Conformational Shift by Mutual Steric Interactions between Two Multiarmed Units

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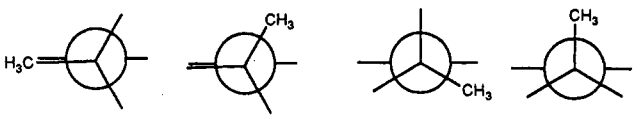
Decakis(bromomethyl)biphenyl (3) has been prepared by reaction of decamethylbiphenyl with Br_2/CCl_4 in the presence of tetrabutylammonium bromide as catalyst. The attempted synthesis of decakis(bromomethyl)benzophenone resulted only in bromopentakis(bromomethyl)benzene (8). X-ray diffraction of a single crystal of 3 shows that the preferred conformation of 3 is not the alternate "up-down" conformation observed for the parent hexakis(bromomethyl)benzene, but a conformation in which the up-down alternation of the CH_2Br groups is disrupted at the meta-para positions of each ring. MM2(85) calculations on 3 indicate that some conformations with disrupted "up-down" alternation of the CH_2Br groups are favored over the all-alternate up-down form. It is suggested that this conformational shift is the result of the mutual steric interactions between arms of different moieties, and that syn interactions between *m*- and *p*-CH_2Br groups operate in order to avoid bromine contacts between ortho groups at different rings. The barrier for Ar-CH_2Br rotation was estimated from dynamic NMR data as 12.5 kcal mol^{-1}.

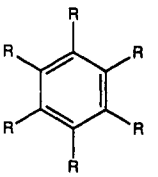
Introduction

Multiarmed organic compounds[1] (sometimes dubbed "octopus molecules")[2] comprise a multiatomic central core (for example, a benzene ring) from which radiate "arms". These arms are usually alkyl or modified alkyl groups in which one or more carbon atoms in the paraffinic chains are substituted by a heteroatom. Multiarmed organic compounds are of interest since they can have liquid crystal properties,[3] can be useful precursors for the synthesis of organometallic compounds,[4] or can display complexing capabilities.[2,5]

The simplest "arm" of stereochemical interest is the ethyl group. When this substituent is attached to a planar frame, several conformations are possible: eclipsed (a), staggered (b and c), and "perpendicular" (d).[6] In general, when several ethyl groups are arranged about a benzene ring, repulsive interactions between the CH_3 group of a given ethyl and its neighboring alkyl groups render the conformations a-c energetically unfavorable. In such systems the ethyl groups are almost exclusively oriented in "perpendicular" (d) conformations.



If possible the molecule will orient the side arms in a way that minimizes the steric interactions of the perpendicular groups. Such an arrangement is the alternate "up-down" arrangement of the alkyl groups shown in Figure 1. This conformation is displayed by hexaethylbenzene[7] (1), hexa-*n*-propylbenzene,[8] and hexakis(bromomethyl)benzene[9] (2), as well as by *all-trans*-1,2,3,4,5,6-hexaethylcyclohexane,[10] in which the six ethyl groups are located at equatorial positions and are alternately disposed "up" and "down" the mean plane of the cyclohexane ring.



1 R = Et
2 R = CH_2Br

The parent compound 1 exists in the alternate "up-down" conformation, but complexation of the molecule with transition metals results in a conformation that depends on the bulk of the other ligands ligated to the metal complex. For example, while the $Cr(CO)_3$ complex of 1 exists in an alternate "up-down" conformation (i.e., identical with the conformation of the free ligand), when 1 is complexed to a $Cr(CO)_2PPh_3$ unit, all six ethyl groups prefer to be located at distal positions, i.e., pointing away from the metal atom.[11]

Although the stereochemistry of several multiarmed systems has been investigated in recent years,[5,7-11] no system has been reported comprising *two* multiarmed moieties in spatial proximity.[12] In order to determine whether the mutual steric interaction between "arms" at different multiarmed moieties can result in a conformational shift, i.e., in a conformational preference different from that of the isolated single moiety, we attempted the

(1) For a review on multiarmed organic compounds, see: Menger, F. M. *Top. Curr. Chem.* **1986**, *136*, 1.
(2) Vögtle, F.; Weber, E. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 814.
(3) See, for example: Praefcke, K.; Kohne, B.; Stephan, W.; Marquardt, P. *Chimia* **1989**, *43*, 380.
(4) For recent work on tentacled iron sandwiches, see: (a) Moulines, F.; Astruc, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1347. (b) Gloaguen, B.; Astruc, D. *J. Am. Chem. Soc.* **1990**, *112*, 4607. (c) Astruc, D.; Hamon, J. R.; Mandon, D.; Moulines, F. *Pure Appl. Chem.* **1990**, *62*, 1165.
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(7) Iverson, D. J.; Hunter, G.; Blount, J. F.; Damewood, J. R., Jr.; Mislow, K. *J. Am. Chem. Soc.* **1981**, *103*, 6073.
(8) Hunter, G.; Weakley, T. J. R.; Weissensteiner, W. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1633.
(9) Marsau, P. *Acta Crystallogr.* **1965**, *18*, 851.
(10) Immirzi, A.; Torti, E. *Atti Accad. Naz. Lincei, Cl. Sci. Fis., Mat. Nat., Rend.* **1968**, *44*, 98.
(11) Hunter, G.; Iverson, D. J.; Mislow, K.; Blount, J. F. *J. Am. Chem. Soc.* **1980**, *102*, 5942.
(12) One exception is 1,2,3,4,5,6,7,8-octakis(bromomethyl)naphthalene described by Hart (Hart, H.; Reilly, J. L.; Jiang, J. B.-C. *J. Org. Chem.* **1977**, *42*, 2684). This system can be formally considered as resulting from linking two tetrakis(bromomethyl)benzene systems side by side in a coplanar fashion. Unfortunately no X-ray data nor slow exchange NMR data was reported for the compound from which the preferred conformation can be inferred.

