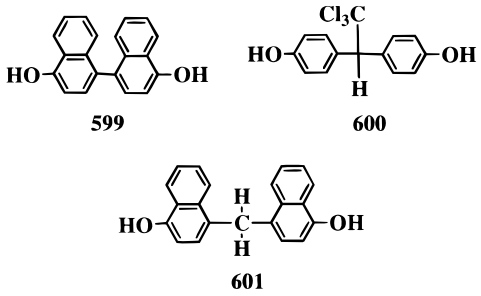


Table 4 lists the molecular weights and the melting points of the resulting copolyesters. Poly(**599-513-597**) had both a higher molecular weight and melting point than the polymer **598** made from *rac*-**12**. In poly(**599-513-597**), the ratio of **599** versus **597** was 50:50. When the ratio of **599** was increased to 75

Scheme 149

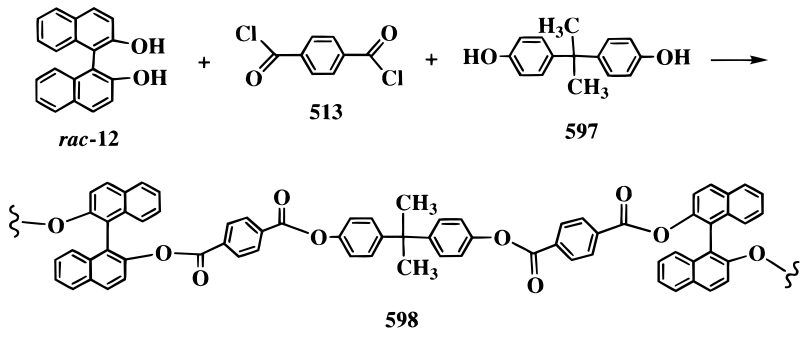


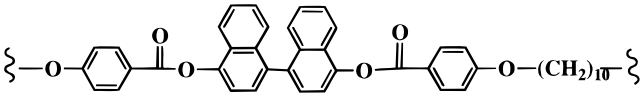
Table 4.

polymer	poly(**599-513-597**)	poly(**599-513-600**)	poly(**599-513-601**)
melting point °C	420	300	240
M_n	11 200	10 900	3 750

mol %, the polymer became only partially soluble. Poly(**599-513-597**) showed ca. 5% weight loss after heating at 250 °C for 180 h in air. Under the same conditions, poly(**599-513-600**) lost ca. 13% of its weight. Both poly(**599-513-597**) and poly(**599-513-600**) had high viscosity and were used to make films and coatings. These two polymer films had surface resistivities of 2.1×10^{15} and 6×10^{16} ohm and tensile strengths of 475 and 865 kg cm^2, respectively. They formed flexible, adhesive coatings on steel, copper, and aluminum. Besides **597**, **600** and **601**, 11 other aromatic diols were also incorporated into the (**599-513**) polyesters. Most of these polymers had high thermal stability but poly(**599-513-597**) proved the most stable. Such high thermal stability may be due to the formation of condensed naphthalene rings at high temperature.

The distribution of the different structural units in the polymer chain of poly(**599-513-597**) was investigated using NMR spectroscopy.[250] The higher the content of the 1,1′-binaphthyl units, the higher the glass transition temperature of the copolymer.[251]

Racemic 1,1′-binaphthyl-based polyester **602** was studied by Jo et al.[252] This polymer consisted of



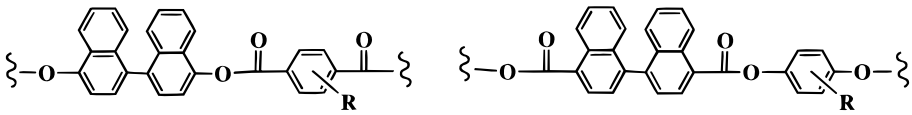
602

mesogenic aromatic units and flexible spacers in the main chain. Its thermotropic properties were investigated. Its melting point was at 224 °C, its liquid crystal-to-isotropic transition temperature (clearing point) was at 248 °C and the mesophase appeared to be nematic.

Although structurally similar, the polymers **603**−**605** lacking the flexible alkyl chains were synthesized by Hohlweg et al. using solution polycondensations (Figure 15).[253] The polyaromatic esters **603b** and **604a,b** were found to be soluble in chloroform, THF, and *p*-chlorophenol, whereas **603a** and **605** were either insoluble or only partially soluble. The T_gs of **603b** and **604a,b** were in the 163−189 °C range. The polymer **604b** was also prepared by Bhowmik et al. using a melt polycondensation.[254] Although this polymer was soluble in *p*-chlorophenol and insoluble in chloroform, polymer **603c** made by the same method proved insoluble in organic solvents. Both their T_gs were ca. 145 °C. Polarizing light microscopy indicated that these polymers had a nematic liquid crystalline appearance. Bhowmik et al. synthesized a series of 1,1′-binaphthyl-4,4′-diol-based polyesters by polymerization and copolymerization with different aromatic dicarboxylic acids.[255,256] Nematic liquid crystalline materials with high T_gs (178−217 °C) and low T_ms (308−360 °C) were among the polymers obtained.

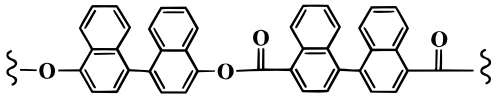
Polymerization of the racemic binaphthylamine **606** with a number of aryl dicarbonyl chlorides **607** or dicarboxylic acids **608** was carried out by Imai and co-workers in 1993 (Scheme 150).[257] Most polymers of the **609** type were soluble in DMF, DMA, *N*-methyl-2-pyrrolidone, DMSO, pyridine and concentrated sulfuric acid but insoluble in acetone and methanol. Their T_gs were in the 266−303 °C range. They were stable up to 370 °C both under nitrogen and in air and are potentially useful as soluble high-temperature materials. Racemic **606** was also polymerized with anhydrides of the **610** type to generate polymers **611** (Scheme 151).[258] The solubility properties and T_gs of the **611** type polymers were similar to those of **609**.

Racemic binaphthyl crown ether **9** in acetonitrile solution was electrochemically polymerized on a platinum disk electrode by Mark, Jr., and co-workers.[259] The resulting polymer film-coated electrode was used as a potentiometric sensor to detect catecholamines such as **612**−**615** (Figure 16). These molecules are known to be important neurotransmitters. The detection limit of this electrode sensor in phosphate buffer solution (0.1 M, pH = 9.4) was ca. 3×10^{-8} M. A linear dynamic range was observed between 1×10^{-7} and 5×10^{-4} M. The presence of inorganic ions or ascorbic acid did not interfere with the selective determination of catecholamines when using the poly(binaphthyl crown ether) electrode. The electrode response in the presence of other arylamines and aryl alcohols were also investigated. However, no structural information on the polymer was obtained. Earlier, Liu et al. studied the inclusion of binaphthyl or bisbinaphthyl crown ethers in polymer films [poly(vinyl chloride)] in the preparation of potentiometric electrode sensors.[260] These binaphthyl-based sensors were used to selectively analyze micinlex, a class of primary amine drugs used for the treatment of heart diseases.



