Polyethylated Aromatic Rings: Conformation and Rotational Barriers of 1,2,3,4,5,6,7,8-Octaethylanthracene, 1,2,3,4,6,7,8-Heptaethylfluorene, and 1,2,3,4,5,6,7,8-Octaethylfluorene

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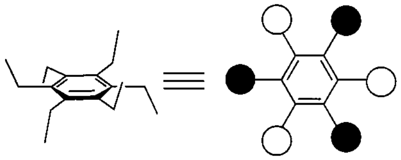
1,2,3,4,5,6,7,8-Octaethylanthracene (**5**), 1,2,3,4,6,7,8-heptaethylfluorene (**7**), and 1,2,3,4,5,6,7,8-octaethylfluorene (**8**) were synthesized by Friedel−Crafts ethylations of 9,10-dihydroanthracene and fluorene. MM3 calculations indicate that the two ethylated six-membered rings of **5** and **7** are conformationally independent. According to the calculations, two low-energy conformers of each compound are possible with the ethyl groups attached to the external aryl rings arranged in an alternated "up−down" orientation. MM3 calculations indicate that in the lowest energy conformation the central fluorene core of **8** adopts a twisted conformation to avoid repulsive steric interactions between the ethyls at the bay region. Two fully alternated up−down conformations are possible for **8**, differing in the orientation ("in" or "out") of the ethyls in the bay region. MM3 calculations predict that the lowest energy conformer is the fully alternated "out" form of C_2 symmetry. The rotational barriers of **5**, **7**, and **8** are in the 8.7−11.3 kcal mol^{-1} range, the largest barrier corresponding to the more crowded octaethylfluorene **8**. Anthracene **5** adopts in the crystal a conformation of approximate C_{2h} symmetry with pairs of *peri* groups on the same edge of the molecule oriented *syn*. The conformations adopted in the crystal by **7** and **8** do not correspond to the calculated lowest energy form. In the conformation of **7** in the crystal the ethyl groups on the trisubstituted ring adopt the unusual all *syn* arrangement. Octaethylfluorene **8** adopts a conformation with a twisted central fluorene core but with a *syn* arrangement of a pair of vicinal ethyl groups.

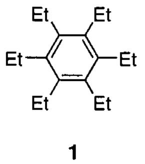
Introduction

Polyethylated aromatic derivatives can be viewed as multiarmed compounds consisting of a central core to which several "arms" are attached.[1,2] These compounds are of stereochemical interest since their conformational behavior is largely determined by the need to avoid repulsive van der Waals interactions between the ethyl arms.

The most thoroughly investigated polyethylated derivative is hexaethylbenzene (**1**) which adopts a fully alternated "up−down" arrangement of the arms, with all ethyl groups oriented perpendicularly to the aryl ring plane (Scheme 1).[3] The destabilizing interaction present when two vicinal ethyl groups are identically oriented in the same sense (i.e., both "up" or "down") is denoted a *syn* interaction. Molecular mechanics calculations indicate that the relative steric energies of the possible conformations of **1** increase with the increased number of *syn* interactions.[3a] In the preferred conformation of **1** the three ethyls on the 1,3,5 positions are oriented toward the same face of the aromatic ring. This conformational preference has been exploited for achieving a convergent arrangement of three binding groups in ligands structurally related to **1**.[4]

Scheme 1





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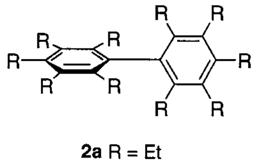

2a R = Et
2b R = H

Aromatic polyethylated derivatives have been the subject of several studies.[5] In the biphenyl analogue of **1** (decaethylbiphenyl, **2a**) the lowest energy conformation possesses one *syn* interaction per ring, involving a pair of ethyls located at the *meta* and *para* positions. This arrangement is adopted to avoid the steric crowding between the ethyl groups located at the *ortho* positions

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(1) Menger, F. M. *Top. Curr. Chem.* **1986**, *136*, 1.

(2) For a review on the conformation of alkyl groups, see: Berg, U.; Sandström, J. *Adv. Phys. Org. Chem.* **1989**, *25*, 1. Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley: Chichester, 1994, ch. 10. See also: Metzger, J. V.; Chanon, M. C.; Roussel, C. M. *Rev. Heteroatom Chem.* **1997**, *16*, 1.

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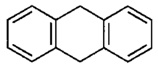
of the two rings which otherwise would be present if in each ring the ethyls adopt the fully alternated up–down arrangement.[5a]

We have reported previously that the crowded **2a** can be prepared in a one-pot reaction by exhaustive ethylation of biphenyl (**2b**) using Friedel–Crafts conditions (EtBr/AlCl$_3$).[5a] The isolation of **2a** indicates that the central Ar–Ar biphenyl bond is not cleaved under the reaction conditions. The aims of the present work were two-fold: (i) To synthesize crowded multiarmed hydrocarbons possessing two polyethylated rings in steric proximity using the exhaustive ethylation route. (ii) To determine the influence of the steric interactions between ethyls *at different rings* on the fully alternated up–down conformation. As the substrates of the alkylation reactions we chose 9,10-dihydroanthracene (**3**) and fluorene (**4**) since their corresponding polyethylated products were expected to possess planar and twisted central cores, respectively.



