Lamellar Racemic Twinning as an Obstacle for the Resolution of Enantiomers by Crystallization: The Case of Me(All)N⁺(CH₂Ph)Ph X⁻ (X = Br, I) Salts

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Received: June 5, 2003; In Final Form: August 30, 2003

Ammonium salts Me(All)N⁺(CH₂Ph)Ph X⁻ (X = Br, 1; X = I, 2) (Asymmetric nitrogen, communication 89, prev. see Kostyanovsky, R. G.; Kostyanovsky, V. R.; Kadorkina, G. K.; Lyssenko, K. A. Mendeleev Commun. 2003, 111) were historically the first compounds with a chiral nitrogen center obtained in optically pure forms via diastereoisomers. We were astonished by the fact that W. J. Pope, who first carried out the resolution (1899), mentioned in his articles that salts have features for conglomerate formation but nowhere did he note the registration of optical activity and manual sorting of left- and right-handed single crystals. We reinvestigated these salts with the help of X-ray diffraction and found that the space groups of both of them are $P2_12_12_1$. However, despite the chiral space group, the enantiomeric composition of the majority of the crystals obtained by crystallization from solutions of racemates was found to be near racemic. Such crystal growth behavior, called lamellar twinning between enantiomers, represents a serious obstacle to the methods of enantiomeric resolution by straightforward crystallization that are used in the chiral industry. The phenomenon probably results from a high concentration in solution of heterochiral growth clusters, which promote the formation of the intergrowth region of twins. To glance experimentally at what might possibly be the first crystal growth units, electrospray ionization FT-ICR mass spectrometry was applied. We were able to register polyionic clusters containing up to five chiral cations. The relative stability of the simplest dimeric clusters (two cations linked by an anion) of 1 with homo- and heterochiral composition was estimated with a B3LYP/SDD calculation, and heterochiral one was found to be more stable by 0.883 kcal/mol.

1. Introduction

Crystallization methodologies are widely used in industry² for large-scale enantiomeric resolution. Among them, the methods of direct crystallization of enantiomers^{3,4} are the most attractive because of their simplicity and low cost. However, these procedures can be applied only to the minority of systems in which the racemate crystallizes to give a mixture of enantiopure crystals (racemic conglomerate).³ Although the frequency of occurrence of conglomerates is rather low (perhaps 10% of all racemates), several promising approaches for the directed prediction and design of these conglomerates were recently proposed.⁵ Nevertheless, once the problem of finding a conglomerate is solved, the resolution may be complicated and fraught with difficulties.⁶ One possible difficulty is lamellar racemic twinning, where instead of the crystal lattice containing only one enantiomer it actually consists of many domains (lamellae) of both enantiomers. The phenomenon has been found and investigated for a variety of compounds: β -phenylglyceric acid,^{7a} helycens,^{7b,c} triazolyl ketone,^{7d} 2-azabicyclo[2.2.1]hept-5-en-3-one,^{7e} methionine, cysteine and valine hydrochlorides,^{7f,g} threonine,^{7h} and 5-ethyl-5-methylhydantoin.^{7i,j} Also, a number of compounds reported in the literature have hints of the same property.8,9

The common feature for the majority of compounds exhibiting lamellar racemic twinning is orthorhombic crystal symmetry (space group $P2_12_12_1$).¹⁰ An orthogonal orientation of crystallographic axes appears to favor the formation of racemic twins with a minimal number of defects.¹¹ For a racemic twin, the structural X-ray investigation proceeds in the same way as for any normal single-crystal analysis; no disorder can be detected,12 and the presence of the second enantiomer can be evaluated only from a refinement of the Flack parameter in the absolute structure determination.¹³ Racemic twinning has been found to affect optical properties; it was shown recently that this phenomenon causes a reduction in the intensity of the secondharmonic generation of nonlinear optical materials.^{10b} It is also well documented that twins usually exhibit birefringence,7d,h which furthermore can be used to discriminate between twinned and nontwinned species. It has also been reported that racemic twinning affects the stereoselectivity of some solid-state reactions.10a,14

In the present paper, we report a reinvestigation of the compounds in which this phenomenon was probably observed historically for the first time. At that time, it was interpreted incorrectly and even caused the generation of an erroneous theory of five-valent nitrogen.

