Separation and Identification of Residual Diastereomers in a Maximally Labeled Triarylamine

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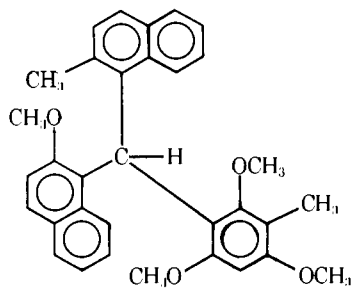
Abstract: Residual diastereoisomerism in a maximally labeled triarylamine, methyl *N*-(biphenyl-2-yl)-*N*-(1-naphthyl)anthranilate, has been demonstrated for the first time. The two stereoisomers were obtained by manual separation of crystals, and their structures were determined by X-ray analysis. Both isomers are molecular propellers, with the three ortho substituents on the triphenylamine skeleton pointing toward the apex of the nitrogen pyramid. Interconversion of the residual diastereomers requires $\Delta G^{\ddagger} = 17.8$ kcal/mol. It is noted that the central nitrogen atom in these systems is a nonstereogenic chiral center.

The notion of residual stereoisomerism was first introduced[2] in the course of studies on the stereochemistry of molecular propellers,[3,4] when we found it necessary to describe a novel type of stereoisomerism in the maximally labeled triarylmethane **1**. The present paper describes the study of residual diastereoisomerism in the maximally labeled triarylamine **2**.



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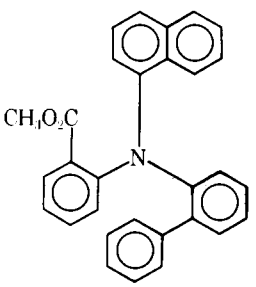

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Maximally Labeled Molecular Propellers. Molecules of the type Ar_3ZX and Ar_3Z resemble three-bladed propellers, in that the aryl rings ("blades") radiating from the central atom Z ("hub") are twisted in the same sense so as to impart a helical (chiral) conformation to the molecule. The highest possible symmetries for such systems are C_3 for Ar_3ZX and D_3 for Ar_3Z, but the greatest potential for useful chemical information is provided by the most highly desymmetrized structures—in accord with Curie's aphorism.[5,6] Such structures, in which the three aryl rings are all different, and in which none possesses a local C_2 axis, are said to be maximally labeled.[4]

A maximally labeled molecule of type Ar_3ZX, such as **1**, contains five stereogenic elements (the three rings, each of which has a pair of differentiable edges, the chiral center Z, and the propeller helicity) and therefore exists in $2^5 = 32$ stereoisomeric forms.[7] This analysis may be extended to maximally labeled molecules of the type Ar_3Z, provided that Z represents a configurationally stable chiral center, e.g., Z = P.[8] However, the situation becomes less straightforward when Z represents a tricoordinate atom with preferred planar equilibrium geometry, e.g., Z = B[9] or N.[11] Let us postulate that Z lies in the plane defined by the three neighboring carbon atoms (the reference plane[7]). Central chirality thus being eliminated, there should be $2^4 = 16$ stereoisomers resulting from the operation of the four remaining stereogenic elements. However, it has been recognized[7] that Z is expected to occupy an equilibrium position in the reference plane if and only if at least one of two conditions is fulfilled: either the plane is also a plane of symmetry, or there is at least one molecular C_2 axis which coincides with one of the Z–C bonds. Neither of these conditions is fulfilled in maximally labeled Ar_3Z, since such molecules, so long as they retain their propeller shape, are necessarily asymmetric. Accordingly, Z is not constrained by symmetry to lie in the reference plane and is therefore expected to form the apex of a trigonal pyramid, contrary to the original postulate.[17] It follows that Z is a chiral center. Nevertheless, as will be discussed below, this element of chirality is not stereogenic. Accordingly, the central atom in maximally labeled triarylamines may be treated *as if* it were located in the reference plane, and only 16 stereoisomers need therefore be considered for such systems.[7,19,20]

In order to provide identifying notation for these stereoisomers, we shall adopt a previous convention,[4] according to which the four permutational rearrangements shown in Figure 1 (*h*, *e*(1), *e*(2), and *e*(3)) are assigned values of either 0 or 1. The resulting ordered quadruples serve as configurational descriptors for the 16 stereoisomers of a maximally labeled triarylamine.

Conformational Dynamics and the Prediction of Residual Diastereoisomerism in Triarylamines. All single-step stereoisomerizations of Ar_3Z and Ar_3ZX systems involve correlated torsional motion of the three rings, resulting in a reversal of propeller helicity. Without known exception, the two-ring flip is the mechanism of lowest energy for this process.[4] This mechanism is one of four, illustrated in Figure 2, in which zero, one, two, or three rings "flip",[21] i.e., rotate through a conformation in which the plane of the ring is perpendicular to the reference plane. The permutational equivalents of these mechanisms[4] consist of suitable combinations of *h* and *e* operations which form sets of rearrangements called modes, as shown in Figure 2. The order of the modes is 1 for the zero- and three-ring flips and 3 for the one- and two-ring flips, and expresses a consequence of correlated rotation: in the zero- and three-ring flips the three rings all rotate in the same direction (clockwise or counterclockwise), whereas in the one- and two-ring flips two of the rings rotate in the same direction while the third rotates in the opposite direction.

The rearrangements *he*(1), *he*(2), and *he*(3), which together constitute the two-ring flip mode (Figure 2), are generators for a group $\mathbf{T} = \{I, he(1), he(2), he(3), e(1)e(2), e(1)e(3), e(2)e(3), he(1)e(2)e(3)\}$. Another set of eight rearrangements, *h*T, may be generated by multiplying all elements in T by *h* ($h\mathbf{T} = \{h, e(1), e(2), e(3), he(1)e(2), he(1)e(3), he(2)e(3), e(1)e(2)e(3)\}$). The union of these cosets forms a group G of order 16, generated by *h*, *e*(1), *e*(2), and *e*(3). Action of G on reference structure (0000) generates all 16 stereoisomers of a maximally labeled triarylamine. Action of T and *h*T on reference structure (0000) generates the two sets of eight stereoisomers (four *dl* pairs) shown in Figure 3. The 16 isomers and their configurational descriptors are shown at the vertices

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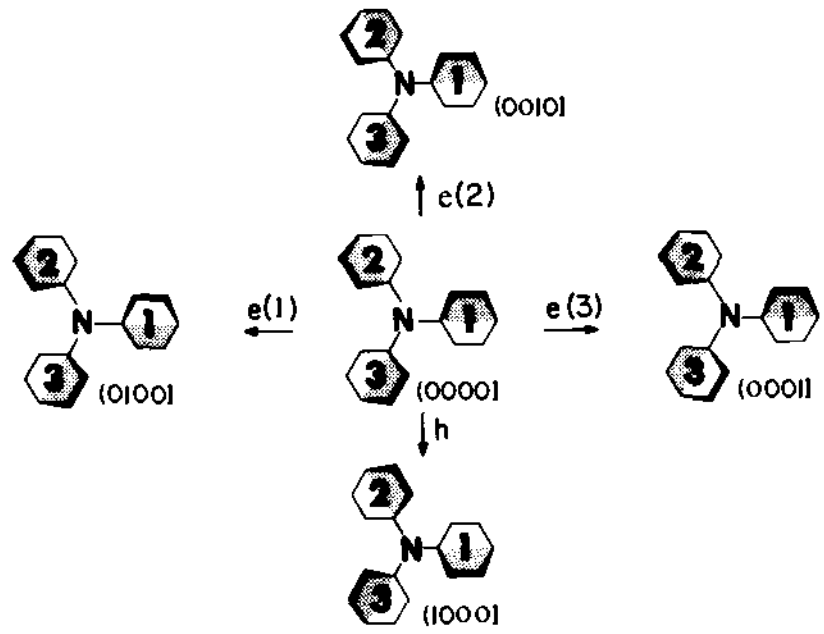


Figure 1. Operation of four permutational rearrangements on reference structure (0000) of a maximally labeled triarylamine. Rings are individually identified by numerals, and each ring has two differentiable edges, one shaded and the other unshaded. Operations designated h, $e(1)$, $e(2)$, and $e(3)$ refer to reversal of propeller helicity (h) and to edge interchanges (e) of the three rings. Configurational descriptors are given as ordered quadruples.

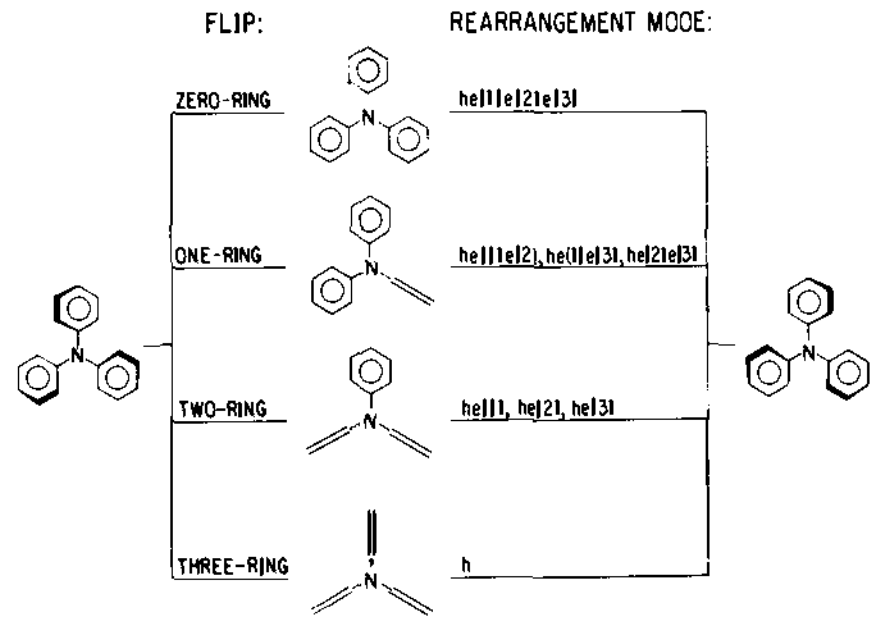


Figure 2. The four flip mechanisms and their permutational equivalents.

of two disjoint graphs, the edges of which represent interconversions by the two-ring flip mechanism. In the particular image chosen for these graphs, enantiomers are related by the diagonals in each cube, and parallel edges represent flips of the same ring (e.g., the four vertical edges in each cube represent *he*(1)). Note that each isomer in one cube has a counterpart in the other from which it differs only in helicity: (0000)/(1000), (1100)/(0100), etc.

