

- (10) Wilson, J. M.; Bayer, R.; Hupe, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 7922.
 (11) Freter, R.; Pohl, E. R.; Wilson, J. M.; Hupe, D. J. *J. Org. Chem.* **1979**, *44*, 1771.
 (12) Stevens, W.; van Es, A. *Recl. Trav. Chim. Pays-Bas* **1964**, *83*, 1294.
 (13) Bax, P.C.; Stevens, W. *Recl. Trav. Chim. Pays-Bas* **1970**, *89*, 265.
 (14) Ellman, G. L. *Arch. Biochem. Biophys.* **1959**, *82*, 70.
 (15) Susi, H.; Zell, T. *Spectrochim. Acta* **1963**, *19*, 1933.
 (16) Pinchas, S.; Lailicht, I. "Infrared Spectra of Labeled Compounds"; Academic Press: New York, 1971; p 132.
 (17) Senatore, L.; Ciuffarin, E.; Fava, A.; Levita, G. *J. Am. Chem. Soc.* **1973**, *95*, 2918.
 (18) Streitwieser, A., Jr.; Jagow, R. H.; Fahey, R. C.; Suzuki, S. *J. Am. Chem. Soc.* **1958**, *80*, 2326.
 (19) Wladislaw, B.; Olivato, P. R.; Sala, O. *J. Chem. Soc. B* **1971**, 2037.
 (20) Knier, B. L.; Jencks, W. P., personal communication.

Chiral Secondary Amides. 2. Molecular Packing and Chiral Recognition

S. Weinstein,* L. Leiserowitz,* and E. Gil-av*

Contribution from the Departments of Organic Chemistry and Structural Chemistry, The Weizmann Institute of Science, Rehovot, Israel. Received June 25, 1979

Abstract: A molecular model which accounts for stereoselective interactions within the series of chiral secondary amides $RCONHCH(CH_3)Ar$ is proposed. It assumes that a guest molecule intercalates between two host molecules in their 5-Å translation H-bonded array to form diastereomeric arrangements for the two enantiomers, differing in stability. The model explains various aspects of chiral recognition: (1) the gas chromatographic separation of enantiomers achieved with *N*-acyl- α -arylethylamines as chiral phases; (2) the difference in solubility of (*R*)- and (*S*)-*N*-trifluoroacetyl- α -(1-naphthyl)ethylamine in solid (*R*)-*N*-lauroyl- α -(1-naphthyl)ethylamine. The packing arrangement of certain diamide molecules was examined in order to reinforce the assumptions on which the explanation of the stereoselective effects was based. Energy computations support the stability relationships which follow from the model.

I. Introduction

The interactions between chiral secondary amides $RCONHCH(CH_3)Ar$ were analyzed in terms of their molecular packing in both the solid and the liquid states in part I.¹ The analyses demonstrated a preference for the formation of stacks in which the molecules are hydrogen bonded along a 5-Å translation axis (Figure 1). The detailed geometry and contacts in this packing motif were revealed by several crystal-structure determinations.¹ The 5-Å translation mode fulfills the requirements for linear hydrogen bonds and for close packing between the aromatic residues whose planes are separated by 3.4 Å. It also generates favorable contacts between the R groups, especially for long hydrocarbon chains. The high stability of this packing mode is further manifested by its retention in the melt.¹

The compounds in this series, when serving as chiral stationary phases in gas-liquid chromatography, separate optical isomers.² Resolution is particularly good when the optical isomers are of the same type ($RCONHCH(CH_3)Ar$) as the chiral phase, with higher retention times for the enantiomer of the same absolute configuration as that of the stationary phase.

It is our purpose to explain on a molecular level the GLC resolutions, as well as other phenomena involving chiral recognition which were found to occur with these amides. The spatial arrangement of the molecules and the contacts between atoms, as observed in the crystal structures, are used to describe the diastereomeric association complexes assumed to be responsible for stereoselectivity.

This approach has been adopted previously. Crystal structure data have been used successfully by Yoneda and co-workers³ to interpret the resolution of racemic metal-coordination compounds by sodium *d*-tartrate solutions. The crystal structures⁴ of the host-guest complexes formed by crown ethers, synthesized by Cram and co-workers,⁵ have been determined to examine the host-guest geometry so as to account for observed stereoselectivity.

