separated and were filtered off: ^{1}H NMR (acetone-d_6) δ 3.94 (s, 3 H), 7.35–8.60 (m, 4 H); mass spectrum, m/e 233 (M^+, ^{80}Se), 202 (M^+ – MeO); UV (60% dioxane) λ_{max} 419 nm (ϵ 3.7 × 10^3).

In the reaction with ethanol all of the solvent was removed and the residue was taken up in hexane. The hexane solution was filtered through a plug of glass wool contained in a disposable pipet, and the hexane was removed under reduced pressure. The residue was kept under high vacuum for 4 h at room temperature to remove the last traces of solvent. This gave 0.047 g (96%) of ethyl *o*-nitrobenzeneselenenate as an orange-red oil: IR (neat) 3092, 3076, 2970, 2926, 2876, 1589, 1566, 1506, 1446, 1325, 1300, 1097, 1024, 833, 731 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 1.30 (t, 3 H), 4.02 (q, 2 H), 7.3–8.6 (m, 4 H); mass spectrum, m/e 247 (M^+, ^{80}Se), 202 (M^+ – EtO); UV (60% dioxane) λ_{max} 418 nm (ϵ 3.7 × 10^3). Anal. Calcd for $C_8H_9NO_3Se$: C, 38.88; H, 3.67. Found: C, 38.75; H, 3.55.

Kinetics. The solvent (3.5 mL), either ethanol or acetonitrile–alcohol, containing the desired amounts of acid catalyst and salt being used to maintain ionic strength, was placed in a 1-cm cell in the thermostated cell compartment of a UV–visible spectrophotometer. There was then added by microsyringe 35 μL of a 10^{-2} M solution of **1** in either ethanol or acetonitrile, and the decrease in the absorbance (A) of the solution with time at 460 nm was recorded. A plot of log ($A - A_\infty$) vs. time for each run was linear.

Hydrolysis of 2b. Kinetics. The same general procedure used to study the kinetics of the esterification of **1** was employed. The selenenate ester (35 μL of a 10^{-2} M solution in either dioxane or acetonitrile) was added to 3.5 mL of either 60% dioxane or acetonitrile–H_2O containing the proper concentrations of buffer (or strong acid) and salt used to maintain constant ionic strength. The progress of the hydrolysis was determined by measuring the increase in the absorbance of the solution at 460 nm.

Reaction of 2b with 1-Butanethiol. Kinetics. A solution of **2b** (10^{-4} M) in either methanol or acetonitrile–MeOH and containing the desired concentrations of trifluoromethanesulfonic acid and sodium trifluoromethanesulfonate was placed in a cell in the spectrophotometer. Once thermal equilibrium was reached, the reaction was initiated by the addition via microsyringe with good mixing of the appropriate amount of a 2 M solution of *n*-BuSH in either methanol or acetonitrile–MeOH. The reaction of the thiol with **2b** was followed by measuring the decrease in optical density at 440 nm.

Reaction of 1 with 1-Butanethiol. Kinetics. The same procedure as just outlined for the reaction of the thiol with **2b** was employed, except that the solvent was acetonitrile–water.

Registry No. **1**, 56790-60-4; **2a**, 99642-70-3; **2b**, 56790-61-5; CH_3CH_2OH, 64-17-5; CH_3OH, 67-56-1; FCH_2CH_2OH, 371-62-0; $HOCH_2CH_2OH$, 107-21-1; $PhCH_2OH$, 100-51-6; $NCCH_2CH_2OH$, 109-78-4; $(CH_3)_2CHOH$, 67-63-0; *n*-BuSH, 109-79-5; *o*-$O_2NC_6H_4SeSBu$-*n*, 81398-78-9; $CH_3CH_2SeC_6H_4$-*p*-NO_2, 65275-58-3; $CH_3CH_2Se(O)C_6H_4$-*p*-NO_2, 65275-45-8.

Supplementary Material Available: Tabulation of results of individual kinetic runs for reaction of *n*-BuSH with **2b** (in MeOH and MeCN–MeOH) and with **1** (MeCN–H_2O) (1 page). Ordering information is given on any current masthead page.

(16) Holzle, G.; Jenny, W. *Helv. Chim. Acta* **1958**, *41*, 331.

Identification of the Rotamers of Hexakis(2-methoxyphenyl)benzene and Hexakis(2-methylphenyl)benzene

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Seven isomers are observed for both hexakis(2-methoxyphenyl)benzene (compound **1**) and hexakis(2-methylphenyl)benzene (compound **2**). Theoretically seven achiral rotamers and one pair of enantiomeric rotamers were predicted, so that eight isomers are expected to be observed by NMR in achiral solvents. From the methoxy (methyl) region of the ^{1}H NMR spectra of **1** (**2**), only pairwise interchangeable assignments can be achieved, since the rotamers have pairwise identical NMR patterns. Thus $2^4 = 16$ global assignments are possible. The molar fractions of the isomers of **1** (**2**) at equilibrium in *o*-dichlorobenzene (kerosene) at 393 K (487 K) were evaluated in terms of the interactions between adjacent pairs of peripheral aryl rings. This resulted in two global assignments, one corresponding to mainly repulsive, the other to mainly attractive steric interactions between these adjacent pairs of peripheral rings. The capacity factors of the isomers upon HPLC on silica allowed a definite choice between the global assignments for **1**, using a Hammett-like equation. In the case of **2**, it was not possible to make a definite choice between the global assignments upon chromatographical grounds.