Although the eight isomers in each set can undergo rapid interconversion by the two-ring flip,[22] the two sets are not interconvertible by this mechanism because T and *h*T are disjoint. It was therefore predicted[7,23] that a maximally labeled triarylamine may exist in two achiral diastereomeric forms (residual diastereoisomerism). The present work was undertaken in order to provide a realization of this prediction. We had previously been able to achieve a partial separation of **1** into two residual diastereomers;[2] however, in this case each residual diastereomer is composed of two enantiomeric sets of eight conformers, and, since interconversion of the sets is prevented by the stability of the chiral center, each residual diastereomer is a potentially resolvable *dl* pair.

Previous studies by Hellwinkel et al.[20,23] had demonstrated residual diastereotopism[19] in tri-ortho-substituted triphenylamines. In these compounds, two of the rings carry the same ortho substituted (R), while the third ring carries a different substituent. Thus all three rings have differentiable edges (since they lack local C_2 symmetry), but, because two of the rings have the same constitution, a degeneracy is introduced which halves the number of stereoisomers relative to a maximally labeled structure. The remaining eight stereoisomers (four *dl* pairs) and their interconversion by the two-ring flip may be represented by either one of the two graphs in Figure 3.[19,24] The two R groups within each of the eight conformers remain diastereotopic even under conditions of rapid two-ring flip interconversion,[25] and site exchange therefore requires another mechanism (e.g., the one- or three-ring flip) with a higher energy barrier. The magnitude of this barrier was found to depend on the steric requirements of R ($\Delta G^{\ddagger}$ = 18–19 and >26 kcal/mol for R = CH_3[23] and $C(CH_3)_2OH$,[20] respectively). Since residual diastereotopism and residual diastereoisomerism are different manifestations of the same phenomenon (in the case of molecular propellers, correlated rotation of the rings under a given flip mechanism),[4,19,26] the work of Hellwinkel et al. provided an encouraging omen for the planned demonstration of residual diastereoisomerism in a maximally labeled triarylamine.

Results and Discussion

Synthesis of a Maximally Labeled Triarylamine. Two essential requirements have to be met in the design of a suitable compound: the substitution pattern of the triarylamine has to conform to the specification of maximum labeling, and the steric effect of the ring substituents has to be such that conformational interconversion proceeds at a slow enough rate so that separation of residual diastereomers becomes feasible under ordinary conditions. Accordingly, the substituents should be placed into ortho positions.[27] In addition, the synthons carrying these substituents should be commercially available (or at least readily synthesized), one or more of the substituents should be amenable to elaboration into derivatives having larger steric requirements (if necessary), and, finally, at least one of the substituents should have an NMR signal in a region removed from that of the aromatic nuclei. The choice of the target molecule, methyl *N*-(biphenyl-2-yl)-*N*-(1-naphthyl)-anthranilate (**2**), was based on a consideration of all the requirements listed above.

The synthetic route followed in the preparation of **2** (Scheme 1) utilized an Ullmann-type copper-catalyzed condensation between aromatic amines and aromatic halogen compounds.[28] The first condensation reaction between methyl anthranilate and 2-iodobiphenyl afforded methyl *N*-(biphenyl-2-yl)anthranilate (**3**), which was then condensed with 1-iodonaphthalene. The second condensation required a significantly longer reaction period (48 vs. 2.5 h), presumably because of increased internal congestion in the transition state leading to the final product. The desired triarylamine **2** was obtained in 18% yield, along with an 11% yield of methyl 2-(9*H*-carbazol-9-yl)benzoate (**4**). This byproduct, identified by independent synthesis from 9*H*-carbazole and methyl 2-iodobenzoate, is evidently formed from **3** by attack of nitrogen on the ortho position of the outer ring of the biphenyl moiety, resulting in five-membered ring closure.

Separation and Interconversion of Two Conformational Isomers. Triarylamine **2** was initially obtained as an oil which solidified upon trituration with *n*-heptane. When this solid was slowly recrystallized from *n*-heptane, it was noticed that two types of crystals had deposited: aggregates of parallelepipeds, mp 161–163 °C (the α form), and rosettes of needles, mp 132–133 °C (the β form). The striking difference in the appearance of the crystals (Figure 4) made it possible to separate these two forms by hand.

The chemical composition of both forms was found to be consistent with that of **2** (elemental analysis; fragmentation

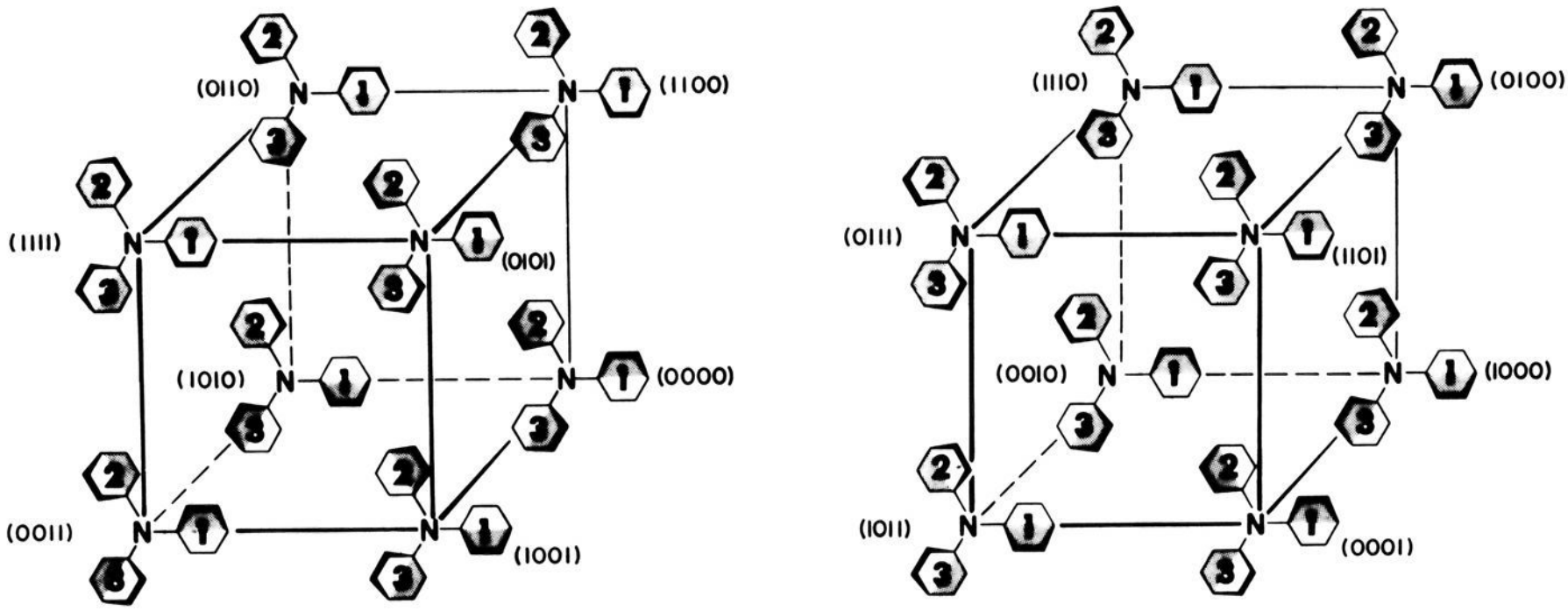
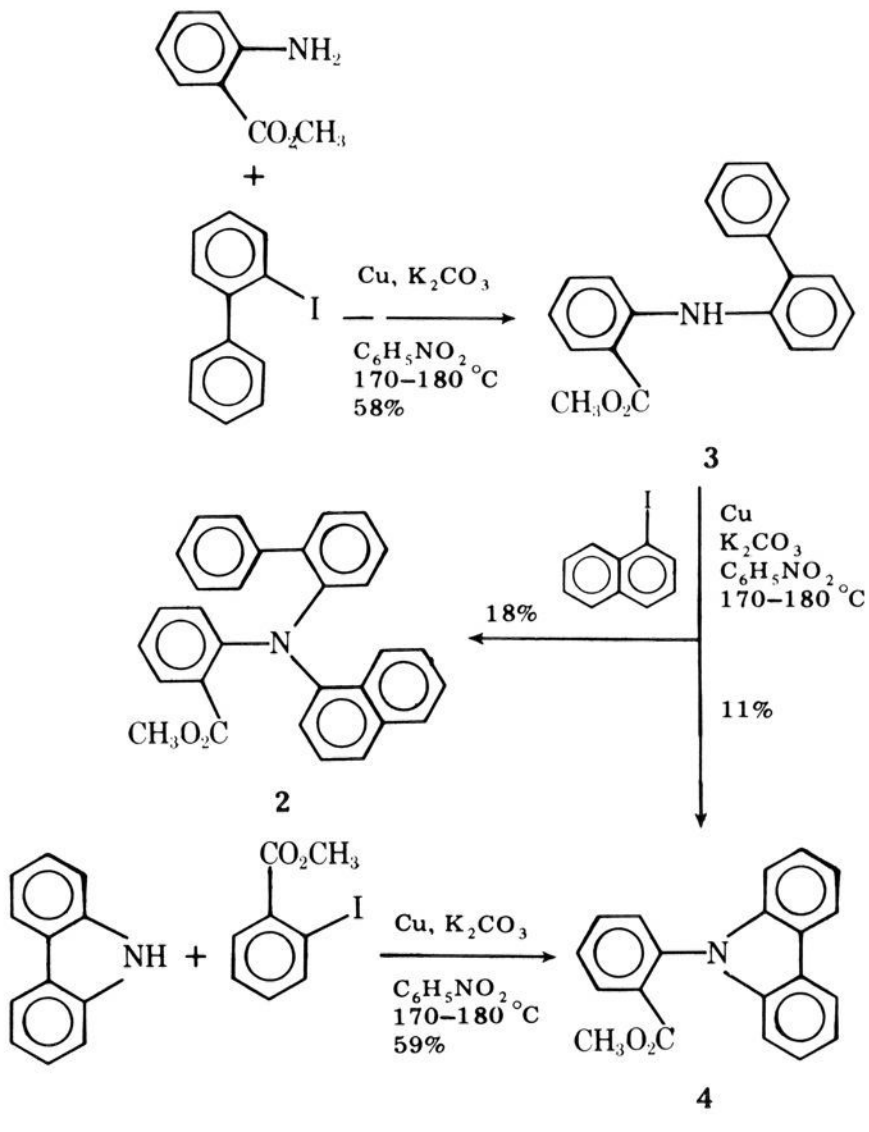