II. Molecular Model of Chiral Recognition

Having demonstrated the stability of the 5-Å translation array in the chiral amides $RCONHCH(CH_3)Ar$, both in the solid and in the melt,¹ we now propose a model which will account for the discrimination in the interactions of these amides with pairs of enantiomers. It is based on the 5-Å translation H-bonding motif, as found in the crystal, and assumes that a guest molecule intercalates within the H-bonded array of the host matrix. The intercalated enantiomers lead to two diastereomeric arrangements, the different stabilities of which account for the stereoselectivity. Within each arrangement, the molecules implement their potential for optimal contacts.

The intercalation model is presented for the particular case of (*R*)-*N*-lauroyl- α -(1-naphthyl)ethylamine (host) and *N*-trifluoroacetyl- α -phenylethylamine (guest). It is seen (Figure 2a) that the guest molecule with a configuration identical with that of the host intercalates in a manner such that the original motif of H bonding is preserved, the aromatic groups make plane-to-plane contacts, and the hydrogen atom linked to the chiral atom of the guest is wedged between two aromatic rings as in the original stack. The methyl group, linked to the chiral carbon atom of the guest, points away from the stack and does not participate in any intrastack contacts. Let us now consider the insertion of a guest molecule of configuration opposite to that of the host while maintaining the host structure, H bonds, and aromatic overlap between host and guest (Figure 2b). This would demand that the methyl group and the hydrogen atom linked to the chiral carbon atom of the guest be interchanged. The methyl group, thus wedged between two naphthyl planes, would lead to severe overcrowding. Another argument against the likelihood of this structure is based on conformational stabilities. The most stable conformation of the isolated molecule according to energy calculations—and also observed in the crystalline state—corresponds to $\phi = 135^\circ$ and $\psi = 109^\circ$ (see Figure 1).⁶ Interchange of the hydrogen atom and methyl group would lead to a conformation in which $\phi = -135^\circ$ and $\psi = -109^\circ$, which is distinctly less stable by about 12 kcal/mol

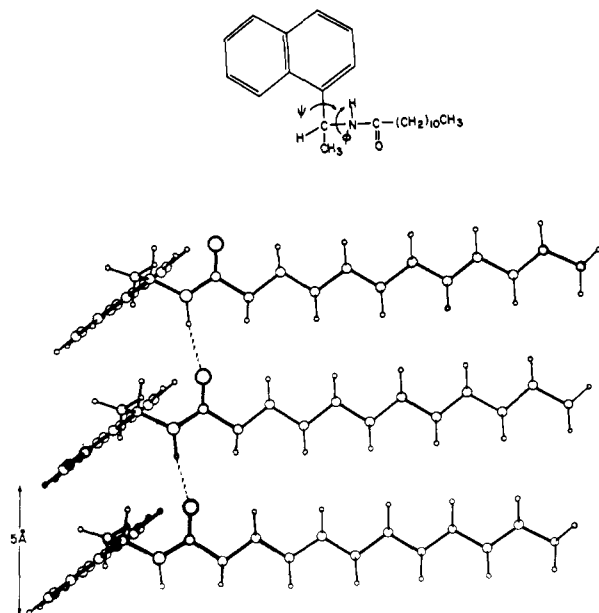


Figure 1. H bonding along a 5-Å translation axis of (*R*)-*N*-lauroyl- α -(1-naphthyl)ethylamine.

according to our calculation.¹

III. Chiral Recognition and the Intercalation Model

In the ensuing sections we interpret chiral recognition in both the solid and liquid states with the help of the proposed model. We shall also describe some systems designed to check the validity of the assumptions on which the model was based.

A. Stereoselectivity in Solid-Solution. The formation of solid-solutions indicates that a guest molecule may pack within the solid matrix of the host without causing major changes in the packing arrangement. The relative fit of two different guest molecules within the host structure should be commensurate with the extent of solid-solution formation.⁷ Thus, the difference in solubility of two enantiomers in a given solid chiral component was taken to be a measure of chiral recognition. The phase diagrams of two diastereomerically related systems were determined.⁸ The solvent in both was (*R*)-*N*-lauroyl- α -(1-naphthyl)ethylamine; the solutes were respectively (*R*)-*N*-trifluoroacetyl- α -(1-naphthyl)ethylamine (*R*-*R'* system) and its enantiomer (*R*-*S'* system).⁹ The results are shown in Figure 3. Solute concentration reached a maximum of 11% in the *R*-*R'* as compared with 5% in the *R*-*S'* system. This observation is indicative of a better fit between solute and solvent of the same configuration, in accord with the model.