603a: R = H
603b: R = C_6H_5
603c: R = Br

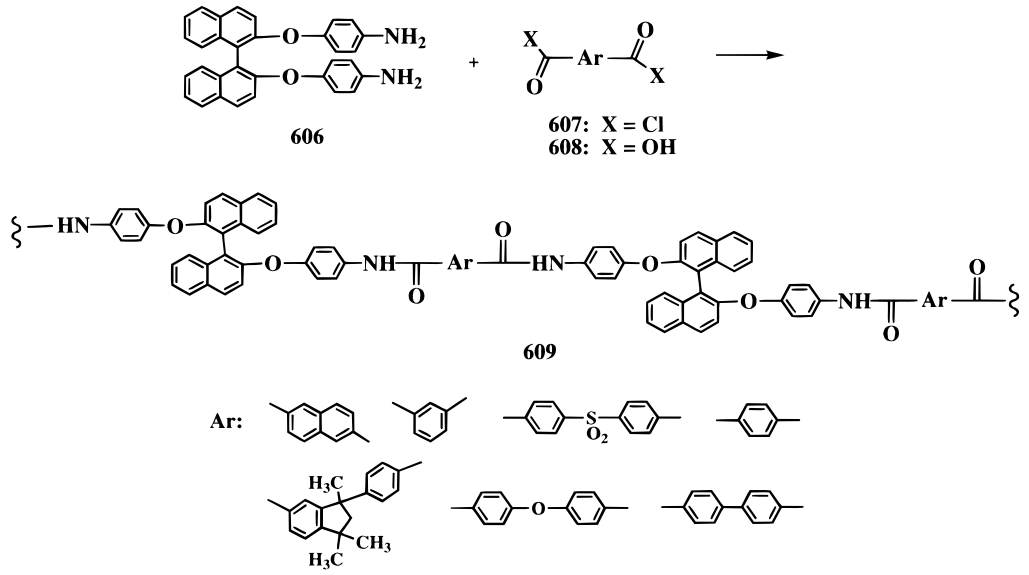
604a: R = H
604b: R = C_6H_5



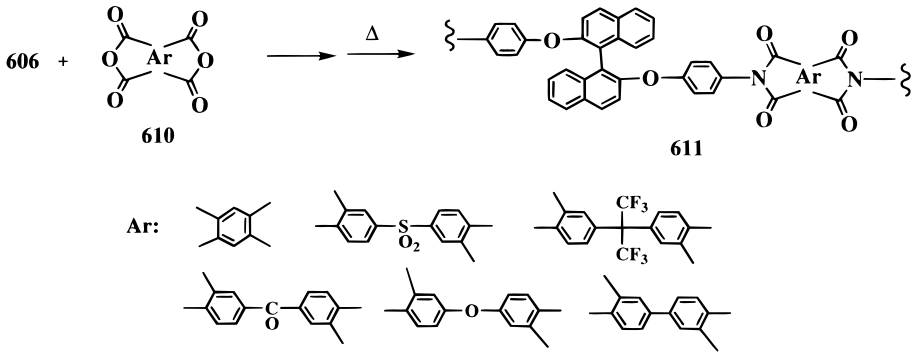
605

Figure 15.

Scheme 150



Scheme 151



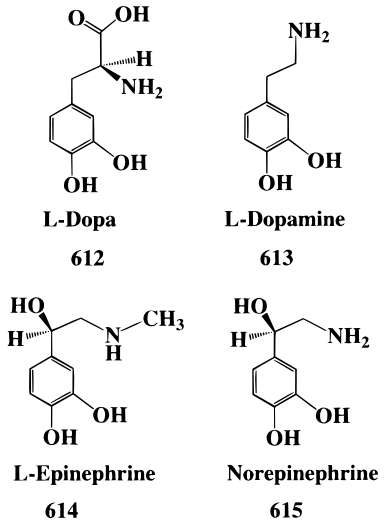


Figure 16.

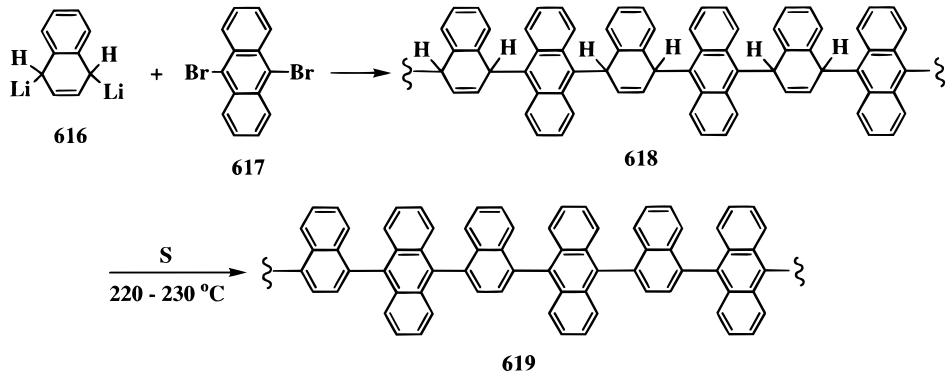
4.2.2. Coupling of Naphthyl Compounds

Lewis acids such as $FeCl_3-H_2O$, $AlCl_3-CuCl_2$, and $MoCl_5$ were used to catalyze the oxidative coupling of naphthalene and 1-chloronaphthalene. The resulting materials contained a mixture of 1,1′-, 1,2′-, or 2,2′-binaphthyl units. The binaphthyl composition depended on both the catalyst and oxidant.[261−264] These naphthyl polymers generally had a dark color (e.g., dark purple) and high spin density, indicative of polynuclear aromatic structure formation during radical cation polymerization.

The condensation of (1,4-dihydro-1,4-naphthalene)-dilithium (**616**) with 1,5-dibromoanthracene (**617**) was carried out to generate the polymer **618** by Paushkin et al. in 1972 (Scheme 152).[265] Dehydrogenation of **618** with sulfur at 220−230 °C gave the conjugated polymer **619**, an analogue of the 4,4′-polymerized binaphthyls. The condensation of naphthalenedilithium or anthracenedilithium with **617**, diiodoethylene, or 1,5-dibromonaphthalene gave the corresponding polymers in yields of 6−68%.

In 1992, Percec et al. synthesized racemic binaphthyl-based aromatic polyethers using the Scholl reaction.[266] The monomers **620**−**623** were polymerized in nitrobenzene in the presence of $FeCl_3$ (Figure 17). Because of its low solubility, the polymerization of **620** required high temperatures. At 115 °C, poly(**620**) was obtained with M_n = 4900 (PDI = 5.8) as measured by GPC. The other polymers were obtained at room temperature. The highest molecular weights were M_n = 90 500 (PDI = 2.4) for poly(**621**), M_n = 34 000 (PDI = 3.2) for poly(**622**), and M_n = 22 400 (PDI = 2.3) for poly(**623**). The glass transition temperatures of these polymers were in the 215−235 °C range. Their NMR spectra supported a 4,4′-coupling structure. A series of monomers **624** con-

Scheme 152



taining a variety of aryl units was studied and a cation−radical polymerization mechanism for these reaction was proposed.[267−271] The monomer **625** was polymerized by using Ni^{II}/Zn catalysts and the highest molecular weight polymer was M_n = 5500 (PDI = 2.4).

The cation radical polymerization of the compounds **626** − **629** in the presence of $FeCl_3$ in nitrobenzene was also studied by Percec et al. in 1992 (Figure 18).[272] The 4,4′-linkage of the binaphthyl units in these polymers was supported by a NMR spectroscopic study. The molecular weights of these polymers were in the range M_n = 2000−4000 as measured by GPC relative to polystyrene standards. Poly(**627**), poly(**628**), and poly(**629**) were soluble in chloroform although poly(**626**) was only partially soluble, and their T_gs were ca. 222−288 °C. They all had a deep red or brown color probably due to the formation of conjugated polynuclear aromatic units in the polymer chain through intramolecular cation−radical cyclization. Poly(**629**) was also synthesized by a $NiCl_2$/Zn-promoted polymerization of **630**.[273] The molecular weight of the polymer obtained by this method was similar to that obtained from **629**; however, its color was white because the nickel(0)-mediated polymerization process could not produce any polynuclear aromatic structures.

