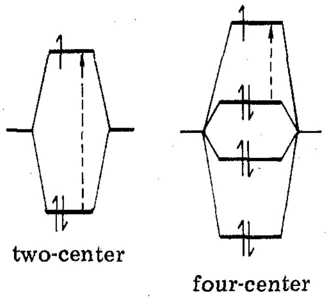
− 1 electrons on *n* energy levels as shown for two- and four-center complexes.



Transitions will predominantly occur between the two upper energy levels and this can satisfactorily explain the low energy IR band as well as the relatively high extinction coefficients of species VIII–XI. Also the large IR contribution to the very broad absorption band (half-width = 1.45 eV) of the intramolecular radical cation from 1,3,5-trithiacyclohexane[3] found in aqueous solutions is in accord with a three-center energy level picture, while the absorption of species XII is to be described by a six-center scheme.

From our experiments no information may, of course, be derived on the spacing of the multicenter energy levels which may well be not equidistant. A similar effect on energy level splitting by resonance interaction of, e.g., Π^* orbitals of a carbonyl group with symmetric benzene orbitals has recently been suggested by Christophorou[19] to explain negative ion resonance spectra.

The odd number of participating electrons ensures an overall binding effect, the magnitude of which, however, may be expected to decrease with increasing number of participating electrons. The latter could possibly explain the reduced lifetime of the 760-nm absorption band of the four-center species X relative to the 530-nm absorption band which is assigned to a two-center complex.

In summary our experiments have shown that stabilization of an oxidized sulfur center may occur by interaction with not only just one other sulfur atom but in a multicenter coordination complex as well. While intramolecular multicenter complexation seems to depend only on structural parameters and little on the nature of the solvent, intermolecular multicenter complexation appears to be facilitated by a low polarity environment.

Acknowledgment. This work was carried out during a visit by K.-D. Asmus to the National Research Council of Canada in Ottawa. The financial support received for this purpose from the NRC is gratefully acknowledged. The authors are also very grateful to Dr. Ch.-H. Fischer and Mrs. E. Darnstädt for help in the synthesis of several sulfur compounds, and D. Bahnemann for assistance in the measurement of the spectra of some intramolecular radical cations.

References and Notes

(1) D. Bahnemann and K.-D. Asmus, *J. Chem. Soc., Chem. Commun.*, 238 (1975).
(2) W. K. Musker and T. L. Wolford, *J. Am. Chem. Soc.*, **98**, 3055 (1976).
(3) K.-D. Asmus, D. Bahnemann, M. Bonifačić, and H. A. Gillis, *Faraday Discuss.*, **63**, 213 (1977).
(4) K.-D. Asmus, D. Bahnemann, Ch.-H. Fischer, and D. Veltwisch, submitted for publication.
(5) (a) B. C. Gilbert, J. P. Larkin, and R. O. C. Norman, *J. Chem. Soc., Perkin Trans. 2*, 272 (1973); (b) B. C. Gilbert, D. K. C. Hodgeman, and R. O. C. Norman, *ibid.*, 1748 (1972).
(6) M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2*, 1618 (1974).
(7) G. Meissner, A. Henglein, and G. Beck, *Z. Naturforsch. B*, **22**, 13 (1967).
(8) M. Bonifačić, H. Möckel, D. Bahnemann, and K.-D. Asmus, *J. Chem. Soc., Perkin Trans. 2*, 657 (1975).
(9) See any textbook on radiation chemistry.
(10) G. G. Teather, N. V. Klassen, and H. A. Gillis, *Int. J. Radiat. Phys. Chem.*, **8**, 477 (1976).
(11) T. K. Cooper, D. C. Walker, H. A. Gillis, and N. V. Klassen, *Can. J. Chem.*, **51**, 2195 (1973).
(12) See, for example: J. M. Warman, K.-D. Asmus, and R. H. Schuler, *Adv. Chem. Ser.*, **No. 82**, 25 (1968).
(13) A. Hummel and W. F. Schmidt, *Radiat. Res. Rev.*, **5**, 199 (1974).
(14) (a) I. A. Taub and H. A. Gillis, *J. Am. Chem. Soc.*, **91**, 6507 (1969); (b) H. A. Gillis, N. V. Klassen, G. G. Teather, and K. H. Lokan, *Chem. Phys. Lett.*, **10**, 481 (1971).
(15) K.-D. Asmus, H. A. Gillis, and G. G. Teather, unpublished results.
(16) M. H. Cohen, *Phys. Rev.*, **101**, 1432 (1956).
(17) W. Rosen and D. H. Busch, *J. Am. Chem. Soc.*, **91**, 4694 (1969).
(18) M. C. R. Symons, *Faraday Discuss.*, **No. 63**, 280–281 (1978).
(19) L. G. Christophorou, M. W. Grant, and D. G. McCorkle, *Adv. Chem. Phys.* **36**, 443 (1977); L. G. Christophorou, private communication.
(20) L. A. Ochrymowycz, C.-P. Mak, and J. D. Michna, *J. Org. Chem.*, **39**, 2079 (1974).

Structural Aspects of Solid Solutions of Enantiomers. The 3-Hydroxymethyl- and 3-Carboxy-2,2,5,5-tetramethylpyrrolidinyl 1-Oxyl Systems as Examples

Bernadette Chion, Janine Lajzerowicz,* Denise Bordeaux,

Laboratoire de Spectrométrie Physique, B.P. 53, 38041 Grenoble Cedex, France

André Collet, and Jean Jacques

Laboratoire de Chimie Organique des Hormones, Groupe de Recherche du CNRS No. 20, Collège de France, 75231 Paris Cedex 05, France *(Received July 26, 1978)*

Enantiomer mixtures of the title compounds 3 and 4 crystallize as solid solutions: a series of continuous solid solutions for 4 and limited solid solutions for 3. The synthesis of enantiomers, the melting point (phase) diagram of 3, solubility diagram of 4 in chloroform, and the crystal structure determination of the racemic solid solution of 4 and of the 40% *R*–60% *S* mixture of 3 are reported. These solid solutions are of static disorder type; cell parameters are close to those of enantiomers; space groups are either identical (3) or supergroup (4) of the enantiomer space groups. General criteria for the formation of solid solutions and special features for compounds 3 and 4, particularly the influence of hydrogen bonding networks, are discussed.