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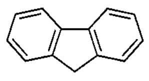

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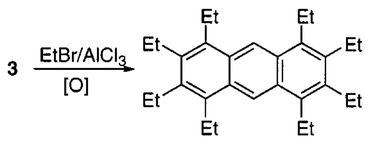
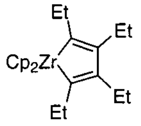
Results and Discussion

Friedel–Crafts Ethylation of 3 and 4. The aromatic substrate **3** was ethylated using the alkylating agent (EtBr) as solvent and adding an almost stoichiometric amount of AlCl$_3$ (7 equiv, eq 1). The reaction yielded



(1)

5



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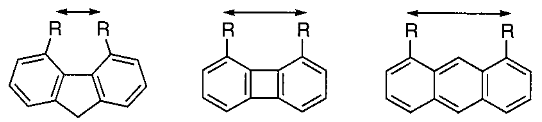
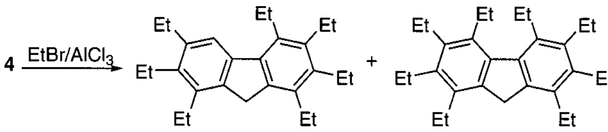
1,2,3,4,5,6,7,8-octaethylanthracene (**5**), indicating that during the course of the reaction ethylated dihydroanthracenes oxidize to the corresponding ethylated anthracenes.[6,7] The progress of the ethylation reaction of **3** was followed by NMR. Even at relatively early stages (ca. trialkylation), the signals for the ring methylenes have disappeared, indicating that aromatization occurs early on. However, the alkylation reaction on anthracene itself is too slow to be synthetically useful. It seems, therefore, that the reaction initially proceeds to a low-alkylated dihydroanthracene mixture, which then air-oxidizes[7] before reaching the peralkylated stage. The *peri* ethyl groups sterically shield the 9 and 10 positions of the anthracene ring system and, as a result, these positions are not further alkylated. Octaethylanthracene **5** has been previously synthesized by reaction of the tetraethylated zircopentadiene **6** with 1,2,4,5-tetraiodobenzene.[6]

Scheme 2



AlCl$_3$-catalyzed ethylation of fluorene was conducted using 10 equiv of AlCl$_3$ and EtBr as solvent. Purification by column chromatography afforded a 2:1 mixture of 1,2,3,4,6,7,8-heptaethylfluorene (**7**) and 1,2,3,4,5,6,7,8-octaethylfluorene (**8**) (eq 2), as judged by ^{1}H NMR.[8] Fluorene **7** was isolated from the mixture by recrystallization while small amounts of pure **8** were obtained by preparative HPLC. The substitution pattern of **7** was determined by means of NMR spectroscopy and X-ray crystallography (see below). Interestingly, the heptaethylated fluorene (**7**) is not converted to **8** by the usual alkylation procedure. Presumably, dialkylation in the bay region must occur early in the reaction sequence for **8** to be formed, otherwise compound **7** is the end product.



7 **8** (2)

Conformational Analysis of the Polyethyl Derivatives 5, 7, and 8. The octaethyl derivatives **5** and **8** differ in the relative dispositions of the two tetraethylphenylene subunits. In **5** the two subunits are fused in parallel fashion, while in **8**, due to the presence of the central five-membered ring, the two external rings are fused in an angular fashion. In ideally planar systems, the latter disposition causes a closer steric proximity between the substituents at the bay area on a fluorene than between pairs of *peri* substituents on the 1 and 8 positions of an anthracene or biphenylene skeleton (Scheme 2).

The steric crowding can be alleviated in **8** if the central skeleton adopts a twisted conformation, as observed for several polyphenyl derivatives of **4** and fluorenone[8] and for octamethylnaphthalene **9**.[9,10] In the case of **7**, a single

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(3) (a) Iverson, D. J.; Hunter, G.; Blount, J. F.; Damewood, J. R.; Jr.; Mislow, K. *J. Am. Chem. Soc.* **1981**, *103*, 6073. (b) Hunter, G.; Blount, J. F.; Damewood, J. R., Jr.; Iverson, D. J.; Mislow, K. *Organometallics* **1982**, *1*, 448. (c) Weissensteiner, W.; Gutierrez, A.; Radcliffe, M. D.; Siegel, J.; Singh, M. D.; Tuohey, P. J.; Mislow, K. *J. Org. Chem.* **1985**, *50*, 5822. (d) For a study of the side chain rotations of **1** in the solid-state, see: Barnes, J. C.; Chudek, J. A.; Hunter, G., Blake A. J., Dyson, P. J., Johnson, B. F. G.; Weissensteiner, W. *J. Chem. Soc., Faraday Trans.* **1995**, *91*, 2149. (e) For a recent paper on the stereodynamics of substituted benzenes structurally related to **1**, see: Kilway, K. V.; Siegel, J. S. *Tetrahedron* **2001**, *57*, 3615.

(4) See for example: (a) Hou, Z.; Stack, T. D. P.; Sunderland, C. J.; Raymond, K. N. *Inorg. Chim. Acta* **1997**, *263*, 341. Bisson, A. P.; Lynch, V. M.; Monahan, M. K. C.; Anslyn, E. V. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2340. Szabo, T.; O'Leary, B. M.; Rebek, J., Jr. *Angew. Chem., Int. Ed.* **1998**, *37*, 3410. Tam-Chang, S.-W.; Stehouwer, F. S.; Hao, J. *J. Org. Chem.* **1999**, *64*, 334.

(5) (a) Marks, V.; Gottlieb, H. E.; Biali, S. E. *J. Am. Chem. Soc.* **1997**, *119*, 9672. (b) Gottlieb, H. E.; Ben-Ari, C.; Hassner, A.; Marks, V. *Tetrahedron* **1999**, *55*, 4003. (c) Taha, M.; Marks, V.; Gottlieb, H. E., Biali, S. E. *J. Org. Chem.* **2000**, *65*, 8621.

(6) Takahishi, T.; Hara, R.; Nishihara, Y.; Kotora, M. *J. Am. Chem. Soc.* **1996**, *118*, 5154.

(7) AlCl$_3$-catalyzed alkylation of 9,10-dihydroanthracene yields in some cases substituted anthracenes, indicating that under the reaction conditions, the dihydroanthracene nucleus is oxidized to anthracene. For example, it has been reported that alkylation of dihydroanthracene (*tert*-butyl chloride/AlCl$_3$) in CH$_2$Cl$_2$ affords a mixture of dialkylated anthracenes (Kaim, W.; Bock, H. *Chem. Ber.* **1978**, *111*, 3585).

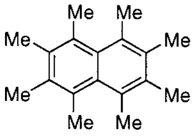
(8) For studies on octaphenylcarbazole, octaphenylfluorenone, and a nonaarylfluorene, see: (a) Qiao, X.; Ho, D. M.; Pascal, R. A., Jr. *J. Org. Chem.* **1996**, *61*, 6748. (b) Tong, L.; Lau, H.; Ho, D. M.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1998**, *120*, 6000.