2. Historical Intrigue

In 1899, Edgar Wedekind summarized his work on the stereochemistry of chiral ammonium salts.¹⁵ He believed that nitrogen had a tetragonal-pyramidal configuration and when bearing five different substituents (according to his model, a covalent bond occurred between the anion and nitrogen) would exist as three enantiomeric pairs. The preparation of each

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Figure 1. (a) Two enantiomorphous crystals of salt **1**, grown by W. J. Pope and A. W. Harvey from aqueous solutions of optically pure enantiomers.^{17b} The faces of the left crystal are assigned with Miller indices; the right one is assigned with the original Pope symbols. (b) Twinned crystal of **1** obtained by us from an aqueous solution of racemic composition. It is interesting that oriented nucleation of the majority of crystals from a glass/ solution or an air/solution interface occurs: most of the crystals grow from one of four possible {110} faces, which finally have a square shape.

stereoisomeric pair would depend on the order of substitutents insertion during the synthesis. When preparing methylallylbenzylphenylammonium bromide **1**, iodide **2**, and later chloride¹⁶ in three different ways, he thought that he had isolated α , β , and γ isomers that had the same elementary composition but differed in melting points, solubilities, and crystal habits.

In the same year, compounds **1** and **2** became the targets for British chemist W. J. Pope and his colleague S. D. Peachey, who resolved them into enantiomers with the help of d- and l-camphorsulfonic acid^{17a} and for the first time proved that the nitrogen atom can be a stereogenic center. They grew crystals of salt **1** from aqueous solutions of optically pure D and L enantiomers^{17b} (Figure 1a) and compared crystallographic parameters of these crystals and those investigated by Wedekind^{16a} and found them to be identical. Pope immediately recognized that Wedekind held in his hands not a simple racemate but "a mere mechanical mixture of the two component salts."^{17b}

When measuring the optical rotation of a solution of partially resolved salt **2**, Pope noticed that crystals precipitated in the polarimetric tube. They were determined later to consist of optically pure salt **2**. The solution, meanwhile, whereas previously it had been able to rotate a plane of polarized light, now suddenly lost its optical activity.^{17a} In this case, Pope correctly explained the result¹⁸ of this experiment; he understood outright that salts **1** and **2** are conglomerates.

However, despite his knowledge of the tetrahedral model of A. Werner, Pope interpreted the results in the context of the "quinquevalent" nitrogen theory.¹⁹ Because he had salts **1** and **2** prepared by one of the three possible ways, he thought that he had correspondingly one enantiomeric pair from three possible pairs. The resolution into enantiomers only strengthened his confidence in this theory. Another aspect of his work seems even more mysterious and strange. Given Pasteur's experiments with sodium-ammonium tartrate tetrahydrate,²⁰ Pope does not mention in his papers the measurement of the optical activity of single crystals of synthetic salts **1** and **2**, or in the other words, he did not perform the classical manual triage of left- and right-handed crystals.²¹

3. Lamellar Racemic Twinning: Structural and Morphological Investigations

To provide an explanation of the activities of scientists of that epoch and in particular the curious omission of the classical manual triage, we again synthesized these compounds (Experimental Section). An X-ray study of monocrystals of salts 1 and 2 was performed, and the structures were found to be chiral and isomorphous (space group $P2_12_12_1$) (Table 1).

However, despite the chiral packing (Figure 2b), the enantiomeric composition of the majority of the crystals was found to be near-racemic, with only a few particles optically enriched. Crystallization from absolute ethanol according to the Wedekind procedure led to series of crystals with different habits in the same crystallization setup (Figure 3). In this experiment, we obtained prisms consisting of equal amount of both enantiomers (Figure 3a) alternating with long thin needles with high enantiomeric purities (Figure 3e). Thus, we were able to demonstrate the racemic twinning (or polyepitaxy) phenomenon.²²

In the case of salt 1, an X-ray investigation was performed for a crystal of the prismatic shape and also one with needlelike morphology (Table 1, columns A and B). We found that all crystallographic parameters in both cases are identical. A refinement of the Flack parameter¹³ led to a direct estimation of the enantiomeric composition. In the case of prismatic crystal, the value x was found to be 0.53 (ee = -6%), whereas for acircular crystal it was equal to 0.12 (ee = 76%). Furthermore, the stereoselective dissolution of a twinned crystal in a solution enriched by one enantiomer clearly demonstrates its lamellar structure (Figure 4).