Most equimolecular mixtures of enantiomers, i.e., racemates, crystallize as racemic compounds, while relatively few (there are ca. 250 inventoried cases[1]) are conglomerates, i.e., cases which permit spontaneous resolution.

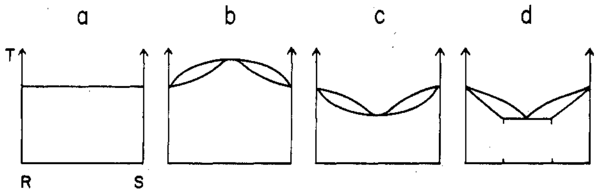
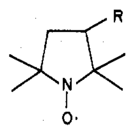


Figure 1. Roozeboom types of phase diagrams of enantiomeric systems forming solid solutions.

The formation of solid solutions of enantiomers is an even more uncommon phenomenon.[2] This work was undertaken with the aim of identifying some of the factors which may be associated with the occurrence of such solid solutions through an investigation of the crystal structures of several racemic and resolved compounds. This analysis is related to similar studies which attempt to explain the occurrence of spontaneous resolution.[3,4]

We have previously published the crystal structures of the enantiomeric and racemic forms of 1 and 2,[5,6] nitroxide free radicals related to 2,2,5,5-tetramethylpyrrolidinyl 1-oxyl. The racemic form of 1 crystallizes as a solid solution whereas racemic 2 is polymorphic and leads either to a conglomerate of *R* and *S* crystals or to a racemic compound. Two other compounds in the same series, 3 and 4, were studied in the work described in this paper. The crystal structures of the enantiomers of 3 and 4 have been determined.[7,8] It appears as a result of our observations that racemic 3 and 4 both crystallize as solid solutions.



1 R = OH

2 R = $CONH_2$

3 R = CH_2OH

4 R = CO_2H

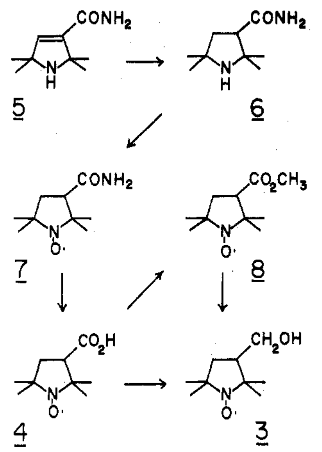
I. General Aspects of Solid Solution Formation between Enantiomers

Several categories of solid solutions can be characterized by way of (i) their phase diagrams and (ii) their crystallographic behavior. It should be emphasized that these two criteria are not necessarily related, in the sense that a given type of phase diagram does not always correspond to a given structural type. The form of the phase diagram enables one to distinguish the four situations[9] shown in Figure 1. Crystallography introduces another classification[5a] which is summarized as follows.

(1) Enantiomers in the solid state are miscible at all concentrations. Within a crystal containing x *R* molecules and $(1 - x)$ *S* molecules the probability of finding a *R* molecule on a given site is proportional to x, and the probability of finding a *S* molecule is proportional to $(1 - x)$. For a racemic composition, this probability is 1/2 and a statistical symmetry element may appear relating the *R* and the *S* molecular positions on the same site; then the space group of the solid solution is a supergroup of the space group of the enantiomer. A further consequence of this situation is the small variations of the cell parameters in the entire range of concentrations.

(2) Continuous miscibility concerns only a part of the crystallographic molecular sites. This possibility may occur when the enantiomer structure contains several independent sites (two, for instance). This situation might be regarded as a continuous solid solution of the enantiomer and the racemate with a disorder concerning only one site and leads, for the racemic composition, to an ordered compound (indistinguishable from an ordinary racemic compound). Categories (1) and (2) can correspond to the phase diagrams shown in Figure 1a–c.

Chart I



Miscibility may occur only in a limited range of concentrations; in the case of a racemic composition, this situation leads to an eutectic of solid solutions: coexistence of two enantiomorphic species of mixed crystals containing *R* and *S* molecules in, e.g., 60:40 and 40:60 ratios (Figure 1d).

In addition, it should be understood that short-range order may be observed in all cases with the exception of those exhibiting phase diagram shown in Figure 1a, and that the latter diagram (ideal solid solution with perfect disorder) may also, but not always, correspond to *plastic crystals*, i.e., solid solutions of enantiomers with both static and dynamic disorder (e.g., camphor).[2]

Relatively few examples of solid solutions of enantiomers are known and even fewer have been subjected to structural studies. Compound 1 is an example of category (1),[5a] as is 4-hydroxyimino-1,2,6,6-tetramethylpiperidinyl 1-oxyl;[10,19] category (2) is illustrated by the carvoxime system.[11]

II. Existence of a Solid Solution for 3 and 4

1. *Preparation of Racemic and Active Compounds.* The racemic forms of nitroxides 3 and 4 were prepared according to the sequence[12] shown in Chart I. Improved procedures were used for several steps. Thus, catalytic hydrogenation of unsaturated amide 5 was carried out without difficulty at room temperature and atmospheric pressure in the presence of palladium on charcoal (instead of Raney nickel at 180 atm). Reduction of ester 8 (obtained from 4 and diazomethane) by lithium aluminum hydride in ether (5 min, 20 °C) to give 3 was found more effective than the one-step reduction of 4 in THF.[12b] Racemic acid 4 was resolved via crystallization of its α-methylbenzylammonium salts[8a] as described in the Experimental Section. Optically pure *S*(−)-4 (mp 204 °C, $[\alpha]_{578}$ −85°) was converted into the crystalline alcohol *S*(−)-3 (mp 118.5 °C, $[\alpha]_{578}$ −136°) via the liquid ester *S*(−)-8 ($[\alpha]_{578}$ −75°). The $S(-)_{578}$ absolute configuration of 3 and 8 is based upon the known stereochemistry of starting compound 4.[8a]

2. *Crystallographic Results.* The similarity of the unit cells of crystals of an enantiomer of 4 and of racemic 4 (Experimental Section) leads to the supposition that the racemic crystal is a solid solution with the space group *Pnma* (supergroup of $P2_12_12_1$). On a site occupied by one molecule in the enantiomer structure, two possible molecular orientations are found in the solid solution structure. These orientations have a mirror image relationship with a probability of 1/2 for each and clearly correspond to *R* and *S* molecules.