The stereochemistry of hexaarylbenzenes has been studied less extensively than that of many other polyaryl systems.[1,10] Only in 1977 Gust[2] pointed out the possibility of isomerism arising from hindered rotation around the bonds between the peripheral aryl rings (P-rings) and the central benzene ring (C-ring), provided at least two P-rings lack local C_2 symmetry. Gust[2,3] was the first to prepare such hexaarylbenzenes and to observe this isomerism. He found two isomers for all the compounds studied, whenever these contain two dissymmetrical, ortho-substituted P-rings. These isomers could be separated at room temperature but were converted into an equilibrium mixture at higher temperatures. He considered these isomers[4] as the rotamers[4] expected if the internal rotation of the ortho-substituted P-rings is slow on the laboratory time scale

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(1) (a) Willem, R.; Pepermans, H.; Hallenga, K.; Gielen, M.; Dams, R.; Geise, H. J. *J. Org. Chem.* **1983**, *48*, 1890. (b) Willem, R.; Pepermans, H.; Hoogzand, C.; Hallenga, K.; Gielen, M. *J. Am. Chem. Soc.* **1981**, *103*, 2297. (c) Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 1535. (d) Mislow, K.; Gust, D.; Finocchiaro, P.; Boettcher, R. J. *Fortschr. Chem. Forsch.* **1974**, *47*, 1. (e) Brocas, J.; Gielen, M.; Willem, R. "The Permutational Approach to Dynamic Stereochemistry"; McGraw-Hill: New York, 1983; pp 262–269, 286–292, 471–533.

(2) Gust, D. *J. Am. Chem. Soc.* **1977**, *99*, 6980.

(3) Gust, D.; Patton, A. *J. Am. Chem. Soc.* **1978**, *100*, 8175.

(4) In general, "rotamer" is just a particular term for an isomer in the case of rotational isomerism. In this paper "rotamer" is used exclusively for the theoretically predicted isomers. In contradistinction, the experimentally observed isomers are named systematically "isomer".

0022-3263/86/1951-0301$01.50/0

Table I. Theoretically Predicted Rotamers r with Their NMR Patterns and Experimentally Detected Isomers of 1 and 2 with Their ^{1}H NMR Data[a]

rotamer r			isomer 1_i			isomer 2_j		
	point group	intensity		chem shift, ppm	intensity		chem shift, ppm	intensity
R^0	C_{6v}	6	*b*			*b*		
$R_{135}{}^3$	D_{3d}	6	1_3	3.479	6	2_7	2.232	6
$R_{14}{}^2$	C_{2v}	2	1_6	3.490	2	2_6	2.076	2
		4		3.453	4		2.147	4
$R_{123}{}^3$	C_{2h}	2	1_1	3.225	2	2_3	1.806	2
		4		3.325	4		2.162	4
$R_{12}{}^2$	C_s	2	1_4	3.258	2	2_2	1.895	2
		2		3.321	2		1.906	2
		2		3.413	2		2.102	2
$R_{124}{}^3/\bar{R}_{124}{}^3$	C_2	2	1_2	3.338	2	2_4	2.016	2
		2		3.438	2		2.057	2
		2		3.566	2		2.202	2
R^1	C_s	1	1_7	3.225	1	2_1	1.920	1
		1		3.392	1		2.016	1
		2		3.353	2		1.974	2
		2		3.372	2		2.162	2
$R_{13}{}^2$	C_s	1	1_5	3.360	1	2_5	1.936	1
		1		3.527	1		2.305	1
		2		3.309	2		2.076	2
		2		3.432	2		2.162	2

[a] This table gives the final assignments. [b] Not detected.

Table II. Theoretically Predicted Rotamers r with the Parameters σ_r, m_r, and n_r, Necessary for the Calculation of the Molar Fractions at Equilibrium in First and Second Approximation, $x_r^{(1)}$ and $x_r^{(2)}$ and Experimentally Detected Isomers of 1 and 2 with Their Molar Fractions at Equilibrium $x^{(exp)}$[a]

rotamer r	σ_r	m_r	n_r	$x_r^{(1)}$	1_i	$x_i^{(exp)}$	$x_r^{(2)}$	2_j	$x_j^{(exp)}$	$x_r^{(2)}$
R^0	6	1	3	0.03	*b*	0.00	0.01	*b*	0.00	0.00
$R_{135}{}^3$	6	1	0	0.03	1_3	0.12	0.12	2_7	0.24	0.24
$R_{14}{}^2$	2	1	1	0.09	1_6	0.14	0.13	2_6	0.12	0.13
$R_{123}{}^3$	2	1	2	0.09	1_1	0.05	0.05	2_3	0.02	0.02
$R_{12}{}^2$	1	1	2	0.19	1_4	0.09	0.09	2_2	0.06	0.05
$R_{124}{}^3/\bar{R}_{124}{}^3$	2	2	1	0.19	1_2	0.27	0.26	2_4	0.27	0.26
R^1	1	1	2	0.19	1_7	0.09	0.09	2_1	0.05	0.05
$R_{13}{}^2$	1	1	1	0.19	1_5	0.24	0.26	2_5	0.24	0.26

[a] This table gives the final assignments. The $x_r^{(2)}$ values are calculated with $\eta_1 = 0.36$ and $\eta_2 = 0.18$. [b] Not detected.