The 2D nucleation of the opposite enantiomer on the growing crystal surface of the original enantiomer requires additional expenses of energy compared with the energy required for the ordinary nucleation of this original enantiomer. This barrier is equal to the difference between attachment energies of layers with the same and opposite chiralities. Therefore, the oscillating nucleation of two enantiomers along the specific direction should reduce the rate of growth in this direction. Figure 5 illustrates how a hypothetical nucleus can grow out into two morphologically diverse crystals depending on the comparative growth rates of different faces. Morphological analysis (Figure 5 and 6) together with measurements of the optical activity led to the assignment of the twin plane to ab or $\{00l\}$.

Thus, the racemic twinning of salts 1 and 2 that was not recognized by Wedekind or Pope did not allow them to observe directly Pasteur-like spontaneous resolution and, moreover, stimulated the development of the erroneous theory of quinquevalent nitrogen. Certainly, crystals with different enantiomeric compositions have different melting points and solubilities and, most importantly, completely different crystal habits. This

TABLE 1: Crystallographic Data for Salts 1 and 2

compound		1		2
formula		C ₁₇ H ₂₀ BrN		C ₁₇ H ₂₀ IN
M (g mol ⁻¹) temperature crystal class space group Z radiation type $a(\text{\AA})$	A 9.185(1)	318.25 298 K orthorhombic $P2_12_12_1$ 4 Mo K α	B 9.190(1)	365.24 140 K ^{<i>a</i>} orthorhombic $P_{2_12_12_1}$ 4 Mo K α 9.410(1)
$ \begin{array}{c} b(A) \\ c(Å) \\ V(Å^3) \\ F(000) \\ \rho_{calc} (gcm^{-1}) \\ \mu (cm^{-1}) \\ \theta (deg) \end{array} $	12.397(1) 13.982(2) 1592.1(3) 1.328 25.70 2.19-29.13	656	12.408(2) 14.015(2) 1598.2(6) 1.323 25.70 2.19-29.13	12.551(2) 14.150(2) 1671.2(4) 728 1.905 19.05 2.17-30.02
reflections measured	17073		17785	19964
independent reflections	4201 (R(int) = 0.0421)		4220 (R(int) = 0.0479)	4875 (R(int) = 0.0263)
reflections $[I > 2\sigma(I)]$	2775		2585	4693
Flack parameter $R(F_{hkl})$: R_1 wR_2 GOF $\rho max/\rho min$ $(eÅ^{-3})$	0.117(9) 0.0246 0.0427 0.916 0.449/-0.275		0.532(8) 0.0260 0.0407 0.915 0.599/-0.190	0.35(2) 0.0278 0.0622 1.017 0.758/-0.798

^{*a*} The investigation of **2** was also performed at room temperature. The structure was refined to wR₂ = 0.0992, R₁ = 0.0405, Flack parameter 0.48(4). Crystallographic parameters are a = 9.409(2) Å, b = 12.709(2) Å, c = 14.280(3) Å, V = 1707.5(5) Å³, density 1.421 g cm⁻¹.



Figure 2. (a) Structure of the *S*-(-)-Me(Ph)N⁺(All)CH₂Ph cation. (b) Packing ([100] projection) of salts **1** and **2** in *P*2₁2₁2₁. Parameters of H bonding (C–H···Hal⁻): H···Br, 2.77–3.09 Å for **1**; H···I, 2.86–3.20 Å for **2**. All C–H distances are normalized to the ideal value of 1.08 Å.

was perceived by Wedekind as direct proof of the existence of α , β , and γ isomers.