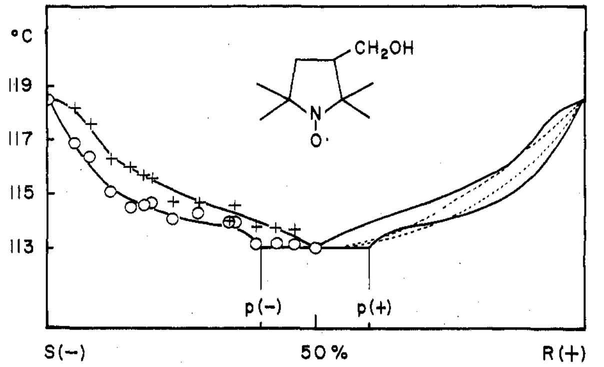


Figure 2. Binary diagram of mixture of (+)- and (−)-**3**: (---) calculated diagram for a series of continuous solid solutions;[13] (–) experimental diagram: O, beginning of melting (solidus); +, end of melting (liquidus).

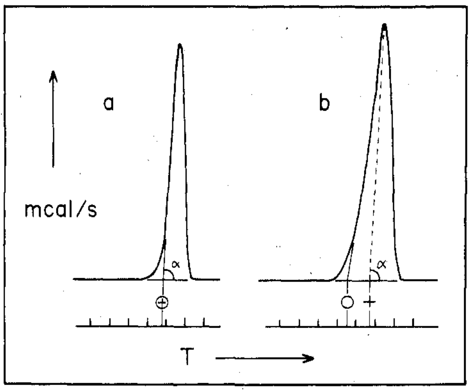


Figure 3. Melting curves of **3** registered via microcalorimetry; (a) pure enantiomer; (b) mixture of 60% optical purity; O, temperature of the beginning of melting; + temperature of the end of melting.

For the same crystallographic reasons, compound 3 is expected to be a solid solution. However, in this case, single crystals obtained from a solution of racemic composition are optically active. Crystals grow generally as twins (twinning plane (100)) which are easily cleaved under a polarizing microscope. Separated crystals exhibit opposite optical rotations of $[\alpha]_D \sim\pm 18°$ (ethanol), which shows that we are dealing with nonracemic mixed crystals with an approximate enantiomer ratio of 60:40 (section I). It implies also that the space group is $P2_1$ and not $P2_1/m$.

3. *Phase Diagrams.* We have confirmed the existence of these solid solutions by establishing the phase diagram for the binary mixtures of (+)- and (−)-3, and in the case of compound 4 which decomposes on melting, the solubility diagram (i.e., ternary phase diagram).

The binary diagram for mixtures of (+)- and (−)-3, established by differential microcalorimetry, is shown in Figure 2. Typical melting curves are shown in Figure 3. Owing to the small difference between the melting points of the racemate (mp = 113 °C) and of the pure enantiomers (mp = 118.5 °C), the examination of experimental points (O, beginning and +, end of melting) does not enable one to distinguish between a continuous series of solid solutions with minimum, and an eutectic mixture of partial solid solutions. The existence of single crystal having opposite optical rotations (as mentioned in the previous paragraph) demonstrates that the second hypothesis is the correct one. This type of diagram is very rare.

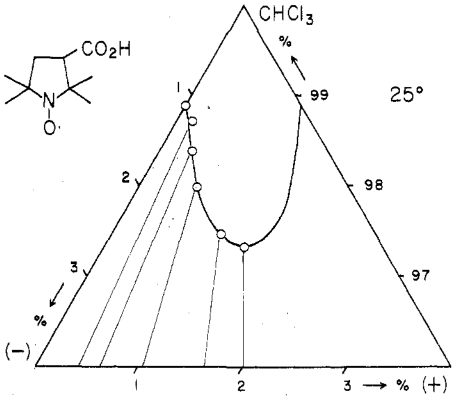


Figure 4. Solubility diagram of mixture of (+)- and (−)-**4** in chloroform (concentrations in g per 100 g of solution; 25 °C).

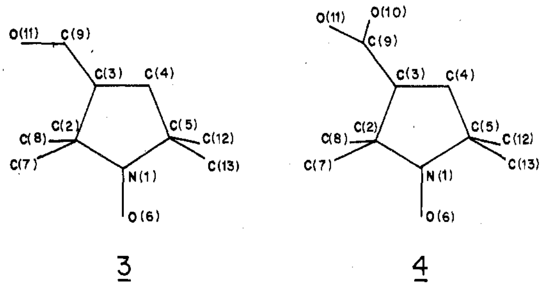


Figure 5. Projections of the molecules on the planes C(2)N(1)C(5).

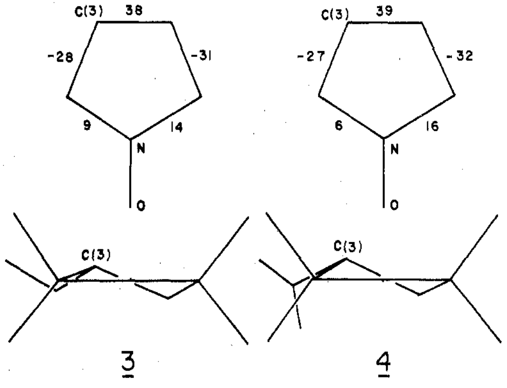


Figure 6. Conformations of the rings: projection on the plane C(2)N(1)C(5) (dihedral angles are shown) and on the plane perpendicular to N(1)O(6).