B. Packing Arrangements of Secondary Diamides as Probes for the Model. The details of packing of the host and guest molecules in the solid solutions discussed above are not easily determined by X-ray diffraction, because of the low solute concentrations. In order to be able to examine the relative stabilities of intercalated *R* and *S* guest molecules in the host matrix, we synthesized the diamide model compounds (**1**) with two chiral moieties CONHCH(CH₃)Ar (Ar = α -naphthyl), identical with those in the monoamides RCONHCH(CH₃)Ar for which the model has been proposed. The study of the molecular packing of the meso *RS* diamide (**1a**) and the chiral *RR* diamide (**1b**) permitted us to characterize the differences in intermolecular interactions due to the alteration in configuration, in a manner analogous to what was done for the monoamides.¹

The *RS* molecule (**1a**) in its crystal ($a = 11.3 \text{ \AA}$, $b = 5.2 \text{ \AA}$, $c = 23.6 \text{ \AA}$, $\beta = 94^\circ$, $Z = 2$, $P2_1/c$, $d_c = 1.25 \text{ g cm}^{-3}$) lies on a center of inversion, and forms H bonds between amide groups and plane-to-plane contacts between naphthyl groups along

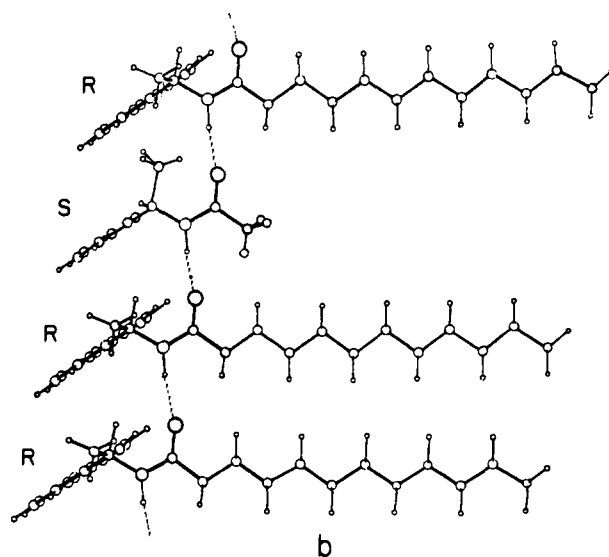
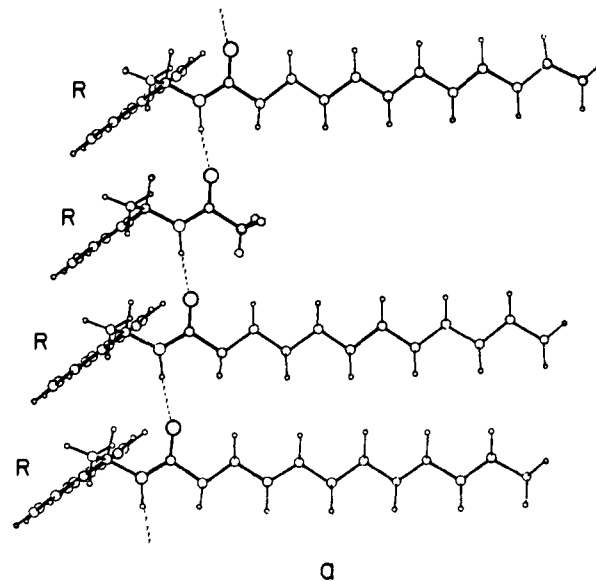
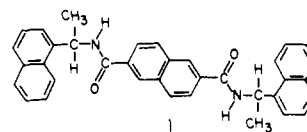


Figure 2. A chiral guest molecule *N*-trifluoroacetyl- α -phenylethylamine inserted into the H-bonded stack of (*R*)-*N*-lauroyl- α -(1-naphthyl)ethylamine: (a) guest of *R* configuration; (b) guest of *S* configuration.



a. *RS* diamide

b. *RR* diamide

the 5.2-Å axis (Figure 4). The 5-Å translation packing requires, because of steric hindrance between the central naphthyl groups, a pronounced deviation from coplanarity¹⁰ of the two amide groups and central naphthyl group in the molecule, leading to a loss in resonance energy. The high stability of the 5-Å translation motif, however, compensates for the loss in resonance energy. In contradistinction, the *RR* molecules (**1b**) do not form the 5-Å translation motif. Rather they crystallize in a tetragonal arrangement ($a = b = 11.8 \text{ \AA}$, $c = 19.9 \text{ \AA}$, $Z = 4$, $P4_12_12$, $d_c = 1.25 \text{ g cm}^{-3}$). A twofold axis which is parallel to the diagonal $a + b$ passes through the molecular center perpendicular to the central naphthyl plane (Figure 5). The amide groups form H bonds about the a_1 axis of length 20 Å, which requires each amide group to lie close to a a_1 axis.¹¹

