A Study of Substituent Effects on Hydrogen-to-Arene Nonbonded Interactions

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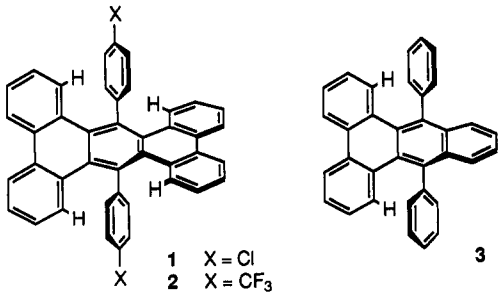
The polycyclic aromatic hydrocarbon 9,14-diphenylbenzo[*b*]triphenylene is strongly twisted due to nonbonded interactions between hydrogen atoms on the polycyclic nucleus and the π systems of the phenyl groups. Ten derivatives of 9,14-diphenylbenzo[*b*]triphenylene, with a wide variety of substituents on the phenyl groups, were synthesized and crystallographically characterized in order to test for the presence of electronic substituent effects on the magnitude of these hydrogen-to-arene nonbonded repulsions. The observed end-to-end twists in these compounds were the following: 9,14-diphenylbenzo[*b*]triphenylene (**3**), 40.4 ± 0.4°; 9,14-bis(4-nitrophenyl)-benzo[*b*]triphenylene (**4**), adopted a nontwisted conformation; 9,14-bis(4-methoxyphenyl)benzo[*b*]triphenylene (**5**), 36.8 ± 1.3°; 9,14-bis[4-(methylthio)phenyl]benzo[*b*]triphenylene (**6**), 40.5 ± 0.6°; 9,14-bis(4-chlorophenyl)-benzo[*b*]triphenylene (**7**), 39.4 ± 0.5°; 9,14-bis(4-bromophenyl)benzo[*b*]triphenylene (**8**), 39.4 ± 0.8°; 9,14-bis-[4-(trifluoromethyl)phenyl]benzo[*b*]triphenylene (**9**), 36.3 ± 1.5° and 33.0 ± 1.5° (two crystallographically independent molecules); 9,14-bis(4-cyanophenyl)benzo[*b*]triphenylene (**10**), 38.2 ± 0.5°; 9,14-bis(4-methylphenyl)benzo[*b*]triphenylene (**11**), 43.1 ± 0.4°; 9,14-bis(4-nitrophenyl)-11-methylbenzo[*b*]triphenylene (**12**), 40.4 ± 0.9° and 33.4 ± 0.9° (two crystallographically independent molecules). The effects of the substituents and of crystal packing forces on the solid-state conformations of these compounds are discussed.

Can substituents on aromatic rings influence the magnitude of nonbonded repulsions involving those rings? During the last few years we have synthesized and crystallographically characterized a variety of aromatic compounds that exhibit severe nonbonded interactions between hydrogens and aromatic rings.[1,2] In one such study, two simple derivatives, **1** and **2**, of the polycyclic aromatic hydrocarbon 9,18-diphenyltetrabenz[*a,c,h,j*]anthracene, which is twisted due to repulsion between the illustrated benzo hydrogens and the phenyl groups, were found to have substantially different end-to-end twists in the solid state: 60.8 ± 1.5° and 69.7 ± 0.8°, respectively.[1c] There was no way to reliably measure the twists of these compounds in solution, and so it remained unresolved whether the observed 9° difference in twists was due to some electronic effect or instead to variations in crystal packing forces. At that time we hypothesized that the para substituents on the phenyl groups might alter the electron density, or at least the polarizability, of these aromatic rings sufficiently to reduce or increase the nonbonded repulsion between the benzo hydrogens and the phenyl groups, with the observable consequence of differing end-to-end twists.



1 X = Cl
2 X = CF_3

3

If the interaction of a benzo hydrogen and an aromatic π system is a simple repulsion of electron clouds, then electron-donating para substituents, by increasing the electron density in the π system, should increase the hydrogen to aromatic ring (H–Ar) repulsion and the observed end-to-end twist. Conversely, electron-withdrawing substituents would be expected to reduce the H–Ar repulsion and consequently the twist. On the other hand, it is extremely common to find simple aromatic compounds packed in crystals so that the hydrogen atoms of one molecule project toward the aromatic π system of another.[3] This edge-to-face or "herringbone" crystal packing pattern for simple aromatics, as well as similar packing of aromatic amino acid side chains in protein crystals, has been proposed to result from favorable H(δ+)-to-C(δ–) interactions.[4] If such an electrostatic attraction is indeed significant, then the substituent effects in the twisted aromatic compounds above might be the reverse of those predicted by a simple repulsive model, i.e., electron-donating para substituents should *reduce* the end-to-end twist by increasing the partial negative charge on carbon and the H–Ar Coulombic attraction.