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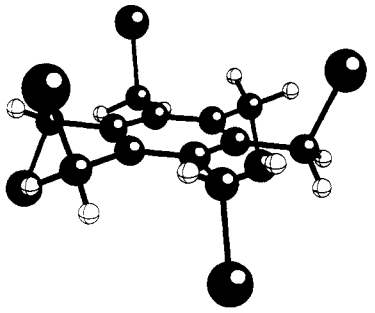
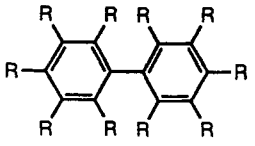
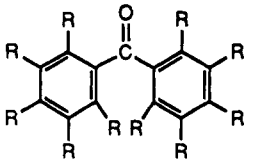


Figure 1. Alternate "up–down" conformation in hexakis(bromomethyl)benzene. The bromomethyl groups are alternately disposed "above" and "below" the phenyl ring plane.

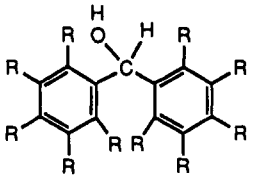
preparation of the multiarmed systems decakis(bromomethyl)biphenyl (**3**) and decakis(bromomethyl)benzophenone (**4**).



3 R = CH_2Br
5 R = CH_3



4 R = CH_2Br
6 R = CH_3



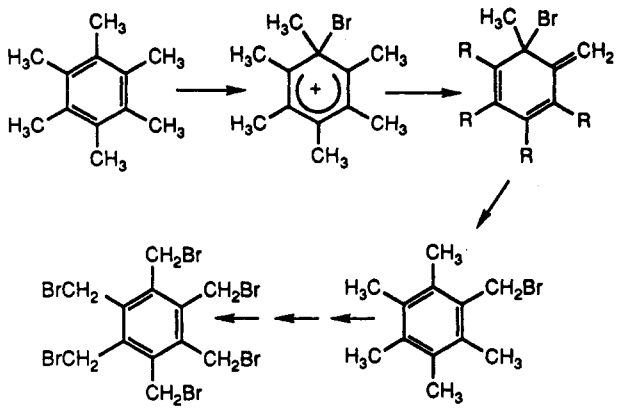
7 R = CH_3

Results and Discussion

The rationale for choosing the bromomethyl group as the side arm was based on several considerations. Firstly, since a bromine atom and a methyl group are of similar size,[13] the CH_2Br group resembles the simplest arm of stereochemical interest, i.e., the ethyl group. Secondly, whereas the preparation of the polyethyl analogues of **3** and **4** should involve a multistep synthesis, the bromomethyl compounds can in principle be prepared in a single-step reaction. By analogy with the preparation of the parent **2**,[14] we figured out that treatment of the synthetically amenable polymethyl compounds **5** and **6** with bromine under *electrophilic* conditions (vide infra) should afford the target compounds. Finally, in principle the bromine atom in the CH_2Br group can be displaced by a host of nucleophiles, and therefore **3** and **4** could be useful synthetic intermediates in the preparation of more complex multiarmed compounds.

Preparation of 3 and Attempted Preparation of 4. The parent hexakis(bromomethyl)benzene (**2**) can be easily prepared by bromination of hexamethylbenzene in dibromoethane.[14] As shown by Baciocchi and Illuminati,[15] this reaction does not occur by a free-radical mechanism like most side-chain brominations but via an electrophilic mechanism in which in the first step a benzenium ion is formed in the rate-determining step, followed by a fast rearrangement of the electrophile from the ring to the side

Scheme I



chain (Scheme I).[15] We reasoned that the polymethyl compounds **5** and **6** could be transformed into **3** and **4** by their treatment with bromine. Both **5**[16] and **6**[17] have been reported in the literature. Biphenyl **5** can be prepared by $CuCl_2$ coupling of (pentamethylphenyl)magnesium bromide[16] while **6** was reported as one of the products of the addition of ethyl formate to the same Grignard reagent.[17] Unfortunately, all our attempts to repeat the literature procedure for the preparation of **6** were unsuccessful. We therefore decided to attempt the synthesis of **6** by oxidation of the known decamethylbenzhydrol (**7**). Preparation of **7** was accomplished by the procedure of Fuson et al.[18] The benzhydrol is acid sensitive, and thus recrystallization of **7** from ethanol without removing traces of acid from the acid hydrolysis of the Grignard adduct resulted in conversion to its ethyl ether derivative. The benzhydrol was oxidized to the benzophenone by pyridinium dichromate (PDC), and the product was characterized by its analytical and spectral properties. The isolated compound (white crystals of mp 205 °C) has different properties than the compound reported by Lapkin (yellow crystals of mp 281–282 °C),[17] and therefore it seems likely that Lapkin's isolated compound was not **6**.