Table III. Experimental Capacity Factors k_i' and k_j' and Those Calculated with Eq 6-9

1_i				2_j			
		k_r'				k_r'	
	k_i'	eq 6	eq 7		k_j'	eq 8	eq 9
1_8[a]		8.6	3.1	2_8[a]		1.3	1.3
1_3	2.0	2.0	2.2	2_7	2.1	2.1	2.1
1_6	3.1	3.2	2.4	2_6	1.8	1.8	1.8
1_1	1.4	1.3	2.7	2_3	1.5	1.5	1.5
1_4	2.1	2.6	2.7	2_2	1.5	1.5	1.5
1_2	1.8	1.6	2.4	2_4	1.8	1.8	1.8
1_7	6.3	5.3	2.7	2_1	1.5	1.5	1.5
1_5	3.0	3.2	2.5	2_5	1.8	1.8	1.8

[a] Not detected.

at room temperature. No assignment of the observed isomers to the predicted rotamers was provided. We prepared hexakis(2-methoxyphenyl)benzene (compound 1) and hexakis(2-methylphenyl)benzene (compound 2); their synthesis will be published elsewhere.[5] We already published a short communication[6] on the stereochemistry of 1 and 2. The aim of this paper is to assign the seven observed isomers of 1 and 2 to the predicted rotamers.

Results

Seven isomers of 1, denoted 1_1–1_7, were isolated from the crude reaction mixture and further purified by repeated preparative HPLC on silica. The indexes *i* in the isomer symbols 1_i are those used in Table 1 of ref 6 in the list of fractions F_i resulting from the HPLC separation. All seven isomers exhibit identical mass spectra, consistent with the one expected for 1. They have unambiguously different ^{1}H NMR spectra in the methoxy region; the chemical shifts and intensities of the methoxy signals of each isomer are listed in Table I. For equilibration studies, a solution of pure 1_2 in *o*-dichlorobenzene was kept at a constant temperature of 393 K for 10 h. Its evolution was monitored by taking samples, which were analyzed by HPLC under the experimental conditions of the separation. This experiment showed that 1_2 was converted into a mixture of 1_1–1_7; after 10 h equilibrium was reached. An analogous experiment on 1_1 resulted in the same final mixture. From the intensities of the methoxy signals in the ^{1}H NMR spectrum of this equilibrium mixture of 1

(5) Pepermans, H.; Willem, R.; Hoogzand, C., manuscript in preparation.
(6) Pepermans, H.; Gielen, M.; Hoogzand, C.; Willem, R. *Bull. Soc. Chim. Belg.* **1983**, *92*, 465.

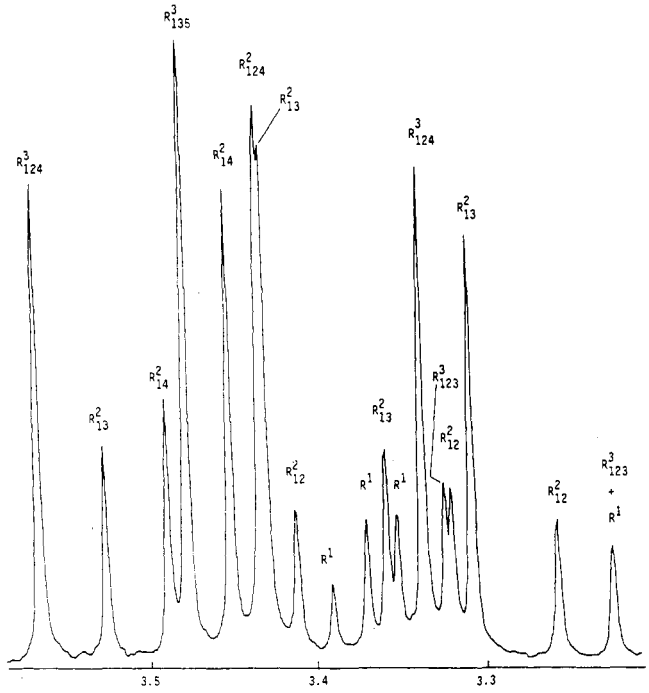

Figure 1. Methoxy region of the ^1H NMR spectrum of the equilibrium mixture of 1 in CD_2Cl_2 at 270 MHz.

(Figure 1), the molar fractions x_i^{exp} of the rotamers were calculated; they are listed in Table II. Monitoring this isomerization, we observed that in the analytical HPLC the capacity factors k' of the isomers $\mathbf{1}_1$–$\mathbf{1}_7$ were sufficiently reproducible to be used for characterization. These capacity factors k_i' are listed in Table III.

Whereas seven pure isomers of **1** could be isolated by HPLC, only four fractions of **2** were obtained. The first fraction consisted of a single isomer $\mathbf{2}_1$, the second of a mixture of $\mathbf{2}_2$ and $\mathbf{2}_3$, the third of a mixture of $\mathbf{2}_4$–$\mathbf{2}_6$, and the fourth of a single isomer $\mathbf{2}_7$. The indexes j in the symbols $\mathbf{2}_j$ are those used in Table 2 of ref 6 in the rotamer symbols R_j'. All four fractions exhibited identical mass spectra, consistent with the one expected for **2**. The composition of the second and third fraction were determined by examining samples having different compositions because they had been treated in different ways: crude, chromatographed, recrystallized, and sublimed samples were examined. The chemical shifts and intensities of the methyl signals of each isomer are listed in Table I. A solution of the third fraction in kerosene was refluxed at 487 K during 44 h. The composition of the resulting equilibrium mixture of $\mathbf{2}_1$–$\mathbf{2}_7$ was calculated from the intensities of the methyl signals in its ^1H NMR spectrum (Figure 2); these molar fractions x_j^{exp} of the isomers of **2** are listed in Table II.

