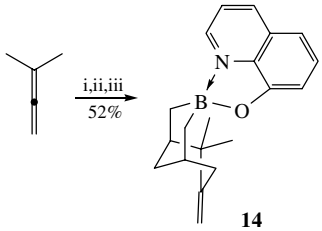


**14**

**Scheme 5** *Reagents and conditions*: i, $All_3B$, 140 °C, 10 h; ii, 20 °C, MeOH, reflux for 3 h; iii, $Et_2O$, 8-oxyquinoline, reflux for 1 h.

‡‡ **14**; 52% yield from 3-methylbuta-1,2-diene; mp 148–152 °C (decomp.). $^1$H NMR (300.13 MHz, $CDCl_3$) $\delta$: 0.56 [br. m, 2H, H(2β), H(4β)], 0.89 [br. m, 2H, H(2α), H(4α)], 1.16 and 1.22 (s, 6H, Me), 1.70 [br. dd, 1H, H(8α), $^2J_{H(8\alpha)-H(8\beta)}$ 6.6 Hz, $^3J_{H(8\alpha)-H(1)}$ 4.4 Hz], 1.79 [br. d, 1H, H(9*syn*), $^3J_{H(9syn)-H(9anti)}$ 4.4 Hz], 2.07 [d, 1H, H(8β), $^2J_{H(8\beta)-H(8\alpha)}$ 6.6 Hz], 2.25 [d, 1H, H(9*anti*), $^3J_{H(9anti)-H(5)}$ 13.2 Hz], 2.33 [br. m, 1H, H(1)], 2.74 [dd, 1H, H(5), $^3J_{H(5)-(H4\beta)}$ 4.4 Hz, $^3J_{H(5)-H(9anti)}$ 13.2 Hz], 4.88 and 4.90 [s, 1H, $CH_2$=], 6.95 [d, 1H, H(7′), $^3J_{H(7')-H(6')}$ 8.1 Hz], 7.09 [d, 1H, H(5′), $^3J_{H(5')-H(6')}$ 8.1 Hz], 7.54 [m, 1H, H(3′)], 7.57 [t, 1H, H(6′), *J* 7.4 Hz], 8.26 [d, 1H, H(4′), $^3J_{H(4')-H(3')}$ 8.1 Hz], 8.39 [d, 1H, H(2′), $^3J_{H(2')-H(3')}$ 5.1 Hz]. $^{13}$C NMR (DEPT-135) (50.32 MHz, $CDCl_3$) $\delta$: 27.0 (Me), 29.4 and 30.2 [C(1) and C(5)], 32.4 [C(9)], 40.5 [C(8)], 41.6 [C(6)], 108.0 [$CH_2$=], 108.7 [C(5′)], 110.5 [C(4′)], 122.5 [C(7′)], 128.1 [C(4a′)], 132.6 [C(6′)], 137.2 [C(3′)], 137.4 [C(2′)], 137.7 [C(8a′)], 153.4 [C(7)], 158.6 [C(8′)]. Found (%): C, 77.98; H, 8.30; B, 3.75. Calc. for $C_{20}H_{24}BNO$ (%): C, 78.70; H, 7.93; B 3.54.

Note that the stereospecificity of allylboron–acetylene condensation leads exclusively to 3-borabicyclo[3.3.1]non-6-enes[1] and compound **13** is the first example of 6-*exo*-methylene derivatives.

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# A helix theory for molecular chirality and chiral interaction†

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**A helix electronic theory shows that complex molecular chiralities can be generalized on the basis of their inherent helicities and effects in stereochemical control conventionally attributed to steric hindrance might instead have an electronic basis.**