In 1996, John, McPherson and co-workers studied the polymerization of 2-naphthol using an enzyme catalysis process in reversed micelles.[274] Bis(2-ethylhexyl) sodium sulfosuccinate (AOT) forms reversed micelles in isooctane to generate microaqueous pools

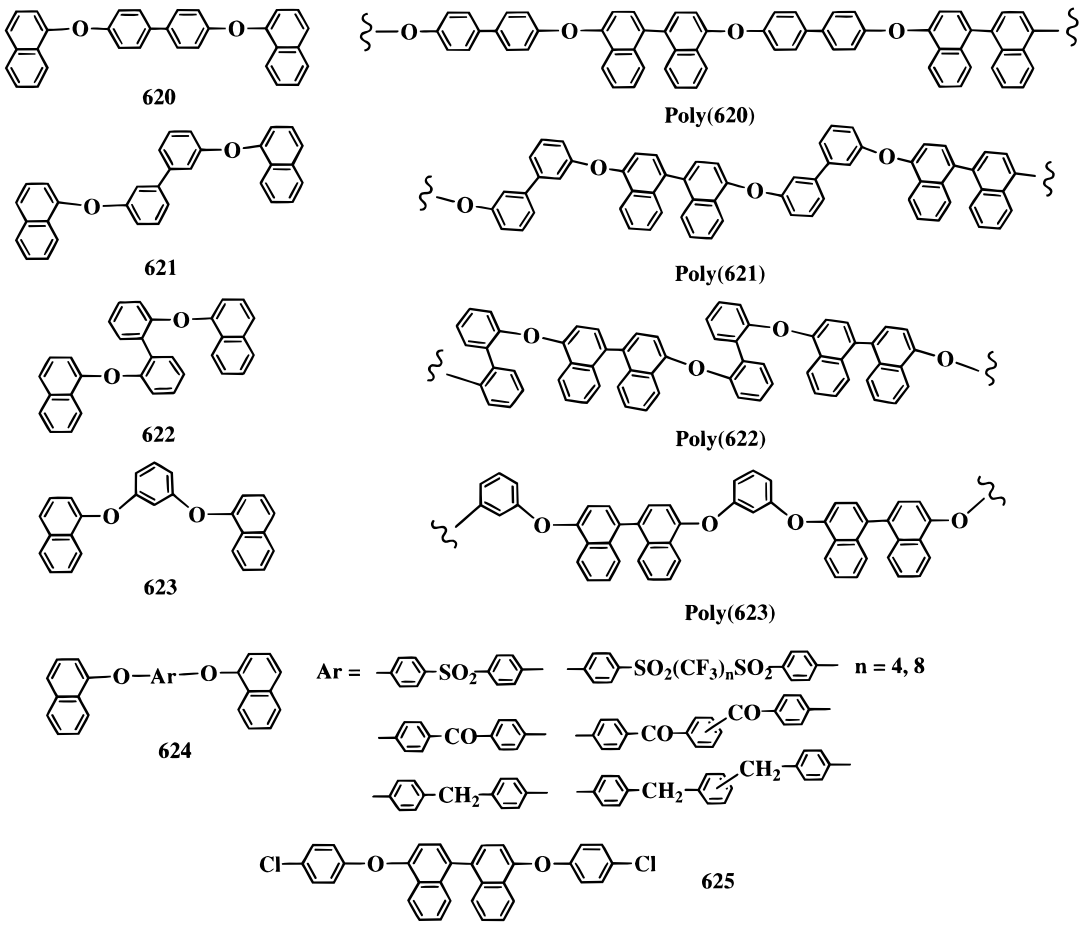


Figure 17.

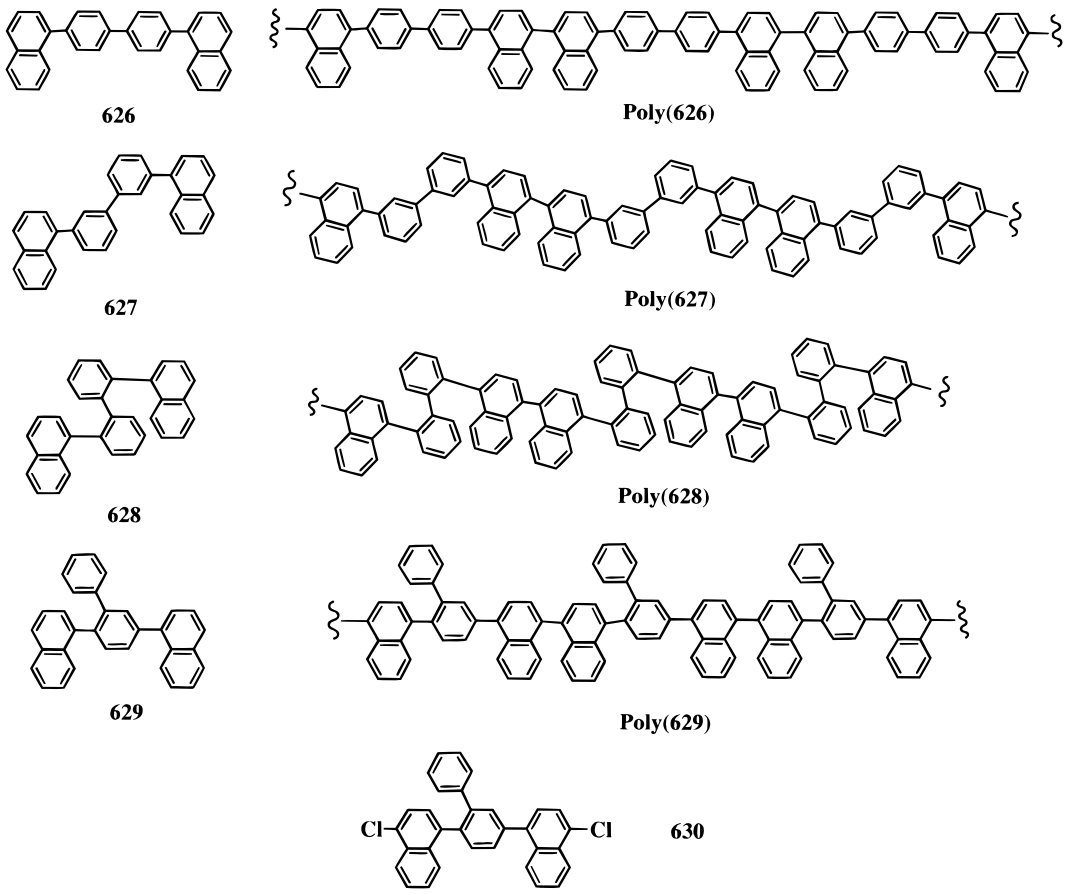
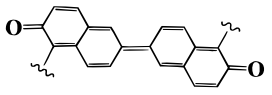


Figure 18.

in the presence of water. Enzymes can be encapsulated into the microaqueous phase and still maintain their activity. In the presence of H_2O_2, horseradish peroxidase (HRP) catalyzed the radical coupling of 2-naphthol in the AOT/isooctane reversed micelles to give poly(binaphthol)s in 95% yield. The molecular weight of the polymer was about 800 as measured by GPC relative to polystyrene standards. This polymer which had a microspherical morphology was soluble in many organic solvents such as acetone, THF, DMSO and benzene but not soluble in water and alkanes. The UV spectrum of the polynaphthol showed $\lambda_{max} = 270$ and 330 nm with weak peaks at 390 and 410 nm. It possibly contains a mixture of 1,1′-, 1,6′-, and 6,6′-binaphthyl structures. Further oxidation of the 6,6′-binaphthol units to quinonoid structures such as **631** could lead to the observed long wavelength absorptions. The fluorescence spectrum of the polymer displayed a strong peak at 375 nm and two weak peaks at 455 and 481 nm when excited at 327 nm. When the polybinaphthol was excited at



631

413 nm, the two peaks at 455 and 481 nm became much stronger. This further supports the proposed formation of rigid planar 6,6′-binaphthyl quinoid structures in the polymer. Although the ^1H and ^{13}C NMR spectra of this polymer were very complex, the IR spectrum showed a peak at 1676 cm^{-1} that could correspond to the C═O vibrations of **631**.