Static Stereochemistry. The C-ring and P-rings of hexaarylbenzenes can safely be considered as rigid, planar, and hexagonal. Therefore the molecular geometry of hexaphenylbenzene is completely defined when the dihedral angles between the P-ring and C-ring planes are known. Crystalline hexaphenylbenzene was shown by X-ray diffraction[7] to consist of a racemic mixture of enantiomeric, propeller-like conformations with a mean dihedral angle of ±65°. The results of an electron diffraction study[8] of hexaphenylbenzene vapor were best fitted by a perpendicular conformation, i.e., a dihedral angle of 90°;

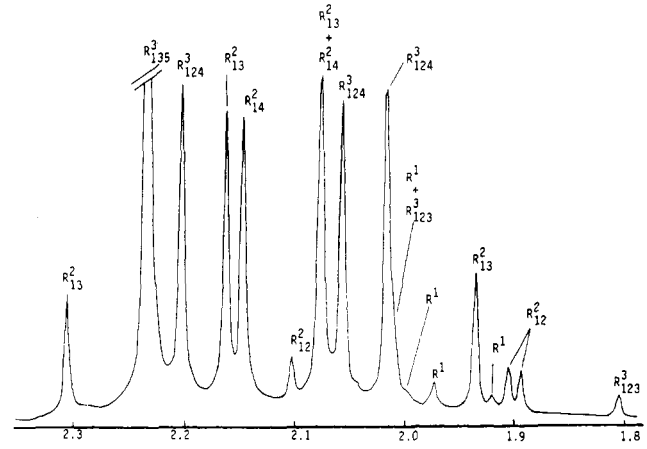

Figure 2. Methyl region of the ^1H NMR spectrum of the equilibrium mixture of **2** in $CDCl_3$ at 270 MHz. The second peak from the left is off scale.

a concerted torsional motion of the six P-rings around their perpendicular position with an amplitude of at least 10° was suggested. The choice between propeller-like and perpendicular conformations in the case of hexaarylbenzenes in solution is therefore not obvious. We present our data in terms of the perpendicular conformation, which allowed Gust to explain his results[2,3] successfully.

Once the skeleton conformation is chosen, the number of rotamers of **1** (**2**), their nature, and in particular their symmetry can be determined by a group theoretical approach.[1e,9] However, for polyaryl systems we prefer the digital approach of Mislow.[10] We used the latter approach on tetrakis(2-methylphenyl)cyclopentadienone[1b] and tetrakis(2-methylphenyl)ethene.[1a] It is advantageous to combine the digital information about the P-rings with a graphical representation of the central unit, rather than storing this information in an array. The D_{6h} perpendicular skeleton conformation of hexaarylbenzenes is accounted for by a picture of the central unit, the D_{6h} benzene ring. By convention, we write a "0" or "1" at the position of each P-ring in the hexagon picture of the central unit to indicate whether the ortho substituent of this P-ring is located respectively below or above the plane of the C-ring.

Since **1** (**2**) is not maximally labeled,[10] the $2^6 = 64$ resulting configurations do not necessarily correspond to different rotamers. Indeed, application of a rotational symmetry operation of hexaphenylbenzene on a starting configuration generates again a configuration of the same rotamer. Application of a reflective symmetry operation of hexaphenylbenzene on the starting configuration generates a configuration of the same rotamer or of its enantiomer, depending whether the starting rotamer was achiral or chiral, respectively. Moreover, the symmetry operations of hexaphenylbenzene leaving a configuration of a rotamer invariant are the symmetry operations of that rotamer. This approach yields with playful ease the static stereochemistry of **1** (**2**). For the perpendicular conformation there are nine rotamers, seven achiral ones and a single pair of enantiomers.

The rotamers are symbolized with mnemotechnical labels in which the upper index indicates the smallest number of *o*-methyl or *o*-methoxy groups lying on the same side of the central benzene ring. Where necessary the lower indexes particularize the relative positions of the peripheral aryl rings on which this smallest number of ortho sub-

(7) Bart, J. C. J. *Acta Crystallogr., Sect. B*, **1968**, *B24*, 1277.
(8) Almenningen, A.; Bastiansen, O.; Skancke, P. N. *Acta Chem. Scand.* **1958**, *12*, 1215.
(9) Hässelbarth, W.; Ruch, E. *Theor. Chim. Acta* **1973**, *29*, 259.
(10) Mislow, K. *Acc. Chem. Res.* **1976**, *9*, 26.

stituents lie. $\bar{R}_{125}{}^3$ appears to be enantiomer of $R_{124}{}^3$ and will therefore be denoted $R_{124}{}^3$. All the other rotamers are achiral.