4. Structural Model for Lamellar Racemic Twinning and Methods for Its Removal

On the basis of the data obtained, we modeled the twinning. When a fragment of the crystal packing, which includes only left-handed ammonium cations, is superimposed on a fragment of right-handed cations, the strongest contacts H••••Hal do not break (Figure 7a). A new symmetry element, a center of inversion, now appears that does not belong to the original space group. Such twins are known as mimetic twins where the twin symmetry is higher than that of the parent enantiomeric crystal.¹¹ The whole crystal consists of alternating lamellae of left- and right-handed crystal domains, each tens of micrometers thick (Figure 8).

The zone of intergrowth (Figure 7a) may be considered to be another polymorphic modification (racemic compound) of the parent left and right enantiomorphs.²² The occurrence of lamellar twinning suggests a negligible energetic gap between the enantiomorphous and racemic crystal lattice. In recent articles,^{7i,j} the estimation of the energies of such crystal lattices was carried out, and the authors found that although the enantiomorphous packing is more stabilized the difference from



Figure 3. Set of crystals with different morphology and enantiomeric composition obtained from ethanol solutions of racemic 1. Crystals: (a) $\Delta\epsilon(212.5 \text{ nm}) 0$, Flack parameter 0.53 (*S/R* 1:1); (b) $\Delta\epsilon(212.5 \text{ nm}) + 0.5$; (c) $\Delta\epsilon(212.5 \text{ nm}) - 3.8$; (d) $\Delta\epsilon(212.5 \text{ nm}) + 7.1$; (e) $\Delta\epsilon(212.5 \text{ nm}) - 9.3$, Flack parameter 0.12 (*S/R* 9:1).



Figure 4. Crystal of **1** with racemic composition starts to dissolve in an aqueous solution of enantiomerically enriched **1**. Here the lamellar structure of the crystal can be clearly recognized.



Figure 5. (a) Crystal nucleus grows into two morphologically different crystals, depending on the relative growth rates of faces A and B. (b) Different morphology of crystals of 1 depending on different growth rates along the c axis.

the modeled racemate is low ($\Delta E = 2.5$ kcal/mol). The authors concluded^{7i,j} that lamellar racemic twinning results from secondary nucleation of the opposite enantiomer on a growing crystal





Figure 6. Assignment of faces for crystals of 1: (a) ee 0%; (b) ee 61%; and 2: (c) ee 0%; (d) ee 18%.

of the first enantiomer and that the impetus for the secondary nucleation is the local supersaturation of the opposite enantiomer.

The use of enantiomerically pure tailor-made auxiliaries,^{7f,g} the addition of wetting reagents,⁷ⁱ and the application of gentle stirring^{7j} have been proposed as means to remove racemic twinning. The first way is convenient for many systems because its application also solves the problem of enantiomeric resolution. However, it does require the often expensive synthesis and preparation of a tailor-made additive in enantiomerically pure form.

We anticipated that in order to avoid twinning during crystal formation, in this case, it is necessary to suppress the growth of the *ab* faces. We designed the substituent-modified methyl-allyl(p-brombenzyl)phenylammonium bromide **3** as an additive that is able to insert stereospecifically into the necessary faces instead of the cations of **1**. It thus blocks these faces for effective growth (Figure 7a) and at the same time prevents the formation of twins.

The crystallizations of 1 with the addition of racemic 3 were performed from aqueous and ethanol solutions. In water, the direction of fastest growth occurs along the crystallographic a axis, whereas the direction of twinning is the c axis. At concentrations of 1-5% (w/w) of 3, there was no noticeable modification of crystal shape; only the addition of 3 at up to 10% (w/w) considerably reduced the rate of growth along the a direction. However, the majority of the crystals were still twinned. In the ethanol solutions, the direction of the most rapid crystal growth coincides with twinning axis c and, as mentioned before, becomes slower when twinning occurs. The addition of **3** at up to 10% (w/w) first inhibited crystallization, but finally, after several days of slow evaporation of the solvent, crystals appeared as asymmetric prisms, which were unusually shortened in length along the c direction and were of homochiral composition.