Figure 3. Two disjoint sets of maximally labeled triarylamine stereoisomers under the operation of the two-ring flip. The set on the left is generated by action of the group **T** on reference structure (0000), and the set on the right by action of $h\mathbf{T}$ on the same structure. The edges in each graph represent interconversions by the two-ring flip mechanism.

and high-resolution mass spectroscopy). In addition to the distinguishing characteristics noted above, the two forms could also be differentiated by their solid-state IR spectra. That the two forms differ not only in crystal morphology but also in molecular structure was conclusively proven by NMR spectroscopy. The ^{1}H NMR spectrum of a solution prepared by dissolving a sample of the α form in CD_2Cl_2 at −40 °C featured one methyl proton singlet at δ 3.03 ppm, whereas the spectrum of a similarly prepared solution of the β form had a corresponding signal at δ 3.38 ppm. When the solution of the α form was warmed to room temperature, a new signal appeared at δ 3.38 ppm and grew in intensity; similarly, starting with the solution of the β form, a new signal at δ 3.03 ppm appeared on warming. At equilibrium, the spectra starting from either direction were indistinguishable, and featured both

Scheme I



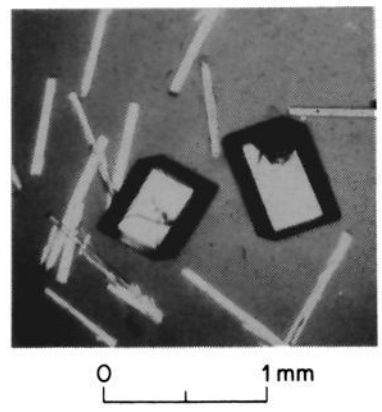


Figure 4. Crystal modifications of **2**. The α isomer forms parellelepipeds (two are shown), and the β isomer elongated needles.

signals in approximately equal intensity. Similar results were obtained from the $^{13}C\{^1H\}$ NMR spectra of the two forms dissolved in $CDCl_3$ at −37 °C. The methyl signal of the α form now appeared at δ 51.5 ppm and that of the β form at δ 52.1 ppm; at ambient temperatures both signals were present and the same equilibrium spectrum was obtained irrespective of the type of crystal initially used to prepare the sample.

From the observations recounted above, it was safe to conclude that the α and β forms were conformational isomers of **2**. The rates of isomerization were determined by monitoring the intensities of the methyl resonances in the ^{1}H NMR spectrum (CD_2Cl_2, −21 °C) as a function of time. The results (Table I) indicated that the isomers differ only very slightly in energy, and that $\Delta G^{\ddagger} = 17.8$ kcal/mol for the isomerization process in either direction. This value was confirmed by dynamic ^{1}H NMR measurements in nitrobenzene-d_5. Coalescence of the methyl proton resonances (δ 3.06 and 3.32 ppm downfield from internal hexamethyldisiloxane for α- and β-**2**, respectively) at 76 °C[29] led to an estimate[30] of $\Delta G^{\ddagger} = 17.7$ kcal/mol; the agreement with the estimate arrived at by nonequilibrium kinetics is excellent, especially in light of the dif-

Table I. Kinetic Parameters for the Interconversion of α- and β-**2** in CD_2Cl_2 at −21 °C

starting isomer of **2**	$K(\alpha/\beta)$[a]	$k \times 10^3$, s^{-1}		$\Delta G^{\ddagger}$, kcal mol^{-1}	
		$\alpha \rightarrow \beta$	$\beta \rightarrow \alpha$	$\alpha \rightarrow \beta$	$\beta \rightarrow \alpha$
α	0.97	1.91	1.86	17.80	17.82
β	0.96	1.72	1.69	17.86	17.87

[a] Equilibrium constant.

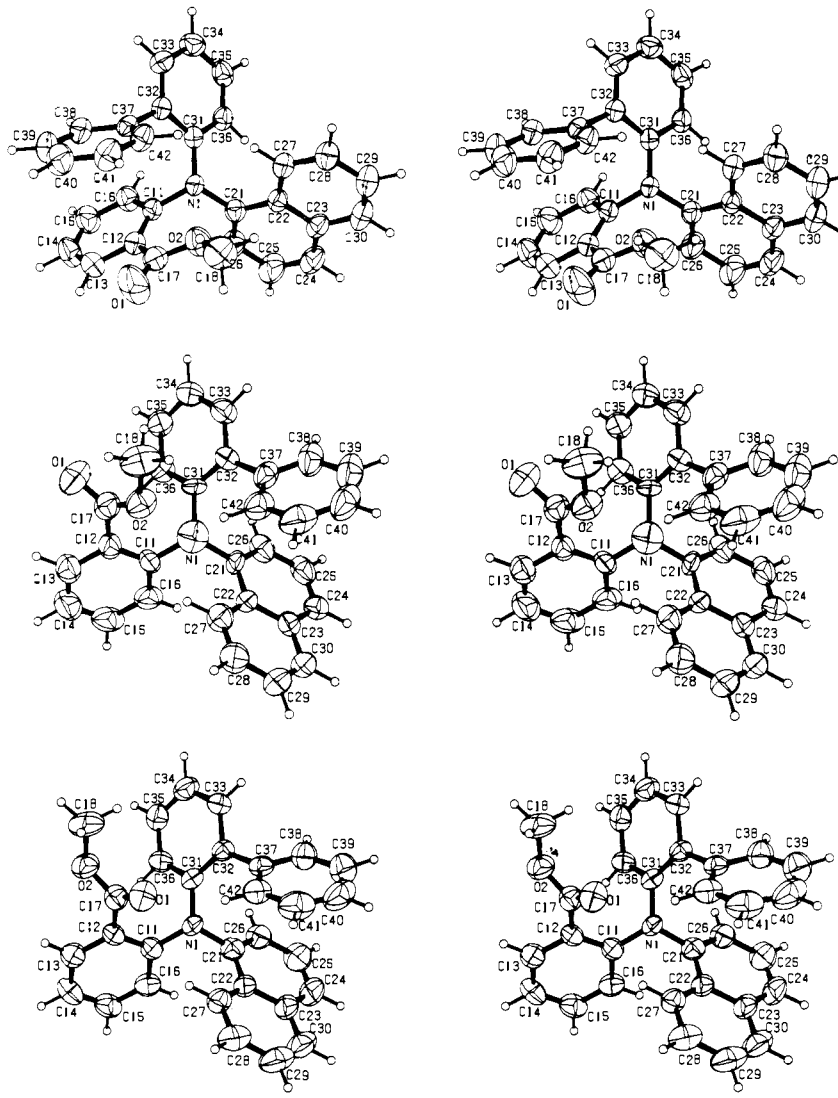


Figure 5. Stereoviews of three conformers of **2**. Only one enantiomer of each is shown. Top: α isomer. Center: β_1 isomer. Bottom: β_2 isomer.

ferent conditions (solvents, temperatures) employed in the two studies.

Identification of Residual Diastereomers. Identification of the two conformational isomers of **2** was achieved by single-crystal X-ray analysis. The α isomer (triclinic) has a centrosymmetric structure, with two enantiomers per unit cell; one enantiomer is shown in Figure 5. For β-**2**, two types of needles were found, both monoclinic. The two modifications differ in that the *b* axis is perpendicular to the needle axis in one of them (β_1) but parallel to it in the other (β_2). Both crystal structures are centrosymmetric, with two pairs of enantiomers per unit cell; one enantiomer of β_1 and β_2 is shown in Figure 5.

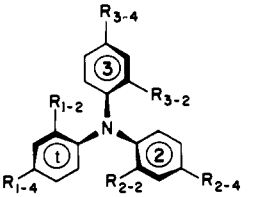
Inspection of the stereoviews in Figure 5 reveals that the three structures have two key features in common: the aromatic rings are arranged in the form of a molecular propeller, and all three ortho substituents are on the same side of the reference plane (shown as projecting toward the observer). Furthermore, the structures of the two β forms differ in only one obvious way: the twists of the carbonyl group, as expressed by the torsion angle C13–C12–C17–O1, are $-41°$ for β_1 and $+127°$ for β_2.[31] It is this feature which is evidently responsible for the observed polymorphism.[32] However, with regard to the two key features noted above, there is nothing to choose between the two β forms; in the subsequent discussion they will therefore be referred to collectively as the β form.

A relationship may now be developed between the structures in Figures 3 and 5, as follows. The structure for the α isomer depicted in Figure 5 corresponds to reference structure (0000) in Figures 1 and 3 if the numerals 1, 2, and 3 are assigned to the 2-methoxycarbonylphenyl, 1-naphthyl, and biphenyl-2-yl groups, respectively, and if the shading represents edges bearing ortho substituents (methoxycarbonyl, benzo, and phenyl in rings 1, 2, and 3, respectively). The structure of the β isomer depicted in Figure 5 differs from that of the α isomer in the same figure in only one essential respect: the helicity of the propeller is reversed. In other words, the α and β isomers are related by the operation *h* (which can be mechanistically pictured in terms of a three-ring flip interconversion; cf. Figure 2), and it follows that the β isomer in Figure 5 corresponds to the structure labeled (1000) in Figures 1 and 3. Accordingly, the enantiomers of the α and β structures shown in Figure 5 are represented in Figure 3 by (1111) and (0111), respectively.

The racemic pairs (0000)/(1111) and (1000)/(0111) belong to the isomeric sets depicted on the left and right side of Figure 3, respectively. Thus α- and β-**2** are conclusively identified as residual diastereomers under the two-ring flip.[33] This is the first example in which residual diastereomers of this type have been structurally identified; in our previous study,[2] separation of the residual diastereomers of **1** was incomplete, and we were therefore unable to effect identification by X-ray analysis.