TABLE I: Circular Dichroism of $S(-)$-3 and $S(-)$-4 in Methanol

$S(-)$-3		$S(-)$-4	
λ, nm	Δε	λ, nm	Δε
205	+2.13	195	+0.93
245	−0.75	238	−0.69
421	−0.31	418	−0.39

The solubility diagram of mixtures of enantiomers of 4 in chloroform is shown in Figure 4. It is known that the ternary diagram is directly related to the binary diagram,[14] the construction of which is made difficult in the case of 4 because of the decomposition of the product close to its melting point (ca. 200 °C). The formation of a continuous series of solid solutions is characterized by the shape of the solubility curve and by the fact that the tie lines do not converge to any solid phase of definite composition.[14]

III. Comparison of the Enantiomer Structures

Crystallographic data for the enantiomers of 3 and 4 are given in ref 6 and 7.

1. *Conformations of the Rings. Circular Dichroism Data.* The rings have very similar conformations in the pyrrolidine nitroxides **1**–**4**[5-8] (Figure 5). They all exhibit a "half-chair" conformation as is shown in Figure 6 with the R group close to the mean plane of the cycle. This conformation is in agreement with the circular dichroism data of compounds $S(-)$-3 and $S(-)$-4 summarized in Table I. In both cases a positive Cotton effect (CE) is observed

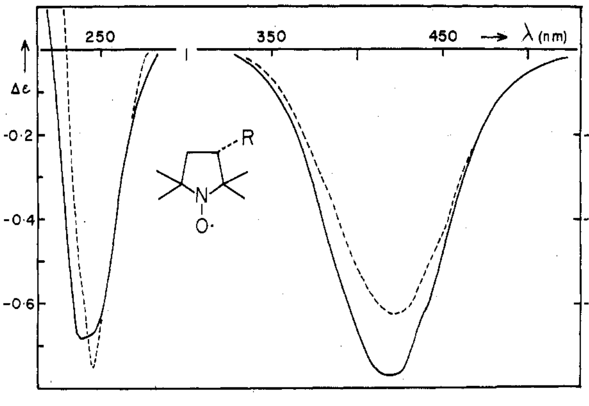


Figure 7. Circular dichroism of $S(-)$-**3** (---) and $S(-)$-**4** (—) in methanol between 220 and 500 nm (Dichrograph II, Roussel-Jouan).

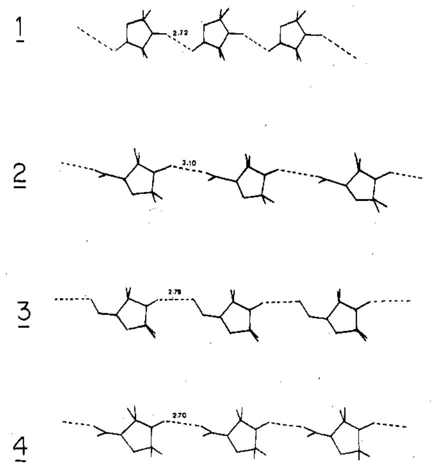


Figure 8. Chains of molecules linked by hydrogen bonding.

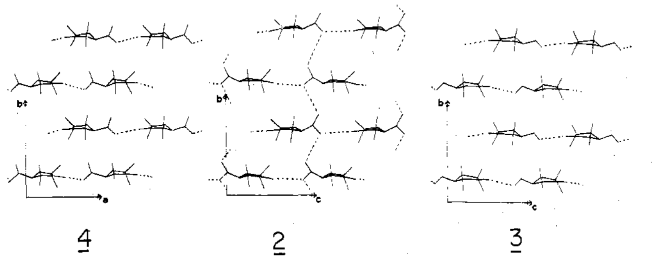


Figure 9. Analogous planes of molecules (stacking of Figure 8 chains).

at 195–205 nm, more intense in the case of **4** than for **3**, and two negative CE around 240 and 420 nm (Figure 7). The latter two bands can be attributed to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, respectively, of the nitroxide chromophore.[15] The same features previously described for **1** are observed.[5b] In all these compounds the negative CE at 420 nm is consistent with the octant rule[15] assuming a pyrrolidine ring in a half-chair conformation and with the R group in a quasi-equatorial position.

2. *Structural Analogies.* The main characteristic of all the crystal structures is the existence of intermolecular hydrogen bonding involving the NO and R groups and leading to similar molecular chains (Figure 8). A binary screw axis 2_1 perpendicular to the chain generates similar molecular planes for **2**–**4** (Figure 9) (in the case of **4** another type of intermolecular hydrogen bonding exists, linking molecules from different chains (Figure 9)). These planes repeated by a lattice translation give isomorphous monoclinic structures for **2** and **3** (for a better comparison a change of unit cell has been done for **2**[6]). For **4**, a 2_1 axis perpendicular to the planes leads to an orthorhombic lattice (Figure 10).

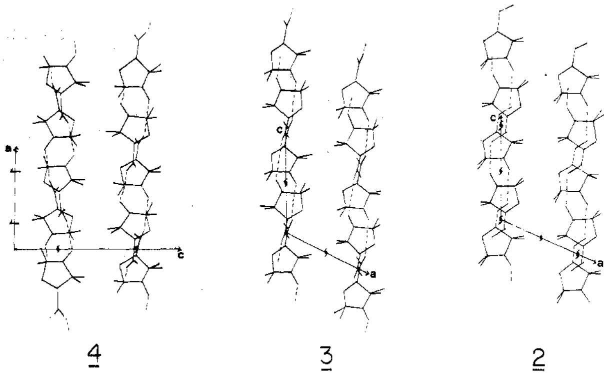


Figure 10. Views of the packing along the $\bar{b}$ axis (the planes of Figure 9 are perpendicular to this picture).