5. Understanding the Racemic Twinning Phenomenon on the Basis of a Cluster Model of Crystal Growth

Recently, new insights that emphasize the embryonic stages of molecular and ionic aggregations in solution were introduced into crystal science.^{23,24} During the nucleation steps in particular, the most significant events can happen, and these determine the macroscopic crystal growth behavior. It has now been illustrated that processes leading to the isolation of a particular crystal phase occur as the result of the formation and selfassembly of clusters. Hence, racemic twinning probably results from rather high concentrations in solution (or melt) of clusters with a heterochiral composition.



Figure 7. (a) Two fragments of the structures of S-(-)- and R-(+)-enantiomers of **1** or **2** can be "stitched" to each other across the {00*l*} crystallographic plane. An auxiliary cation of salt **3** (see text) is adsorbed onto faces {00*l*} and inhibits their effective growth. (b) Three types of neutral ionic dimeric clusters, which are formed in the supersaturated solution and are probably responsible for the macroscopic crystal growth picture; C_S and C_R are chiral left-handed and right-handed ammonium cations, respectively, and **A** is an achiral bromide or iodide anion.



Figure 8. Picture illustrating the alternation of left and right domains in a lamellar racemic twin.

The growth blocks for ionic crystals are polyionic aggregates.²⁵ Thus, if the stereogenic center is a cation, then in the simplest case, in a supersaturated solution, three types of dimeric clusters can be formed: $\{(C_S \cdot A \cdot C_S)^+ A^-\}, \{(C_R \cdot A \cdot C_R)^+ A^-\}, and \{(C_S \cdot A \cdot C_R)^+ A^-\}, where C_S and C_R are chiral cations and$ A is an achiral anion (Figure 7b). The first two can be consideredto be responsible for aggregation into larger homochiral domainsand, finally, for the formation of chiral crystals. The heterochiralthird, in fact, can be the cause for the creation of a heterochiralstructural fragment, which in twins is between the two enantiomorphic lamellae of opposite configuration.

It has been shown that mass spectrometry (MS) can be used as an analytical tool for the investigation of the aggregation of molecules and ions in solution.²⁶ The technique seems to have incontestable advantages such as the simplicity of the interpretation of results and its comparability with synchrotron methods.²⁷ Currently, with the help of MS, several attempts to investigate the clustering in solution that are relevant to crystallization have been reported. In the first one,²⁸ the liquid adiabatic expansion technique for sample input followed by electron impact ionization was used to explain the cocrystallization of pyridinepyrrole (1:1) complexes. The authors found that peaks corresponding to clusters with the same stoichiometry predominate in the mass spectra, and from these results they were able to draw conclusions about the structural motif of the growth unit. However, the method of ionization that they used raises doubts concerning the application to fragile noncovalent associates with high molecular weight.

With electrospray ionization (ESI), Cooks et al.²⁹ and another group³⁰ reported that serine tends to form magic number clusters composed of eight molecules with strong chiral discrimination. ESI is a soft ionization device; however, the disadvantage is that during this process a large number of transformations and rearrangements may occur and completely distort the structure of agglomerates existing in solution.

A more optimistic point of view was demonstrated in the ingenious work of Beauchamp et al.³¹ These authors postulated that the clusters of serine registered after ESI are not the same as that in solution but they do reflect their original structure and properties. With ion-mobility spectrometry accompanied by DFT calculations, they deduced the cubic structure of the serine octamer. However, later calculations led to confusion because of the absence of a preference for homochirality in such structural fragments. The preference, however, was found for the H-bonded chain structural motif derived from the crystal structure of L-serine. The presence in solution of such linear homochiral associates, which may serve as precursors for the gas-phase clusters detected by MS, explains the origin of their homochiral composition; their transformation to the cubic motif was proposed to happen within the ESI sample inlet. Thus, in attempting to explain the origin of the chiral discrimination effect in clusters in the gas phase, the authors obtained interesting information about the crystal growth units in solution.



Figure 9. ESI FT-ICR mass spectra demonstrating the clustering of 1 and 2 (the letter N⁺ indicates the ammonium cation Me(Ph)N⁺(All)CH₂Ph). (a) Single-charged clusters containing up to five cations were registered for 1. The complex-type signals are conditioned by a combination of ions with different isotopes, and the picture is complicated by the natural isotopic abundance of bromine (⁷⁹Br 50.54%, ⁸¹Br 49.46%). (b) Clusters with up to four cations were obtained for 2. In all cases, the average and whole values for m/z are given.