The barrier of 17.8 kcal/mol for the interconversion of the residual diastereomers, by a one- or three-ring flip,[33] is surprisingly low. In their study of residual diastereotopism in

Table II. Pyramidality of Nitrogen in Triarylamines



entry	method[j]	ref	R_{1-2}	R_{2-2}	R_{3-2}	R_{1-4}	R_{2-4}	R_{3-4}	$\sum$(C-N-C)[l]	pyramidality[m]
1[a]	XR	12a	Cl	Cl	Cl	Cl	Cl	Cl	360.00	0.000
2[b]	XR	12e	H	H	H	Ph	Ph	Ph	359.98	0.014
3[c]	XR	12d	H	H	H	C(CN)C=C(CN)$_2$	H	H	359.98	0.015
4[d]	XR	12b	H	H	H	I	I	I	359.89	0.027
5	XR	12b	H	H	H	F	F	F	359.87	0.029
6[e]	XR	12c	H	H	H	C(CN)C=C(CN)$_2$	H	H	359.55	0.056
7[f]	XR	12b	H	H	H	I	I	I	357.55	0.130
8[g]	XR	present work	CO_2CH_3	(C_4H_4)[k]	Ph	H	H	H	354.65	0.197
9[h]	XR		CO_2CH_3	(C_4H_4)[k]	Ph	H	H	H	353.96	0.205
10[i]	XR		Ph	(C_4H_4)[k]	CO_2CH_3	H	H	H	349.81	0.267
11	ED	16	H	H	H	H	H	H	348 ± 6	0.288 ± 0.085

[a] Data refer to perchlorotriphenylamine. [b] Free-radical cation. [c] Monoclinic modification. [d] Molecule no. 1 of two in the asymmetric unit. [e] Orthorhombic modification. [f] Molecule no. 2 of two in the asymmetric unit. [g] β_1 form of **2**. [h] β_2 form of **2**. [i] α form of **2**. [j] XR = single-crystal X-ray diffraction. All studies were performed on centrosymmetric crystals. With the exception of perchlorotriphenylamine (C_2 symmetry), all structures are asymmetric. Data refer to the structure depicted above. ED = gas-phase electron diffraction. [k] Aryl group is 1-naphthyl. [l] Sum of three bond angles (deg). [m] Perpendicular distance from nitrogen atom to reference plane (Å).

triarylamines, Hellwinkel et al.[23] found that coalescence of the two ortho methyl groups in methyl *N,N*-bis(2-methylphenyl)anthranilate requires 18.7 kcal/mol; it thus appears that the steric requirements of the 1-naphthyl and biphenyl-2-yl groups are slightly less than those of *o*-tolyl in the one- or three-ring flip transition state. This conclusion may be extended to the two-ring flip transition state. Hellwinkel et al.[23] had observed barriers of ca. 12–13 kcal/mol for this process in compounds closely related to the above. In the present work it was found that the upfield methyl signal in the ^{1}H NMR spectrum of **2** (δ 3.42 and 3.12 ppm, $CHFCl_2$, 32 °C) broadens at ca. −50 °C, and at −80 °C the spectrum features three methyl signals (δ 3.48, 3.38, and 2.84 ppm) in a ratio of ca. 2:1:2. Further cooling to −115 °C leads to no further changes. Apparently, at ca. −50 °C the two-ring flip begins to freeze out, and a barrier ($\Delta G^{\ddagger}$) of roughly 11–12 kcal/mol may be estimated for this process. The $\Delta\Delta G^{\ddagger}$ of ca. 5 kcal/mol for the two- and one- (or three-) ring flips found in the present work is thus in complete accord with similar findings by Hellwinkel et al.[23] It should be noted, however, that some alternative interpretations of these observations, e.g., freezing out of the $\beta_1 \rightleftarrows \beta_2$ site exchange process, cannot be rigorously excluded.

Structures of the Residual Diastereomers in Relation to Those of Other Triarylamines. A meaningful description of the α and β structures is best rendered by comparing key features in these molecules with those in other triarylamines for which the appropriate information is available. We have therefore listed in Tables II and III nitrogen pyramidality, aryl ring tilt angles,[34] C–N bond lengths, and C–N–C bond angles for α- and β-**2**, along with the corresponding quantities for other triarylamines.[35]

Table II lists the perpendicular displacement of the central atom from the reference plane, i.e., the pyramidality at nitrogen. Among triarylamines whose structures have been determined by X-ray analysis,[36] the conformers of **2** (entries 8–10) are seen to have the highest pyramidality. Although pyramidalization of the nitrogen atom in **2** is to be expected on grounds of symmetry alone (see above), the extent of this effect requires further comment.

On the basis of NMR evidence, and by analogy with other, related systems, Hellwinkel et al.[20,23] suggested that in the ground state of such systems the three ortho substituents and the nitrogen atom are all on the same side of the reference plane, i.e., that the three substituents point toward the apex of a nitrogen pyramid.[37] Our results are fully in accord with this analysis, for which they serve to provide the first direct structural evidence. The magnitude of the deviation from planarity may be taken as a measure of the imbalance in nonbonding interactions above and below the reference plane; it follows that the bulkier the ortho substituents, the greater the pyramidalization. Whether tri-ortho-substituted triarylamines adopt other conformations as well seems to depend on the particular system. Thus, the low-temperature ^{1}H NMR spectrum of **2** indicates the presence of other conformations at the slow exchange limit of the two-ring flip, whereas Hellwinkel et al.[20,23] were unable to find any evidence for the presence of other conformations.

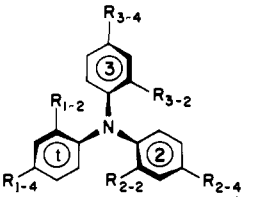
Among the conformational isomers of **2**, the α form has the most pyramidal nitrogen atom, suggesting that the steric interactions of the ortho substituents are relatively severe. This assessment is consistent with a number of abnormal structural features found in this isomer.

First, as seen by inspection of Table III, the tilt angle of the methoxycarbonylphenyl ring in α-**2** is only 29°, the smallest such value in the collection. Second, the inter-ring dihedral (twist) angle in the biphenyl moiety is 74 ± 0.5°, as compared to 49 ± 1° for the β_1 and 58 ± 2° for the β_2 isomer. Third, the dihedral angle between the methoxycarbonyl group and the phenyl ring within the methoxycarbonylphenyl moiety is 9 ± 1.5°, as compared to 43 ± 2° for the β_1 and 52 ± 0.5° for the β_2 isomer. The last two effects seem to be closely related: as revealed by an examination of molecular models, the methoxycarbonylphenyl group and the outer phenyl ring of the biphenyl-2-yl moiety in the α isomer are stacked in almost parallel planes.

The β_1 form is the least pyramidal among the isomers of **2**. It is therefore noteworthy that the C–N bonds in this conformer are significantly longer than those of other triarylamines (Table III). Apparently, bond stretching affords an additional mechanism for the reduction of repulsive interactions between the ortho substituents.

None of three conformers of **2** shows any evidence for unusual resonance interaction between the central nitrogen and the aryl rings. Where such interaction occurs, the effect on the

Table III. Tilt Angles of Aryl Rings, C-N Bond Lengths, and C-N-C Bond Angles in Triarylamines



entry[a]	tilt angle, deg[b,c] ring 1	ring 2	ring 3	r(C-N), Å ring 1	ring 2	ring 3	C-N-C, deg[g] ring 1	ring 2	ring 3
1	40	40	35	1.430	1.430	1.414	119.2	119.2	121.6
2	64	45	47[d]	1.386	1.418	1.421	117.1	122.0	120.9
3	73[e]	41	37[f]	1.371	1.446	1.448	117.3	121.3	121.4
4	56	47[d]	46	1.423	1.421	1.440	119.1	120.8	120.0
5	59	31	58	1.411	1.431	1.417	118.6	122.5	118.8
6	70[d]	35[f]	40	1.403	1.425	1.446	117.1	121.1	121.3
7	63[d]	33	38	1.425	1.413	1.431	120.1	118.7	118.8
8	52[f]	41[d]	48	1.451	1.466	1.468	118.1	118.5	118.1
9	51	39[f]	50	1.426	1.431	1.424	118.4	117.3	118.3
10	51	45	29	1.426	1.439	1.433	115.8	115.6	118.4
11	47 ± 5	47 ± 5	47 ±5	1.42 ± 0.04	1.42 ± 0.04	1.42 ± 0.04	116 ± 2	116 ± 2	116 ± 2

[a] See footnotes *a–k*, Table II. [b] Absolute values of tilt angles, as defined in ref 34. [c] Mean deviation ±≤0.5° unless otherwise indicated. [d] Mean deviation ≤±1.0°. [e] Mean deviation ≤±1.5°. [f] Mean deviation ≤±2.0°. [g] The angle opposite the specified ring, e.g., the C(ring 2)-N-C(ring 3) angle in the column headed ring 1.

structure is seen in unusually large tilt angles, short C-N bonds, and decreased C-N-C bond angles (ring 1, entries 2, 3, and 6 in Table III).

The structural details discussed above serve to account for the spectral properties of the α and β isomers. In contrast to the β form, the methoxycarbonyl group and the phenyl ring in the α form are almost coplanar, consistent with the carbonyl stretch frequencies of 1715 and 1729 cm^{-1} observed for α- and β-**2**, respectively. Furthermore, the methyl group in the α isomer is located above the plane of the naphthalene ring, and is therefore more strongly shielded than the methyl groups in the β isomer. On the assumption that the conformers depicted in Figure 5 also predominate in solution, one might therefore expect an upfield shift of the α relative to the β methyl group. This expectation is fulfilled by the observation that δ (CD_2Cl_2) is 3.03 and 3.38 ppm for the α and β isomer, respectively.

Nonstereogenic Chiral Centers. The pyramidal nitrogen atom in **2** is attached to three different substituents and therefore formally qualifies as a chiral center.[42] In the conformers depicted in Figure 5, this center has the *R* configuration. A fifth two-valued configurational descriptor is thus introduced, and, according to the convention adopted in this paper, the configurations of these conformers may be described as (*R*)-(0000) and (*R*)-(1000).[43] The question which immediately arises concerns the existence of conformers with (*S*)-(0000) and (*S*)-(1000) configurations; beyond that, the larger question arises whether one should consider 2^5 instead of only 2^4 stereoisomers.

Before we proceed to address this question, we must reemphasize that the chirality at nitrogen in these conformers is not a trivial deformation arising from crystal packing forces, such as is probably the case for most of the other triarylamines in Table II.[11] Instead, the underlying cause is the absence of symmetry constraints in the free molecule, i.e., the absence of a plane or a twofold axis of symmetry. The essence of the phenomenon is thus seen to be the symmetry nonequivalence of the two faces of the reference plane. Expressed otherwise, in an asymmetric molecule such as **2** there is bound to be an imbalance of nonbonding interactions above and below the reference plane, and it is this imbalance which enforces pyramidality at nitrogen in the ground state.[46]

We therefore recognize a fundamental distinction between systems of the type Ar_3Z in which a double-well potential with a barrier significantly greater than RT[49] results in stereoisomerism due to pyramidality at Z (as in phosphines and arsines), and those systems in which the barrier separating the two energy wells has been replaced by an energy minimum, or has been reduced to less than RT,[49] so that the "natural" ground state is one in which Z is planar (as in triarylamines, boranes, and carbenium ions). In the first case, a central atom with three suitably different ligands will function as a stereogenic element, and will give rise to stereoisomers differing in configuration at Z. In the second case, however, the deformation from planarity which makes Z a chiral center is solely induced by the symmetry nonequivalence of the two faces of the reference plane, i.e., the configuration at Z depends entirely on that of the rest of the molecule. It follows that Z is incapable of giving rise to stereoisomerism in its own right, i.e., Z is not a stereogenic element.[50] This being the case for the maximally labeled triarylamine **2**, (*S*)-(0000) and (*S*)-(1000) do not correspond to minima on the conformational potential energy hypersurface, and the number of stereoisomers is thus limited to 16.