In order to attempt the preparation of **3**, we reacted biphenyl **5** with excess Br_2 in CCl_4 under reflux conditions. However, whereas treatment of hexamethylbenzene under similar conditions resulted in its clean conversion into **2**, the reaction of **5** resulted in a mixture of products. We therefore decided to add tetrabutylammonium bromide to the reaction, since it was shown by Dakka and Sasson that this compound (commonly used as a phase-transfer catalyst) can function as a Friedel–Crafts aromatic bromination catalyst.[19] Indeed, addition of the catalyst resulted in a cleaner conversion of **5** to **3**.

Treatment of **6** with $Br_2/Bu_4N^+Br^-$ under different conditions resulted exclusively in the isolation of a product that displayed three signals in the ^1H NMR spectrum (200 MHz, room temperature, $CDCl_3$) at δ 4.81, 4.74, and 4.67 with an integration ratio of 2:2:1. This compound was identified as bromopentakis(bromomethyl)benzene (**8**).[20]

(13) For a discussion, see: Hounshell, W. D.; Iroff, L. D.; Iverson, D. J.; Wroczynski, R. J.; Mislow, K. *Isr. J. Chem.* **1980**, *20*, 65.
(14) Backer, H. J. *Recl. Trav. Chim. Pays-Bas* **1935**, *54*, 745.
(15) Baciocchi, E.; Ciana, A.; Illuminati, G.; Pasini, C. *J. Am. Chem. Soc.* **1965**, *87*, 3953. Baciocchi, E.; Illuminati, G. *Tetrahedron Lett.* **1962**, 637. For a review, see: Hartshorn, S. R. *Chem. Soc. Rev.* **1974**, *3*, 167.
(16) (a) Smith, L. I.; Nichols, J. *J. Org. Chem.* **1941**, *6*, 489. (b) Biali, S. E.; Kahr, B.; Okamoto, Y.; Aburatani, R.; Mislow, K. *J. Am. Chem. Soc.* **1988**, *110*, 1917.
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(18) Fuson, R. C.; Jackson, H. L. *J. Am. Chem. Soc.* **1950**, *72*, 351. Smith, H. A.; Thompson, R. G. *J. Am. Chem. Soc.* **1955**, *77*, 1778.
(19) Dakka, J.; Sasson, Y. *J. Chem. Soc., Chem. Commun.* **1987**, 1421; *J. Org. Chem.* **1989**, *54*, 3224.
(20) Bromopentakis(bromomethyl)benzene has been described in a patent as a useful compound for flameproofing of polymers (Jenkner, H.; Buettgens, W. Ger. Offen. 2435,457; *Chem. Abstr.* **1976**, *84*, 135265v). The compound was prepared by catalytic (iodine) bromination of pentakis(bromomethyl)benzene.

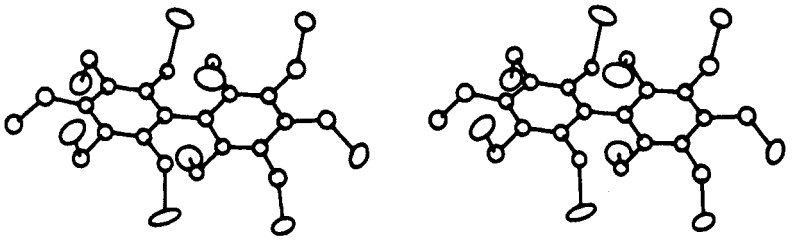
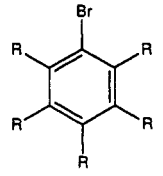
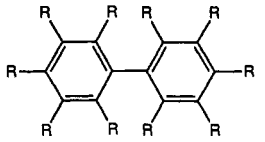


Figure 2. Stereoview of the X-ray structure of decakis(bromomethyl)biphenyl (3).

Further proof for the structure of 8 came from its independent synthesis by reacting pentamethylbenzene with $Br_2/Bu_4N^+Br^-$. It seems likely that, under the reaction conditions, one of the intermediates in the formation of 4 is cleaved at the Ar–CO bond and therefore the final product is 8 instead of the expected 4.



8 R = CH_2Br



9 R = $CHCl_2$

Static Stereochemistry of 3. Hexaethylbenzene exists in eight stereoisomeric forms resulting from the different possible arrangements of the perpendicular ethyl groups "above" and "below" the phenyl ring plane. Biphenyl 3 should in principle exist in a larger number of conformations due to the presence of 10 CH_2Br groups. These conformers should belong to one of the subgroups of the point group of the biphenyl skeleton (i.e., D_{2d}, D_2, C_{2v}, S_4, C_2, C_s, or C_1). Since the bromomethyl groups at the para positions destroy the C_2 axis along the biphenyl axis, and the perpendicular orientations of the bromomethyl groups destroy both σ planes which pass through the two aryl rings, the only possible symmetries for the conformers of 3 are C_2 and C_1. All possible conformers are therefore chiral and exist in two enantiomeric forms. Biphenyl 3 as well as the previously studied[16b] decakis(dichloromethyl)biphenyl (9) represent examples of biphenyl substituted by 10 identical substituents but which nevertheless exist in chiral conformations due to the arrangements of the side chains.