Any object is said to be 'chiral' if it cannot be superimposed upon its mirror image. The term chirality was first coined in 1893, four years before the electron was discovered, by Lord Kelvin (W. Thomson): 'I call any geometrical figure, or group of points, chiral, and say it has chirality if its image in a plane mirror, ideally realized, can not be brought to coincide with itself".[1] Application of this concept to asymmetric molecules leads to the definition of molecular chirality. Since then, molecular chirality has been understood as a purely geometrical property, and therefore the stereochemical interactions of chiral molecules are usually analyzed by means of steric size-based considerations.[2] While it is true that chiralities in the molecular world and chiral objects in the everyday macroscale world share a geometrical link, it is intriguing to ask whether in the former there are electronic consequences that are also resulted from the degradation of symmetry. We recently developed a helix electronic theory for molecular chirality and chiral interaction.[3–6] The work shows that structurally diverse chiralitites can be generalized on the basis of their inherent helicities. This helix approach suggests that effects conventionally attributed to steric hindrance might instead have an electronic basis, and that a new electronic effect, which we call homohelical interaction, generally controls the stereochemical course of chiral processes. We herein present an overview of the major points of this theory.

Although the basic quantum mechanical theory of optical activity has long been known,[7] its quantitative implementation to real molecules has proven to be very difficult. From a more practical structural approach, much effort has been focused on relating the optical activities of chiral molecules to their structures because such a relationship, if generally identified, would allow one to deduce molecular conformation and absolute configuration simply from optical rotation, which is highly desirable. Many models along this line had been developed in the past two centuries.[8–10] It was first suggested by Fresnel in 1827 that a chiral microstructure, possibly helical in nature, is required for a chiral substance to have different refractive indices for right- and left-circular polarized light and thus to exhibit optical activity.[11] Tinoco and Woody elegantly showed in 1964 that an electron constrained to move on a helix, which is probably the simplest chiral potential, does lead to optical rotation, and the sign is positive at long wavelengths when the helix is right-handed.[12] The essence of this conclusion, as pointed out by Brewster,[8(a)] enters, explicitly or implicitly, into all major theoretical models for optical activity. Such an electron-on-a-helix model subsequently gained firm support at the macroscale level: it was experimentally demonstrated that collections of randomly distributed copper wire helices are indeed capable of rotating the plane of polarized radio-frequency electromagnetic radiation.[13]

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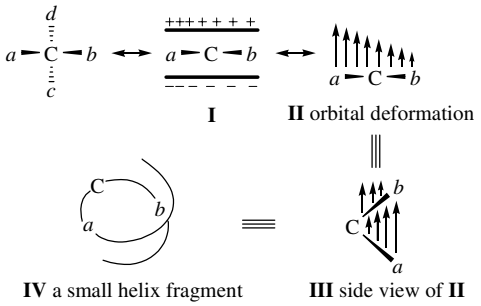


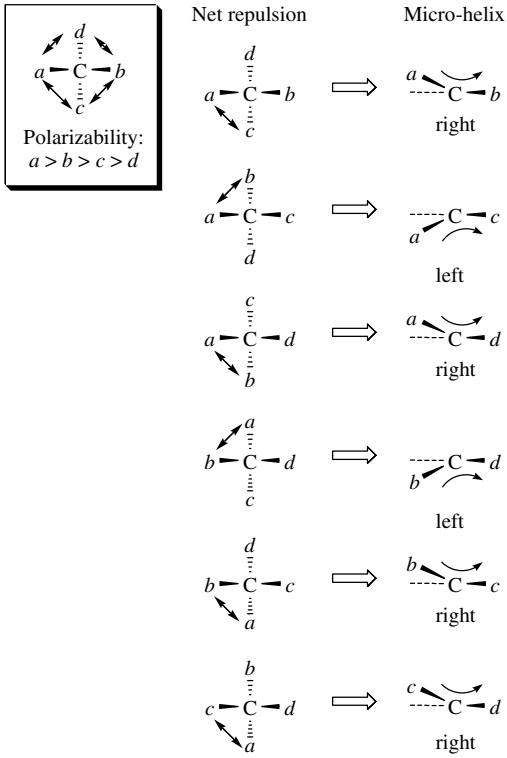

**Scheme 1** Helical deformation of a covalent bond pair in dissymmetric electronic environment.

Despite the helix model's successes, there seems to be a considerable gap between theory and molecular reality because, for example, for a simple five-atom chiral molecule such as C*HFBrCl the helix is hard to identify. However, helical electronic structures can be visualized and analyzed in these and other molecules by supposing that unbalanced electronic repulsions, measured by group polarizabilities, deform the bonds into helices. The polarizability characterizes the distortion a group's electrons experience in an electric field. This idea is an outgrowth of many earlier attempts to identify helical electronic paths in chiral molecules.[8(a)–(c)]