The preceding considerations lead to the conclusion that, in processes involving interconversion among conformers of **2**, the energy requirement for nitrogen inversion is relatively high. Consider, for example, the enantiomerization of (*R*)-(0000) to (*S*)-(1111), which requires a minimum of three two-ring flips.[22] The overall result is inversion at nitrogen, but, whichever step or steps in the three-step sequence are responsible (an odd number, one or three, is required), it takes a two-ring flip to effect inversion at nitrogen. We have estimated an energy barrier of 11–12 kcal/mol for this process in **2**, a value which is well above the inversion barriers of typical acyclic trialkylamines, let alone aromatic amines.[14,52,53]

Experimental Section

Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N.Y. Infrared spectra were recorded on a Perkin-Elmer 467 spectrometer. NMR spectra were recorded on a Varian XL-100 spectrometer equipped wth variable-temperature accessories, operating in the Fourier transform mode, and refer to solutions in the appropriate solvent containing tetramethylsilane (Me_4Si) as internal reference (unless specified otherwise). Temper-

ature measurements were made with a Wilmad T-811 NMR probe thermometer and are believed accurate to ±1 °C. Mass spectra were measured on an AEI MS-9 high-resolution mass spectrometer, with an ionizing voltage of 70 eV. Melting points were measured in a Thomas-Hoover apparatus in capillary tubes and are corrected. TLC analyses were performed on Whatman MK6F silica gel plates and were developed using an eluent of 10% acetone–90% hexanes (v/v). Preparative chromatography was performed on silica gel columns prepared in petroleum ether (60–80 °C), and eluted with an increasing gradient of $CHCl_3$ in petroleum ether (60–80 °C).

Methyl *N*-(Biphenyl-2-yl)-*N*-(1-naphthyl)anthranilate (2). A mixture of methyl anthranilate (3.73 g, 25 mmol), 2-iodobiphenyl (7.0 g, 25 mmol), copper-bronze powder (0.75 g, BDH Chemicals Ltd.), anhydrous K_2CO_3 (3.5 g, 25 mmol), and nitrobenzene (12 mL) was heated at 170–180 °C for 2.5 h. TLC analysis of the reaction mixture showed 2-iodobiphenyl (R_f 0.72), a new spot (R_f 0.55), and methyl anthranilate (R_f 0.30). (After standing overnight, the new spot developed a yellow color on the TLC plate.) The nitrobenzene was removed by steam distillation, and chloroform (50 mL) was added to the residue. The separated organic layer was added to chloroform extracts from the aqueous layer, dried over anhydrous $MgSO_4$, and filtered, and the solvent was distilled at reduced pressure. The residue was dissolved in the minimum quantity of chloroform, and then chromatographed. All chromatography fractions shown by TLC analysis to exhibit the new spot were combined, and the solvent was distilled at reduced pressure to yield 4.4 g (58%) of **methyl *N*-(biphenyl-2-yl)anthranilate (3)** as an oil: ^1H NMR ($CDCl_3$) δ (ppm) 3.72 (s, 3 H, OCH_3), 6.67 (m, 2 H, aromatic H), 7.35 (m, 10 H, aromatic H), 7.88 (m, 1 H, aromatic H), 9.14 (broad s, 1 H, NH); IR ν_{max} (thin film) (cm^{-1}) 3320 (N–H), 1687 (C=O), 1510 (N–H).

A mixture of methyl *N*-(biphenyl-2-yl)anthranilate (4.2 g, 13.8 mmol), 1-iodonaphthalene (4.3 g, 16.9 mmol), copper–bronze powder (0.5 g), anhydrous K_2CO_3 (2.0 g, 14.5 mmol), and nitrobenzene (6 mL) was heated at 170–180 °C for 48 h. TLC analysis of the reaction mixture showed 1-iodonaphthalene (R_f 0.70), methyl *N*-(biphenyl-2-yl)anthranilate (R_f 0.55), and two new spots (R_f 0.49 and 0.44). (After standing overnight, the R_f 0.55 spot developed a yellow color, and the R_f 0.49 spot developed a brown color.) The nitrobenzene was removed by steam distillation, and the residue was worked up as described above. All chromatography fractions shown by TLC analysis to exhibit the new spot at R_f 0.44 were combined. Distillation of the solvent at reduced pressure yielded 460 mg (11%) of a white, crystalline solid whose melting point and IR and ^1H NMR spectra were found to be identical in all respects with those of authentic methyl 2-(9*H*-carbazol-9-yl)benzoate (see below). The characterization was additionally confirmed by a mixture melting point using an authentic sample of methyl 2-(9*H*-carbazol-9-yl)benzoate.

Further elution of the column afforded fractions shown by TLC analysis to exhibit the new spot at R_f 0.49. Distillation of the solvent at reduced pressure yielded 750 mg (14%) of **methyl *N*-(biphenyl-2-yl)-*N*-(1-naphthyl)anthranilate** as an oil, which solidified upon addition of *n*-heptane. Slow recrystallization from hot *n*-heptane produced a mixture of two types of crystals: aggregates of parallelepipeds and rosettes of needles (Figure 4). The morphologically different crystals were found to be present in approximately equal quantities, and were separated by hand. The parallelepipeds and the needles were designated as α and β isomers, respectively.

α Isomer: mp 161–163 °C; ^1H NMR (CD_2Cl_2, −40 °C) δ (ppm) 3.03 (s, 3 H, OCH_3), 7.40 (m, 20 H, aromatic H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, −37 °C) δ (ppm) 51.5 (OCH_3); IR ν_{max} (KBr) 1715 cm^{-1} (C=O); MS *m/e* (rel intensity) 429 (M^+, 100), 398 ($M^+ - OCH_3$, 3), 370 ($M^+ - CH_3O_2C$, 9), 319.2 (M*); MS (high resolution) *m/e* 429.172 796 (429.172 869 calcd for $C_{30}H_{23}NO_2$).

Anal. Calcd for $C_{30}H_{23}NO_2$: C, 83.89; H, 5.40; N, 3.26. Found: C, 83.28; H, 5.70; N, 3.24.

β Isomer: mp 132–133 °C; ^1H NMR (CD_2Cl_2, −40 °C) δ (ppm) 3.38 (s, 3 H, OCH_3), 7.40 (m, 20 H, aromatic H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, −37 °C) δ (ppm) 52.1 (OCH_3); IR ν_{max} (KBr) 1729 cm^{-1} (C=O); MS *m/e* (rel intensity) 429 (M^+, 100), 398 ($M^+ - OCH_3$, 3), 370 ($M^+ - CH_3O_2C$, 14), 319.2 (M*); MS (high resolution) *m/e* 429.172 826 (429.172 869 calcd for $C_{30}H_{23}NO_2$).

Anal. Calcd for $C_{30}H_{23}NO_2$: C, 83.89; H, 5.40; N, 3.26. Found: C, 83.78; H, 5.46; N, 3.36.

At ambient temperature each isomer gave ^1H and $^{13}C\{^1H\}$ NMR spectra with the same resonances: ^1H NMR (CD_2Cl_2, ambient temperature) δ (ppm) 3.08 (s, 1.5 H, α-OCH_3), 3.40 (s, 1.5 H, β-OCH_3), 7.40 (m, 20 H, aromatic H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, ambient temperature) δ (ppm) 51.1 (α-OCH_3), 51.7 (β-OCH_3).

Table IV. Final Atomic Parameters for the α Isomer of **2**[a]

atom	*x*	*y*	*z*	*B*
O(1)	0.3372(3)	0.4761(3)	0.9536(2)	*b*
O(2)	0.4732(2)	0.3627(2)	0.8368(2)	*b*
N(1)	0.3337(2)	0.2026(2)	0.7451(2)	*b*
C(11)	0.2045(3)	0.2278(3)	0.8246(2)	*b*
C(12)	0.2117(3)	0.3108(3)	0.8971(2)	*b*
C(13)	0.0794(4)	0.3289(3)	0.9717(2)	*b*
C(14)	−0.0560(4)	0.2692(4)	0.9750(3)	*b*
C(15)	−0.0625(3)	0.1890(4)	0.9036(3)	*b*
C(16)	0.0673(3)	0.1680(3)	0.8298(2)	*b*
C(17)	0.3452(3)	0.3903(3)	0.8994(2)	*b*
C(18)	0.6029(4)	0.4457(4)	0.8311(3)	*b*
C(21)	0.4342(3)	0.0955(3)	0.7803(2)	*b*
C(22)	0.5890(3)	0.1053(3)	0.7252(2)	*b*
C(23)	0.6861(3)	−0.0034(3)	0.7603(2)	*b*
C(24)	0.6277(4)	−0.1139(3)	0.8498(3)	*b*
C(25)	0.4805(4)	−0.1176(4)	0.9021(3)	*b*
C(26)	0.3827(3)	−0.0127(3)	0.8663(3)	*b*
C(27)	0.6521(3)	0.2171(3)	0.6370(2)	*b*
C(28)	0.8008(3)	0.2185(3)	0.5850(2)	*b*
C(29)	0.8950(3)	0.1096(3)	0.6187(3)	*b*
C(30)	0.8382(3)	0.0021(3)	0.7041(3)	*b*
C(31)	0.3109(3)	0.2138(3)	0.6427(2)	*b*
C(32)	0.2566(3)	0.3434(3)	0.5915(2)	*b*
C(33)	0.2340(3)	0.3509(3)	0.4922(2)	*b*
C(34)	0.2673(3)	0.2386(3)	0.4414(2)	*b*
C(35)	0.3209(3)	0.1128(3)	0.4921(2)	*b*
C(36)	0.3418(3)	0.1012(3)	0.5913(2)	*b*
C(37)	0.2230(3)	0.4702(3)	0.6403(2)	*b*
C(38)	0.0750(3)	0.5058(3)	0.6799(2)	*b*
C(39)	0.0438(4)	0.6239(3)	0.7254(3)	*b*
C(40)	0.1587(4)	0.7078(3)	0.7300(3)	*b*
C(41)	0.3058(4)	0.6742(3)	0.6898(3)	*b*
C(42)	0.3370(3)	0.5546(3)	0.6457(2)	*b*
H(13)	0.085	0.386	1.026	5.0
H(14)	−0.151	0.288	1.030	6.0
H(15)	−0.162	0.141	0.905	6.0
H(16)	0.063	0.108	0.777	5.0
H(18)A	0.695	0.417	0.780	8.0
H(18)B	0.625	0.433	0.901	8.0
H(18)C	0.589	0.552	0.803	8.0
H(24)	0.697	−0.191	0.876	6.0
H(25)	0.441	−0.198	0.966	6.0
H(26)	0.272	−0.017	0.905	6.0
H(27)	0.586	0.299	0.613	4.0
H(28)	0.843	0.296	0.519	6.0
H(29)	1.006	0.113	0.580	6.0
H(30)	0.908	−0.074	0.729	6.0
H(33)	0.190	0.442	0.456	5.0
H(34)	0.252	0.248	0.368	6.0
H(35)	0.347	0.028	0.456	6.0
H(36)	0.381	0.009	0.630	5.0
H(38)	−0.011	0.445	0.676	5.0
H(39)	−0.066	0.649	0.754	6.0
H(40)	0.133	0.793	0.766	7.0
H(41)	0.392	0.738	0.691	6.0
H(42)	0.446	0.528	0.618	5.0

[a] Standard deviations in parentheses. [b] Anisotropic thermal parameters are recorded in the supplementary material.