TABLE II: Atomic Coordinates (Å) Used for the Solid Solution Structure Determination (See Experimental Section)

	3			4		
	x	y	z	x	y	z
N(1)	0.00	0.00	0.00	0.00	0.00	0.00
C(2)	−0.78	1.28	−0.03	−0.76	1.28	−0.04
C(3)	−2.19	0.74	0.28	−2.16	0.73	0.33
C(4)	−2.21	−0.67	−0.33	−2.20	−0.66	−0.28
C(5)	−0.81	−1.23	−0.03	−0.80	−1.24	−0.04
C(6)	1.28	0.00	0.00	1.27	0.00	0.00
C(7)	−0.25	2.21	1.05	−0.21	2.24	0.98
C(8)	−0.61	1.86	−1.42	−0.64	1.85	−1.46
C(9)	−3.37	1.59	−0.23	−3.31	1.61	−0.12
O(10)				−3.93	1.45	−1.12
O(11)	−3.36	2.82	0.46	−3.52	2.63	0.66
C(12)	−0.31	−2.16	−1.16	−0.34	−2.13	−1.17
C(13)	−0.73	−1.91	1.33	−0.67	−1.95	1.30

IV. Structure of the Solid Solutions

The refinement of the coordinates of atomic sites in a solid solution is impossible because these sites are too close. A technique of rigid body refinement is used (ORION program[16]). The molecular model is that of the enantiomer structure; the position of the center of gravity and the orientation of the molecules are refined. Thermal parameters are also refined with a block technique using TLS tensors.

3. As has already been mentioned (section II.2), the crystals obtained from a racemic solution do not have a racemic composition. On the site occupied by one molecule in the enantiomer structure we now have two possible molecular orientations related by a mirror, but, the probabilities being 0.4–0.6 (hence not equal), there is not really a statistical mirror on this site. Therefore the space group remains $P2_1$ and not $P2_1/m$. Nevertheless the refinement was conducted with the $P2_1/m$ group ($P2_1$ with 0.4–0.6 probabilities does not improve the result). Table II gives the coordinates of the atoms in a system attached to the molecular group (Experimental Section). Table III gives the orientations and positions of the groups in the enantiomer and in the solid solution structures; they are very close. The van der Waals intermolecular contacts remain correct (the smallest is 3.42 Å for a C ↔ C contact).

4. The molecular model of the enantiomer structure did not give a good refinement and we had to slightly modify the orientation of the COOH group to improve the agreement. The angle between the COOH plane and the mean plane of the ring differs by 7° between the enantiomer structure and the solid solution structure. A problem appeared also with the oxygen atom of C=O. Refinements with TLS tensors including all the atoms did not work. This oxygen atom has a very large and very

TABLE III: Molecular Orientations θ (deg) and Positions u (Å) (See Experimental Section)

		θ_1	θ_2	θ_3	u_1	u_2	u_3
3	enantiomer	−87.4	−31.7	−179.5	0.951	0.233	0.339
	solid solution	−85.5 −94.5	−32.4 −32.4	178.9 −178.9	0.956 0.956	0.245 0.255	0.342 0.342
4	enantiomer	−92.6	−31.3	0.6	1.358	0.254	0.289[a]
	solid solution	−93.5 −86.5	−32.1 −32.1	1.9 −1.9	1.356 1.356	0.258 0.242	0.038 0.038

[a] There is a (001/4) translation between $P2_12_12_1$ and $Pnma$.

TABLE IV: Intermolecular Hydrogen-Bonding Geometry

		O(6)-O′(11), Å	N(1)-O(6)-O′(11), deg	O(6)-O′(11)-C′(9), deg
3	enantiomer	2.80	139.9	114.5
	solid solution	2.76 2.79	139.7 137.4	112.9 111.2
4	enantiomer	2.70	137.2	118.0
	solid solution	2.74 2.68	136.0 138.5	117.4 121.1

anisotropic thermal vibration in the enantiomer structure. The refinement went much better when we excluded this atom from the TLS group and assigned anisotropic thermal parameters to it. Table II gives the coordinates of the atoms in a system attached to the molecular group. Table III gives the orientation and position of the molecular group in the crystallographic cell for the enantiomer structure and the corresponding two positions and orientations for the solid solution. Once again they are very close. The smallest intermolecular contact is between an oxygen and a carbon atom (ca. 3.0 Å). It is significant that the hydrogen bonding schemes are not at all perturbed by the formation of the solid solutions in both **3** and **4** (Table IV).

V. Discussion

The reasons for which a mixture of enantiomers crystallizes in one form rather than another (racemic compound, conglomerate, or solid solution) are still difficult to understand. Several factors can influence the mode of crystallization: (a) the shape of the molecule and the relative importance of the volume of the chiral group with respect to the volume of the molecule; (b) intermolecular bonding; (c) the compacity of packing; (d) the symmetry of the crystal lattice.

1. *General Criteria for the Formation of Solid Solutions.* Solid solutions of enantiomers are a special case of solid solutions of molecules A and B and the arguments proposed by Kitaigordoskii concerning the possible existence of solid solutions can be applied to them.[17] Let us recall briefly that the necessary conditions for the formation of a series of continuous solid solutions are as follows: (a) the *isomorphism* of the crystal structures of the A and B compounds, i.e., very close cell parameters, identical space groups and Z, and similar molecular packing; (b) the *isosterism* of A and B molecules, i.e., a strong analogy of the shapes and volumes of molecules.

In the case of solid solutions of enantiomers, a difficulty appears immediately as a consequence of the contradiction between isomorphism and enantiomorphism; although the enantiomorphous crystalline structures are identical in distances and angles they are not superimposable. It is probably for this reason that these solid solutions are so rare. It remains for us to examine the conditions of isosterism of enantiomeric molecules. Here also isosterism and enantiomerism seem to be incompatible. One realizes that the relative importance of chirality in the geometry of enantiomeric molecules has a very important bearing on the possibility of interchanging enantiomers in a crystal. For a solid solution of molecules A and B, a degree of isosterism ϵ has been defined[17] by

$$\epsilon = 1 - V_{no}/V_o \qquad (1)$$

where V_o is the maximum overlapping volume of superimposed A and B molecules, and V_{no} is the corresponding nonoverlapping volume.