For a simple point-chiral molecule C*$abcd$, in which substituents $a$, $b$, $c$ and $d$ are attached to central chiral atom C*, let's focus on the $a$–C*–$b$ bond pair and investigate its deformation through an animation sequence shown in Scheme 1. The method is based on a procedure proposed by Yin.[14] Because $c \neq d$, the actual situation of $a$–C*–$b$ in such a dissymmetric electronic environment is equivalent to placing it in a non-uniform electric field as illustrated in **I**. Furthermore, because $a \neq b$, electron densities along $a$–C*–$b$ must be forced to move at different extents, depending on how polarizable the electronic density at each individual position is: more polarizable electrons are more prone to move as visualized in **II** by the length of the arrowed lines. One could more clearly view this from **III**. It then can be readily recognized that the $a$–C*–$b$ moiety has deviated from co-planarity and twisted into a helix as shown in **IV**, a small helix, but a helix nevertheless!

For the enantiomer of C*$abcd$ in Scheme 1, suppose that the polarizabilities of the substituents follow the sequence $a > b > c > d$. Because distortion increases with group polarizability, as in earlier models,[8] the strength of electronic interaction (represented by the double arrowed lines in Scheme 2) between any two groups can be expected to follow the sequences $a$–$c$ > $b$–$c$, and $a$–$d$ > $b$–$d$. Hence, for the $a$–C*–$b$ bond pair, the $a$–C* bond should twist up more than the $b$–C* bond. The $a$–C*–$b$ will thus twist into a right-handed micro-helix. Similarly, as summarized below for the other five bond pairs, the $a$–C*–$d$, $b$–C*–$c$, and $c$–C*–$d$ bonds will twist into right-handed micro-helices and the $a$–C*–$c$ and $b$–C*–$d$ bonds, into left-handed micro-helices. Since there are more right-handed than left-handed structures, the molecule has a net right-handed helicity. This might account for its having dextro-rotatory at long wavelengths.[7,8] It can be shown that if any two groups are the same, the molecule's net helicity disappears, hence its optical rotation.

It is clear from this analysis that for C*$abcd$ to be optically active, that the four groups must be different from each other is not just a symmetry-breaking geometrical requirement as commonly appreciated, but is also a critical electronic basis. The roles played by this electronic property of chirality in chiral induction and recognition have been previously examined[3–6] through many experiments and will be highlighted in a later part. It is also evident that the unbalanced electronic interactions should arise largely from the bonds and atoms that are directly attached to the chiral center. Therefore, in agreement with Brewster's suggestion,[8(b)] the polarizability ranking of multi-atom groups should be assigned according to the polarizabilities of the atoms or moieties directly attached to the chiral center,

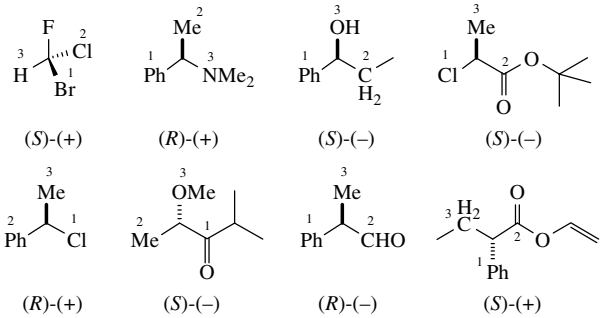



**Scheme 2** Helical structures in a typical point-chiral molecule C*$abcd$ of a group polarizability sequence $a > b > c > d$.