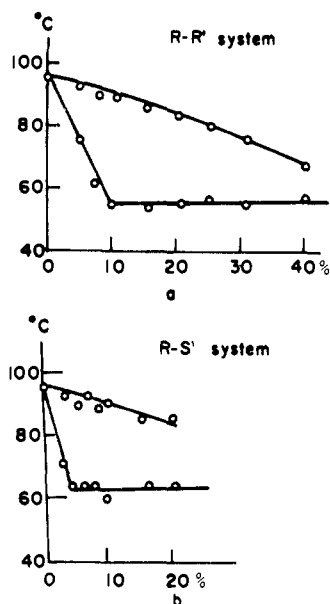


Figure 3. Phase diagrams of (*R*)-*N*-lauroyl- α -(1-naphthyl)ethylamine with *R'* and *S'* solutes of *N*-trifluoroacetyl- α -(1-naphthyl)ethylamine: (a) *R'* solute; (b) *S'* solute.

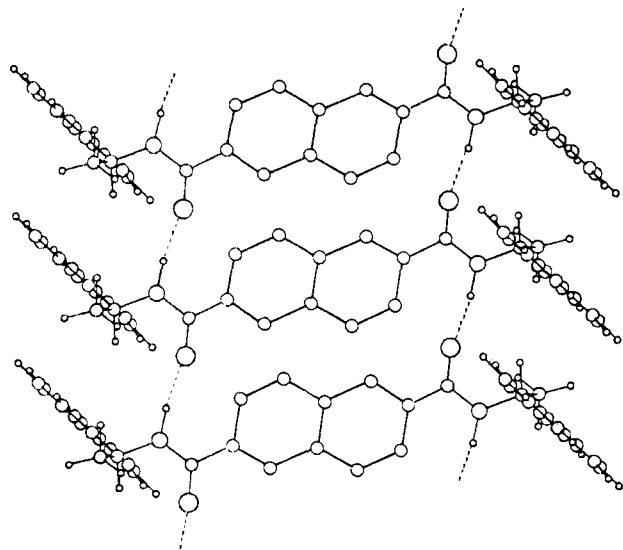


Figure 4. Postulated H-bonding arrangement of the *RS* diamide (**1a**) viewed perpendicular to the amide planes.

It is observed almost without exception that centrosymmetric molecules pack in centrosymmetric crystal structures in which the molecular and lattice centers of inversion coincide.¹² Indeed the centrosymmetric meso compound (**1a**) behaves accordingly. The *RR* molecule (**1b**) could pack almost isomorphously with the *RS* molecule (**1a**) were the *RR* crystal structure derived from that of the *RS* structure by the interchange of the hydrogen atom and methyl group on one chiral carbon atom. This would result in a 5-Å translation packing in which, at the unmodified end of the molecule, the hydrogen linked to the asymmetric carbon atom would be wedged between two naphthalene rings, whereas at the modified end the methyl group would be so wedged, thus leading to pronounced steric hindrance. This speculative molecular packing contains in one stack the essential elements of both diastereomeric arrangements of the intercalation mode (Figure 2). The fact that this packing arrangement has not been found is in accord with the lesser stability of the hydrogen-bonded stack with a guest molecule of opposite configuration.