Methyl 2-(9*H*-Carbazol-9-yl)benzoate (4). A mixture of 9*H*-carbazole (3.46 g, 20.7 mmol), methyl 2-iodobenzoate (7.86 g, 30 mmol), copper–bronze powder (0.90 g), anhydrous K_2CO_3 (4.14 g, 30 mmol), and nitrobenzene (2 mL) was heated at 170–180 °C for 40 h. TLC analysis of the reaction mixture showed no unreacted carbazole (R_f 0.30), a new spot (R_f 0.45), and methyl 2-iodobenzoate (R_f 0.55). The reaction mixture was cooled, and chloroform (50 mL) was added followed by water (50 mL). The separated organic layer was added to chloroform extracts from the aqueous layer, dried over anhydrous $MgSO_4$, and filtered. The solvent was distilled at reduced pressure. The residue was dissolved in the minimum quantity of chloroform and

Table V. Final Atomic Parameters for the β_1 isomer of **2**[a]

atom	x	y	z	B
O(1)	−0.0427(3)	0.6311(2)	0.6936(5)	b
N(1)	0.1658(3)	0.6564(2)	0.4288(5)	b
O(2)	0.0750(3)	0.5640(2)	0.6501(5)	b
C(11)	0.0776(4)	0.6512(3)	0.3478(7)	b
C(12)	0.0064(4)	0.6310(3)	0.4327(8)	b
C(13)	−0.0781(4)	0.6329(3)	0.3527(9)	b
C(14)	−0.0904(4)	0.6517(4)	0.1929(10)	b
C(15)	−0.0193(5)	0.6699(3)	0.1097(7)	b
C(16)	0.0652(4)	0.6705(3)	0.1870(7)	b
C(17)	0.0105(4)	0.6096(3)	0.6035(8)	b
C(18)	0.0846(4)	0.5456(3)	0.8180(7)	b
C(21)	0.2413(3)	0.6491(4)	0.3315(6)	b
C(22)	0.2522(4)	0.5807(3)	0.2515(6)	b
C(23)	0.3270(4)	0.5750(3)	0.1617(7)	b
C(24)	0.3874(4)	0.6338(4)	0.1580(6)	b
C(25)	0.3743(4)	0.6978(4)	0.2384(7)	b
C(26)	0.2995(4)	0.7057(3)	0.3239(6)	b
C(27)	0.1965(3)	0.5191(3)	0.2589(7)	b
C(28)	0.2126(4)	0.4561(3)	0.1784(8)	b
C(29)	0.2858(5)	0.4517(4)	0.0846(8)	b
C(30)	0.3419(4)	0.5098(4)	0.0773(7)	b
C(31)	0.1780(4)	0.6988(3)	0.5788(6)	b
C(32)	0.2466(3)	0.6807(3)	0.6944(7)	b
C(33)	0.2516(4)	0.7225(3)	0.8349(7)	b
C(34)	0.1926(4)	0.7783(3)	0.8602(7)	b
C(35)	0.1277(4)	0.7957(3)	0.7407(8)	b
C(36)	0.1210(3)	0.7566(3)	0.5989(7)	b
C(37)	0.3135(4)	0.6219(4)	0.6791(6)	b
C(38)	0.4014(5)	0.6395(3)	0.7155(7)	b
C(39)	0.4661(4)	0.5861(5)	0.7087(8)	b
C(40)	0.4439(6)	0.5155(5)	0.6669(9)	b
C(41)	0.3551(6)	0.4976(3)	0.6287(7)	b
C(42)	0.2897(4)	0.5508(4)	0.6346(7)	b
H(13)	−0.133	0.620	0.417	7.0
H(14)	−0.154	0.651	0.134	8.0
H(15)	−0.030	0.683	−0.012	8.0
H(16)	0.118	0.687	0.123	7.0
H(18)A	0.136	0.510	0.849	10.0
H(18)B	0.030	0.521	0.859	10.0
H(18)C	0.098	0.590	0.891	10.0
H(24)	0.444	0.629	0.094	6.0
H(25)	0.419	0.742	0.233	6.0
H(26)	0.287	0.755	0.384	6.0
H(27)	0.140	0.523	0.322	6.0
H(28)	0.172	0.411	0.188	7.0
H(29)	0.298	0.405	0.017	7.0
H(30)	0.397	0.507	0.010	6.0
H(33)	0.301	0.711	0.926	6.0
H(34)	0.196	0.807	0.968	6.0
H(35)	0.083	0.838	0.759	6.0
H(36)	0.074	0.771	0.509	6.0
H(38)	0.420	0.693	0.744	7.0
H(39)	0.532	0.599	0.738	8.0
H(40)	0.492	0.475	0.662	8.0
H(41)	0.338	0.444	0.594	8.0
H(42)	0.223	0.537	0.610	7.0

[a,b] See Table IV.

Table VI. Final Atomic Parameters for the β_2 isomer of **2**[a]

atom	x	y	z	B
O(1)	0.9952(3)	0.0446(6)	0.3709(3)	b
O(2)	0.8785(3)	0.0106(7)	0.3800(3)	b
N(1)	0.9864(3)	0.2856(8)	0.2220(3)	b
C(11)	0.9518(3)	0.1367(10)	0.1881(5)	b
C(12)	0.9252(3)	0.0113(10)	0.2442(4)	b
C(13)	0.8875(4)	−0.1259(11)	0.2109(5)	b
C(14)	0.8800(4)	−0.1525(10)	0.1237(5)	b
C(15)	0.9091(4)	−0.0333(12)	0.0689(4)	b
C(16)	0.9445(4)	0.1103(10)	0.1004(4)	b
C(17)	0.9374(4)	0.0254(10)	0.3369(5)	b
C(18)	0.8840(4)	0.0348(11)	0.4723(4)	b
C(21)	1.0374(4)	0.3713(11)	0.1706(4)	b
C(22)	1.1022(4)	0.2819(11)	0.1526(4)	b
C(23)	1.1545(5)	0.3735(13)	0.1055(5)	b
C(24)	1.1419(6)	0.5436(15)	0.0812(5)	b
C(25)	1.0798(6)	0.6227(12)	0.0999(5)	b
C(26)	1.0273(4)	0.5361(11)	0.1440(4)	b
C(27)	1.1179(4)	0.1133(11)	0.1806(4)	b
C(28)	1.1812(5)	0.0373(11)	0.1623(5)	b
C(29)	1.2313(5)	0.1277(16)	0.1148(6)	b
C(30)	1.2198(5)	0.2881(15)	0.0884(5)	b
C(31)	0.9488(4)	0.3842(9)	0.2828(4)	b
C(32)	0.9843(3)	0.4843(9)	0.3428(4)	b
C(33)	0.9436(4)	0.5726(9)	0.4042(4)	b
C(34)	0.8704(4)	0.5629(10)	0.4021(5)	b
C(35)	0.8357(3)	0.4686(10)	0.3411(5)	b
C(36)	0.8749(4)	0.3829(9)	0.2804(4)	b
C(37)	1.0626(4)	0.5036(12)	0.3485(4)	b
C(38)	1.0903(4)	0.6680(12)	0.3425(5)	b
C(39)	1.1626(6)	0.6974(13)	0.3476(5)	b
C(40)	1.2074(5)	0.5591(18)	0.3544(6)	b
C(41)	1.1814(6)	0.3973(15)	0.3612(5)	b
C(42)	1.1084(5)	0.3692(11)	0.3565(4)	b
H(13)	0.865	−0.209	0.251	6.0
H(14)	0.854	−0.256	0.101	6.0
H(15)	0.905	−0.051	0.006	6.0
H(16)	0.965	0.196	0.060	6.0
H(18)A	0.836	0.020	0.497	8.0
H(18)B	0.902	0.153	0.485	8.0
H(18)C	0.917	−0.053	0.497	8.0
H(24)	1.179	0.608	0.049	7.0
H(25)	1.072	0.745	0.082	7.0
H(26)	0.981	0.596	0.156	6.0
H(27)	1.082	0.049	0.214	6.0
H(28)	1.192	−0.083	0.183	7.0
H(29)	1.277	0.070	0.101	7.0
H(30)	1.257	0.350	0.056	7.0
H(33)	0.968	0.643	0.450	5.0
H(34)	0.842	0.626	0.446	6.0
H(35)	0.783	0.462	0.340	6.0
H(36)	0.849	0.318	0.234	5.0
H(38)	1.057	0.768	0.334	6.0
H(39)	1.182	0.818	0.346	7.0
H(40)	1.260	0.578	0.354	8.0
H(41)	1.215	0.298	0.370	7.0
H(42)	1.089	0.249	0.359	6.0

[a,b] See Table IV.

then chromatographed. All fractions shown by TLC analysis to exhibit the new spot were combined, the solvent was distilled at reduced pressure, and the crystalline residue was recrystallized from *n*-heptane to yield 3.7 g (59%) of white crystals: mp 150–151 °C; ^{1}H NMR ($CDCl_3$) δ (ppm) 3.16 (s, 3 H, OCH_3), 7.35 (m, 9 H, aromatic H), 8.10 (m, 3 H, aromatic H); IR ν_{max} (KBr) 1738 cm^{-1} (C=O); MS *m/e* (rel intensity) 301 (M^+, 100), 270 ($M^+ - OCH_3$, 13), 242 ($M^+ - CH_3O_2C$, 7), 241 (16); MS (high resolution) *m/e* 301.110 208 (301.110 272 calcd for $C_{20}H_{15}NO_2$).