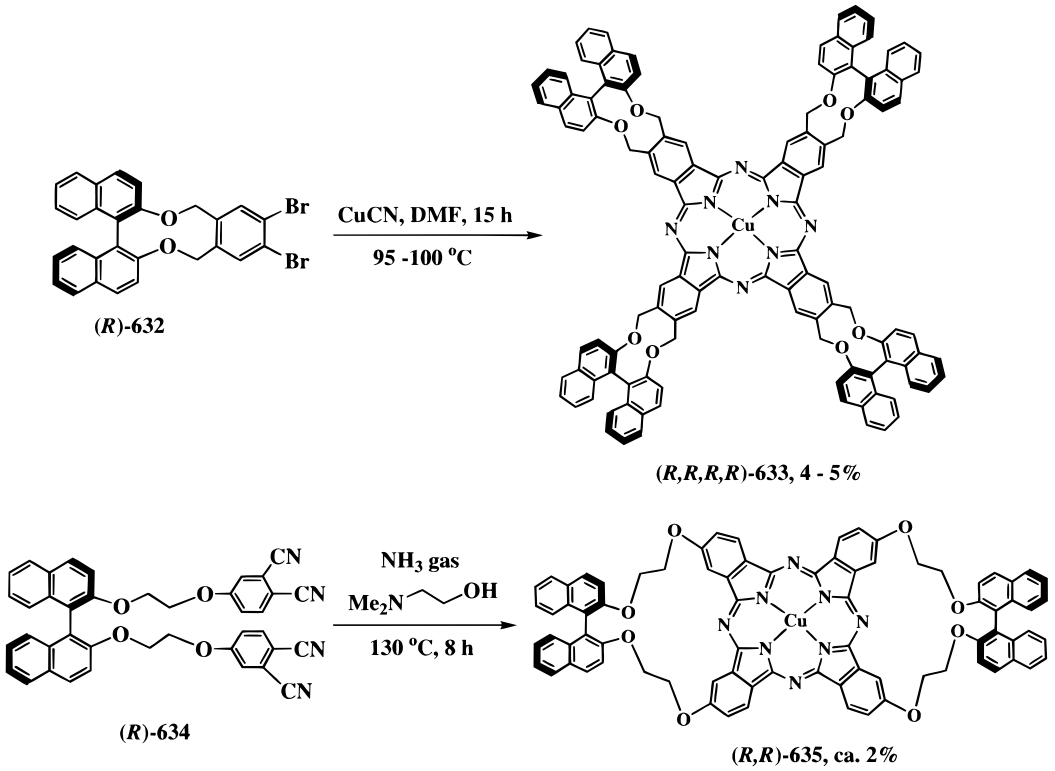
5. Miscellaneous Binaphthyl Oligomers

Multibinaphthyl molecules that are not easily classified into previous sections are summarized here. This includes chiral binaphthyl-substituted phthalocyanines, the preparation of chiral tetranaphthalenes, the Mitsunobu reaction of BINOLs with a chiral alcohol and natural products bearing structures similar to the multibinaphthyls. A stereocontrolled cross-coupling of a naphthyl Grignard reagent with naphthyl dibromides is also described. In this reaction, a chiral ferrocene ligand is used to generate a chiral nickel complex which catalyzes the enantioselective synthesis of optically active oligonaphthyl compounds. This process is potentially useful in the enantioselective synthesis of chiral binaphthyl polymers. A few optically inactive multibinaphthyl molecules are also summarized.

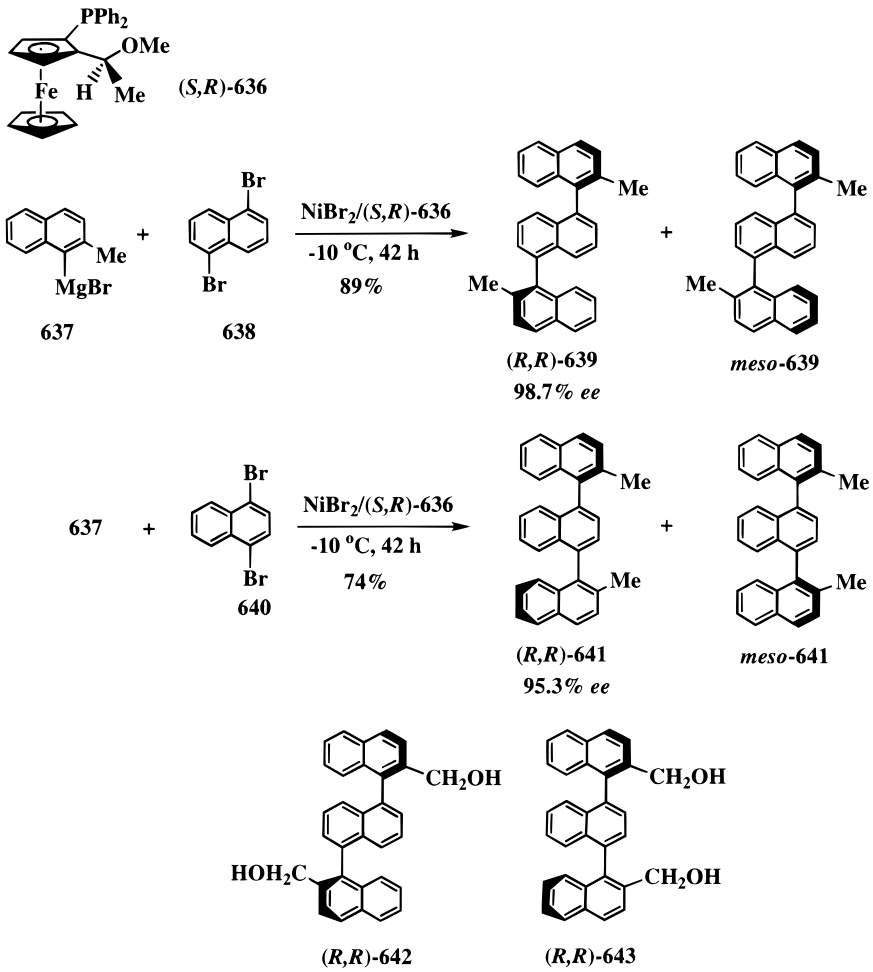
5.1. Optically Active Multibinaphthyl Molecules

Binaphthyl-based optically active phthalocyanines were reported by Kobayashi et al. in 1993.[275] When (*R*)-**632** was heated with CuCN in DMF, (*R*,*R*,*R*,*R*)-**633** was produced in 4−5% yield (Scheme 153). The corresponding (*S*,*S*,*S*,*S*)-**633** was synthesized from (*S*)-**632**. The reaction of (*R*)-**634** with ammonia in