The number of isomers for each possible symmetry can be readily calculated by using configurational matrices.[21] This method, introduced by Willem et al.,[21] has been previously used for the calculation of the number of isomers of 9[16b] and of octakis(dichloromethyl)anthracene.[22] Each conformation of 3 is represented by a 10-digit, one-dimensional configurational matrix. Each digit can adopt one of two possible values (0 or 1) representing the two possible perpendicular arrangements ("up" or "down") of a given CH_2Br group. As in the case of biphenyl 9, there exist 2^{10} (1024) distinct configurational matrices. Some of the matrices represent the same isomer; four equivalent matrices exist for structures of C_1 symmetry, while two equivalent matrices exist for conformations of C_2 symmetry.[23] The number of matrices representing isomers of C_2 symmetry is $2^5 = 32$, indicating that 16 conformers of C_2 symmetry exist. The number of conformers of C_1 symmetry is therefore $(1024 - 32)/4 = 248$. Since all conformations are chiral, it can therefore be concluded that 3 exists in 264 conformations which relate as 132 enantiomeric pairs. It is interesting to note that, as in the case of the hexaisopropylbenzene/hexaethylbenzene pair,[24] the number of isomers for biphenyls 3 and 9 is identical, and therefore a one-to-one mapping between the two sets of isomeric structures is possible.

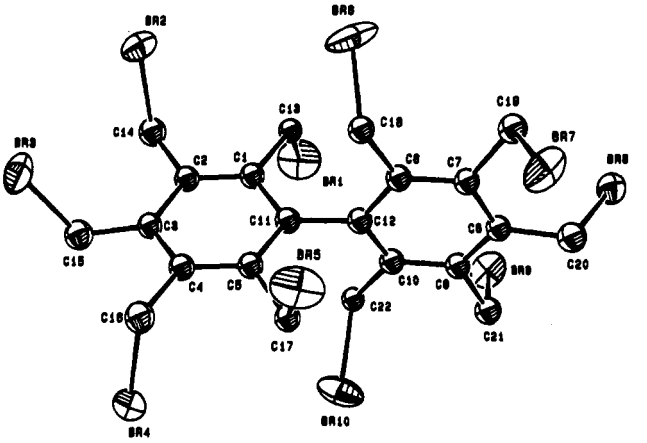


Figure 3. Numbering scheme for biphenyl 3.

Solution and Crystal Conformation of Biphenyl 3. The ^1H NMR spectrum of 3 at room temperature (200 MHz, $CDCl_3$) displays one sharp and two broad signals. Raising the temperature to 360 K in $C_6D_5NO_2$ resulted in sharpening of the signals, and three singlets with an integration ratio of 2:1:2 were observed at δ 4.95, 4.91, and 4.36. The high-field signal can be assigned to the *o*-CH_2Br protons, since these protons should be under the shielding influence of the neighboring phenyl ring. Lowering the temperature down to 190 K in $CDCl_3/CD_2Cl_2$ resulted in a decoalescence process followed by resharpening of the signals. Since all possible conformations of 3 are chiral, the two protons of any CH_2Br groups reside in diastereotopic environments. Due to the symmetry nonequivalence of the methylenic protons, a C_2 conformation should display in the NMR spectrum 10 doublets, while a C_1 conformation should display 20 doublets. Unfortunately, the large overlap of the NMR signals does not allow the interpretation of the slow-exchange NMR spectrum, and therefore the favored conformation cannot be deduced from the NMR data.

In order to determine the preferred conformation of 3 in the solid state, we grew a single crystal of 3. The structure was solved and refined in the space group $P\bar{1}$ with two molecules in the unit cell. The crystal conformation has C_1 symmetry. A stereoview of the X-ray structure and the numbering scheme are shown in Figures 2 and 3. Positional parameters for 3 are listed in Table I, and selected bond lengths, bond angles, and torsional angles are collected in Table II.

(21) Willem, R.; Pepermans, H.; Hoogzand, C.; Hallenga, K.; Gielen, M. *J. Am. Chem. Soc.* **1981**, *103*, 2297.

(22) Biali, S. E.; Buda, A. B.; Mislow, K. *J. Org. Chem.* **1988**, *53*, 1289.

(23) The number of the distinct configurational matrices describing a given conformation is inversely proportional to its symmetry number. For a mathematical demonstration, see: Brocas, J.; Gielen, M.; Willem, R. *The Permutational Approach to Dynamic Stereochemistry*; McGraw-Hill: New York, 1983; Chapter 8.

(24) Siegel, J.; Gutiérrez, A.; Schweizer, W. B.; Ermer, O.; Mislow, K. *J. Am. Chem. Soc.* **1986**, *108*, 1569.

Table I. Positional Parameters and Estimated Standard Deviations for 3[a]