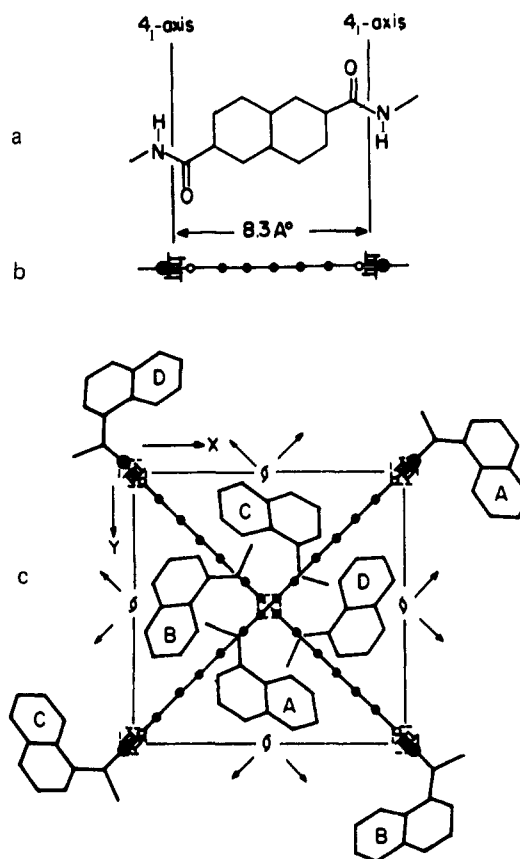


Figure 5. Postulated H-bonding arrangement of the *RR* diamide (**1b**). (a) The molecule is viewed along the molecular twofold axis perpendicular to the central naphthyl plane. (b) Projection of the molecule onto the *ab* plane. The central naphthyl ring is seen edge on. The 4₁ axes are shown. (c) The structure is viewed along the H-bonding 4₁ axis. The two outer naphthyl rings belonging to the same molecule are labeled with the same letter. (○) O and C (amide) eclipsed; (●) N; (◐) O, C (amide), and N of a neighboring molecule eclipsed (◑) C; (---) H bonds.

These findings support the conclusions as to the relative stabilities indicated by the intercalation model.

C. Resolutions by Gas-Liquid Chromatography. Having demonstrated the existence of short-range order involving the 5-Å translation packing in the melt,¹ application of the intercalation model to the liquid state is valid. The model explains the separation of pairs of enantiomers observed in our gas-chromatographic experiments, conducted with (*R*)-*N*-lauroyl- α -(1-naphthyl)ethylamine as the chiral liquid phase.^{2,13}

(i) The order of emergence of the enantiomers from the chromatographic column is the same for all the *N*-acyl- α -arylethylamines studied. The isomers with the same configuration as the stationary phases (termed "solvent") have the longer retention times, indicating stronger interaction between molecules of the same configuration, in accord with the model.

(ii) Substituting a phenyl by 1-naphthyl in the molecules undergoing separation (termed "solutes") improves the resolution appreciably.¹³ This observation can be ascribed to greater overlap between the aromatic groups of solute and solvent, when both have naphthyl rings as compared with phenyl-naphthyl overlap, when the aromatic group of the solute is a phenyl. Substituting a trifluoroacetyl by the large pivaloyl group, as the acyl moiety in the solute, results in a pronounced improvement in resolution.¹³ This could be due to better contacts of a *tert*-butyl than of a trifluoromethyl group with the acyl chains of the solvent. These results are compatible with the requirement of the model for optimum aromatic overlap and contacts between the acyl groups in the

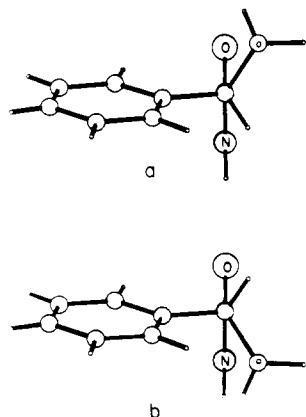


Figure 6. Molecular conformations of α -phenylpropionic acid *tert*-butylamide in the intercalation model. The Newman projection is viewed along the C(amide)–C(chiral) bond. For clarity, the *tert*-butyl group has not been drawn. (a) S' guest molecule. (b) R' guest molecule.

intercalation of the solute within the stack. Enhancement of these interactions lends more weight to the type of association assumed to be responsible for stereoselectivity.

Substituting a phenyl by a cyclohexyl group in the solute to give *N*-acyl- α -cyclohexylethylamine results in reduced resolution,² which may be explained as follows. The cell constants of *S*-trifluoroacetyl- α -cyclohexylethylamine ($a = 14.4 \text{ \AA}$, $b = 16.3 \text{ \AA}$, $c = 5.0 \text{ \AA}$, $\beta = 94^\circ$, $P2_1$, $Z = 4$, $d_c = 1.25 \text{ g cm}^{-3}$) reveal the 5- \AA translation H-bonding mode. This fact justifies the assumption that the cyclohexyl derivative can also intercalate between the host molecules. The effective thickness of the cyclohexyl group is, however, larger than that of the phenyl. Hence, the distance between the plane of the naphthyl ring and the mean plane through the cyclohexyl ring must be larger than the distance of 3.4 \AA between the naphthyl and phenyl rings. Thus, when intercalating the cyclohexyl derivatives of opposite configuration to that of the host, there is less difficulty, relative to the phenyl analogue, to accommodate the methyl group of the asymmetric carbon. It follows that differentiation between the two intercalated enantiomers of the cyclohexyl derivative is less pronounced. This description is in agreement with the experimental facts, i.e., the same order of emergence for the enantiomers of the phenyl and cyclohexyl analogues, but reduced resolution for the latter.