Considering the fact that HPLC on an achiral adsorbent and with an achiral eluent cannot separate enantiomers, one can separate at most eight isomers, corresponding to the seven achiral rotamers and to the one pair of enantiomeric rotamers expected. The number of seven actually isolated isomers implies that one isomer is absent or remained undetected.

The pattern expected in the methoxy (methyl) region of the NMR spectrum of any rotamer of 1 (2) is readily deduced from its symmetry. This leads to four patterns, each occurring twice: a single line, two lines (with relative intensities 2:4), three lines (2:2:2), and four lines (1:1:2:2). The assignments of Table I, II, and III are obtained by the complete assignment argumentation developed in this paper. Indeed, from the qualitative NMR considerations presented up to now, the assignment of 1_3 (2_7) to $R_{135}{}^3$ instead of R^0 is purely arbitrary, while the assignments of respectively 1_1 and 1_6, 1_2 and 1_4, 1_5 and 1_7 (respectively 2_1 and 2_5, 2_2 and 2_4, 2_3 and 2_6) are each pairwise interchangeable. Thus, combination of the four independent pairwise assignments of isomers with identical NMR patterns leads to $2^4 = 16$ *global* assignments of the seven isomers to the eight rotamers.

Equilibrium Model. In order to choose between these 16 global assignments, we studied the equilibrium mixture of 1 (2) and compared experimental molar fractions x_i of the isomers with the a priori calculated ones x_r of the rotamers. We calculate the molar fraction x_r of a rotamer r from the free enthalpies G_r of *all* the rotamers[11] eq 1.

$$x_r = \frac{\exp(-G_r/RT)}{\sum_{r'} \exp(-G_{r'}/RT)} \tag{1}$$

In a first approximation, we assume that the free enthalpies G_r of all rotamers r of 1 (2) are equal, except for the contributions associated with their rotational symmetry ($+RT \ln \sigma_r$, in which σ_r represents the symmetry number of rotamer r) and the mixing entropy of the pair of enantiomeric rotamers ($-RT \ln m_r$, in which m_r equals 2 for this pair and 1 for the other, achiral rotamers). The resulting expression for the molar fraction $x_r{}^{(1)}$ in this first approximation is given as eq 2. The values of σ_r, m_r, and

$$x_r{}^{(1)} = \frac{\dfrac{m_r}{\sigma_r}}{\sum_{r'} \dfrac{m_{r'}}{\sigma_{r'}}} = \left(\frac{3}{16}\right)\left(\frac{m_r}{\sigma_r}\right) \tag{2}$$

$x_r{}^{(1)}$ are listed in Table II. From this it appears that the rotamers with the *same* NMR pattern have equal molar fractions. Neither the isomers of 1, nor those of 2, display this feature. Moreover, none of the isomers of 1 or 2 has a molar fraction agreeing within the experimental error with the predicted value.

In a second approximation, we introduce an explicit contribution to the free enthalpy associated with the interaction within each pair of P-rings in an ortho position on the C-ring. Depending whether the substituents on these P-rings are located on the same side or on opposite sides of the plane of the C-ring, we call this interaction a cis or trans interaction and associate with it the respective free enthalpy contributions ΔG^{cis} or ΔG^{trans}. The number

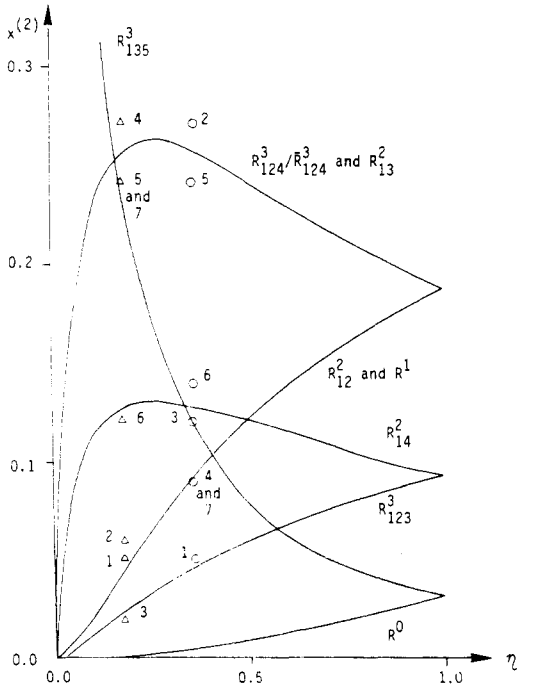

Figure 3. Molar fraction $x_r{}^{(2)}$ of the rotamers r in second approximation as a function of η. The circle i markes the experimental value of the molar fraction of the isomer 1_i and the triangle j that of 2_j.

of times they occur is expressed by the parameter n_r listed in Table II as respectively $2n_r$ and $6 - 2n_r$. Introducing the variable $\eta = \exp[-2(\Delta G^{cis} - \Delta G^{trans})/RT]$, the expression for the molar fraction $x_r{}^{(2)}$ in this second approximation is given as eq 3, in which $P(\eta)$ is the polynomial

$$x_r{}^{(2)} = \frac{\dfrac{m_r \eta^{n_r}}{\sigma_r}}{\sum_{r'} \dfrac{m_{r'} \eta^{n_{r'}}}{\sigma_{r'}}} = \frac{x_r{}^{(1)} \eta^{n_r}}{P(\eta)} \tag{3}$$