Scheme 153

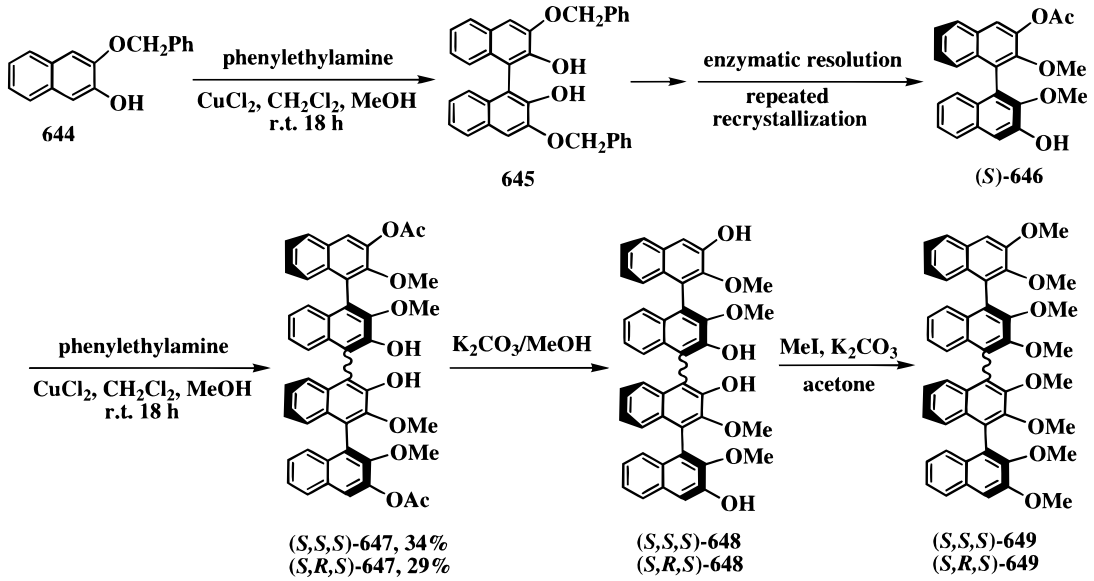


Scheme 154

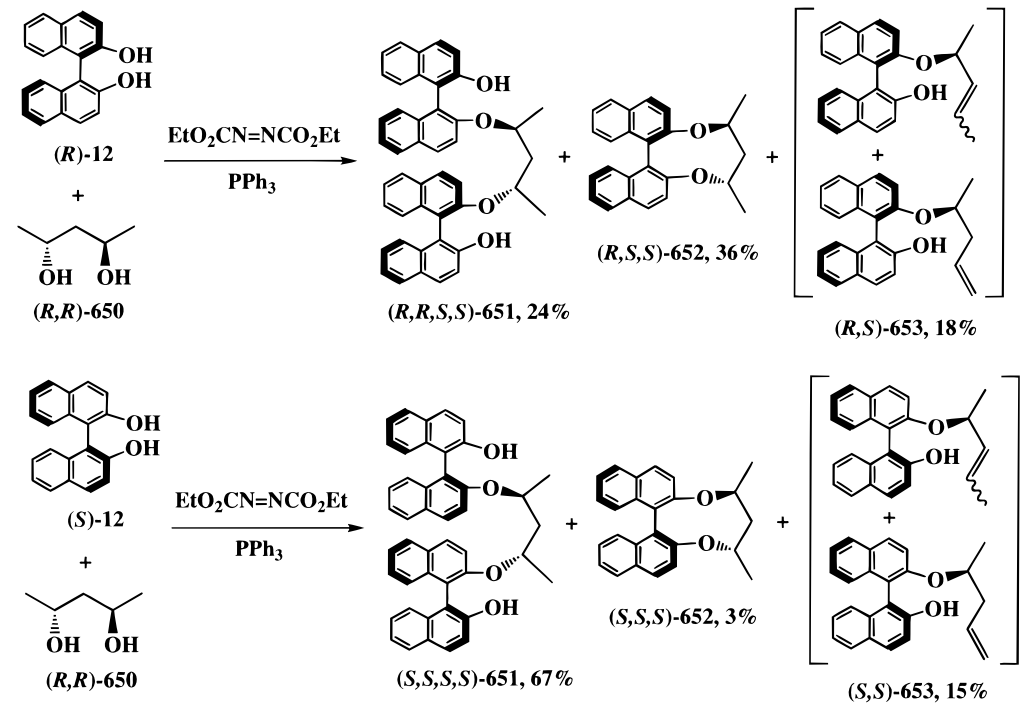


refluxing (*N*,*N*-dimethylamino)ethanol gave (*R*,*R*)-**635** in ca. 2% yield and (*S*)-**634** gave (*S*,*S*)-**635**. The chiral phthalocyanines **633** and **635** were characterized using FAB mass spectroscopy, NMR spectros-

Scheme 155

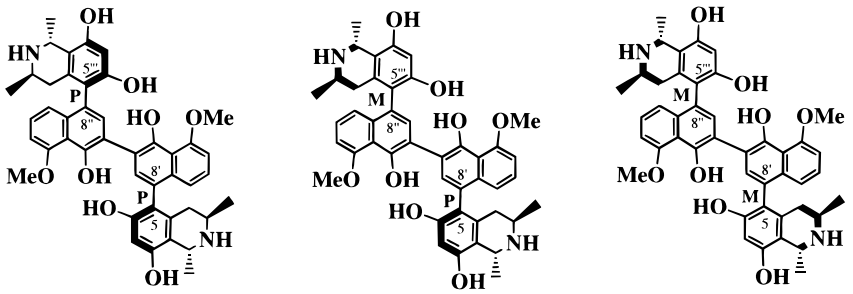


Scheme 156



copy as well as their CD spectra. (*R*,*R*,*R*,*R*)-**633** exhibited only positive CD signals and (*S*,*S*,*S*,*S*)-**633** gave only negative signals. All peaks and shoulders in their CD spectra corresponded exactly with those in their absorption spectra. Since BINOL (*S*)-**12** is a right-handed conformer and (*R*)-**12** is a left-handed conformer, the negative CD signals of (*S*,*S*,*S*,*S*)-**633** were induced in the field of the right-handed conformer and the positive CD signals of (*R*,*R*,*R*,*R*)-**633** in the field of the left-handed conformer. A UV spectroscopic study of (*R*,*R*)-**635** and (*S*,*S*)-**635** indicated that these molecules probably exist as $\pi-\pi$ stacking dimers in solution. On the basis of UV and CD spectroscopic studies, it was proposed that two opposite helical dimers are formed in solution, most probably right-handed for (*S*,*S*)-**635** and left-handed for (*R*,*R*)-**635**.

A highly enantioselective cross-coupling synthesis of ternaphthalenes was reported by Hayashi, Ito and co-worker in 1989.[276] In the presence of 2 mol % of $NiBr_2$/(*S*,*R*)-**636**, the 2-methylnaphthyl Grignard reagent **637** cross-coupled with 1,5-dibromonaphthalene (**638**) to give an optically active ternaphthalene (*R*,*R*)-**639** with 98.7% ee (Scheme 154). The ratio of (*R*,*R*)-**639** to *meso*-**639** was 84:16. The coupling of **637** with 1,4-dibromonaphthalene (**640**) gave (*R*,*R*)-**641** with 95.3% ee. The ratio of *meso*-**641** to (*R*,*R*)-**641** was 14:86. The optical purities of **639** and **641** were determined by HPLC analysis of **642** and **643** made by brominating **639** and **641** with NBS followed by hydrolysis. The reactions catalyzed by (*S*,*R*)-**636** to produce optically active (*R*,*R*)-**639** and (*R*,*R*)-**641** are potentially useful for the enantioselective syn-