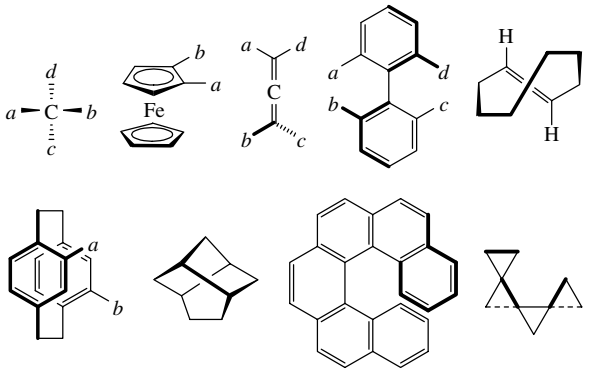
*i.e.*, local polarizabilities, and not according to the polarizabilities of the whole group.

The correlation of helix handedness with sign of rotation agrees with theories of optical activity, as well as earlier empirical formulations.[8(a)] Although at the present stage rotational strengths cannot be evaluated quantitatively, the signs of rotation can be predicted because the polarizability sequences can often be readily deduced, which enables absolute stereochemistries to be assigned on the basis of rotation signs.[3] Scheme 3 provides some illustrations. The group local polarizabilities in each of them follow the sequence 1 > 2 > 3 > H > F. Because this method does not address the rotation contributions of the helical structures that may arise from molecular conformations,[3] it is effectively applicable only to small and conformationally flexible molecules whose rotations are preferably measured in non-polar solvents.[3] Despite these limitations, the method is worth considering by practicing chemists because it is so simple to apply. It complements the current computational approaches to optical rotation.[10]

As disclosed previously,[3] helical structures can also be identified in axial, planar, and other chiralities. This is summarized in Scheme 4. Complex chiralities differ merely in their helical parameters, which include radius, pitch, length and electronic polarizability on the helix. Helices in point-chiral molecules are small, so the rotations of such molecules are tiny, often below 100°. Helices in axial-chiral molecules are usually larger, and




**Scheme 3** Absolute stereochemical assignments on the basis of rotation signs at $Na_D$ line.



All chiralities feature helical structures: chirality ≡ helicity

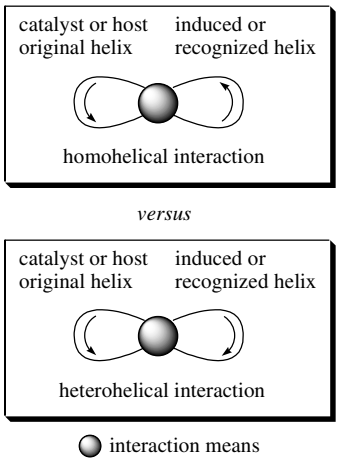
**Scheme 4** Helical structures in all types of molecular chiralities.

the rotations of them are frequently around a few hundreds of degrees. Helices in helicenes, as visualized from the largely skewed, highly polarized π-electron skeletons, are very large, and therefore the rotations of these molecules can reach several thousands of degrees.