According to Kitaigorodskii no solid solution should be possible if ϵ is less than 0.8 (0.9 for an ideal solid solution). Another coefficient is also important: the packing coefficient C of the enantiomer structure defined by

$$C = vZ/V \qquad (2)$$

where v is the volume of the molecule and V the volume of the unit cell containing Z molecules.

We obtained the coefficient ϵ in two different ways: by the *calculation* of molecular volumes and overlapping volumes or by their *experimental evaluation* from the structures of enantiomers and solid solutions. The first method is that of Kitaigorodskii.[17] These calculations are difficult to carry out (how can one evaluate properly the overlapping volume without carrying out elaborate computations?). In the second method, a sphere has been assigned to each atom corresponding to its van der Waals radius. Volumes were evaluated by a graphical measurement of the surface of successive sections made every 0.5 Å through the molecule (or through the set of two molecules positioned on one site for the solid solution). The results are summarized in Table V.

With respect to the packing coefficient C we note that the lowest coefficient is that of **1** (ideal solid solution) and the highest is **3** (partial solid solution). In other words, the highest is the packing coefficient for the enantiomer

TABLE V: C and ϵ Coefficients

	mol vol, Å^3			V_{no}, Å^3		ϵ	
compd	calcd[a]	meas	packing coeff C[b]	calcd[c]	meas	calcd[c]	meas
1	161	167	0.72	23	51	0.85	0.64
3	176	189	0.76	55	50	0.63	0.69
4	178	187	0.74	52	56	0.66	0.65

[a] Method and data in ref 17 and 18. [b] Calculated from the measured molecular volume. [c] The nonoverlapping volume corresponds to (molecular volume − volume (R) + volume (H)).

structure, the most difficult to realize is the solid solution.

We find very similar values (~0.65) for the theoretical and the experimental ϵ coefficients except for **1**. For both compounds **3** and **4** the values are much smaller than the limit fixed by Kitaigorodskii for the existence of a solid solution (0.8). For **1**, the volume of the R group is smaller than for **3** and **4** and the theoretical value of ϵ is 0.8. Nonetheless, the experimental value obtained for **1** is similar to that for the two other compounds. We conclude that a value of 0.65 for ϵ is sufficient for the existence of a solid solution. In fact, for **1**, a solid solution is formed even with four possible molecular orientations on one site.

2. *Special Features of Solid Solution Formation for the Compounds Studied in This Work.* (a) We have found that for all the compounds (**1**, **3**, and **4**) which form solid solutions, the shape of the molecule in the crystal structure of the enantiomer almost has a symmetry plane (Figure 6).

(b) Hydrogen bonding plays a very important role in the crystal structure of compounds liable to form such bonding. If the formation of a solid solution is not compatible with the hydrogen bonding network existing in the enantiomer structure, the solid solution is not likely to exist. Such a situation is found for **2**. Although the enantiomer crystal structure of **2** is isomorphous with the structure of **3**, the racemic form of **2** is not a solid solution.[6] In this case, a solid solution could only form by breaking the hydrogen bonding which exists between chains (section III and Figure 9). On the other hand, if a solid solution can accomodate the hydrogen bonding scheme of the enantiomer structure, then their existence is likely to strongly influence the formation of a solid solution even if the steric conditions are not excellent (as in **1**, **3**, and **4**). In order to confirm this assertion, we intend to determine the crystal structures of chiral pyrrolidine nitroxide in which there are no possibilities of hydrogen bonding.

(c) Another question arises: why does **4** form a series of continuous solid solutions over the entire range of concentrations whereas **3** does not? Several explanations can be given. (i) The molecular conformation of **4** is more flexible and may change slightly to fit the available site, allowing the formation of mixed crystals (section IV). (ii) The space group $P2_12_12_1$ of **4** leads to the group *Pnma* for its solid solution, the latter being much more convenient from the packing point of view than is $P2_1/m$, the solid solution group expected for racemic **3**.

The existence of a solid solution for 4-hydroxyimino-2,2,6,6-tetramethylpiperidinyl 1-oxyl has been mentioned.[10,19] We note that in this case also the molecule almost has a symmetry plane and the solid solution disorder is compatible with a hydrogen bonding scheme.

Finally, a last characteristic of the solid solution of **4** must be mentioned. The diffuse reflections observed on the X-ray photographs shows that this solid solution is partially ordered. There is a short-range order within the (001) plane with an alternation of *R* and *S* molecules and no correlation between the planes. We intend to study this phenomenon further.

Experimental Section

2,2,5,5-Tetramethylpyrrolidine-3-carboxamide (**6**). Hydrogenation of 1 g of unsaturated amide **5**[12a] was carried out at room temperature and atmospheric pressure in the presence of 0.3 g of 5% palladium on charcoal and with 10 mL of ethanol as solvent. The absorption of H_2 was complete in ca. 1 h and the yield of pure **6**, mp 127 °C, was nearly quantitative (Lit.[12a] mp 128–129 °C).

Resolution of (±)-**4**. Racemic acid (±)-**4** (4.4 g) and 0.45 equiv (1.3 g) of (+)-α-methylbenzylamine ((+)-MBA) were mixed and dissolved in 70 mL of hot acetone. After ca. 1.5 h at 20 °C a first crop of 1.72 g of A1 crystals was collected. Evaporation to dryness of the mother liquor furnished mixture B1 (containing the impure more soluble salt and the unreacted acid) which was decomposed with a calculated amount of 0.5 N sodium hydroxyde. Extraction with methylene chloride afforded the amine; acidification of the aqueous solution (slight excess of 1.2 N HCl) followed by extraction with ether yielded 3.4 g of partially resolved (+)-**4**. This compound was combined with 1.3 g of (−)-MBA in 70 mL of acetone to give, after 2 h, 1.90 g of crystals C1 and the corresponding D1 from the mother liquor.

Mixture D1 was worked up like B1 and furnished 2.25 g of partially resolved (−)-**4**, which was treated with 0.8 g of (+)-MBA in 40 mL of acetone to give 1.22 g of crystals A2 and mixture B2.