atom	x	y	z
Br(1)	0.2982 (3)	0.3385 (3)	0.1713 (3)
Br(2)	0.0514 (3)	0.5843 (2)	0.2196 (3)
Br(3)	−0.2997 (3)	0.3575 (3)	0.0475 (3)
Br(4)	−0.3743 (3)	−0.0813 (3)	0.0236 (3)
Br(5)	−0.1360 (3)	0.1476 (3)	0.4853 (3)
Br(6)	0.2759 (4)	0.5797 (3)	0.6029 (3)
Br(7)	0.2954 (3)	0.3317 (3)	0.8613 (3)
Br(8)	0.6206 (2)	0.2640 (2)	0.6960 (3)
Br(9)	0.4773 (3)	0.0935 (3)	0.3344 (3)
Br(10)	0.0258 (3)	−0.1084 (3)	0.1622 (3)
C(1)	0.094 (2)	0.324 (2)	0.253 (2)
C(2)	−0.002 (2)	0.324 (2)	0.161 (2)
C(3)	−0.132 (2)	0.242 (2)	0.123 (2)
C(4)	−0.163 (2)	0.168 (2)	0.189 (2)
C(5)	−0.065 (2)	0.165 (2)	0.279 (2)
C(6)	0.220 (1)	0.315 (2)	0.538 (2)
C(7)	0.314 (2)	0.303 (2)	0.620 (2)
C(8)	0.356 (2)	0.207 (2)	0.578 (2)
C(9)	0.304 (2)	0.131 (2)	0.447 (2)
C(10)	0.212 (2)	0.145 (2)	0.363 (2)
C(11)	0.065 (2)	0.241 (2)	0.313 (2)
C(12)	0.166 (2)	0.233 (2)	0.404 (2)
C(13)	0.231 (2)	0.405 (2)	0.292 (2)
C(14)	0.028 (2)	0.415 (2)	0.105 (2)
C(15)	−0.237 (2)	0.230 (2)	0.008 (2)
C(16)	−0.304 (2)	0.089 (2)	0.158 (2)
C(17)	−0.098 (2)	0.073 (2)	0.335 (2)
C(18)	0.168 (2)	0.411 (2)	0.582 (2)
C(19)	0.381 (2)	0.399 (2)	0.765 (2)
C(20)	0.441 (2)	0.185 (2)	0.676 (2)
C(21)	0.347 (2)	0.031 (2)	0.400 (2)
C(22)	0.163 (2)	0.065 (2)	0.221 (2)

[a] Estimated standard deviations in the least significant digits are shown in parentheses.

Table II. Selected Experimental and Calculated Structural Parameters for the Crystallographic Conformation of 3[a]

atoms	exptl (X-rays)	calcd (MM2(85))
C(11)–C(12)	1.45 (3)	1.52
C(13)–Br(1)	1.94 (2)	1.95
Br(1)–C(13)–C(1)	113 (2)	111
C(13)–C(1)–C(11)	117 (2)	119
C(1)–C(11)–C(12)–C(6)	89	90
Br(1)–C(13)–C(1)–C(11)	100	100
Br(2)–C(14)–C(2)–C(1)	−82	−86
Br(3)–C(15)–C(3)–C(2)	−86	−94
Br(4)–C(16)–C(4)–C(3)	90	89
Br(5)–C(17)–C(5)–C(4)	−86	−80
Br(6)–C(18)–C(6)–C(12)	−97	−100
Br(7)–C(19)–C(7)–C(6)	94	90
Br(8)–C(20)–C(8)–C(7)	−103	−87
Br(9)–C(21)–C(9)–C(8)	−100	−95
Br(10)–C(22)–C(10)–C(9)	82	80

[a] Bond lengths in angstroms; bond and torsional angles in degrees.

As shown in the figures, *the preferred conformation is not the alternate "up–down", but a conformation in which the up–down alternation of the CH_2Br groups is disrupted at one meta–para position of each ring.* The two phenyl rings are almost perpendicular (φ = 89°). The CH_2Br groups differ in their C(Ar)–C(Ar)–C–Br torsional angles: most of the them have angles of 80°, while the two *m*-CH_2Br groups both neighbors of which are oriented in an alternate fashion are oriented nearly perpendicularly. It is interesting to note that the biphenyl axis is almost linear, whereas in the related (and more crowded) biphenyl **9** there is a cant of the two rings relative to each other.[16b] The Ph–Ph bond is somewhat short (1.45 Å), but this abnormal value is probably due to poor refinement of the structure.

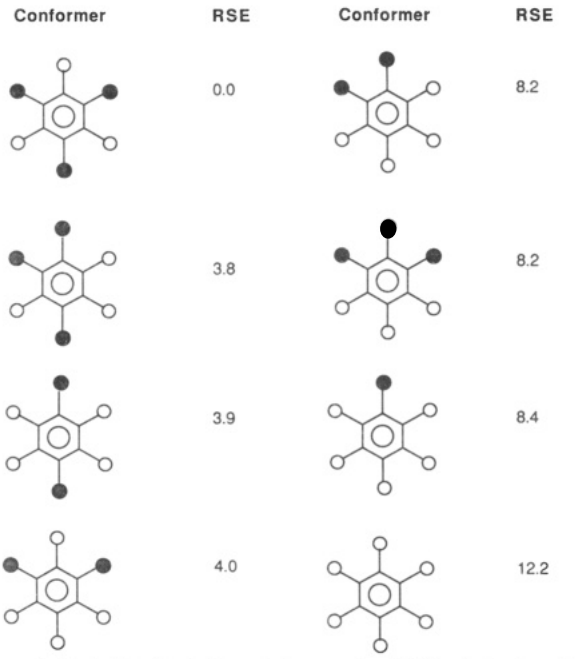


Figure 4. Calculated relative steric energies (RSEs, in kcal mol^{-1}) of the conformers of hexakis(bromomethyl)benzene. Bromomethyl groups pointing toward or away from the observer are represented by filled or empty circles, respectively.

In order to obtain some insight into the reasons for the conformational preferences of **3**, we performed molecular mechanics calculations. The results of the calculations are described in the next section.