(iii) Another significant observation is that the secondary amide chiral phases resolve α -phenylalkanoic acid amides,² $\text{RC}^*\text{H}(\text{C}_6\text{H}_5)\text{CONHR}'$ ($\text{R} = \text{CH}_3, \text{C}_2\text{H}_5$) with a reversal of the order of emergence in comparison with the *N*-acyl- α -arylethylamines, $\text{ArC}^*\text{H}(\text{CH}_3)\text{NHCOR}$. This indicates a stronger interaction between host and guest of opposite configuration. Satisfactory interpretation of this behavior is an appropriate test for the validity and scope of the model. In the α -phenylalkanoic acid amides the asymmetric atom is attached to the carbonyl, whereas in the *N*-acyl- α -arylethylamines it is linked to the NH group. The required host–guest interactions can only be achieved by inserting the guest amide group anti-parallel to those of the host, and choosing the conformation of the guest $\text{CH}(\text{CH}_3)\text{C}_6\text{H}_5$ moiety such that the phenyl plane is parallel to the naphthyl planes.

The molecular conformation of the guest was derived using the atomic coordinates from the crystal structure of *N*-*tert*-butyl- α -phenylpropionic acid amide, determined experimentally.¹⁴ In order to obtain a suitable conformation for intercalation, the torsion angles about the C(amide)–C(chiral) and C(chiral)–C(phenyl) bonds had to be adjusted as depicted in Figure 6 for the S' and R' guest molecules. As seen in Figure 6, the R' molecule is derived from S' by an interchange of the hydrogen atom and the methyl group linked to the chiral carbon atom. The conformation of this S' molecule is as stable as

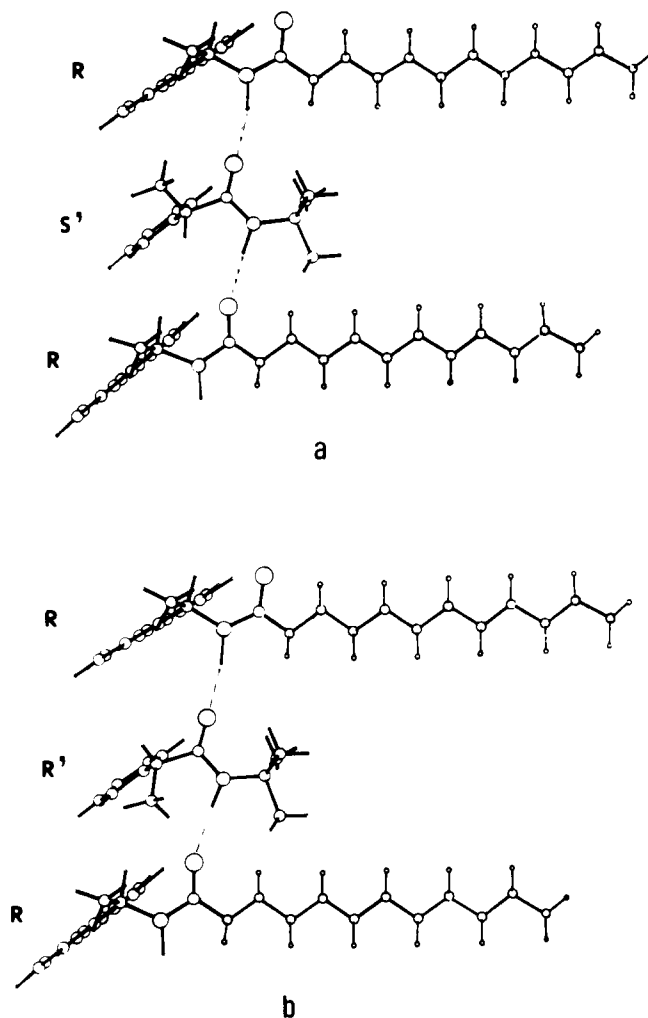


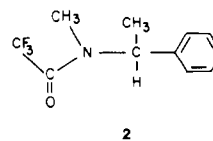
Figure 7. A molecule of α -phenylpropionic acid *tert*-butylamide, of configuration S or R (labeled S' and R'), inserted into the H-bonded stack of (R)-*N*-lauroyl- α -(1-naphthyl)ethylamine: (a) $RS'R$; (b) $RR'R$.

that found in the crystal, and is certainly more stable than that of the R' molecule, since the latter contains too short a distance between the NH group and the methyl linked to the chiral center.