$(\eta^3 + 15\eta^2 + 15\eta + 1)/32$. Figure 3 shows all $x_r{}^{(2)}$ for $0 \leq \eta \leq 1$. The limiting cases are safely excluded. The case $\eta = 0$ ($\Delta G^{cis} \gg \Delta G^{trans}$) implies that at equilibrium 1 (2) exists as the pure rotamer $R_{135}{}^3$ and not as the observed mixture. In the case $\eta = 1$ ($\Delta G^{cis} = \Delta G^{trans}$), the second approximation is reduced to the first and is therefore invalid. For $0 < \eta < 1$, the relations between the values of $x_r{}^{(2)}$ demonstrated in Figure 3 allow to select the global assignment presented in Tables I and II. This is accomplished by using the pairwise assignments already made and considering the inequalities between the molar fractions of the rotamers with the same NMR pattern valid for $0 < \eta < 1$ (Figure 3):

$$x_{R^0}{}^{(2)} < x_{R_{135}{}^3}{}^{(2)}$$

$$x_{R_{123}{}^3}{}^{(2)} < x_{R_{14}{}^2}{}^{(2)}$$

$$x_{R_{12}{}^2}{}^{(2)} < x_{R_{124}{}^3/\bar{R}_{124}{}^3}{}^{(2)}$$

$$x_{R^1}{}^{(2)} < x_{R_{13}{}^2}{}^{(2)}$$

From Figure 3, we derive graphically for each rotamer of 1 (2) which values of η give a calculated value of $x_r{}^{(2)}$ agreeing within the experimental error of ± 0.02 with the $x_i{}^{exp}$ of the assigned isomer i. The intersection of the ranges of η obtained for all rotamers of 1 (2) is $0.31 \leq \eta_1 \leq 0.41$ ($0.16 \leq \eta_2 \leq 0.20$). The values of $x_r{}^{(2)}$ presented in Table II are calculated with the mean value $\eta_1 = 0.36$ ($\eta_2 = 0.18$). The corresponding value of $\Delta G^{cis} - \Delta G^{trans}$ is 400

(11) Glasstone, S.; Lewis, D. "Elements of Physical Chemistry"; Macmillan: London, 1961.

± 60 cal/mol (840 ± 60 cal/mol). The fit between the experimental molar fractions and those calculated with this second approximation is satisfactory for all isomers of **1** (**2**). Nevertheless, it is based on the unproven assumption $0 < \eta < 1$ ($\Delta G^{cis} > \Delta G^{trans}$). The alternative case $\eta > 1$ ($\Delta G^{cis} < \Delta G^{trans}$) cannot be excluded, neither on physical nor on numerical grounds. Physically it calls for attractive steric interactions, less common than their repulsive counterparts, though not unreported.[12] Numerically, the case $\eta > 1$ is completely analogous to the case $0 < \eta < 1$ since $x_r^{(2)}(\eta) = x_{r'}^{(2)}(1/\eta)$, in which r' is the other rotamer with the NMR pattern of r. Compared to the argumentation with $0 < \eta < 1$, this results in the pairwise interchange of *all* assignments of rotamers with the same NMR pattern, in the reciprocal values for η and in the opposite values for $\Delta G^{cis} - \Delta G^{trans}$.

Chromatographical Model. In order to discriminate between both remaining global assignments, we examined the retention times t_i (t_j) of the isomers **1** (**2**), looking for correlations with stereochemical parameters of the assigned rotamers. In Table III the more convenient, flow rate independent capacity factors k_i' (k_j') of the isomers are listed, rather than the retention times themselves. They are calculated from the latter by[13] eq 4,

$$k_i' = \frac{t_i - t_0}{t_0} \tag{4}$$

in which t_0 is the time needed by the eluent to flow through the column.

For compound **1** on one hand, we find that if we use the global assignment corresponding with the repulsive interaction between the substituents, the capacity factors k_i' of the isomers $\mathbf{1}_i$ are related to the number of substituents on each side of the C-ring: first the rotamers with the 3:3 distribution leave the column, then those with the 4:2 distribution, and finally the one with the 5:1 distribution. Within both the first and the second set, it is observed that the rotamers with larger n_r leave the column earlier. On the contrary, if we use the complementary global assignment, the one corresponding to the attractive interaction between the substituents, we find no relation of this kind. For compound **2** on the other hand, the rotamers leave the column in three fractions when hexane/CH_2Cl_2 is used as an eluent. With both global assignments, each fraction contains all rotamers with some n_r value. The only difference is that with the "repulsive" assignment, the rotamers with the larger n_r value leave the column *earlier*, whereas with the "attractive" one, they leave it *later*. Hence in contrast to compound **1**, the capacity factors k_j' of the rotamers $\mathbf{2}_j$ appear to be independent of the number of substituents on each side of the C-ring.