Because it was available, we tested the solutions of salts 1 and 2 with ESI Fourier transform ion-cyclotron resonance (FT-ICR) MS and were able to detect several positively charged ionic agglomerates along with the single ammonium cation (Figure 9).^{32,33} These clusters are possibly relevant³⁴ to polyionic growth blocks existing in solution. The B3LYP/SDD calculation of the homo- and heterochiral dimeric clusters of 1 (two cations and one anion) has revealed that they have practically the same

energy with a slightly lower value (by 0.883 kcal/mol) for the heterochiral cluster. The theoretically obtained geometries (Figure 10) are quite close to the experimental ones from the X-ray investigation. The Br···H contacts vary from 2.65-2.81 and 2.69-2.79 Å for the homo- and heterochiral clusters, respectively. For comparison, corresponding values for the same structural fragment of the crystal structure of **1** are 2.73-2.99 Å.



Figure 10. Geometries of (a) homo- and (b) heterochiral clusters of 1 optimized with the B3LYP/SDD calculation. The energy of the heterochiral cluster is 0.883 kcal/mol lower than that of the homochiral alternative.

6. Conclusions

Lamellar racemic twinning of chiral ammonium salts 1 and 2 was found and investigated. Despite the chiral space group, determined by an X-ray study of single crystals grown from synthetic nonresolved material, the enantiomeric composition of the crystals was racemic. Morphological study and molecular modeling led to the identification of the twinning plane as $\{00l\}$. Auxiliary salt 3 was designed to be stereospecifically absorbed onto the $\{00l\}$ faces, thus blocking them from effective growth and concurrently avoiding twin formation. The crystalline fragment along the twinning plane is probably formed by polyionic growth units with a heterochiral composition existing in supersaturated solution. To investigate clustering in solution directly, we applied ESI FT-ICR mass spectrometry and detected clusters containing up to five ammonium cations with four anions. These agglomerates are possibly relevant to elementary building blocks existing in solution.

Whereas methods for the investigation of nucleation processes on the surface are well-established, the corresponding technique for 3D bulk solutions is still lacking. The most promising approach, as was shown above, is mass spectrometry. Keeping in mind the key problem of the experimental registration of the critical nucleus (hundreds of molecules) and leaving the technical details for specialists, we can dream about an apparatus that not only will have a soft ionization setup and a lowtemperature sample inlet but also will allow the delivery of large and heavy clusters to the detector and so permit work with concentrated (supersaturated) solutions. When working under these conditions, we can expect little damage and maximum retention of the structural features of solution associates responsible for crystal growth.

In conclusion, the lamellar racemic twinning is an undesirable obstacle to the resolution into enantiomers by crystallization (entrainment methods, crystallization with deficiency of conglomerator^{9a}). The future understanding of this phenomenon as well as the development of new and simple methods for its prevention will noticeably increase the number of resolvable compounds and will have an impact on an exiting area of crystal nucleation research.

7. Experimental Section

¹H and ¹³C NMR spectra were recorded using Bruker DRX-500 and Bruker WM-400 spectrometers. Optical activities were determined by polarimetry and CD methods (polarimeter Polamat A and CD spectrometer Jasco-500A). Optical rotations were measured for aqueous or ethanol solutions (0.03-0.04 M) at 23-25 °C in a 1-dm tube. Optical purities were estimated by comparing with values of resolved 1 and 2.17b Melting points were measured with a Stuart Scientific SMP-3 apparatus. Mass spectra were obtained using an experimental plant based on the ion-cyclotron resonance Bruker Spectrospin CMS-47 mass spectrometer (Superconducting magnet 4.7 T, vacuum 8×10^{-8} Torr). The settings that were used were a source voltage of 2 kV, a capillary voltage of 100 V, a capillary temperature of 125 °C, and an electrospray tip inner diameter of 89 µm. Samples were electrosprayed using a 50:50 methanol/water mixture with a concentration of $1 \times 10^{-3} - 5 \times 10^{-3}$ M at a flow rate of 500 nL/min from a 25-µL Hamilton syringe.