(9) Sim, G. A. *Acta Crystallogr., Sect B.* **1982**, *B38*, 623.

(10) For studies on the synthesis and reactions of polymethylated aromatic compounds, see: Hart, H.; Oku, A. *J. Org. Chem.* **1972**, *37*, 26; Hart, H.; Ryge, B. *Tetrahedron Lett.* **1977**, *36*, 3143, Hart, H.; Oku, A. *J. Org. Chem.* **1972**, *37*, 4274, Sy, A.; Hart, H. *J. Org. Chem.* **1979**, *44*, 7; Hart, H.; Nwokogu, G. *J. Org. Chem.* **1981**, *46*, 1251. For a short synthesis of octamethylnaphthalene, see: Hart, H.; Teuerstein, A. *Synthesis* **1979**, 693.

ethyl group is present in the bay area, and as a result of the less severe crowding, it could be expected that the central fluorene core adopts a planar or nearly planar conformation.

The analysis of the static stereochemistry of **5** can be conducted assuming that in all the ideal conformers the ethyl groups are perpendicularly oriented to a planar anthracene skeleton. Under this assumption, the number of ideal conformers and their symmetries should be analogous to those calculated for **10**[5c] since the central skeletons of **5** and **10** share identical symmetries (D_{2h}) and identical dispositions of the ethyl groups. Thirty-four enantiomeric pairs and eight achiral forms are possible for **5,** resulting from the different up–down orientations of the ethyls. These include four forms (two enantiomeric pairs) of D_2, four isomers of C_{2h}, two of C_{2v}, 12 forms of C_2, four of C_s, two of C_i, and 48 of C_1 symmetries.



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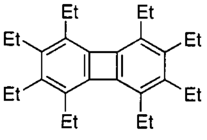

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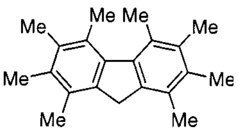

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Similarly, the number of ideal conformers of **7** can be readily calculated assuming that in all low-energy conformers the ethyl groups are perpendicular to a planar fluorene skeleton. As a result of this arrangement, no symmetry plane can coexist with the fluorene core, and all conformers must possess C_1 symmetry and are therefore chiral. On the basis of the configurational matrix method[11] it can be readily calculated that 128 forms (64 enantiomeric forms) are possible for **7**.[12]

MM3 calculations of 1,2,3,4,5,6,7,8-octamethylfluorene (**11**) indicate that a twisted conformation of the fluorene core of C_2 symmetry lies 7.8 kcal mol^{-1} below a planar conformation of C_s symmetry, the latter form representing a saddle point (one negative eigenvalue in the vibrational matrix). For the conformational analysis of **8** we assumed, by analogy to **11**, that the central fluorene core adopts a chiral twisted conformation of C_2 symmetry. The nonplanar nature of the central scaffold renders the two faces of a given six-membered ring diastereotopic, increasing the number of potential up–down forms. The conformations of **8** can be analyzed as resulting from the superposition of two independent stereogenic elements: the up–down pattern of the ethyl groups and the two enantiomeric helical arrangements of the central fluorene core. If the up–down pattern of the ethyl groups is achiral, the formal introduction of the two possible twisted arrangements of the fluorene skeleton should yield two enantiomeric forms. However, if the up–down pattern is chiral, the introduction of the helicity will result in two diastereomeric forms. This can be exemplified by the fully alternated up–down arrangement. In contrast to the systems with a central planar core (e.g., **1**, **5**, and **9**) *two different fully alternated up–down arrangements of the ethyl groups are possible* for a given twisted conformation (Figure 1). For nomenclature purposes, the two fully alternated diastereomeric forms of C_2 symmetry will be designated by describing the orientation of the substituents at the bay region. These conformations will be dubbed "in" or "out" depending whether when looking along the axis bisecting the Ar–Ar bond and the central methylene group, the methyl is pointing toward the ring (in) or to the external surface of the molecule (out).

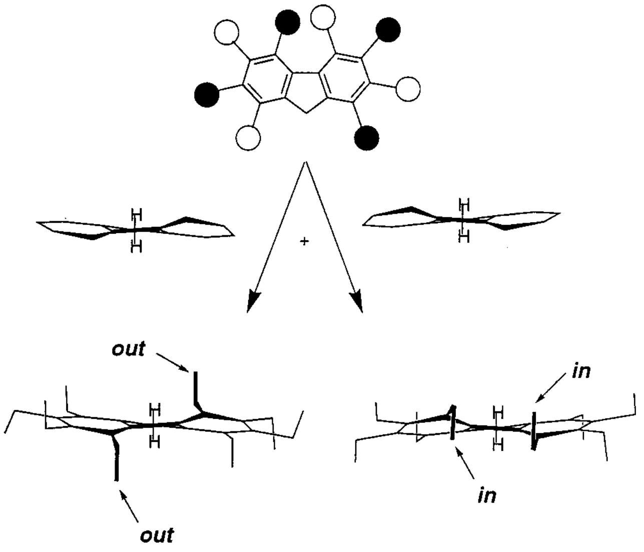

Figure 1. Two diastereomeric forms resulting from the formal superposition of a chiral perfectly alternated up–down arrangement of the ethyl groups and the two possible helical conformations of the central fluorene core. The molecules at the bottom are viewed along an axis bisecting the Ar–Ar bond and the central methylene group.

Molecular Mechanics Calculations. 1. Octaethylanthracene 5. MM3 calculations were conducted on selected conformers of **5** possessing at most a single *syn* interaction per ring. The results of the calculations are collected in Figure S1 (Supporting Information). The lowest energy conformations correspond to the forms of D_2 and C_{2h} symmetries (**5a** and **5b**, respectively) in which the ethyls within each phenylene ring are perfectly alternated. Single point MP2(full) calculations were also conducted using the fully optimized RHF-6-31G* geometries of **5a** and **5b**. Similarly to the MM3 calculations, the MP2 ab initio calculations predict that both forms should possess nearly identical energies. The similar energies between **5b** (with two *syn–peri* interactions) and **5a** (lacking any *syn* interaction) suggests that the two tetraethylphenylene subunits are sterically isolated from each other and are conformationally independent.