Anal. Calcd for $C_{20}H_{15}NO_2$: C, 79.72; H, 5.02; N, 4.65. Found: C, 79.51; H, 5.36; N, 4.83.

Crystallography. The α isomer (parallelepipeds) is triclinic: $P\bar{1}$; a = 9.225 (2) Å, b = 9.562 (2) Å, c = 13.447 (2) Å, α = 77.08 (1)°, β = 74.89 (1)°, γ = 87.74 (1)°; d_{calcd} = 1.278 g cm^{-3} for Z = 2 ($C_{30}H_{23}NO_2$, mol wt 429.52); μ(Cu Kα) = 6.4 cm^{-1}. The β isomer (needles) exhibits conformational polymorphism. The β_1 modification (b axis perpendicular to needle axis) is monoclinic: $P2_1/n$; a = 15.189 (3) Å, b = 18.209 (3) Å, c = 8.341 (2) Å, β = 94.87 (2)°; d_{calcd} = 1.241 g cm^{-3} for Z = 4; μ(Cu Kα) = 6.2 cm^{-1}. The β_2 modification (b axis parallel to needle axis) is monoclinic: $P2_1/a$; a = 18.844 (3) Å, b = 7.777 (1) Å, c = 15.717 (2) Å, β = 91.08 (1)°; d_{calcd} = 1.238 g cm^{-3} for Z = 4; μ(Cu Kα) = 6.2 cm^{-1}. For α, β_1, and β_2, crystals measuring approximately 0.10 × 0.20 × 0.30, 0.04 × 0.05 × 0.5, and 0.06 × 0.08 × 0.7 mm, respectively, were used for data collection. All intensity data were measured on Hilger-Watts automated four-circle diffractometers (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse height discrimination). A total of 3003 (α), 2152 (β_1), and 2167 (β_2) reflections were measured for θ < 57° (α), <48° (β_1 and β_2), of which

2299 (α), 1329 (β_1), and 1203 (β_2) were considered to be observed ($I > 2.5\sigma(I)$). The structures were solved by a multiple solution procedure[54] and refined by full-matrix least squares. No absorption correction was made. In the final refinement anisotropic thermal parameters were used for the heavier atoms and isotropic temperature factors were used for the hydrogen atoms. The final discrepancy indices are $R = 0.042$ (α), 0.047 (β_1), 0.053 (β_2) and $wR = 0.049$ (α), 0.041 (β_1), 0.044 (β_2) for the 2299 (α), 1329 (β_1), 1203 (β_2) observed reflections. The final difference maps have no peaks greater than ±0.1 e Å^{-3} for all three structures. Stereoviews of the final structures are given in Figure 5, and the final atomic parameters for the α, β_1, and β_2 isomers are given in Tables IV–VI.

Equilibration Studies on 2. CD_2Cl_2 was added to a thin-walled NMR tube containing α or β isomer, cooled in a dry ice–acetone bath. After the solid had completely dissolved, the cooled tube was rapidly transferred to the NMR spectrometer (probe temperature preset at −21 °C using the Wilmad NMR-probe thermometer), and the spectrum in the methoxy region was recorded as a function of time. The values of the k ($\alpha \rightarrow \beta$) and k ($\beta \rightarrow \alpha$) rate constants for the equilibration of the diastereomers at −21 °C were calculated by use of eq 1, which is an adaptation[55] of the usual expression[56] for a reversible first-order reaction, where R is the ratio of diastereomers at time t and K is the equilibrium constant (i.e., R at t_∞).

$$\ln [(R - K)/(1 + R)] = -(k(\alpha \rightarrow \beta) + k(\beta \rightarrow \alpha))t \qquad (1)$$

The ratio (R) of the two diastereomers was determined from the relative peak areas of the methoxy proton absorptions as a function of time. In order to determine the equilibrium constant, the NMR tube was removed from the probe and kept at ambient temperature for 0.5 h. The spectrum was recorded after the tube was returned to the probe (−21 °C) and thermal equilibrium had been reached. The value of K (α/β) was found to be the same, within experimental error, starting from either the α or the β isomer. A value of K (α/β) = 0.975 ± 0.005 was found at −21 °C. A least-squares treatment (correlation coefficient 0.997) of ln [$(R - K)/(1 + R)$] vs. t (eq 1) using seven data points over a time interval of 11 min and the value of K, together with the Eyring equation,[57] gave the values of $\Delta G^{\ddagger}_{-21}$ for **2** reported in Table I.

Acknowledgment. We thank the National Science Foundation (CHE77-07665) for support of this work.

Supplementary Material Available: Bond lengths (Table IM), bond angles (Table IIM), and final anisotropic thermal parameters for the three isomers (α, β_1, and β_2) (Tables IIIM–VM) of **2** (5 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) Princeton University. (b) On leave from the Department of Chemistry, Ben-Gurion University of the Negev, Israel. (c) Hoffmann-La Roche, Inc.
(2) Finocchiaro, P.; Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 8172; **1974**, *96*, 3198.
(3) Mislow, K.; Gust, D.; Finocchiaro, P.; Boettcher, R. J. *Top. Curr. Chem.* **1974**, *47*, 1.
(4) Mislow, K. *Acc. Chem. Res.* **1976**, *9*, 26.
(5) "C'est la dissymétrie qui crée le phénomène" (Curie, P. *J. Phys. (Paris)* **1894**, *3*, 393).
(6) Desymmetrization may be said to "complicate the problem in an informative way" (Cotton, F. A.; Hanson, B. E.; Jamerson, J. D. *J. Am. Chem. Soc.* **1977**, *99*, 6588).
(7) Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 1535.
(8) The pyramidal stability of triarylphosphines has been demonstrated by the optical resolution of phenyl-*m*-carboxyphenyl-*p*-biphenylylphosphine (Luckenbach, R. *Z. Naturforsch. B* **1976**, *31*, 1135).
(9) The boron atom in triphenylborane[10a] and trimesitylborane[10b] lies in the plane of the three neighboring carbon atoms.
(10) (a) Zettler, F.; Hausen, H. D.; Hess, H. *J. Organomet. Chem.* **1974**, *72*, 157. (b) Blount, J. F.; Finocchiaro, P.; Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 7019.
(11) The nitrogen atom in perchlorotriphenylamine lies in the plane of the three neighboring carbon atoms;[12a] displacement from this plane in other reported X-ray structures of triarylamines[12b-f] is so slight (≤ca. 0.1 Å; cf. Table II) that nonplanarity in these cases may be ascribed to the accident of crystal packing.[13] Although electric dipole moment[15] and gas-phase electron-diffraction[16] measurements on triphenylamine seem to indicate that the nitrogen atom is slightly pyramidal (C–N–C = 114°[15] or 116°[16]), it has been noted[16] that the nitrogen atom in triphenylamine may be planar in the ground state but appear pyramidal because of a shallow thermal bending potential.
(12) (a) Hayes, K. S.; Nagumo, M.; Blount, J. F.; Mislow, K. *J. Am. Chem. Soc.*, **1980**, preceding paper in this issue. (b) Freeman, G. R.; Levy, H. A.; Brown, G. M. *Acta Crystallogr., Sect. A, Suppl.* **1969**, *25*, 145. Brown, G. M., private communication. (c) Popova, E. G.; Chetkina, L. A.; Kotov, B. V. *Zh. Strukt. Khim.* **1976**, *17*, 510. (d) Chetkina, L. A.; Popova, E. G.; Vozzhennikov, V. M.; Kotov, B. V. *Ibid.* **1976**, *17*, 114. (e) Brown, G. M.; Freeman, G. R.; Walter, R. I. *J. Am. Chem. Soc.* **1977**, *99*, 6910. (f) Irngartinger, H., unpublished results, cited in Hellwinkel, D.; Melan, M. *Chem. Ber.* **1974**, *107*, 616.
(13) The inversion barrier for such shallow pyramids is estimated[14] to be less than 0.1 kcal/mol.
(14) Stackhouse, J.; Baechler, R. D.; Mislow, K. *Tetrahedron Lett.* **1971**, 3437.
(15) Leonard, N. J.; Sutton, L. E. *J. Am. Chem. Soc.* **1948**, *70*, 1564.
(16) Sasaki, Y.; Kimura, K.; Kubo, M. *J. Chem. Phys.* **1959**, *31*, 477.
(17) We have commented that "a priori, any system is asymmetric unless constrained to be otherwise".[18] Although accidental planarity cannot be ruled out on grounds of logic, the probability of such an event becomes vanishingly small as the limits of experimental error become vanishingly small.
(18) Mislow, K.; Bickart, P. *Isr. J. Chem.* **1977**, *15*, 1.
(19) Finocchiaro, P.; Gust, D., Mislow, K. *J. Am. Chem. Soc.* **1974**, *96*, 3205.
(20) Hellwinkel, D.; Melan, M.; Egan, W.; Degel, C. R. *Chem. Ber.* **1975**, *108*, 2219.
(21) Kurland, R. J.; Schuster, I. I.; Colter, A. K. *J. Am. Chem. Soc.* **1965**, *87*, 2279.
(22) We have noted[4] that enantiomerization by this mechanism, which requires a minimum of three two-ring flips,[7] cannot proceed by way of an achiral structure, so that (by the principle of microscopic reversibility), enantiomeric pathways always exist, e.g., (0000) → (1001) → (0011) → (1111) and (1111) → (0110) → (1100) → (0000).
(23) Hellwinkel, D.; Melan, M.; Degel, C. R. *Tetrahedron* **1973**, *29*, 1895.
(24) If the rings numbered 2 and 3 are constitutionally indistinguishable (i.e., if they have the same ortho substituent R), the following eight pairs of isomers become rotationally equivalent: (0100)/(0011), (1101)/(1001), (0001)/(0101), (1000)/(1111), (1110)/(1010), (0111)/(0000), (1011)/(1100), and (0010)/(0110).
(25) Enantiomerization by this mechanism does not equivalence R_2 and R_3 (the ortho substituents in rings 2 and 3)[24] since R_2 in any one structure and R_3 in the corresponding enantiomer are diastereotopic. Because the four *dl* pairs are mutually diastereomeric, R_2 and R_3 retain their diastereotopic relationship.
(26) Finocchiaro, P.; Hounshell, W. D.; Mislow, K. *J. Am. Chem. Soc.* **1976**, *98*, 4952.
(27) Lack of local C_2 symmetry is assured by unsymmetrical placement of substituents in the ortho and/or meta positions. However, substituents in the meta positions exert a negligible, or at most a minor, effect (e.g., through buttressing) on the rates of conformational interconversion.
(28) Ullmann, F. *Ber.* **1903**, *36*, 2382.
(29) The coalescence was found to be reversible, showing that decomposition cannot account for the observed process.
(30) Gutowsky, H. S.; Holm, C. H. *J. Chem. Phys.* **1956**, *25*, 1228. This method is applicable in the present case since the deviation of the isomer population ratio from unity is negligible (Table I).
(31) For the α structure in Figure 5, the value of this torsion angle is −8°.
(32) Conformational polymorphism in triarylamines has been reported previously.[12c,d]
(33) The one- or three-ring flips lead to diastereomerization of maximally labeled triarylamines differing only in helicity, such as α- and β-**2** (Figure 5).[4] The zero ring flip leads to eight residual diastereomers,[4] and it is in principle conceivable that the isolated α and β forms happen to be two of these. However, while this alternative cannot be rigorously excluded, it is highly unlikely on other grounds: this mechanism has been strictly ruled out in the conformational isomerization of related systems,[4] and the transition state is expected to involve severe internal congestion, leading to an energy barrier well above that observed in the present case.
(34) The ring tilt angle is defined as the dihedral angle between the average plane of the aromatic ring and a line which passes through the central nitrogen atom normal to the reference plane.
(35) Parameters listed in Tables II and III which were derived from other sources[12,15] are calculated from the data given in the cited references.
(36) The electron-diffraction result (entry 11) is open to question.[11]
(37) This ground-state conformation is adopted by tris(2-methylphenyl)phosphine and its oxide,[38] by tris(2,5-dimethylphenyl)arsine,[39] by tris(2-methylphenyl)germane,[40] and by tris(2-methylphenyl)silane.[41]
(38) Halpern, E. J.; Mislow, K. *J. Am. Chem. Soc.* **1967**, *89*, 5224. Shaw, R. A.; Woods, M.; Cameron, T. S.; Dahlén, B. *Chem. Ind. (London)* **1971**, 151. Cameron, T. S.; Dahlén, B. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1737.
(39) Trotter, J. *Acta Crystallogr.* **1963**, *16*, 1187.
(40) Cameron, T. S.; Mannan, K. M.; Stobart, S. R. *Cryst. Struct. Commun.* **1975**, *4*, 601.
(41) Hummel, J. P.; Zurbach, E. P.; DiCarlo, E. N.; Mislow, K. *J. Am. Chem. Soc.* **1976**, *98*, 7480.
(42) Cahn, R. S.; Ingold, C.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385.
(43) By *configuration* we mean[44] "the relative position or order of the arrangement of atoms in space which characterizes a particular stereoisomer"; this definition accords with the sense (i.e., relative spatial arrangement of component parts in a system) in which the term is used in general scientific discourse. For each set of stereoisomers, there exists a set of configurational descriptors which are mapped one-to-one onto the set of stereoisomers and thus serve as characteristic labels of the configurations. All other considerations are regarded as irrelevant. Accordingly, *R*, *S*, D, L, *E*, *Z*, exo, endo, axial, equatorial, anti, gauche, *M*, *P*, etc., are all configurational descriptors or, in a convenient ellipsis, configurations of the appropriate stereoisomers. This usage, though unorthodox, can boast of three advantages: it is simply applied to all stereoisomers regardless of their mutual relationship (enantiomers, diastereomers, invertomers, ro-