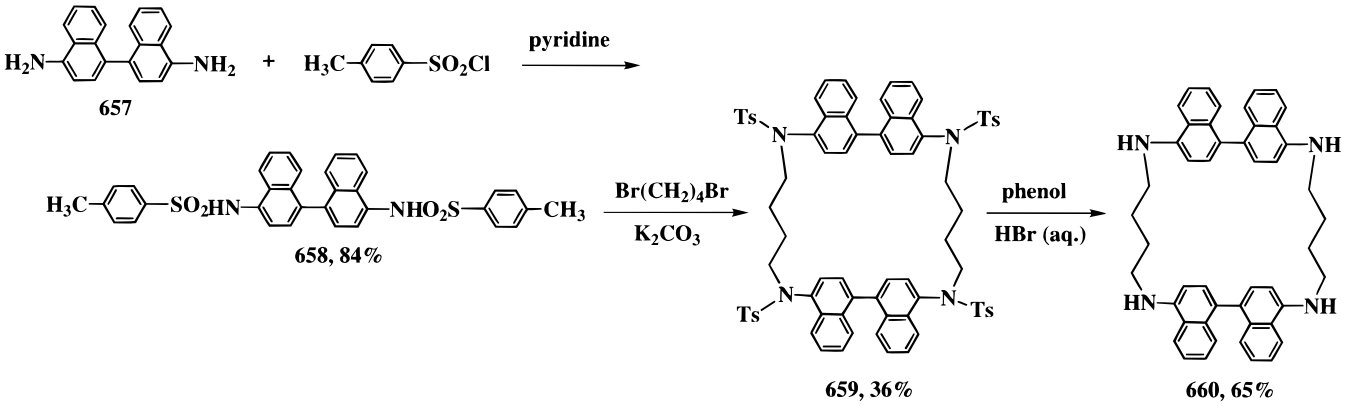
michellamine A
654a

michellamine B
654b

michellamine C
654c

Figure 19.

Scheme 157



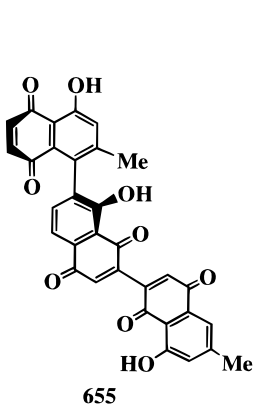
thesis of binaphthyl polymers from achiral naphthalene starting materials.

A stepwise construction of chiral tetranaphthalenes linked at the 1,4-positions was reported by Tanaka et al.[277] Oxidative coupling of **644** gave **645** that was subsequently converted to an optically pure binaphthyl molecule (*S*)-**646** after a series of protection/deprotection steps and enzymatic resolution (Scheme 155). Oxidative coupling of (*S*)-**646** produced two diastereomers (*S*,*S*,*S*)-**647** and (*S*,*R*,*S*)-**647** in 34% and 29% yields, respectively. Hydrolysis of **647** under basic conditions gave **648**. A single-crystal X-ray analysis of (*S*,*S*,*S*)-**648** established the absolute stereochemistry of this tetranaphthalene molecule. The dihedral angles between each of the naphthalene rings were 74.7°, 79.7°, and 113.0°, respectively. (*S*,*S*,*S*)-**648** and (*S*,*R*,*S*)-**648** were methylated to give **649**. Stepwise coupling of (*S*)-**646** with **644** gave trimers and then tetramers, various diastereomers of which were isolated and characterized. Stereochemical assignment was supported by their CD spectra.

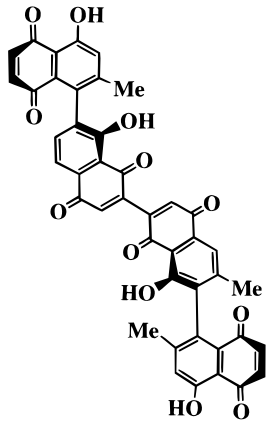
Ogasawara and co-worker studied the Mitsunobu reaction of (*R*)- and (*S*)-**12** with (*2R*,*4R*)-2,4-pentanediol [(*R*,*R*)-**650**].[278] Because of different stereochemical environments, different product distributions were observed. From the reaction of (*R*)-**12** with (*R*,*R*)-**650**, a dimeric compound (*R*,*R*,*S*,*S*)-**651** was obtained in 24% yield (Scheme 156). The reaction of (*S*)-**12** with (*R*,*R*)-**650** gave a dimeric compound (*S*,*S*,*S*,*S*)-**651** in 67% yield. Other monobinaphthyl compounds including (*R*,*S*,*S*)-**652**, (*R*,*S*)-**653**, (*S*,*S*,*S*)-**652**, and (*S*,*S*)-**653** were also isolated from both of the reactions.

The michellamines A, B, and C, **654a**−**c**, are natural product analogues of highly functionalized bisbinaphthyl molecules (Figure 19). These molecules are stereoisomers with respect to the restricted rotation around the bonds at 5−8′ and 8″−5‴. They were isolated from the Cameroonian liana *Ancistrocladus korupensis* and found to be active against the HIV virus. Their total syntheses was accomplished by several research groups.[279−281]

The trimeric naphthoquinone galpinone (**655**), isolated from *Euclea natalensis*,[283] and the tetrameric naphthoquinone bisisodiospyrin (**656**), isolated from *Diospyros lotus*,[284] are also optically active naturally occurring compounds.[282−284]



655

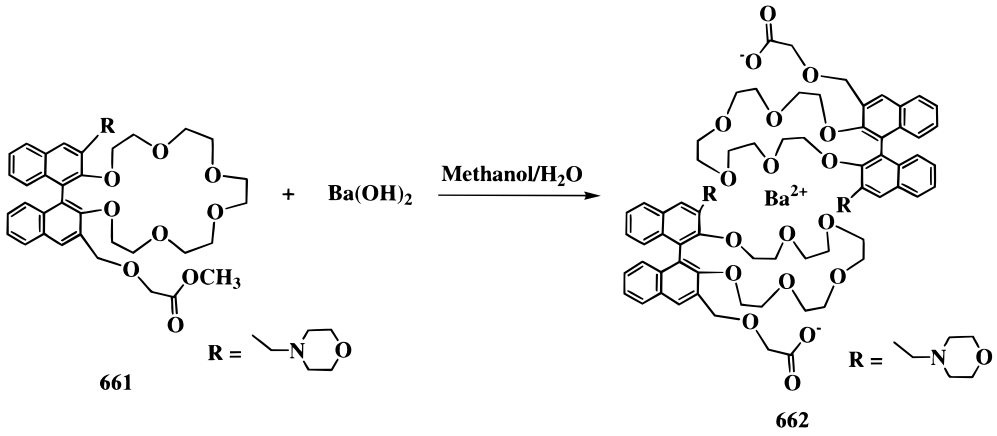


656

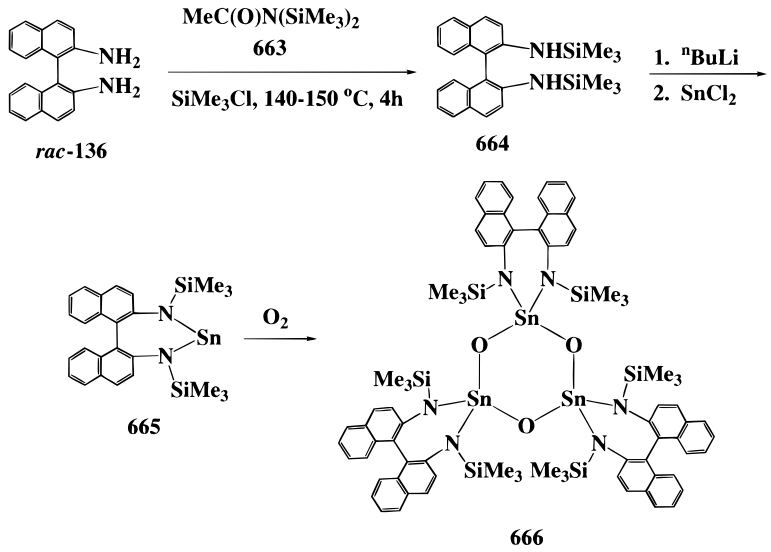
5.2. Optically Inactive Multibinaphthyl Molecules