Similar work up of B2 afforded 1.47 g of impure (+)-**4**, which was combined with 0.7 g of (−)-MBA to give 0.85 g of crystals C2.

The corresponding crops A1 + A2 were recrystallized from 80 mL of acetone to yield A3, 1.96 g.

Similar treatment of C1 + C2 afforded C3, 1.7 g.

The decomposition of A3 ($NaOH/CH_2Cl_2$ followed by HCl/ether) gave 1.13 g of (−)-**4**: mp 204 °C (decomp); $[\alpha]^{30}_{578}$ −85°, $[\alpha]^{30}_{546}$ −117°, $[\alpha]^{30}_{364}$ +384° (ethanol, c = 0.37). In the same way, decomposition of C3 yielded 0.96 g of (+)-**4**: $[\alpha]^{25}_{578}$ +83° (ethanol, c = 0.38).

(±)-*3-Hydroxymethyl-2,2,5,5-tetramethylpyrrolidinyl 1-Oxyl* (**3**). Esterification of racemic acid (±)-**4** with a slight excess of an ethereal solution of diazomethane afforded, after usual work up, 535 mg of the ester (±)-**8** as an orange-yellow oil, pure by TLC. This ester in 3 mL of ether was added dropwise, but rapidly, to a stirred suspension of lithium aluminum hydride (100 mg) in 3 mL of ether. After stirring for 5 min at room temperature hydrolysis was conducted at 0 °C with a limited amount of water until separation of alumina was complete. The yellow solution was dried (Na_2SO_4) and evaporated to dryness to yield 435 mg (95 %) of (±)-**3**. Subsequent crystallization from ether at −20 °C afforded 310 mg of pale yellow crystals, mp 113 °C.

S(−)-*3-Hydroxymethyl-2,2,5,5-tetramethylpyrrolydinyl 1-Oxyl* (**3**). The esterification of 705 mg of optically pure *S*(−)-**4** with diazomethane as described for the racemate furnished 665 mg of *S*(−)-**8**, orange-yellow oil, $[\alpha]^{25}_{578}$ −75° (ethanol, c = 0.7). Lithium aluminum hydride reduction of this ester (ether, 5 min, 20 °C) afforded 573 mg of a solid which was recrystallized from ether at −20 °C: yield 450 mg of *S*(−)-**3**, mp 118.5 °C, $[\alpha]^{25}_{578}$ −136°, $[\alpha]^{25}_{546}$ −180°, $[\alpha]^{25}_{364}$ +431° (ethanol, c = 0.55).

Binary Phase Diagram for (+)- *and* (−)-**3**. The mixtures required for the construction of the phase diagram where prepared from optically pure (−)-**3** and (±)-**3**, and weighed on a microbalance with a precision of 10^{-6} g. Each mixture consisted of ca. 10 mg overall. The melting curves (see Figure 3) were scanned on a Perkin-Elmer DSC 2 microcalorimeter. The samples (0.5–1 mg in sealed aluminum pans) were heated at a rate of 2.5 °C/min.

Solubility Diagram of (+)- *and* (−)-**4**. Mixtures of (+)- and (±)-**4** (ca. 100 mg total) and chloroform (ca. 2 g, analytical grade, stabilized with 0.5% ethanol) were placed in stoppered flasks and equilibrated for several days at 25 ± 0.1 °C with agitation (thermostatted bath). The compositions of the saturated solutions were determined by measurement of optical rotations of weighed aliquots. The tie lines, which indicate the composition of the solid phases in equilibrium with the saturated solutions, were obtained by the method of Schreinmakers.[14]

Crystallographic Data for **3** *and* **4**. **3**. The crystals of enantiomer are monoclinic[7] with a = 6.766 Å, b = 9.949 Å, c = 8.121 Å, β = 114.62°; space group $P2_1$, Z = 2. The crystals of racemate are monoclinic with a = 6.743 Å, b = 10.025 Å, c = 8.085 Å, β = 114.20°. The space group is either $P2_1$ or $P2_1/m$, Z = 2.

4. The crystals of enantiomer are orthorhombic[8b] with a = 8.089 Å, b = 10.097 Å, c = 12.404 Å; space group $P2_12_12_1$, Z = 4. The crystals of racemate are orthorhombic with a = 8.037 Å, b = 10.119 Å, c = 12.488 Å. The space group is either $Pnma$ or $Pna2_1$, Z = 4.

Refinement of the Solid Solution Structures.[20] The enantiomer molecular model is used. A coordinate system S is attached to the molecular group and defined as follows: origin N(1); Ox parallel to N(1)–O(6); Oy parallel to C(2)–C(5). The position of the group in the cell is given by the crystallographic coordinates $u_1u_2u_3$ of the origin of S and three orientation angles $\theta_1\theta_2\theta_3$. S being in coincidence with the cell system, a rotation of θ_1 around $\vec{a}$ then θ_2 around $\vec{b}$ and θ_3 around $\vec{c}$ lead S to its real orientation in the cell.

Intensity data were collected on the Siemens four-circle diffractometer of the Laüe-Langevin Institute (Grenoble). The final R value are for **3**: R = 0.10, R_w = 0.11 (700 intensities, 27 parameters, unit weights) and for **4**: R = 0.09, R_w = 0.09 (600 intensities, 36 parameters, unit weights).

References and Notes

(1) (a) Collet, A.; Brienne, M. J.; Jacques, J. *Bull. Soc. Chim. Fr.* **1972**, 127; (b) *ibid.* **1977**, 494; (c) Secor, R. M. *Chem. Rev.* **1963**, *63*, 297.

(2) A compilation of ca. 60 examples of solid solutions of enantiomers is being prepared for publication.

(3) Cesario, M.; Guilhem, J.; Pascard, C.; Collet, A.; Jacques, J. *Nouv. J. Chim.* **1978**, *2*, 343.

(4) Leiserowitz, L.; Weinstein, M. *Acta Crystallogr., Sect. B* **1975**, *31*, 1463.