tomers, etc.), it is in harmony with the breadth of meaning implied by the etymology of the term as much as by its widespread usage in technological fields outside of chemistry, and, last but not least, it renders redundant and thus superfluous the term "configurational isomer", whose contradistinction to "conformational isomer" has saddled stereochemistry with a needless dichotomy.[45]
(44) Mislow, K. "Introduction to Stereochemistry"; W. A. Benjamin: New York, 1965; p 82.
(45) (a) A more detailed examination of these and related fundamental questions is reserved for future discussion. (b) For a different approach to the definition of "stereochemical configuration", see: Drozd, V. N.; Zefirov, N. S.; Sokolov, V. I.; Stankevich, I. V. *Zh. Org. Khim.* **1979**, *15*, 1785.
(46) The same absence of symmetry constraints or, expressed in physical terms, imbalance of bonding or nonbonding interactions is responsible for the pyramidality at other tricoordinate atoms whose "natural" ground state is planar. Calculations on carbocations amply bear this out. For example, the carbenium ion center in ethyl cation is pyramidal in a conformation in which a plane of symmetry bisects the H–C^+–H bond angle.[47] Similarly, the improbability of meeting the symmetry requirements for a planar ground state[17] is the underlying reason for pyramidality at the carbenium ion center in asymmetric tricyclic carbocations.[48]
(47) Lathan, W. A.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 808.
(48) Bach, R. D.; Siefert, J. H.; Tribble, M. T.; Greengard, R. A.; LeBel, N. A. *J. Am. Chem. Soc.* **1973**, *95*, 8182.
(49) Eliel, E. L. *Isr. J. Chem.* **1977**, *15*, 7.
(50) By extension of the same argument to other systems in the literature, it is easily seen that nonstereogenic chiral elements are widespread in organic chemistry. As in the present case, where such elements are centers they may have to be treated *as if* they were coplanar, a step which becomes necessary if the model of the molecule is to serve a useful function in the enumeration of stereoisomers. Of particular interest in this connection are two substituted biphenyls studied by Helmchen et al.,[51] biphenyl-2,2′,6,6′-tetracarboxylic acid tetra-(*S*)-α-phenylethylamide (D_2 symmetry) and 2′,6′-dimethoxycarbonylbiphenyl-2,6-dicarboxylic acid di-(*S*)-α-phenylethylamide (C_2 symmetry), neither of which has axial chirality since no permutation of the ligands on the biphenyl framework which maintains the constitution of the molecule can lead to stereoisomerism. However, although the chirality of these compounds is thus determined by the chirality of ligands and not by the chirality of the biphenyl moiety, the latter is expected to be chiral in the ground-state conformation of the molecule, on the basis of symmetry arguments similar to those adduced in connection with the chirality at nitrogen in **2**. A configurational descriptor (e.g., *P* or *M*, whichever applies) may therefore be attached to the biphenyl moiety in this compound. Nevertheless, since this moiety is not stereogenic, it may be treated *as if* it had local D_{2d} symmetry.
(51) Helmchen, G.; Haas, G.; Prelog, V. *Helv. Chim. Acta* **1973**, *56*, 2255.
(52) Lehn, J. M. *Top. Curr. Chem.* **1970**, *15*, 311. Rauk, A.; Allen, L. C.; Mislow, K. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 400. Lambert, J. B. *Top. Stereochem.* **1971**, *6*, 19.
(53) An increase in the size of the ortho substitutents brings about an increase in the two-ring flip barrier,[20] and therefore also in the barrier to inversion at nitrogen.
(54) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A* **1971**, *27*, 368.
(55) Gutowsky, H. S.; Jonas, J.; Siddall, T. H. III *J. Am. Chem. Soc.* **1967**, *89*, 4300.
(56) Laidler, K. J. "Chemical Kinetics", 2nd ed.; McGraw-Hill; New York, 1965; p 19.
(57) The transmission coefficient was assumed to be unity.

Photochemical Kinetics of Salicylidenaniline

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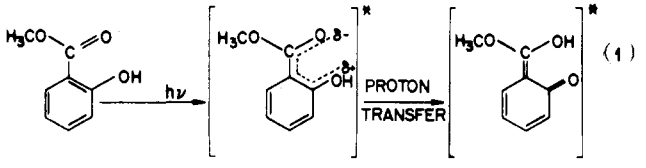
Abstract: The nanosecond and picosecond photochemical kinetics of quinoid fluorescence produced by excitation of the enol form of salicylidenaniline have been investigated in various environments. An excited state tautomeric proton transfer occurs within 5 ps at temperatures above 4 K in both protic and aprotic solvents. Bimodal fluorescence kinetics observed at low temperature appear to represent excited state vibrational relaxation occurring on the 10-ps time scale.

Introduction

The acidities of functional groups in excited electronic states are often strongly different than in ground electronic states. pK_a increases as large as 6 pK_a units have in fact been observed.[1] These large changes often induce proton-transfer reactions upon absorption of a photon. This type of photochemical reaction occurs in small molecules such as aromatic ketones[2] and fluorescent indicators,[3] as well as in complex biological systems such as rhodopsin.[4] In excited states, phenols, amines, and protonated amines usually become more acidic, while ketones, esters, carboxylic acids, amides, and azo groups become more basic.

The case where functional groups with opposite pK_a tendencies occupy nearby sites within one molecule is particularly interesting because the proton may move from one group to the other generating either transient or permanent tautomers of the original molecule. An example of this phenomenon is found in methyl salicylate (eq 1). Weller[5] first studied the

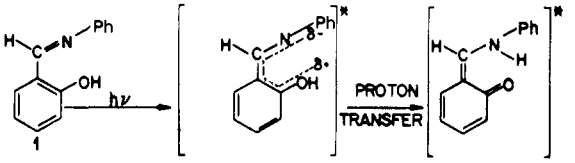


(1)

absorption and emission spectra of this compound, and concluded that the large fluorescence Stokes shift was the result of proton translocation. This proposal was supported by the absence of the unusually large Stokes shifted fluorescence in 2-methoxybenzoate. It was thought that a tautomer of the initially excited state[6,7] is generated as shown in eq 1. Recent work shows that the proton transfer is completed very rapidly without any evidence for a double minimum potential along the reaction coordinate in the excited state.[8,9]

Another class of compounds with similar proton-transfer properties are the salicylenanilines. These compounds have attracted much interest because of their additional ability to produce stable photochromic isomers of the initially colorless compound.[10-17]

This paper deals with the fluorescent properties of salicylidenaniline (**1**) and its derivatives, which exhibit very large



1

Stokes-shifted fluorescence.[14,15] Our purpose is to probe the excited state reaction dynamics of **1**, that is, to determine the time scale for excited-state proton transfer and to identify the intermediate species appearing before the photochromic species. The experimental techniques employed are time and wavelength resolved picosecond and nanosecond emission spectroscopy.

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