Molecular Mechanics Calculations of 3. For the molecular mechanics calculations we used Allinger's MM2(85) program.[25] We first calculated the relative energies of the eight conformers of the parent **2**. The results of the calculations are summarized in Figure 4. As in the case of **1**[7] and hexapropylbenzene,[8] the calculated conformation of lowest energy corresponds to the alternate "up–down" form (Figure 1). All other conformations have higher relative steric energies (RSEs), which roughly increase with the increased number of syn interactions.

As showed in the previous section, 132 conformations (264/2) must be considered for the full characterization of the conformational behavior of **3**. In order to limit the number of calculations, we considered the all-alternate "up–down" conformation and all conformations with no more than two syn interactions (i.e., with no more than two pairs of vicinal CH_2Br groups pointing in the same direction) and with no more than a single syn interaction per ring. The results of the calculations are summarized in Figure 5. The calculated structural data for the crystallographic conformation are included in Table II. The calculations reproduce satisfactorily the structure of the crystallographic conformation. It should be noted that the calculations predict a normal Ph–Ph bond length (1.52 Å) in contrast with the experimental value (1.45 (3) Å). It seems therefore highly likely that the abnormal crystallographic Ph–Ph bond length is due to poor refinement.

Several conclusions can be extracted from the calculations. In contrast with **2**, the relative destabilization of the conformers of **3** is not dictated exclusively by the number of syn interactions. For example, the conformer without any syn interaction (i.e., the conformer in which in both rings the CH_2Br groups exist in an alternate up–down conformation) lies 1.7 kcal mol^{-1} above a confor-

(25) Allinger, N. L. QCPE MM2(85), 1986.

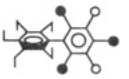
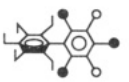
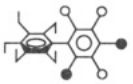
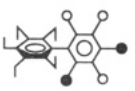
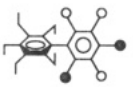
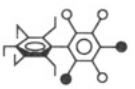
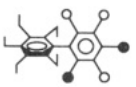
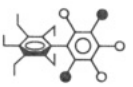
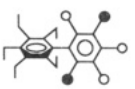
Conformer	N Syn	Br/Br	RSE	Conformer	N Syn	Br/Br	RSE
	0	1	1.70				
	1	1	2.64		1	1	2.74
	1	1	2.74		1	1	2.78
	2	0	0.0		2	2	7.34
	2	2	7.47		2	0	0.0
	2	0	0.16		2	2	7.04
	2	2	7.03		2	0	0.17
	2	0	0.20		2	2	6.90
	2	2	6.91		2	0	0.21

Figure 5. Relative steric energies (RSEs, in kcal mol^{-1}) of selected conformers of biphenyl **3**. Bromomethyl groups at the phenyl ring coplanar to the page are represented by filled circles (CH_2Br groups pointing toward the observer) or empty circles (CH_2Br groups pointing away from the observer). "N Syn" and "Br/Br" represent the numbers of syn interactions and bromine/bromine clashings, respectively. The crystallographic conformation is the one with a RSE of 0.20 kcal mol^{-1} (first column, second entry from the bottom).

mation with two such interactions. As indicated by the X-ray data and corroborated by the calculations, the spatial proximity between the two multiarmed moieties results in a conformational shift, i.e., in a conformational predilection different from that of a single isolated moiety. The reason for this conformational shift can be rationalized in terms of the avoidance of bromine–bromine contacts between *o*-CH_2Br groups at different rings. Since the biphenyl rings are substituted by an odd number of CH_2Br groups, a complete up–down alternation of the groups results in two terminal *o*-CH_2Br groups pointing in the same direction ("up" or "down"). These orientations of the CH_2Br groups must led to a clash with one *o*-CH_2Br group of the neighboring ring, irrespective of its orientation. The Br/Br clashing is energetically more costly than a syn interaction, and therefore in order to avoid these Br/Br contacts the molecule adopts a conformation in which two syn interactions are present, one at each ring. The introduction of a syn interaction at each ring results in an alternate orientation of the *o*-CH_2Br groups and allows the existence of arrangements devoid of Br/Br contacts. According to the calculations, each of the two syn interactions can be located at any two vicinal positions of the biphenyl ring without an appreciable contribution to the steric energy of the conformer.

Dynamic NMR Data of 3. Although the complexity of the slow-exchange ^1H NMR spectrum of **3** precluded its analysis, we were able to estimate roughly the rotational barrier of the CH_2Br groups in **3**. Lowering the temperature of a solution of **3** in 1:1 $CDCl_3/CD_2Cl_2$ resulted in broadening of the high-field singlet, followed by its decoalescence into two signals (Figure 6). From the coalescence temperature (T_c = 266 K) and the chemical shift difference between the exchanging protons ($\Delta\nu$ = 121 Hz), a barrier of 12.5 kcal mol^{-1} was calculated.[26] This barrier is ascribed to the rotation of the side chains, since, as estimated for biphenyl **9**, the phenyl–phenyl bond rotation barrier should be higher than 30 kcal mol^{-1}.[16b] Further support for our suggestion that the measured barrier should be ascribed to side-chain rotation comes from the dynamic NMR data of **8**. Lowering the temperature of a solution of **8** in 1:1 $CDCl_3/CD_2Cl_2$ resulted in broadening and decoalescence of the high-field singlet into two doublets. From the coalescence data ($\Delta\nu$ = 43 Hz, T_c = 258 K), a barrier of 12.6 kcal mol^{-1} was calculated for the Ar–CH_2Br rotation in **8**.[26] The similarity in rotational barriers found for **3** and **8** further supports our claim that the measured barrier for **3** can be ascribed to Ar–CH_2Br rotation.