The conformational behavior of **5** is different from that of **10**, in which according to MM3, semiempirical and ab initio calculations, the C_{2h} form **10b** with two *syn* interactions is 1.5–2.0 kcal mol^{-1} higher in energy than the alternated D_2 conformer **10a** (Scheme 3). The different conformational behavior is the result of the larger distance between the two tetraethylphenylene subunits in **5** than in **10**. In the case of **5** the central six-membered ring acts as a spacer, increasing the separation between the two tetraethylphenylene subunits and reducing their mutual steric interactions (cf. Scheme 2).[9]

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(11) Willem, R.; Pepermans, H.; Hoogzand, C.; Hallenga, K.; Gielen, M. *J. Am. Chem. Soc.* **1981**, *103*, 2297. See also: Biali, S. E.; Buda, A. B.; Mislow, K. *J. Org. Chem.* **1988**, *53*, 1289.

(12) In the case of **7**, each ideal conformer can be described by a matrix consisting of seven binary digits, in which a "0" or "1" describes the up or down orientation of an ethyl group. Since there are seven binary digits, 2^7 (i.e., 128) different matrixes are possible. The calculated number of different matrixes corresponds to the number of ideal up–down conformers of **7** since each conformer is represented by a single matrix.

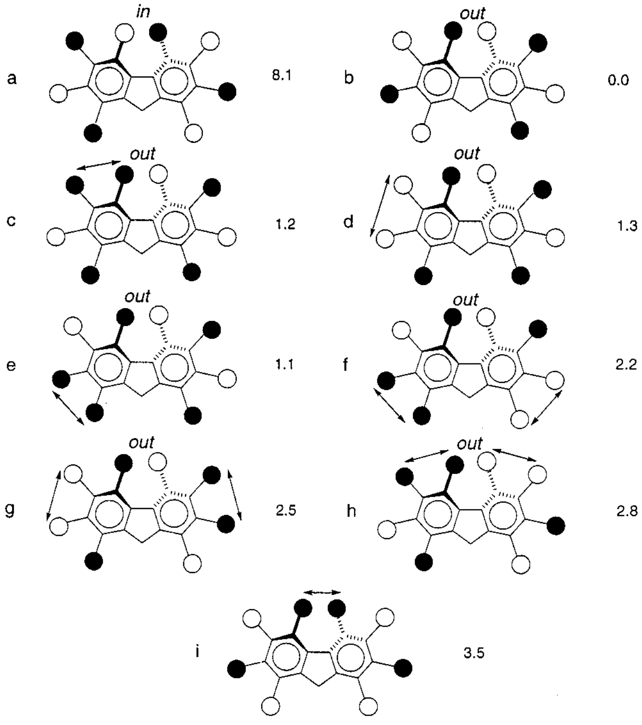
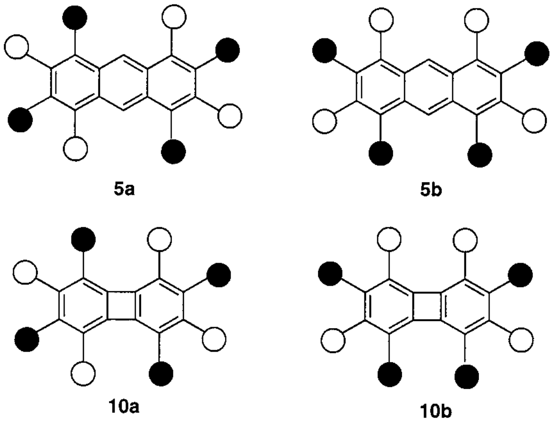


Figure 2. Calculated (MM3) relative steric energies of selected conformers of **8**.

2. Heptaethylfluorene 7. MM3 calculations of conformers of **7** possessing at most a single *syn* interaction or two *syn* interactions in the trisubstituted ring are collected in Figure S2 (Supporting Information). All calculated conformers possess a nearly planar fluorene skeleton. The calculations indicate that the lowest energy conformations are those lacking any *syn*–*ortho* interaction. Among the conformers possessing a single *syn* interaction, the largest steric energy was calculated for conformers "i" and "j". Their higher energy is probably due to the buttressing effects of the two neighboring ethyls at the 1 and 4 positions on the groups oriented *syn*. As in the case of **5**, the nearly identical calculated steric energies of the two alternated forms "a" and "b" (Figure S2) suggest that due to the large mutual separation, the two polyethylated rings are conformationally independent.

3. Octaethylfluorene 8. MM3 calculations performed on **8** indicate that the fully alternated "out" form of C_2 symmetry (Figure 2) is the global minimum. The central fluorene core in the lowest energy conformer is nonplanar, and the calculated torsional angle between the four carbons at the bay region is 34.5°. Ab initio RHF 6-31G* calculations (assuming C_2 symmetry) predict a somewhat smaller twist (29.2°). According to the MM3 calculations, the conformation with a mirror symmetric up–down pattern of ethyls ("i") lies 3.5 kcal mol^{-1} above the lowest energy conformation.[13] Structures with a single *syn* interaction between *ortho* ethyls are destabilized by only 1.1–1.3 kcal mol^{-1}. The fully alternated "in" conformer is 8.1 kcal mol^{-1} more strained than the "out" form. The higher energy of the "in" form is due to the steric repulsions between ethyls facing across the Ar–Ar bond.

Scheme 3



These groups, although formally oriented differently (one pointing "up" and one "down") are in the "in" form in close proximity.

NMR Analysis. The room temperature ^1H and ^{13}C NMR data for compounds **5**, **7**, and **8** are summarized in Table 1. The number of signals in the spectra is consistent with a fast rotation of the ethyl side chains on the NMR time-scale at room temperature. This is in agreement with previous measurements in similar systems.[3,5] The assignment of the signals of each compound was performed with the aid of two-dimensional techniques such as COSY, HMQC, and HMBC.