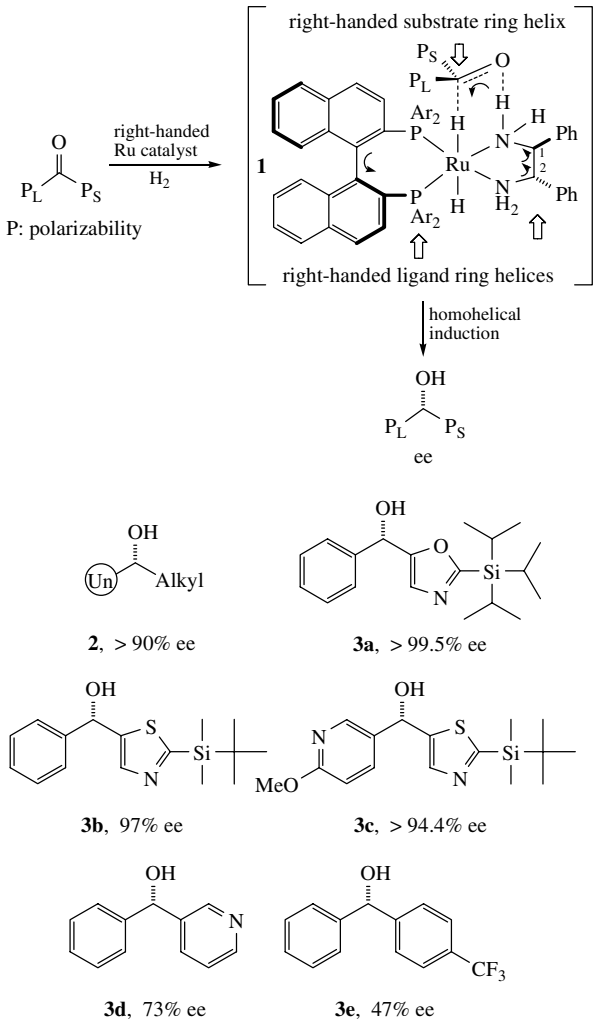
It becomes clear that structurally diverse molecular chiralities can be generalized on the basis of their inherent helical identities, being either right- or left-handed. Once again, it merits a note that this chirality-helicity equivalence suggests a structural basis that relates theories of optical activity to real molecules in a unified helix framework.[7,8] This generalization may not come as a surprise. Indeed, in the everyday macroscale world, biologically manifested helical or spiral phenomena are ubiquitous;[15] deep down in the molecular world, self-assembled and self-organized architectures often express themselves as helical,[16] proteins are helical, and DNAs are helical...;[17] If helicity were, as long held, only a special form of chirality,[9] it would not be without ambivalence to accept why nature chooses such a special tool to fulfill her universal genetic missions.

The identification of helicity as the hallmark of molecular chirality significantly simplifies the stereochemical pictures of complex chiral induction and recognition events. Since fundamentally there are only two molecular chiralities, right- and left-handed helicity, any diastereomeric interactions between a catalyst and a substrate, or between a host and a guest, can be described as either homohelical (when the interacting helices have the same handedness) or heterohelical (when they don't), as shown in Scheme 5. The interesting question is which one is energetically more favorable.

By employing the classical electron-on-a-helix model of Tinoco and Woody,[12] it can be shown that a homohelical electronic interaction, which constitutes a helix expansion, is always lower in energy than its diastereomeric heterohelical electronic interaction, which constitutes a helix compression.[5] Indeed, numerous experiments show that homohelical interactions always seem to




**Scheme 5** Homohelical and heterohelical electronic interactions.




**Scheme 6** General homohelical induction rationale in Ru-catalyzed hydrogenation of simple ketones. $P_L$: the ketone substituent of larger polarizability; $P_S$: the ketone substituent of smaller polarizability; Ar = 3,5-$Me_2C_6H_3$, Un = unsaturated group; Alkyl: alkyl group.

be favored.[3–6] *A chiral catalyst prefers inducing the chiral product, and a chiral host prefers recognizing the chiral guest, that allows the catalyst or host to preserve its electronic helicity – or handedness – in the transition state.* This principle of conservation of helical asymmetry enables a facile deducing of the favourable reaction pathway thus the stereochemical outcome under a known reaction mechanistic framework without necessarily involving numeric calculations. It is readily applicable since helicity analysis is often easy. Of the many examples previously discussed,[3,4] the diphosphine–diamine–Ru complexes-catalyzed asymmetric transfer hydrogenation of Noyori *et al.*[18] is used here to illustrate the principle.

The mechanism involves the pericyclic transfer of hydrogens from ligand nitrogen to substrate oxygen and from ruthenium to substrate carbon. The helices in the ligand–metal chelate rings in Scheme 6 are critical in executing asymmetric induction. Catalyst **1** has right-handed helicity both in its diphosphine ring, *i.e.*, helix –P–C–C–C–C–P– from the atropisomeric skew, and in its diamine ring, *i.e.*, helices –N–$C^1$*–$C^2$*– at the $C^1$* center and –$C^1$*–$C^2$*–N– at the $C^2$* center (both analyzed by two local polarizability sequences: Ph > H and C* > N. Note that a knowledge of the complete polarizability sequence of the four groups around each chiral center, *i.e.*, Ph, H, C* and N here, is unnecessary since usually only one particular helix around the chiral center is concerned). Therefore, the homohelical induction principle requires the hydride to attack to C=O preferentially as shown, because only with this enantiofacial selection can the substrate ring helix, *i.e.*, –H–C*–O– (polarizability sequences: O > H and $P_L > P_S$), also develop right-handed helicity in the