Crystallographic data and parameters of the refinement for the crystal structure determination of salts 1 and 2 are presented in Table 1. The data collection was carried out on a SMART 1000 CCD using ω -scan mode with a 0.3° step in ω and a 10-s exposure per frame. All structures were solved by direct methods and refined by full-matrix least squares against F^2 in the anisotropic (H atoms are isotropic) approximation using the SHELXTL-97 package. The data were processed with the use of the SAINT PLUS program package. The absorption correction and the merging of reflections were applied using the SADABS program. The positions of hydrogen atoms were located from the Fourier electron density synthesis and were included in the refinement in the isotropic riding model approximation. The absolute structure was determined on the basis of the Flack parameter. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary no. CCDC-209797 for 1 A, 209798 for 1 B, and 209798 for 2. Copies of the data can be obtained free of charge upon application to the CCDC (12 Union Road, Cambridge CB2 1EZ U.K. Fax: (internat.) +44-1223/336-033; E-mail: deposit @ccdc.cam.ac.uk). The habits of crystals represented in Figures 5 and 6 were measured either on the diffractometer or with an optical goniometer.

Calculations of homo- and heterodimeric clusters were performed with the Gaussian 98 program package³⁵ at the B3LYP level. Full optimization was carried out with the SDD basis set starting from the X-ray structural data. As convergence criteria, the extremely tight threshold limits of 2×10^{-6} and 6×10^{-6} au were applied for the maximum force and displacement, respectively.

Compound 1, obtained as colorless crystals, was prepared from 15 g (0.102 mol) of Me(All)NPh and 17.45 g (0.102 mol) of PhCH₂Br (one week at 22 °C, in the dark). The obtained solid was first washed with benzene-hexane (1:1) for 1 day, yield of crude product 29.85 g (92%). Then it was recrystallized three times from water at 5 °C, yield 6.5 g (20%). Obtained crystals were analytically pure, mp 165-166 °C (decomp). Solubility (20 °C) in H₂O: (w/w) 3.8%. Anal. Calcd for C₁₇H₂₀NBr: C, 64.16; H, 6.33. Found: C, 64.21; H 6.28. ¹H NMR (500.13 MHz, CD₃OD): δ 3.44 (3H, s, Me), 4.54 (1H, dd, H_a, ${}^{2}J_{ab} = -13.4$ Hz, ${}^{3}J_{ac} = 7.7$ Hz), 5.03 (1H, dd, H_b, ${}^{2}J_{ab}$ = -13.4 Hz, ${}^{3}J_{bc} = 5.4$ Hz), 5.21 (2H, dd, CH₂-Ph, AB spectrum, ${}^{2}J = -12.7$ Hz, $\Delta \nu = 42.3$ Hz), 5.68 (dd, 1H, H_d, $_{2J_{de}}$ =2.0 Hz, $^{3}J_{dc}$ =9.7 Hz), 5.69 (1H, m, H_c), 5.72 (1H, dd, H_{e} , ${}^{2}J_{ed} = 2.0$ Hz, ${}^{3}J_{ec} = 16.4$ Hz), 7.08 (2H, d, o-Bn), 7.30 (2H, t, m-Bn), 7.46 (1H, t, p-Bn), 7.60 (3H, m, p,m-Ph), 7.72 (2H, m, o-Ph).



¹³C {¹H} NMR (125.03 MHz, CD₃OD): δ 46.81 (Me), 70.60 (-CH₂--C₂H₃), 73.82 (CH₂Ph), 123.26 (*o*-Ph), 125.86 (-CH=), 128.25 (*ipso*-Bn), 128.74 (CH₂=-C₂H₃--), 129.52 (*m*-Bn), 131.17 (*m*-Ph), 131.44 (*p*-Ph), 131.52 (*p*-Bn), 133.43 (*o*-Bn), 142.60 (*ipso*-Ph). The assignment of carbon signals to the appropriate proton signals was performed by 2D HSQC and HMBC correlations. UV (1.05 × 10⁻³ M, H₂O), $\epsilon(\lambda$, nm): 2855 (203), 10 945 (220.6), 628 (262); CD spectrum of needlelike crystal (1.1 × 10⁻³ M, EtOH), $\Delta\epsilon(\lambda$, nm): 9.3 (212.5).