1. Octaethylanthracene 5. As the temperature of a CD_2Cl_2 or CD_2ClF solution of **5** is lowered, two effects are apparent in the ^1H NMR spectrum. First, the quartets of the methylene protons decoalesce, as each geminal pair becomes diastereotopic. Second, the aromatic CH signal splits into two singlets of unequal intensities, indicating the presence, in solution, of more than one conformer. The low-temperature ^{13}C spectrum shows that only two conformers are significantly populated (a 73/27 ratio, corresponding to a $\Delta G° = 0.3$ kcal mol^{-1} at 145 K) and that in both forms the four *peri* ethyl groups (as well as the ethyls at positions 2, 3, 5, and 7) are symmetry related. We assign these forms to the lowest energy conformers **5a** and **5b** (Scheme 3). However, since both conformers possess identical calculated steric energies, the individual identities of the major and minor conformers (**5a** or **5b**) cannot be individually assigned. From the line-shape changes of the signal of carbon 8a (δ ca. 128 ppm, the carbon with the largest chemical shift difference between the two conformers, $\Delta\delta = 29$ Hz at 150.9 MHz), as a function of the temperature, a barrier of 8.8 ± 0.1 kcal mol^{-1} was determined for the major → minor conformer interconversion process (see Table 2).

Computational studies indicate that the rotation of the side chains in all the polyethylated arenes studied so far involves noncorrelated rotation of the ethyls.[3,5b] Stepwise 180° rotation of the four ethyl groups on one of the aromatic rings of conformer **5a** (or **5b**) should lead to **5b** (or **5a**). Full topomerization would then require the rotation of the remaining four side-chains. This analysis predicts that the process that renders the methylene protons of the major conformer isochronous should have the same barrier as the major → minor conformer interconversion process.[14] However, the *rate* of topomerization of the methylene protons of an ethyl group of the major conformer (a major → minor → major* process)

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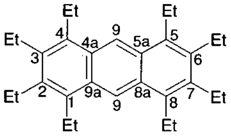
[13] This chiral conformation is asymmetric. In the bay region, one of the pair of ethyls facing the Ar–Ar bond is oriented "in" while the second is oriented "out".

Table 1. NMR Data for Compounds 5, 7, and 8[a]

	^{1}H[b]			^{13}C[d]		
	5	**7**[c]	**8**[c]	**5**	**7**	**8**
1	3.26, 1.41	2.77, 1.24	3.04, 1.03	134.74, 21.98, 15.50	135.62, 23.50, 14.78	135.22, 25.36, 16.15
2	2.89, 1.29	2.74, 1.22	2.73, 1.24	136.65, 22.98, 15.92	137.77, 22.11, 16.10[e]	139.69, 21.94, 16.13
3	2.89, 1.29	2.77, 1.23	2.82, 1.24	136.65, 22.98, 15.92	138.70, 21.67, 16.28	137.77, 22.46, 16.78
4	3.26, 1.41	3.11, 1.35	2.77, 1.24	134.74, 21.98, 15.50	135.23, 22.43, 14.54	134.70, 23.33, 14.84
4a	–	–	–	128.80	137.77	140.49
5a	–	–	–	128.80	140.30	140.49
5	3.26, 1.41	7.61	2.77, 1.24	134.74, 21.98, 15.50	121.22	134.70, 23.33, 14.84
6	2.89, 1.29	2.77, 1.31	2.82, 1.24	136.65, 22.98, 15.92	140.67, 26.40, 16.13[e]	137.77, 22.46, 16.78
7	2.89, 1.29	2.75, 1.20	2.73, 1.24	136.65, 22.98, 15.92	136.80, 21.43, 15.82	139.69, 21.94, 16.13
8	3.26, 1.41	2.82, 1.24	3.04, 1.03	134.74, 21.98, 15.50	137.67, 23.43, 14.73	135.22, 25.36, 16.15
8a	–	–	–	128.80	140.02	140.25
9	8.73	3.73	3.72	119.30	34.59	35.23
9a	–	–	–	128.80	140.30	140.25

[a] At rt, in $CDCl_3$ (referenced to internal TMS). [b] Chemical shifts for the ethyl groups are reported in the order CH_2, CH_3. [c] When identical chemical shifts are reported for heterotopic groups, the $\Delta\delta$ values are typically a few ppb. [d] Chemical shifts for ethylated positions are reported in the order C, CH_2, CH_3. [e] Signals may be interchanged.

For simplicity, the following numbering scheme was used for the three compounds:



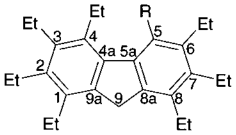


Table 2. Dynamic NMR-Derived Rates of Conformational Processes for 5, 7, and 8 (see text)

T/K[a]	k/s^{-1}	$\Delta G^‡$/kcal mol^{-1}	K
5 (averaging of two conformers, ^{13}C NMR, $CDCl_2F$)			
145.0			2.7
160.0	4	8.7 ± 0.2	2.7
173.0	20	8.9 ± 0.3	2.7[b]
5 (AB → A_2, ^{1}H NMR, CD_2Cl_2)[c]			
176.0	4	9.4 ± 0.5	
197.5	50	9.6 ± 0.7	
210.0	300	9.5 ± 0.7	
7 (AB → A_2, ^{1}H NMR, CD_2Cl_2)			
197.0	100	9.6 ± 0.1	
207.6	300	9.6 ± 0.2	
218.3	600	9.9 ± 0.2	
228.9	1200	10.0 ± 0.2	
239.6	2400	10.2 ± 0.2	
8 (AB → A_2, ^{1}H NMR, CD_2Cl_2)			
191.1	30	9.8 ± 0.2	
212.7	85	10.5 ± 0.2	
235.8	300	11.1 ± 0.3	
249.7	700	11.3 ± 0.3	

[a] Temperatures are believed to be accurate to ± 1 K for **5** and ± 0.5 K for **7** and **8**. [b] Extrapolated from the value at the two lowest temperatures. [c] For the calculation of $\Delta G^‡$ the Eyring equation was used with $\kappa = 0.5$ (see text).

should be half the rate of the major → minor process, since there are equal chances that the minor form will revert to the major conformer with or without concomitant topomerization of the methylene protons. For simplicity, a line-shape analysis for the methylene protons was performed taking into account only the coalescence of the methylene protons for each of the two conformers. This approximate treatment, after multiplying the rates by a factor of 2 (Table 2) gives a barrier similar (within experimental error) to that derived for the major → minor process.