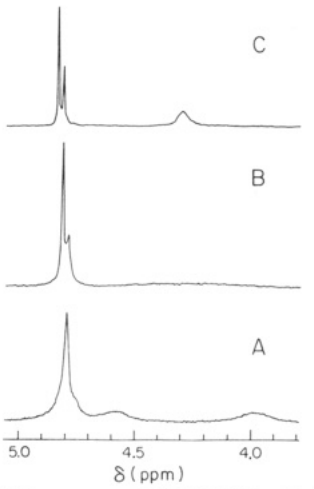


Figure 6. ^1H NMR spectra of **3** (200 MHz, 1:1 $CDCl_3/CD_2Cl_2$) at different temperatures: A, 241 K; B, 266 K; C, 292 K.

Conclusions. Organic molecules formally comprising two multiarmed moieties (such as **3**) can display conformational preferences different from those of a single isolated multiarmed moiety. In the case of biphenyl **3**, the preferred conformation of the side chains at each ring is not the alternate up–down but a conformation that includes two syn interactions in order to avoid contacts between the bromine atoms of the *o*-CH_2Br groups.

Experimental Section

NMR spectra were recorded on a Bruker WP 200-MHz pulsed FT spectrometer. Pentamethylbenzene and pyridinium dichromate were purchased from Aldrich.

Decakis(bromomethyl)biphenyl (3). Decamethylbiphenyl (0.6 g, 2.05 mmol) and 0.33 g of tetrabutylammonium bromide were dissolved in 300 mL of CCl_4. To this solution was added with stirring 12 mL of bromine (37.2 g, 233 mmol), and the mixture was heated to reflux for 2 days. After standing for 2 days at room temperature, the solid that precipitated was filtered and washed with ethanol. The compound was purified by recrystallization from 1,4-dioxane, yielding 1.54 g (69%) of slightly impure material. The compound was purified by repeated recrystallizations from 1,4-dioxane and toluene to afford a material of mp 285 °C: ^1H NMR ($C_6D_5NO_2$, room temperature) δ 4.32 (CH_2, 8 H, br), 4.93 (CH_2, 4 H), 4.97 (CH_2, 8 H); ^{13}C NMR ($CDCl_3$, room temperature)

(26) The rate of exchange at the coalescence temperature for **3** was calculated by using the Gutowsky–Holm approximation (Gutowsky, H. S.; Holm, C. H. *J. Chem. Phys.* **1956**, *25*, 1228) while for **8** Kurland's equation was used (Kurland, R. J.; Rubin, M. B.; Wise, W. B. *J. Chem. Phys.* **1964**, *40*, 2426).

δ 24.0, 24.3, 28.5 (3 CH_2Br), 136.1, 138.7, 139.1, 139.3 (4 C_{ar}); MS (70 eV), m/z 1082.8 (M, $C_{22}H_{20}{}^{79}Br_6{}^{81}Br_4$, 3%), 342 (B, $C_8H_8{}^{81}Br^{79}Br_2$). Anal. Calcd for $C_{22}H_{20}Br_{10}$: C, 24.39; H, 1.86. Found: C, 24.65; H, 1.95.

Single-Crystal X-ray Structure of Biphenyl 3. A single crystal of the biphenyl **3** suitable for X-ray diffraction was prepared by slow evaporation of a toluene solution of **3**. Data were measured on a PW1100/20 Philips four-circle computer-controlled diffractometer. Mo Kα (λ = 0.71069 Å) radiation with a graphite crystal monochromator in the incident beam was used. Intensities were corrected for Lorentz, polarization, and absorption effects. Crystal data: formula, $C_{22}H_{20}Br_{10}$; M = 1083.4; space group, $P\bar{1}$; a = 12.037 (3); Å; b = 12.254 (3) Å; c = 12.020 (3) Å; α = 108.02 (4)°; β = 106.09 (4)°; γ = 108.51 (5)°; V = 1453.7 Å^3; Z = 2; ρ(calcd) = 2.48 g cm^{-3}; μ(Mo Kα) = 135.26 cm^{-1}; R = 0.077; R_w = 0.112.

Bromopentakis(bromomethyl)benzene (8). Pentamethylbenzene (1.32 g, 10 mmol), and 1.65 g of tetrabutylammonium bromide were dissolved in 250 mL of CCl_4. To the stirred solution was added 4 mL of bromine (12.4 g, 78 mmol). After the mixture was refluxed for 5 days, it was cooled, and the solid that precipitated was filtered and washed (EtOH). Recrystallization from chloroform gave 4.65 g (73%) of **8**: mp 245 °C; ^{1}H NMR ($CDCl_3$, room temperature) δ 4.67 (2 H), 4.74 (4 H), 4.81 (4 H); ^{13}C NMR ($CDCl_3$, room temperature) δ 24.1 (CH_2), 25.0 (CH_2), 29.8 (CH_2), 130.8 (C_{ar}), 136.9 (C_{ar}), 138.7 (C_{ar}); MS (70 eV), m/z 622 (M, $C_{11}H_{10}{}^{81}Br_3{}^{79}Br_3$, 4%), 141 (B). Anal. Calcd for $C_{11}H_{10}Br_6$: C, 21.25; H, 1.62. Found: C, 21.32; H, 1.71.