The resulting diastereomeric arrangements $RS'R$ and $RR'R$ are shown in Figure 7. Both structures show nearly linear N–H...O bonds and almost parallel aromatic groups separated by $\sim 3.4 \text{ \AA}$. $RS'R$ exhibits favorable contacts, whereas in the other diastereomeric structure $RR'R$ the methyl group bonded to the chiral carbon atom of the guest approaches the host oxygen atom too closely (2.5 \AA).

These considerations explain the chromatographic results and also increase the confidence in the validity of the model.

(iv) The resolution factor is very low¹³ for the tertiary amide *N*-trifluoroacetyl-*N*-methyl- α -phenylethylamine, $\text{CF}_3\text{CON}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{C}_6\text{H}_5$ (**2**), on the secondary amide



phases. The same is true for resolution of secondary amides on the tertiary amide phase *N*-lauroyl-*N*-methyl- α -(1-naphthyl)ethylamine.¹³ Since in these two cases only one N–H...O bond is possible between host and guest, the complete hydrogen-bonded array cannot be formed. Consequently, the

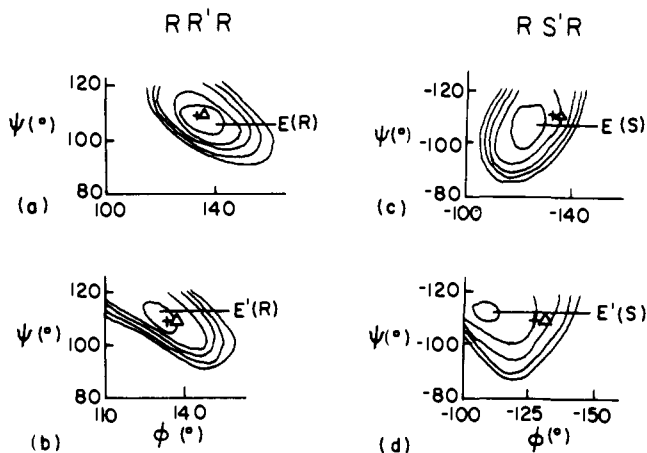


Figure 8. Variation in energy of the two diastereomeric trimers $RR'R$ and $RS'R$ formed between host (R) and guest (R' or S') molecules as a function of the conformation of the guest. To obtain the conformation of S' which is the mirror image of R' , the ϕ and ψ angles of the latter are reversed in sign. (a and c) Inter- + intramolecular energy variation. (b and d) Intermolecular energy variation. The symbols Δ and $+$ indicate the ϕ and ψ values in the chiral crystals N -trifluoroacetyl- and N -acetyl- α -(1-naphthyl)ethylamine, respectively. Contour interval is 2 kcal/mol. Lowest energy values are indicated by $E'(R)$, $E'(R)$, $E(S)$, $E'(S)$ where $E(S) = E(R) + 12$ kcal/mol, $E'(S) = E'(R) + 9$ kcal/mol.

constraints imposed by intercalation, as required by the model, are reduced, compatible with the low resolution observed.

D. Analysis of the Intercalation Model by Energy Computations. Energy computations on the intercalation model were performed on ensembles of N -acetyl- α -(1-naphthyl)ethylamine molecules. Torsional and van der Waals nonbonded energy terms, using pairwise atom-atom potentials, were computed by the QCFF/PI program.¹⁵ It was assumed that intercalation of the guest molecule within the host array does not change the host structure. Therefore, only the energy difference between one guest molecule and its two flanking host molecules in the two diastereomeric arrangements needs to be considered. The crystallographic data of (R)- N -acetyl- α -(1-naphthyl)ethylamine¹ were used to construct the model from three molecules related by 5-Å translation and in which the central molecule represents the guest. The guest was given a configuration either identical with, resulting in the trimer $RR'R$, or opposite to, $RS'R$, that of the two host molecules.⁹ The amide groups were kept fixed throughout all operations, while the conformation of the guest molecule was changed by varying ϕ and ψ (ref 6) in steps of 10° and the energy of each resulting structure was calculated.¹⁶

The energy map for the system $RR'R$ (Figures 8a,b) displays a minimum which includes the trimer in which the conformation of the guest molecule (R'_{\min}) is identical with that of the host molecule, namely, the three molecules are related by translation.