2. Heptaethylfluorene 7. The molecular mechanics-based prediction for this substance is very similar to that for **5**: two conformers with the same energy should be dominant (forms “a” and “b” in Figure S2). These would interconvert by the stepwise rotation of the three ethyl groups on the trisubstituted ring.

Upon lowering the temperature, decoalescence of the methylene protons could be clearly observed indicating slow ethyl rotation on the NMR time scale. The most convenient site for the line shape analysis (see results in Table 2) is the ethyl group located in the bay area (the substituent at C-4), which is not only deshielded by the proximity of the adjacent aromatic ring but also shows a quite large geminal $\Delta\delta$ value of 0.35 ppm at 165 K. Notably, this methylene shows a NOE interaction in the room-temperature NOESY spectrum with the unique aromatic proton. Line shape analysis indicated that the topomerization barrier of **7** is 9.9 kcal mol^{-1} (at 218.3 K). We could not find any splitting of lines in the lowest temperature ^{13}C spectrum (165 K, CD_2Cl_2). Therefore, either the $\Delta G°$ between the two conformers is severely underestimated by the MM3 calculations, or the two conformers are accidentally isochronous in the NMR spectrum.

3. Octaethylfluorene 8. Molecular mechanics calculations predict only one significantly populated conformer for this material, the fully alternating conformer “b” in Figure 2. In agreement with the calculations, the lowest temperature ^{13}C spectrum (171 K, CD_2Cl_2) shows only one set of lines (but, of course, this could be due to accidental isochrony of two conformers). In the low temperature ^{1}H NMR spectrum the methylene protons of the ethyls at the bay region (shifted downfield from the other methylenes) were anisochronous while the methylene protons at the central five-membered ring remained unchanged. This spectrum is consistent with a frozen (on the NMR time scale) conformer of C_2 symmetry. From a simulation of the coalescence process of the methylenes of the groups at the bay area the topomerization barrier of the molecule was determined

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(14) If the lowest energy topomerization pathway of the major conformer does not involve passing through the minor conformer, the topomerization barrier should be lower than the barrier for the major → minor interconversion.

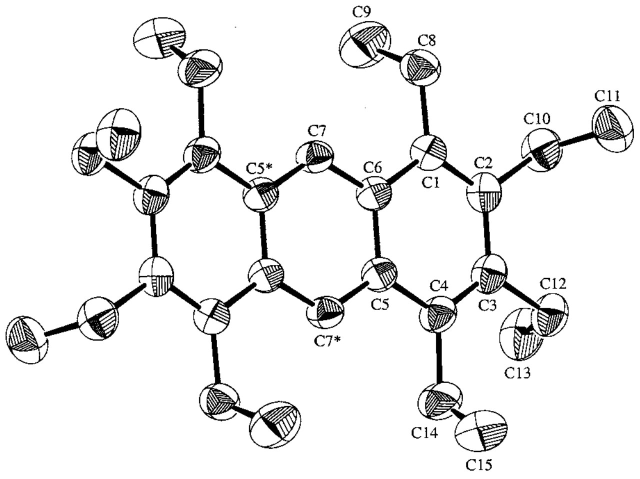

Figure 3. X-ray structure and numbering scheme of 1,2,3,4,5, 6,7,8-octaethylanthracene (**5**).

(Table 2).[15] It should be mentioned that due to the twisted conformation of its central core, a formal 180° rotation of all the ethyl groups of **8** would lead to the all-alternating "in" form "a" (Figure 2) and not to topomerization of the pair of methylene protons within a given ethyl group. This process requires, in addition, reversal of the helical sense of the central fluorene scaffold. MM3 calculations indicate that the fully alternated form with a planar fluorene core lies 8.7 kcal mol^{-1} above the global minimum (only slightly above conformer "a"). This form corresponds to a saddle point as indicated by the frequency analysis (one negative eigenvalue).

Interestingly, the barrier for the rotation of the ethyl groups in octaethylfluorene is the highest we have found in our studies with ethylated aromatic compounds.[5] The high barrier must be due to the buttressing effect in the transition state of one substituted ring onto the other across the bay area. In addition, as observed for decaethylbiphenyl[5a] the ethylated fluorenes **7** and **8** show a significant negative entropy of activation for the ethyl rotation process as indicated by the increase in $\Delta G^{\ddagger}$ with the temperature. These three hydrocarbons have in common a close interaction between an ethyl side-chain and an adjacent aromatic ring.

X-ray Crystallography. Single crystals of the polyethylated derivatives suitable to X-ray crystallography were grown from *n*-hexane/EtOH (**5** and **7**) or ether/MeOH (**8**) (Figures 3−5). Anthracene **5** adopts in the crystal a conformation (corresponding to **5b**) with an alternated up−down arrangement of the ethyl groups within each ring (Figures 3 and S3). Although the conformation possesses C_i symmetry, the deviation from C_{2h} symmetry is not large. Pairs of ethyls located at vicinal *peri* positions are oriented *syn*. Such an arrangement was previously observed in the crystal structure of octaethylbiphenylene. Molecular mechanics and ab initio calculations (see above) indicate that the conformations **5a** and **5b** possess nearly identical energies.

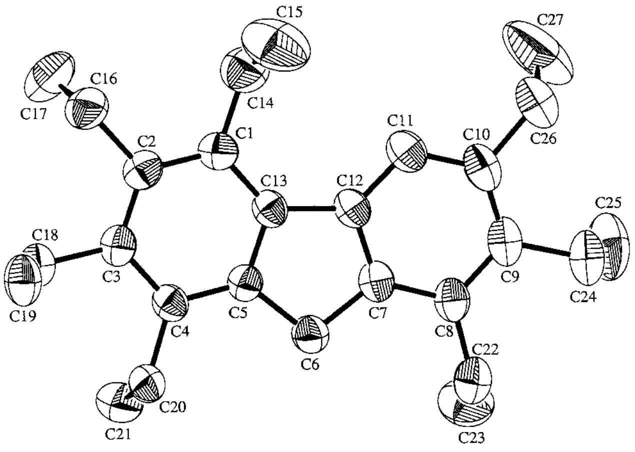

Figure 4. X-ray structure of 1,2,3,4,6,7,8-heptaethylfluorene (**7**).