Compound **2**, colorless crystals, precipitated from an aqueous solution of **1** and an equimolar quantity of NaI with quantitative yield, mp 143–147 °C (decomp), has the same NMR, UV, and CD properties. Anal. Calcd for $C_{17}H_{20}NI$: C, 55.90; H, 5.52. Found: C, 55.91; H, 5.48.

Compound **3**, colorless crystals, was prepared from *p*-BrC₆H₄-CH₂Br and Me(All)NPh. The reaction was performed without solvent for 1 week at room temperature. The obtained oily product was solidified with dry ethyl acetate and then recrystal-lized two times from acetonitrile/ethyl acetate (1:1), mp 99.5–100.5 °C. Anal. Calcd for C₁₇H₁₉NBr₂: C, 51.41; H, 4.82. Found: C, 51.47; H, 4.98. ¹H NMR (400.14 MHz, CD₃OD): δ 3.48 (3H, s, Me), 4.61 (1H, dd, H_a, ²J_{ab} = -13.1 Hz, ³J_{ac} = 6.5 Hz), 5.05 (1H, dd, H_b, ²J_{ab} = -13.1 Hz, ³J_{bc} = 4.3 Hz), 5.14 (2H, dd, CH₂-Ph, AB spectrum, ²J = -12.8 Hz, $\Delta \nu$ = 67.2 Hz), 5.52–5.67 (3H, m, H_d, H_c), 6.99 (2H, d, *o*-C₆H₄-Br), 7.42 (2H, d, *m*-C₆H₄Br), 7.60–7.64 (3H, m, *p*,*m*-Ph), 7.77–7.79 (2H, m, *o*-Ph).

Acknowledgment. We are grateful to Professor M. Lahav (Weizmann Institute of Science, Rehovot, Israel) for valuable discussions and advice. V.Y.T. gratefully acknowledges the Weizmann Institute for the support that allowed him to work at the Materials and Interfaces Department during the summer of 2002. We acknowledge the help of Dr. Yu. A. Strelenko (N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences) with NMR measurements. This work was supported by the Russian Academy of Sciences (programs of academicians O. M. Nefedov and Yu. A. Zolotov), the Russian Foundation for Basic Research (RFBR) (grant nos. 03-03-32019, 03-03-06526, 02-03-32311, and 03-03-04010), and INTAS (grant no. 99-00157). We also thank the two referees for their invaluable comments on this paper.

Supporting Information Available: CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) In ref 7j, the authors proposed the use of the term lamellar epitaxy instead of the term lamellar twinning for the description of cases of twinning of opposite enantiomers of the same chemical compound. They based this idea on the definition of J. D. Dunitz (Acta Crystallogr., Sect. B 1995, 51, 619) that enantiomeric crystals of a conglomerate and a racemate are three different chemical substances if the enantiomerization rate is low and can be considered to be polymorphs if the enantiomerization rate is high. It is seems that the authors solved the confusion because even the same enantiomer can form lamellar twinned crystals, whereas the crystal growth of one substance on crystals of the other it is accepted as epitaxy. However, the confusion arises again if we take into consideration the fact that under certain conditions the enantiomerization rate can be high (for example, the presence of a catalyst or high temperature, which can increase the enantiomerization rate), whereas under another set of conditions the rate will be low. Therefore, in the first case the term twinning is appropriate, but in the second we should use the term epitaxy. We are inclined to take another point of view. Racemate-conglomerate polymorphism takes place when crystallization occurs from solution or in a melt of racemic composition and molecules or ions can assemble equiprobably into racemic crystals (racemic compound) or mechanical mixture of left- and right-handed crystals (conglomerate). To distinguish the ordinary twinning of crystals of the same enantiomer from the twinning of alternating lamellae of two opposite enantiomers leading to crystals of racemic composition, we suggest that the term lamellar racemic twinning be used. We refer readers also to ref 13a, where the term twinning by inversion for twinning between the two opposite enantiomers is proposed.

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