A binaphthyl cyclophane **660** containing two racemic 1,1′-binaphthyl-4,4′-diamino units was prepared

Scheme 158



Scheme 159

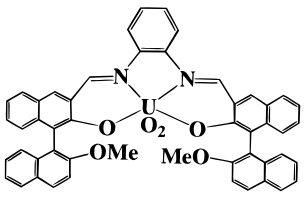


by Faust et al. in 1960 (Scheme 157).[285] The reaction of racemic 4,4′-diamino-1,1′-binaphthyl (**657**) with tosyl chloride gave **658** in 84% yield. This compound was reacted with 1,4-dibromobutane in the presence of potassium carbonate to form the macrocycle **659** in 36% yield. Removal of the tosylate groups by treatment with phenol/HBr (aqueous) gave the final product the tetraamino cyclophane **660**.

Monomeric binaphthyl crown ethers were found to form dimeric complexes with Ca^{2+} and Ba^{2+} by Cram and co-workers.[59,60] For example, hydrolysis of **661** in the presence of $Ba(OH)_2$ in methanol/water solution gave the dimeric complex **662** (Scheme 158), which was stable to sulfuric acid and purified by chromatography on silica gel, demonstrating that the complexed Ba^{2+} was unavailable for interacting with other ions or solvent.[59]

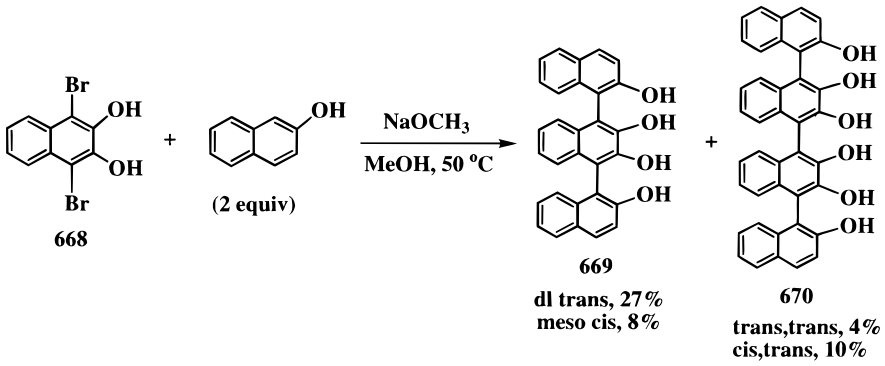
A cyclotristannoxane molecule obtained by Drost et al. from racemic 1,1′-binaphthyl-2,2′-diamine (*rac*-**136**) reacted with *N*,*N*-bis(trimethylsilyl)acetamide (**663**) in the presence of trace amounts of $SiMe_3Cl$ to give **664** which was then converted to the tin(II) amide **665** after treatment with *n*-butyllithium and $SnCl_2$ (Scheme 159).[286] Slow diffusion of oxygen into a pentane solution of **665** at room temperature produced a few pale yellow crystals of **666** whose structure was established by X-ray analysis. Two of the binaphthyl dihedral angles (*RR*) in **666** were 72° and the dihedral angle of the third binaphthyl was 69°. Although the authors did not comment on the stereoselectivity of the formation of the binaphthyl trimer, it appeared to be nonselective since an ORTEP of (*R*,*R*,*S*)-**666** was reported.

A bisbinaphthyl salophen uranyl complex **667** has also been prepared.[287,288] From the racemic binaphthyl starting material, **667** was obtained as a mixture of the meso and the racemic diastereomeric complexes.

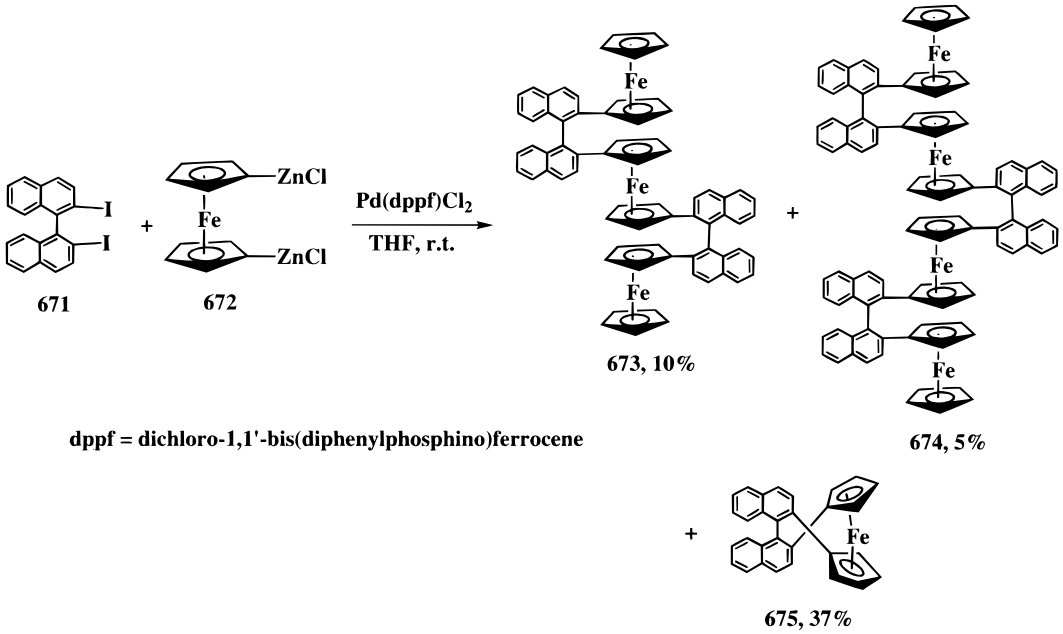


Závada and co-workers synthesized racemic 1,4-linked tetranaphthalene molecules.[289] They found that when **668** was treated under very mild conditions (25−50 °C) with 2-naphthol in the presence of sodium methoxide, a diastereomeric mixture of the trimer and tetramer, **669** and **670**, were produced

Scheme 160



Scheme 161



(Scheme 160). The meso isomer, *cis*-**669**, and the *dl* isomer, *trans*-**669**, were obtained in 8% and 27% yields, respectively. Whereas *trans,trans*-**670** and *cis,trans*-**670** gave yields of 4% and 10%. A single-crystal X-ray analysis established the stereochemistry of *trans*-**669** and *cis*-**669**. Refluxing either compound in pyridine gave an almost equimolar mixture of both isomers, indicating that their equal thermodynamic energies led to interconversion at higher temperatures. Optically active forms of the ternaphthols and quaternaphthols were not obtained.

Binaphthyl-based ferrocenes were obtained by Foxman et al.[290] A mixture of binaphthyl ferrocene complexes were obtained from the reaction of racemic 2,2′-diiodo-1,1′-binaphthyl (**671**) with the dimetalated ferrocene **672** in the presence of a palladium catalyst (Scheme 161). The complexes **673**−**675** were isolated by column chromatography in yields of 10%, 5%, and 37%, respectively. Although the diastereomeric mixture of **673** was only partially separated and that of **674** remained unseparated, all compounds were characterized by mass spectroscopy. In addition, a single-crystal X-ray structure of the monobinaphthyl ferrocene **675** was obtained.