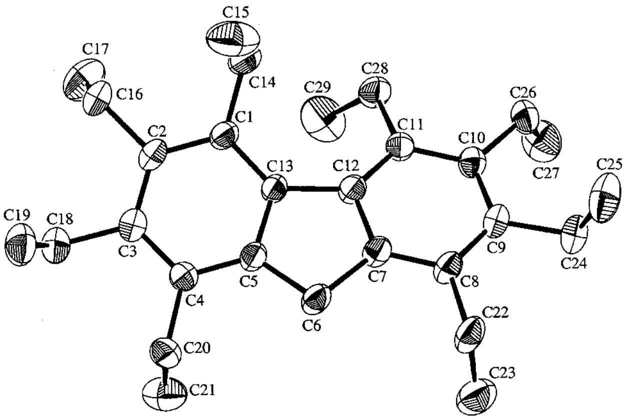

Figure 5. X-ray structure and numbering scheme of 1,2,3,4,5, 6,7,8-octaethylfluorene (**8**).

Notably, in the crystal conformation of **7** the ethyl groups in the trisubstituted ring are oriented in the same direction, while in the tetrasubstituted ring they adopt the normal up−down arrangement (Figures 4 and S4). MM3 calculations indicate that the crystal conformation (which corresponds to form "m" in Figure S2) lies ca. 1.9 kcal mol^{-1} above the lowest energy conformations. The central fluorene subunit is nearly planar and the torsional angle between the four carbons at the bay region is 2.5° (calculated (MM3): 4.8°).

Octaethylfluorene **8** adopts in the crystal a conformation with a *syn* interaction between a pair of vicinal ethyl groups located at the 3 and 4 positions (cf. Table 1) with the ethyl groups on the bay region oriented "out" (Figures 5 and S5). The central fluorene core is non planar and the torsional angle between the four carbons at the bay region (C1, C13, C12, C11) is 29.6°, a value similar to that reported by Pascal for octaphenylfluorenone (33.2°).[8b] According to the MM3 calculations, the crystal conformation (which corresponds to the form "c" in Figure 2) lies 1.1 kcal mol^{-1} above the fully alternated form. The MM3 calculations satisfactorily reproduce the structural parameters of the conformation, the largest deviation corresponding to the torsional angle (C12−C11−C28−C29) of one of the ethyl groups at the bay region which significantly deviates from a perpendicular arrangement (X-ray: 50.1°, MM3: 69.5°).

The high energy conformations of **7** and **8** present in the crystal (also observed in the crystal structure of **10**)[5c] are most likely the result of packing forces. These conformations are preferred in the crystal since they probably allow for a better self-fitting, and/or a denser

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[15] The line-shape calculations were performed using a computer program based on the equations in the following paper: Alexander, S. *J. Chem. Phys.* **1962**, *37*, 967.

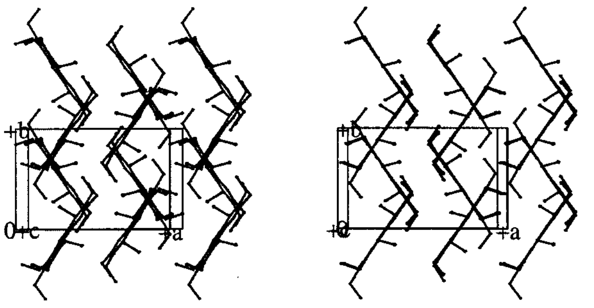

Figure 6. Stereoview of the packing of the molecules in the unit cell of **7**.

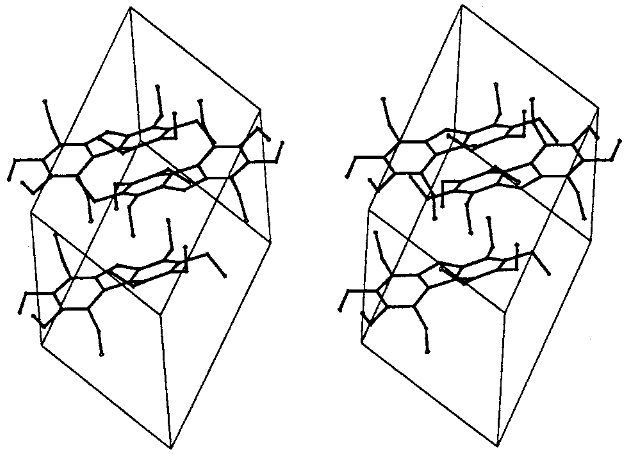

Figure 7. Stereoview of the packing of **8** in the unit cell.

packing. In **7**, the three vicinal ethyl groups pointing toward one of the aryl faces render the opposite face sterically accessible. These ethyls in a vicinal molecule are on top of the exposed face with the C(sp^3)−C(sp^3) bonds oriented nearly parallel to it (Figure 6). The *syn* orientation of three vicinal ethyls apparently facilitates the perpendicular packing of a vicinal molecule. In the case of **8** the two vicinal *syn* ethyls together with the additional ethyl on the same ring oriented in the same direction delimit a “cleft”. Toward this cleft are oriented the pair of *syn* ethyl groups of a second molecule related by the crystallographic inversion center (Figure 7). A less speculative analysis of the reasons for the preference of high-energy conformers of **7** and **8** in the solid state will have to be postponed until more crystallographic data on similar systems become available.

Experimental Section

NMR Spectroscopy. NMR spectra were run on a Bruker DMX-600 spectrometer operating at 600.1 (^{1}H) and 150.9 (^{13}C) MHz. $CDCl_2F$ was prepared according to the literature.[17] Probe temperatures were measured with a calibrated Eurotherm 840/*T* digital thermometer.