Decamethylbenzhydrol (7). The carbinol was prepared according to the literature procedure[18] and recrystallized from petroleum ether: mp 189 °C (lit. mp 190 °C); ^{1}H NMR ($CDCl_3$, room temperature) δ 1.83 (1 H, d, J = 4 Hz, OH), 2.19 (12 H, s, CH_3), 2.20 (12 H, s, CH_3), 2.25 (6 H, s, CH_3), 6.54 (1 H, d, J = 4 Hz, ArC*H*Ar).

When **7** was recrystallized from ethanol in the presence of acid, the ethyl ether of the carbinol was isolated: mp 160 °C; ^{1}H NMR ($CDCl_3$, room temperature) δ 1.20 (3 H, t, J = 7.0 Hz, OCH_2CH_3), 2.14 (12 H, s, CH_3), 2.20 (12 H, s, CH_3), 2.25 (6 H, s, CH_3), 3.34 (2 H, q, J = 7.0 Hz, OCH_2CH_3), 5.92 (1 H, s, ArC*H*Ar); MS (70 eV), m/z 352 (M, 4%), 175 (B, $C_6(CH_3)_5CHCH_3$). Anal. Calcd for $C_{25}H_{36}O$: C, 85.17; H, 10.29. Found: C, 85.06; H, 10.17.

Decamethylbenzophenone (6). Decamethylbenzhydrol (0.109 g, 0.34 mmol) and pyridinium dichromate (0.264 g, 0.7 mmol) were dissolved in 25 mL of dry CH_2Cl_2, and the mixture was stirred at room temperature for 24 h. Ether (125 mL) was added, and the solid that separated was filtered. Evaporation of the organic solvents resulted in a solid, which was recrystallized from $CHCl_3$/EtOH, yielding 0.056 g (50%) of **6**: mp 205 °C; ^{1}H NMR ($CDCl_3$, room temperature) δ 2.08 (CH_3, 12 H), 2.18 (CH_3, 12 H), 2.25 (CH_3, 6 H); ^{13}C NMR ($CDCl_3$, room temperature) δ 16.4 (CH_3), 17.2 (CH_3), 17.8 (CH_3), 131.6 (C_{ar}), 133.2 (C_{ar}), 136.9 (C_{ar}), 141.1 (C_{ar}), 205.2 (CO); MS (70 eV), m/z 322 (M, $C_{23}H_{30}O$, 41%), 307 (B, M − CH_3). Anal. Calcd for $C_{23}H_{30}O$: C, 85.66; H, 9.38. Found: C, 85.29; H, 9.25.

Attempted Synthesis of Decakis(bromomethyl)benzophenone (4). Decamethylbenzophenone (0.040 g, 0.12 mmol), tetrabutylammonium bromide (74.5 mg), and 0.12 mL of bromine (2.4 mmol) were dissolved in 5 mL of CCl_4, and the mixture was stirred at room temperature for 48 h. The mixture was treated with a saturated aqueous Na_2SO_3 solution, the phases were separated, and the organic phase was dried ($MgSO_4$) and evaporated, yielding 68 mg (0.11 mmol, 46%) of bromopentakis(bromomethyl)benzene (**8**).

Acknowledgment. We thank Professors Kurt Mislow and Yoel Sasson for helpful discussions and Dr. Shmuel Cohen for the X-ray structure determination. This work was supported by a grant of the United States–Israel Binational Science Foundation, to which we are grateful.

Supplementary Material Available: Tables of bond lengths and angles for **3** (2 pages). Ordering information is given on any current masthead page.

Stereochemical Course of the Base-Promoted Aldol Self-Coupling of Racemic 5-Norbornen-2-one and 2-Norbornanone

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The enolate anions of 5-norbornen-2-one and 2-norbornanone enter into self-coupling with their conjugate acids in a manner that exhibits diastereomeric discrimination. The major products obtained from aldol reactions conducted at low temperature are those where bonding has occurred preferentially to the ketone of like absolute configuration. Structural assignments rest on X-ray crystallographic analyses and chemical interconversions. When the reactions are effected at higher temperatures, dehydration also occurs spontaneously. All indicators point to adherence by these bicyclic systems to molecular recognition in these condensation reactions as well. The aldol products, which are stable to the conditions under which they are formed, have been evaluated for their inherent levels of total energy and strain energy by molecular mechanics methods. These data, when taken in conjunction with assumed reaction trajectories, suggest the possible causes that underlie this interesting selectivity.

Molecular recognition need not be an exclusive feature of biochemical systems and should be observable in situations involving smaller molecules. The criterion need only be that a given reagent recognize a specific reaction partner in the presence of alternative compounds before the pair advance into C–C bond formation or some alternative reaction. A capacity for discrimination has been uncovered several times, often serendipitously, in the context of various studies involving the enolate ions of ketones possessing a bicyclo[2.2.1]heptene framework. Perhaps the earliest example to come to light is due to Cristol and Freeman,[2] who noted that heating (±)-5-norbornen-2-one (**1**) with a solution of potassium *tert*-butoxide in *tert*-butyl

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(2) Cristol, S. J.; Freeman, P. K. *J. Am. Chem. Soc.* **1962**, *83*, 4427.

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