The observed relations can be changed into quantitative correlations by considering that the capacity factor k' describes the distribution of the sample between the stationary and the mobile phases.[13] Since k_r' is a heterogeneous equilibrium constant for the adsorption–desorption reaction of the romater r, ln k_r' can be expressed in a Hammett-like equation as a linear function[14] of the parameters n_r and d_r (eq 5), where d_r is half the difference

$$\ln k_r' = a + bn_r + cd_r \tag{5}$$

of the numbers of substituents on both sides of the C-ring and thus represents the substituent distribution. For **1**, the repulsive and attractive assignments give respectively as best fit eq 6 and 7. For **2**, this becomes respectively eq 8 and 9. Table III gives the experimental capacity factors

$$\ln k_r' = 0.68 - 0.20n_r + 0.69d_r \tag{6}$$

$$\ln k_r' = 1.12 - 0.13n_r + 0.02d_r \tag{7}$$

$$\ln k_r' = 0.75 - 0.17n_r + 0.00d_r \tag{8}$$

$$\ln k_r' = 0.23 + 0.18n_r - 0.01d_r \tag{9}$$

k_i' of $\mathbf{1}_i$ and k_j' of $\mathbf{2}_j$ together with the capacity factors k_r' calculated with eq 6–9. This table shows that for **1** only the repulsive assignment leads to a satisfactory fit. This result argues in favor of this assignment rather than the attractive one. For **2**, both global assignments lead to satisfactory fits, and thus no choice among them is possible. The results of these correlations confirm the qualitative observations described at the beginning of this part.

A possible explanation for the relatively important value of the coefficient c of d_r in eq 1 is the stabilization of adsorbed molecules **1** due to the interaction between their dipole moment and the polar interface between adsorbent and solvent. This stabilization is proportional to the dipole moment D_r of rotamer r and hence to d_r. The larger proportionality constant for **1** than that for **2** is not unexpected in view of the large dipole moment of a 2-methoxyphenyl ring than that of a 2-methylphenyl one. Measurements of the dipole moments of the isomers of **1** could easily confirm this explanation and the resulting assignments,[16] provided sufficient material had been isolated. Further, the coefficient b can be related to very small changes (~50 cal/mol) in the free enthalpy contributions ΔG^{cis} and ΔG^{trans} upon adsorption.

Experimental Section

The HPLC separations and analyses were performed on a preparative Du Pont 830 apparatus, equipped with a six-way high-pressure injection valve, a variable wavelength UV detector, and a three-way fractionating valve. The column (L = 250 mm, D = 22.7 mm) was packed with Lichrosorb Si 60/7 silica and was conditioned with the eluent. The eluent was always a mixture of hexane with CH_2Cl_2 or $CHCl_3$, all of solvent grade, but redistilled before use. The flow rate was always 20 mL/min at about 300 psi. The reported capacity factors are related to an internal standard, *o*-dichlorobenzene for **1** and CCl_4 for **2**.

The mass spectra were recorded on an AEI MS 902 S instrument, with electron impact at 70 eV as ionization source. The ^1H NMR spectra were recorded on a Bruker HX 270 instrument at 270 MHz and room temperature. All chemical shifts are given in ppm relative to Me_4Si.

Preparative Separation of 1. The separated samples of **1** resulted from various reactions[5] and were prepurified by gravitational LC on silica (Woelm 63-200) using CH_2Cl_2 as eluent. They were dissolved in the HPLC eluent CH_2Cl_2/hexane (70:30 v/v) and injected in samples of up to 10 mL. The separation was monitored by UV at 254 or 285 nm. All products were reinjected until they showed a single peak. Thus seven fractions of **1** were obtained (weight in mg):F_1 (15), F_2 (68), F_3 (6), F_4 (48), F_5 (29), F_6 (8), and F_7 (about 1). All fractions F_i exhibited identical mass spectra: as base peak the parent peak at m/e 714 with the expected isotopic distribution and no other peaks with intensities larger than 5%. Their ^1H NMR spectra showed that each fraction

(12) Carter, R. E.; Nilsson, B.; Olsson, K. *J. Am. Chem. Soc.* **1975**, *97*, 6155.

(13) Snyder, L. R.; Kirkland, J. J. "Introduction to Modern Liquid Chromatography", 2nd ed.; Wiley-Interscience: New York, 1979.

(14) Wells, P. R. "Linear Free Energy Relationships"; Academic Press: London, 1968.

(15) The addition of CH_2Cl_2 is necessary because of the low solubility of **1** in *o*-dichlorobenzene at room temperature. In a blank experiment on a mixture of 2 mL of CH_2Cl_2 and 20 mL of *o*-dichlorobenzene at 393 K, the weight loss after 24 h was about 0.5%. Thus the possible influence of the changing of the solvent during reaction is negligible.

(16) We thank one of the referees for bringing this point to our attention.

F_i consisted of a single pure isomer 1_i.

Equilibrium Mixture of 1. In a 25-mL flask was dissolved 11.6 mg of 1_2 in 1 mL of CH_2Cl_2 and brought to 25 mL with o-dichlorobenzene.[15] This solution was transferred into an open reacting tube and placed in an oil bath thermostated at 393 K. After several reaction times, every 15–30 min at the beginning and every 40–60 min later on, aliquots of 0.5-mL were removed, quenched to room temperature, and analyzed by HPLC in the conditions of the preparative separation. After 5.5 h the peak areas of all isomers remained constant within experimental error, indicating that equilibrium was reached. After 7.5 h the remaining reaction mixture was quenched. The solvent was removed at 1 mmHg and at room temperature on a rotavapor. The solid residue was dissolved in 0.5 mL of CD_2Cl_2; the methoxy region of the ^1H NMR spectrum of this solution is shown in Figure 1. An analogous experiment starting from pure 1_1 resulted in the same final mixture.