The energy analysis for the system $RS'R$ (Figures 8c,d) shows that in the trimer of lowest energy the conformation of S' (S'_{\min}) is similar to the conformation of R'_{\min} since their

corresponding ϕ and ψ torsion angles are approximately equal in magnitude and opposite in sign. The intercalated S'_{\min} and R'_{\min} molecules in these two trimers are close to being related by a mirror plane which coincides with the amide group. The $RS'_{\min}R$ structure does not contain aromatic overlap between guest and host; rather, the methyl group of the guest is positioned between two naphthyl rings, whereas its naphthyl group is placed in between methyls. If aromatic overlap is imposed as discussed in section II for the intercalation model, the resulting structure is even less stable than $RS'_{\min}R$ according to the calculation.

The pertinent result of the energy analysis (Figure 8) is that the $RR'R$ trimer of minimum energy is appreciably more stable than any $RS'R$ trimer,¹⁷ in keeping with the observations of stereoselectivity reported here.

Acknowledgments. The authors are indebted to Hue-Cheng Chang for assistance with the measurement of the X-ray data. Thanks are due to the Stiftung Volkswagenwerk for partial support of the research.

References and Notes

- (1) S. Weinstein and L. Leiserowitz, *Acta Crystallogr., Sect. B*, in press.
- (2) S. Weinstein, B. Feilbush, and E. Gil-Av, *J. Chromatogr.*, **126**, 97 (1975).
- (3) Y. Kushi, M. Kuramoto, and H. Yoneda, *Chem. Lett.*, 339 (1976).
- (4) I. Goldberg, *J. Am. Chem. Soc.*, **99**, 6049 (1977).
- (5) E. P. Kyba, K. Koga, L. E. Sousa, M. G. Siegel, and D. J. Cram, *J. Am. Chem. Soc.*, **95**, 2691 (1973), and subsequent publications.
- (6) The torsion angles ϕ [C(carbonyl)-N-C(chiral)-C1(naphthyl)] and ψ [N-C(chiral)-C1(naphthyl)-C2(naphthyl)] are defined as follows for the system A-B-C-D: looking along the vector B→C the angle is zero when A and D are eclipsed. A positive angle designates clockwise rotation of the C-D bond with respect to the A-B bond. The torsion angles refer to a molecule of R configuration.
- (7) A. I. Kitaigorodskii in "Molecular Crystals and Molecules", Academic Press, New York, 1973, p 94.
- (8) The measurements were made on a Perkin-Elmer DSC-1 differential scanning calorimeter.
- (9) The absolute configurations of the guest molecules are defined by R' and S' .
- (10) L. Leiserowitz and M. Tuval, *Acta Crystallogr., Sect. B*, **34**, 1230 (1978).
- (11) The two amide groups of a molecule must span the distance of 8.3 Å between two 4₁ axes, which is half the $a + b$ diagonal. This value is very close to the intramolecular distance of 7.9 Å between the carbon atoms of the amide groups, in accordance with the postulated packing (Figure 5).
- (12) A. I. Kitaigorodskii in "Organic Chemical Crystallography", Consultants Bureau, New York, 1955, p 102.
- (13) S. Weinstein, Ph.D. Thesis, submitted to the Feinberg Graduate School, The Weizmann Institute of Science, Rehovot, Israel, 1977.
- (14) Hue-Cheng Chang, L. Leiserowitz, and S. Weinstein, to be published.
- (15) (a) A. Warshel and M. Karplus, *J. Am. Chem. Soc.*, **94**, 5613 (1972); (b) A. Warshel and M. Levitt, Quantum Chemistry Program Exchange, No. 247, Indiana University, 1974; (c) A. Warshel and S. Lifson, *J. Chem. Phys.*, **53**, 582 (1970).
- (16) The amide H and O atoms participating in the N-H...O bond were treated as an alkyl H atom and C atom, respectively, and so the short (N)H...O distance of ~1.9 Å led to apparent repulsion. Moreover, the attractive Coulomb forces, which are rather significant for N-H...O bonds, were not considered. Thus the energies obtained are all high by a constant value. Still, the comparative study is altogether reliable because the amide groups were kept fixed and unaltered throughout the calculations.
- (17) The difference in energy between $RR'_{\min}R$ and $RS'_{\min}R$ is 9 kcal/mol, according to the calculation, a value which would correspond to much higher stereoselective effects than observed.¹⁸ The reason thereof is that in reality the "diastereomers" are not as rigid in atomic positions, as imposed by the model. In addition there is an inaccuracy in the calculated energy due to the approximate nature of the potential parameters used in the calculations.¹
- (18) B. Feilbush and E. Gil-Av, *Tetrahedron*, **26**, 1361 (1970).