transition state. Note that it is not the sizes of the substituents that are important, but their local polarizabilities, which accords with experiments, for only aromatic and unsaturated ketones of generic structure **2**, which are characterized by a significant π-*versus*-σ local electronic polarizability distinction, have been found to give high enantiomeric excess (ee).[2,18]

Hydrogenations with an analogous catalyst[19] lead to **3a–e**. The substituent polarizabilities in **3a–d** are known to follow benzene > pyridine > thiazole > oxazole, and for **3e** benzene is more polarizable than another benzene that is electron-withdrawn by a *para*-$CF_3$ group.[3] The hydrogenations all proceed with expected stereochemistries. More interestingly, it can be seen that the higher the polarizability distinction, the higher the ee. Steric consideration, in contrast, does not obviously account for the results: in **3d** it is difficult to apply because the substituents are nearly equal in size, and in **3a–c** and **3e** it seems to yield wrong enantiomers because in each case the group on the right is larger than the one on the left. An extensive survey shows that this homohelical induction rationale is generally held.[3] Steric effects appear to be less significant in stereochemical control, and they alone, that is, in reactions employing dialkyl ketones for instances, do not give high enantioselectivities in general even when the alkyl groups differ appreciably in bulk.[2,18] This helical electronic approach to understanding reaction stereochemical course is powerfully predictive, as demonstrated in many other processes.[3] We have further showed that the homohelical-*versus*-heterohelical electronic interaction energetic difference can be maximized, thus the ee can be *ca*. 100%, only when the helical characters, or in a more clear energy language, the local energies of electrons, of the interacting helices are equal to each other.[4,5] In short, they must be helically matched. This conclusion highlights the importance of polarizability matching in three-dimensional chiral space and is essentially a chiral version of the classical hard and soft acid–base theory.[20]

In summary, we have developed a helix theory for chirality and chiral interaction and illustrated various aspects of its applications in real molecular systems. It merits a comment here that, although the discussion herein placed an emphasis on asymmetric synthesis, one could envision broader implications of the work in other areas in which the roles of chirality are decisive, such as in chiral chromatography,[21] chiral molecular self-assembly, express and amplification of chirality in liquid crystals,[16] and protein folding.[22] We believe that the helicity conservation and helical characters matching principles will find utilities in the discovery of efficient chiral catalysts. It is expected that, in conjunction with steric considerations, the development of a computational strategy that can quantitatively address such local helical electronic effects would enable rational design.

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# New [4 + 4] photodimerization of 5-chloro-2-pyridone to the *meso-cis-syn* dimer as an inclusion complex with 1,2,4,5-benzenetetracarboxylic acid

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As the first example of the [4 + 4] *cis-syn* dimer of 2-pyridone, the *meso-cis-syn* dimer of 5-chloro-2-pyridone was prepared by photoirradiation of a 1:4 inclusion complex of a 1,2,4,5-benzenetetracarboxylic acid host and 5-chloro-2-pyridone in the solid state, and the steric course of the reaction was studied by X-ray analysis.

In relation to damage to DNA by photodimerization of its basic components in nucleotide, photodimerization reactions of 2-pyridone derivatives are very important. However, the photodimerization of 2-pyridones **1** has not been successful, since **1** exists as an equilibrium mixture with corresponding enol forms **2**. For example, the photoirradiation of an equilibrium mixture of **1a** and **2a** in solution for 72 h gave *trans-anti* dimer **3a** in 40% yield.[1] In the crystal, only keto form **1a** exists,[2] but its photoirradiation in the solid state does not give any photodimer. In the case of 5-chloro-2-pyridone **1b**, photoirradiation