(5) (a) Chion, B.; Lajzerowicz, J.; Collet, A.; Jacques, J. *Acta Crystallogr., Sect. B* **1976**, *32*, 339; (b) Collet, A.; Jacques, J.; Chion, B.; Lajzerowicz, J. *Tetrahedron* **1976**, *31*, 2243.

(6) Chion, B.; Lajzerowicz, J. *Acta Crystallogr., Sect. B* **1975**, *31*, 1430.

(7) Chion, B. *Cryst. Structure Commun.*, **1978**, *7*, 395.

(8) (a) Ament, S. S.; Wetherington, J. B.; Moncrieff, J. W.; Flohr, K.; Mochizuki, M.; Kaiser, E. T. *J. Am. Chem. Soc.* **1973**, *95*, 7896; (b) Wetherington, J. B.; Ament, S.; Moncrieff, J. W. *Acta Crystallogr., Sect. B* **1974**, *30*, 568.

(9) Roozeboom, H. B. W. *Z. Phys. Chem.* **1899**, *28*, 494.

(10) Bordeaux, D.; Lajzerowicz, J. *Acta Crystallogr., Sect. B*, **1977**, *33*, 1837.

(11) (a) Baert, F.; Fouret, R. *Cryst. Structure Commun.* **1974**, *4*, 307; (b) Kroon, J.; Van Gurp, P. R. E.; Onk, H. A.; Baert, F.; Fouret, R. *Acta Crystallogr., Sect. B* **1976**, *32*, 2561; (c) Oonk, H. A.; Kroon, J. *Ibid.* **1976**, *32*, 500.

(12) (a) Rozantzev, E. G. "Free Nitroxyl Radicals" (English translation); Plenum Press: New York, 1970; p 203; (b) Berliner, L. "Spin Labelling"; Academic Press: New York, 1976; p 183.

(13) The liquidus and solidus curves corresponding to a continuous solid solution (dotted line Figure 2) were calculated using the following data: enthalpy of fusion and melting point of the pure enantiomers, $\Delta H_A{}^f$ = 6.3 kcal mol^{-1}, $T_A{}^f$ = 391.5 K; melting point of the racemic form, $T_R{}^f$ = 386 K. Details on this calculation will be given in a later publication.

(14) Jacques, J.; Gabard, J. *Bull. Soc. Chim. Fr.* **1972**, 342.

(15) Ramasseul, R.; Rassat, A.; Rey, P. *Tetrahedron*, **1974**, *30*, 265.

(16) Andre, D.; Fourme, R.; Renaud, M. *Acta Crystallogr., Sect. B* **1971**, *27*, 2371.

(17) Kitaigorodskii, A. I. "Organic Chemical Crystallography", Consultant Bureau, New York, *1961*, p. 230.

(18) Bondi, A. "Physical Properties of Molecular Crystals, Liquids and Glasses"; Wiley: New York, 1968; p 453.

(19) The crystals of this solid solution contain equimolecular populations of right- and left-handed *conformations* of the molecule; a fast *conformational exchange in solution precludes the actual resolution* of this compound.

(20) Lists of intensity data, hydrogen coordinates, and thermal parameters are available on request.

Calculation of Activities in the System $KO_{0.5}$–$AlO_{1.5}$–SiO_2

Isaac Eliezer,* Naomi Eliezer, Reed A. Howald, and Mary C. Verwolf

Department of Chemistry, Montana State University, Bozeman, Montana 59715 (Received April 10, 1978)

Publication costs assisted by the U.S. Department of Energy

The vapor pressure of potassium has been measured as a function of temperature in the $AlO_{1.5}$- and SiO_2-rich regions of the $KO_{0.5}$–$AlO_{1.5}$–SiO_2 system. Combining this data with the known solubility relations in the system and mathematical analyses of activities in the binary subsystems leads to calculated activities for all three species as a function of temperature and composition for liquids in the system $KO_{0.5}$–$AlO_{1.5}$–SiO_2. These calculations provide refinements in the phase diagram and in the thermodynamic properties of $K_2Si_4O_9$, $KAlO_2$, sanidine, leucite, and $KAlSiO_4$.

Introduction

A ternary system can be analyzed thermodynamically if the activity of one component can be measured over the full range of compositions. We have measured potassium pressures over SiO_2-rich liquids in the $KO_{0.5}$–$AlO_{1.5}$–SiO_2 system using atomic absorption measurements of the vapor diffusing from a sample cell. The technique and apparatus are described in an earlier paper on the $KO_{0.5}$–SiO_2 binary system.[1] However no single technique can provide accurate vapor pressure measurements over the range of pressures covered in this ternary system at a single temperature, or over the whole range of temperatures required by the high melting points of leucite, $KAlSiO_4$, $KAlO_2$, corundum, and mullite. Our vapor pressure measurements over systems of three coexisting solids in the high $AlO_{1.5}$ region of the phase diagram have confirmed the stability[2] of the leucite–corundum–orthorhombic $KAlSiO_4$ set of three solids, which shows an activity of $10^{-5.92}$ for liquid $KO_{0.5}$ at 1700 K. Shairer and Bowen[2] have found that this set of three solids is in equilibrium with the liquid ternary of composition $X_{KO_{0.5}}$ = 0.2514, $X_{AlO_{1.5}}$ = 0.3303 at 1826 K, at which point the three liquid activities are calculated to be $a_{KO_{0.5}} = 10^{-5.46}$, $a_{AlO_{1.5}}$ = 0.522, and a_{SiO_2} = 0.360. It is thus possible to obtain all three activities at temperatures and compositions for the liquid where it is in equilibrium with three solids, and the thermodynamic analysis of the liquid should include this data.

We have analyzed the liquids in the binary subsystems $KO_{0.5}$–SiO_2,[1] $KO_{0.5}$–$AlO_{1.5}$,[3] and $AlO_{1.5}$–SiO_2[4] using the Redlich–Kister power series with terms through the fourth

0022-3654/78/2082-2688$01.00/0