Calculations. MM3(94) calculations were performed using the Alchemy 2000 program.[18] All stationary points were characterized as minima by the absence of imaginary frequencies in the frequency matrix. Ab initio calculations were conducted using the Gaussian 98 Program.[19]

Crystallography. The X-ray diffraction data were measured with an ENRAF−NONIUS CAD-4 or a PW1100/20 Philips four-Circle computer controlled diffractometers. CuK$_\alpha$ (λ = 1.54178 Å) or MoK$_\alpha$ (λ = 0.71069 Å) radiation with a graphite crystal monochromator in the incident beam was used. All crystallographic computing was done on a VAX 9000 computer using the teXsan structure analysis software. Crystal data for **5**: $C_{30}H_{42}$, space group $P2_1/c$, a = 9.681(2) Å, b = 14.645(3) Å, c = 8.704(4) Å, β = 95.29(3)°, V = 1228.8(6) Å^3, Z = 2, ρ_{calc} = 1.09 g cm^{-3}, μ(Cu Kα) = 4.44 cm^{-1}, no. of unique reflections = 2437, no. of reflections with I ≥ 2 σ_I = 1832, R = 0.060, R_w = 0.080. Crystal data for **7**: $C_{27}H_{38}$, space group $P2_1/c$, a = 14.123(5) Å, b = 8.728(6) Å, c = 18.584(7) Å, β = 105.53(3)°, V = 2207(2) Å^3, Z = 4, ρ_{calc} = 1.09 g cm^{-3}, μ(Cu Kα) = 4.45 cm^{-1}, no. of unique reflections = 3529, no. of reflections with I ≥ 2 σ_I = 2392, R = 0.067, R_w = 0.105. Crystal data for **8**: $C_{29}H_{42}$, space group $P\bar{1}$, a = 11.463(3) Å, b = 12.406(2) Å, c = 9.332(1) Å, α = 106.51(1)^0, β = 97.09(2)°; γ = 71.54(2)°; V = 1206.4(4) Å^3, Z = 2, ρ_{calc} = 1.08 g cm^{-3}, μ(Mo Kα) = 0.60 cm^{-1}, no. of unique reflections = 6303, no. of reflections with I ≥ 3 σ_I = 3578, R = 0.068, R_w = 0.090.

The analytical HPLC separation of **7** and **8** was performed on a Waters Gradient System equipped with a Waters 717-Plus autosampler, a Waters 600 intelligent pump, a Waters 996 photodiode array detector and the system was piloted with Millenium software from Waters. The system was coupled to an automated fraction collector 202 from Gilson. Mobile phases were (A) H_2O (0.1% TFA) and (B) MeCN (0.08% TFA). Separation conditions were as follows: Analytical column C18 218TP54 from Vydac, gradient [A/B]: 3 min [20/80], 3−10 [0/100]. 10−35 [0/100], flow = 1 mL/min: Retention times for **7** and **8** were 20.21 and 20.95 min, respectively. Semipreparative column C18 218TP10 from Vydac, gradient [A/B]: 3 min [20/80], 3−10 [0/100]. 10−50 [0/100], flow = 10 mL/min; samples eluting from the semipreparative column between 9 and 15 min were reanalyzed using the analytic conditions, and pure fractions were pooled.

Preparative HPLC purification of **8** from a mixture of **8** and **7** was done in a Waters 600 system using a Waters Spherisorb 20 × 250 mm RP-18 column with 100% methanol as eluent. Using a flow of 9 mL/min the retention times for **8** and **7** were 28.75 and 31.52 min, respectively. The fraction containing pure **8** was evaporated and dissolved in an ether−MeOH mixture. Slow evaporation of the solvent mixture afforded crystals of **8** suitable for X-ray crystallography.

Preparation of 1,2,3,4,5,6,7,8-Octaethylanthracene (5). A 1.8 g (0.01 mol) amount of dihydroanthracene was dissolved in 20 mL of EtBr, and to the stirred solution was added in small portions during 30 min 8 g (0.07 mol) of $AlCl_3$. After stirring for 18 h at room temperature, the mixture was poured into ice. After extraction with ether, the organic phase was washed with brine, followed by drying and evaporation. Chromatography of the residue (silica, eluent: *n*-hexane) afforded 0.95 g (23%) of **5**, which was recrystallyzed from *n*-hexane/ethanol, mp 200 °C. Anal. Calcd for $C_{30}H_{42}$: C, 89.49; H, 10.51. Found: C, 89.22; H, 10.11.

Preparation of 1,2,3,4,6,7,8-Heptaethylfluorene (7) and 1,2,3,4,5,6,7,8-Octaethylfluorene (8). A solution of 1.7 g of fluorene (0.01 mol) dissolved in 20 mL of EtBr was treated with 13.4 g of $AlCl_3$ (0.1 mol). After stirring for 18 h, the crude mixture of products was worked up as described above. Chromatography of the crude product (silica, eluent: *n*-hexane) afforded 0.89 g (22%) of a 2:1 mixture of **7** and **8**. From this

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(16) Allinger, N. L.; Yuh, Y. H.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551.

(17) Siegel, J. S.; Anet, F. A. L. *J. Org. Chem.* **1988**, *53*, 2629.

(18) Alchemy 2000. Tripos Inc., St. Louis, MO 63144.

(19) *Gaussian 98, Revision A.8*, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1998.

mixture we could crystallize (*n*-hexane/ethanol) pure **7**. The mixture of the two products was separated by HPLC (see above). **7**, mp 102 °C, CI MS *m*/*z* 363.3 (MH^+), Anal. Calcd for $C_{27}H_{38}$: C, 89.44; H, 10.56. Found: C, 89.32; H, 10.35. **8**, mp 105 °C, HRMS calcd for $C_{29}H_{42}$: *m*/*z* 390.3286. Found: *m*/*z*: 390.3273.

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Supporting Information Available: Calculated (MM3) relative energies of selected up−down conformers of **5** and **7**, stereoviews of the conformations of **5**, **7**, and **8** in the crystal, crystallographic data for **5**, **7**, **8**, ^{1}H NMR spectra of **5**, **7**, and **8**, and calculated (RHF-6-31G(d)) energies and final coordinates for **5** and **8**. This material is available free of charge via the Internet at http://pubs.acs.org. .

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