6. Summary

Chiral macrocycles, metal complexes, linear oligomers, and polymers all based on the 1,1′-binaphthyl structure have been synthesized and their applications explored. All the optically active multibinaphthyl materials have substituents at the 2,2′-positions of the 1,1′-binaphthyl units which lead to the generation of highly stable chiral configurations for their atropisomers. The stable chiral configuration of these materials is essential for many of their applications.

Multibinaphthyl-based chiral macrocycles have been prepared mainly for the purpose of chiral recognition of organic molecules. These macrocyclic hosts show enantioselective binding with chiral molecules such as amino acids and sugars. As shown in Cram's study, the cooperation of the two binaphthyl units in molecular hosts such as (*R,R*)-**19** leads to more efficient enantioselective discrimination. However, the incorporation of more binaphthyl units does not necessarily guarantee better chiral recognition. The complementary host−guest binding is most important in the design of efficient chiral hosts.

The bifunctional chiral crown ether host (*S,S*)-**118** reported by Yamamoto and co-workers represents an

interesting extension of Cram's work. In (*S,S*)-**118**, the two crown ether rings form two binding sites for guest molecules containing two amine groups. Such multifunctional recognition has led to enhanced chiral discrimination. Chiral hosts such as (*R,R,R,R*)-**80** synthesized by Diederich and co-workers also have multiple binding sites for sugar hydroxyl groups. The development of hosts with multiple chiral units as well as multiple binding sites appears very promising for the recognition of molecules of increasing complexity. Although the main binding mode of crown ether hosts with guest molecules is through hydrogen bonding, other binding forces are utilized in the binaphthyl-based macrocycles. For example, chiral cyclophanes such as (*R,R*)-**92** capable of recognition through $\pi-\pi$ interactions have been studied by Stoddart and co-workers. The hemicarcerand (*R,R,R,R*)-**65** is capable of encapsulating guest molecules in its hollow interior through van der Waals interaction. Stang and co-workers have demonstrated that transition metal complexes containing chiral binaphthyl ligands can carry out stereospecific self-assemblies, leading to interesting chiral structures such as (*R*)-**112a,b**.

Among current studies of multibinaphthyl molecules, the most active area is that of asymmetric catalysis. Using the binaphthyl units, chiral ligands with very diverse structures have been constructed. Binaphthyl ligand-based chiral catalysts have been applied to the catalysis of many organic reactions and several highly enantioselective multibinaphthyl catalysts have been developed. Shibasaki's heterometallic system has shown excellent chiral induction in reactions such as nitro aldol reactions and Michael additions. In a Shibasaki's catalyst, two or three BINOL units are coordinated with either a Ln(III) element or a group III metal center as well as an alkaline cation. Heterometallic catalysts such as (*S,S,S*)-**140** can act as both Lewis acids and Lewis bases. This dual functionality cooperating with the multiple chiral units has produced high enantioselectivity in asymmetric catalysis. Using two chiral binaphthyl units and a chiral diamino unit, Katsuki and co-workers synthesized a new class of manganese salen complexes, e.g., (*R,R,S,S*)-**296**, that can catalyze the asymmetric epoxidation of unfunctionalized *cis*-olefins with excellent enantioselectivity. Matching the binaphthyl chirality with the chirality of the diamino units is critical for stereoselectivity. On the basis of a bisbinaphthyl phsophinephosphite ligand, Takaya and co-workers developed highly enantioselective hydroformylation catalysts such as (*R*)-**380** in which the two inequivalent phosphorus atoms lead to two different coordination sites. In the addition of H_2 and CO to alkenes, these inequivalent coordination sites, the asymmetric ligand environment as well as matching chirality between the two binaphthyl units are all important factors for high asymmetric induction.

Binaphthyl-based polymeric chiral catalysts such as (*R*)-**461** and (*R*)-**468** are reported by Pu and co-workers. These polymers have shown excellent enantioselectivity in the reaction of aldehydes with diethylzinc. Promising results are also obtained for the asymmetric reduction of ketones, the asymmetric epoxidation of α,β-unsaturated ketones, and the asymmetric hetero-Diels−Alder reaction of aldehydes with conjugated dienes using the polybinaphthyl-based chiral catalysts. Because of the rigid and stereoregular polybinaphthyl structure, these novel polymeric catalysts are expected to have a much better defined microenvironment at the catalytic sites than the traditionally prepared polymer-supported chiral catalysts. In the traditional approach to preparing polymeric chiral catalysts, a highly enantioselective monomeric catalyst is first developed which is then anchored to a flexible and sterically irregular polymer backbone. This approach often leads to a significant decrease in stereoselectivity on going from the monomer to the polymer catalyst. This indicates that the microenvironment of the catalytic sites in the polymer is important for catalyst efficiency. However, because of the flexibility and the steric irregularity of traditional polymer supports, the microenviornment cannot be systematically modified in order to improve their catalytic properties. Studies using polymers (*R*)-**449**, (*R*)-**456**, (*R*)-**461**, and (*R*)-**468** as well as the monomer (*R*)-**464** have demonstrated two new strategies for the development of enantioselective polymer catalysts: (1) Highly enantioselective polymeric catalysts can be obtained by systematically modifying the microenvironment of the catalytic sites of rigid and sterically regular polymers. (2) Enantioselective monomeric catalysts can be converted to polymer catalysts with the same catalytic properties by incorporating the monomeric catalysts into rigid and sterically regular polymer backbones. This strategy ensures greater preservation of the catalytic environment of the monomeric catalysts as long as the catalytically active species are not aggregates of the monomers. The advantages of using the polymer catalysts in asymmetric synthesis include easy recovery and reuse of the chiral catalysts, simplified product purification, and the possibility of carrying out flow reactor and flow membrane reactor synthesis. They may also allow the introduction of different catalytic sites into one polymer to carry out multiple asymmetric reactions.

The incorporation of chiral binaphthyl units into conjugated polymer chains by Pu and co-workers led to a class of conjugated polymers with inherently chiral main chains. These materials such as (*R*)-**552** and (*R*)-**556** to (*S*)-**561** are different from the chiral conjugated polymers made by anchoring optically active substituents to the conjugated main chain. In contrast to these polymers in which the main chain chiral conformation changes with respect to temperature, solvent, or other external factors, the binaphthyl-based chiral conjugated polymers possess very stable main chain chiral configuration. They are potentially useful for asymmetric electrosynthesis, enantioselective sensing, polarized light emission, and nonlinear optics. For example, by utilizing the rigid chiral binaphthyl structure, polymers such as (*R*)-**569** and (*R*)-**587** with novel propeller-like chain structures have been prepared as potential nonlinear optical materials.

Other researchers have used chiral binaphthyls to custom-build polymers such as using polyamides like (*S*)-**517** in enantioselective chromatography. These polymers can separate the enantiomers of certain racemic aryl amides and aryl carbamates. Binaphthyl-based crown ether polymers such as (*S*)-**525** are prepared for chiral recognition purposes. Other potential applications of binaphthyl polymers in areas such as liquid crystalline materials, electrochemical sensors, thermally stable coatings, and soluble high-temperature materials have also been explored.

In summary, the unique C_2 symmetric binaphthyl structure, the diverse functionalities of the binaphthyl molecules as well as their stable chiral configuration have allowed the construction of molecules and macromolecules with both fascinating structures and properties. Apart from the continuous interest in the design of binaphthyl-based chiral hosts and catalysts for chiral recognition and asymmetric synthesis, the use of binaphthyls in materials science is emerging as a promising field. The rigidity, chirality, and conjugation of such binaphthyl molecules offer great opportunity in the design of new materials with potentially exciting applications.

7. Acknowledgments

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