Preparative Separation of 2. The separated[5] sample of 175 mg of **2** was prepurified by gravitational LC on silica (Woelm 63-200) using hexane/benzene (50:50 v/v) as an eluent. In a first HPLC separation with hexane/CH_2Cl_2 (85:15 v/v) as eluent, three fractions of **2** were collected: 64 mg of F_1' ($k' = 1.5$), 52 mg of F_2' ($k' = 1.8$), and about 2 mg of F_3' ($k' = 2.1$). In a second HPLC separation with hexane:$CHCl_3$ (97:3 v/v) fraction F_1' was separated into 8 mg of F_{11}' ($k' = 1.1$) and 42 mg of F_{12}' ($k' = 1.2$); no further separation of F_2' was detected. These four fractions exhibited identical mass spectra: as base peak the parent peak at m/e 618 with the expected isotopic distribution and no other peaks with intensities larger than 5%. From the methyl region of their ^1H NMR spectra, it was deduced that F_{11}' consisted of 2_1, F_{12}' of 2_2 and 2_3, F_2' of 2_4–2_6, and F_3' of 2_7.

Equilibrium Mixture of 2. In a 50-mL reaction flask was dissolved 16 mg of **2** (containing all isomers) in 10 mL of kerosene (Fluka purum), redistilled before use [bp 100–108 °C (11 mmHg)]. The flask was equipped with a water condensor, flushed with argon, and heated in a metal bath. The reaction mixture was refluxed during 44 h at 487 K. The kerosene was distilled off in a bulb-to-bulb apparatus [95–100 °C (13 mmHg)]. The solid residue was purified by TLC on silica (Merck Kieselgel 60 F_{254}) with hexane/benzene (50:50 v/v). The methyl region of the ^1H NMR spectrum of the 16 mg of recovered **2** is shown in Figure 2.

Registry No. 1, 86933-45-1; 2, 86933-46-2.

Diazafulvenones. Thermal Isomerizations and Eliminations in Alkoxycarbonyl and Anilinocarbonyl Derivatives of Imidazole

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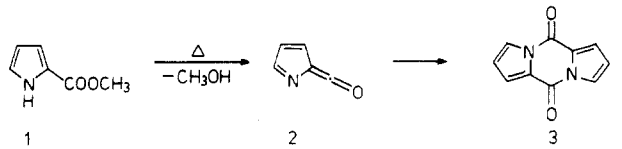
4-Carbonyl-4*H*-imidazole (**10**) and 2-carbonyl-2*H*-imidazole (**11**) are formed by flash vacuum pyrolysis of methyl 4- and 2-imidazolecarboxylates, respectively. **10** and **11** dimerize to diketopiperazines **14** and **16**, respectively. The same products are also obtained from 4- and 2-(anilinocarbonyl)imidazoles, respectively. Methyl imidazole-1-carboxylate (**4**) on pyrolysis gives a ca. 1:1 mixture of the same ketenes **10** and **11**, which dimerizes to a 1:2:1 ratio of diketopiperazines **14–16**. In contrast, ethyl imidazole-1-carboxylate gave CO_2, ethylene, and imidazole as the major products. The pyrolysis reactions were monitored by low-temperature infrared and high-temperature mass spectrometry.

The formation of 2-carbonyl-2*H*-pyrrole (1-azafulven-6-one, **2**) by flash vacuum pyrolysis of pyrrole-2-carboxylic acid or its methyl ester (**1**) was reported recently.[2] The



1 2 3

ketene **2** was directly observed by IR[2] and mass spectrometry,[3] trapped with methanol to regenerate the starting material (**1**), and isolated in the form of the dimer **3**.

We now wish to report the formation of diazafulvenones **10** and **11** on pyrolysis of the imidazole derivatives **4**, **8**, **9**, **12**, and **13**, their direct detection by IR and mass spectrometry, and their dimerization to give diketopiperazine derivatives **14–16**.

The pyrolysis of methyl imidazole-4-carboxylate (**8**) at 750–820 °C (10^{-4} torr) with isolation of the products on a KBr window at −196 °C resulted in the formation of two new species, absorbing at 2245 and 2150 cm^{-1}. The latter absorption disappeared on warming to −40 °C and is ascribed to 4-carbonyl-4*H*-imidazole (**10**) because in a preparative experiment (see Experimental Section) carried out at the same temperature (750 °C) the dimer **14** was isolated in 20% yield. The strucutre of **14** is based on the IR, ^1H NMR, mass and high-resolution mass spectra, and elemental analysis.

The same IR results were obtained on pyrolysis of the anilide **9** at 800 °C. Here, too, the dimer **14** was isolated in 20% yield after a preparative pyrolysis. Thus, the ketene **10** is formed by elimination of methanol from **8**,

(1) (a) Université Mons. (b) Universidad Complutense. (c) CSIC. (d) AKZO. (e) Marburg. (f) Permanent address: University of Queensland.
(2) (a) Gross, G.; Wentrup, C. *J. Chem. Soc., Chem. Commun.* **1982**, 360. (b) Wiersum, U. E. *Recl.: J. R. Neth. Chem. Soc.* **1982**, *101*, 365.
(3) Gross, G.; Wentrup, C.; Maquestiau, A.; Flammang, R., unpublished results. Gross, G. Ph.D. Thesis, University of Marburg, 1983.

0022-3263/86/1951-0306$01.50/0