Additional structural data were required to test theses hypotheses, and we chose the synthetically more accessible, highly crystalline, twisted polycycle 9,14-diphenylbenzo-[*b*]triphenylene (**3**) as the molecular framework for examination of substituent effects on hydrogen-to-arene nonbonded interactions. There have been numerous investigations that demonstrate the existence of electronic substituent effects on bond angles in substituted benzene rings,[5] but to our knowledge there has been no systematic effort to study electronic effects on the magnitude of

(1) (a) Pascal, R. A., Jr.; McMillan, W. D.; Van Engen, D. *J. Am. Chem. Soc.* **1986**, *108*, 5652-5653. (b) Pascal, R. A., Jr.; Van Engen, D. *Tetrahedron Lett.* **1987**, *28*, 293-294. (c) Pascal, R. A., Jr.; McMillan, W. D.; Van Engen, D.; Eason, R. G. *J. Am. Chem. Soc.* **1987**, *109*, 4660-4665. (d) Pascal, R. A., Jr.; Van Engen, D.; Kahr, B.; McMillan, W. D. *J. Org. Chem.* **1988**, *53*, 1687-1689. (e) Smyth, N.; Van Engen, D.; Pascal, R. A., Jr. *J. Org. Chem.* **1990**, *55*, 1937-1940.

(2) (a) Pascal, R. A., Jr.; Grossman, R. B. *J. Org. Chem.* **1987**, *52*, 4616. (b) Pascal, R. A., Jr.; Grossman, R. B.; Van Engen, D. *J. Am. Chem. Sco.* **1987**, *109*, 6878-6880. (c) Pascal, R. A., Jr.; Winans, C. G.; Van Engen, D. *J. Am. Chem. Soc.* **1989**, *111*, 3007-3010.

(3) Kitiagorodsky, A. I. *Molecular Crystals and Molecules*; Academic: New York, 1973; pp 38-48.

(4) (a) Burley, S. K.; Petsko, G. A. *Science* **1985**, *229*, 23-28, and references cited therein. (b) Burley, S. K.; Petsko, G. A. *J. Am. Chem. Soc.* **1986**, *108*, 7995-8001, and references cited therein.

(5) Selected examples: (a) Domenicano, A.; Murray-Rust, P. *Tetrahedron Lett.* **1979**, 2283-2286. (b) Domenicano, A.; Murray-Rust, P.; Vaciago, A. *Acta Crystallogr., Sect. B* **1983**, *39*, 457-468. (c) Krygowski, T. M. *J. Chem. Res., Synop.* **1984**, 238-239. (d) Krygowski, T. M.; Hafelinger, G.; Schule, J. *Z. Naturforsch.* **1986**, *41b*, 895-903. (e) Anulewicz, R.; Hafelinger, G.; Krygowski, T. M.; Regelmann, C.; Ritter G. *Z. Naturforsch.* **1987**, *42b*, 917-927. (f) Domenicano, A.; Schultz, G.; Hargittai, I.; Colapietro, M.; Portalone, G.; George, P.; Bock, C. W. *Struct. Chem.* **1989**, *1*, 107-122.

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Table I. Crystallographic Data for Compounds 3–12

	3 (H)	4 (NO_2)	5 (OMe)	6 (SMe)	7 (Cl)	8 (Br)	9 (CF_3)	10 (CN)	11 (Me)	12 (NO_2Me)
formula	$C_{34}H_{22}$	$C_{34}H_{20}N_2O_4$	$C_{36}H_{26}O_2$	$C_{36}H_{26}S_2$	$C_{34}H_{20}Cl_2$	$C_{34}H_{20}Br_2$	$C_{36}H_{20}F_6$	$C_{36}H_{20}N_2$	$C_{36}H_{26}$	$C_{35}H_{22}N_2O_4$
space group	$P2_1/c$	$Pbcm$	$C2/c$	$P2_1/n$	$P2_1/c$	$P2_1/c$	$P\bar{1}$	$P2_1$	$Pccn$	$P2_1/n$
a (Å)	10.159 (2)	5.795 (2)	16.218 (3)	12.589 (3)	10.975 (2)	11.080 (3)	12.234 (4)	11.544 (2)	15.474 (2)	11.230 (3)
b (Å)	12.611 (2)	15.929 (7)	18.712 (4)	16.819 (4)	23.448 (3)	23.865 (5)	15.813 (3)	8.771 (2)	17.127 (3)	19.132 (11)
c (Å)	18.404 (4)	27.099 (11)	16.675 (5)	12.656 (3)	9.978 (1)	9.960 (2)	16.094 (5)	13.309 (3)	18.523 (3)	24.645 (14)
β (deg)	105.47 (2)	90.0	96.34 (2)	94.38 (2)	108.75 (1)	107.59 (2)	a	108.550 (14)	90.0	92.58 (3)
Z	4	4	8	4	4	4	4	2	8	8
V (Å^3)	2272.5 (8)	2501 (2)	5029 (2)	2672 (1)	2431.3 (6)	2510.6 (9)	2734 (2)	1277.6 (4)	4909 (1)	5290 (4)
D_{calc} (g cm^{-3})	1.26	1.38	1.30	1.30	1.36	1.56	1.38	1.25	1.24	1.34
crystal size (mm)	0.20 × 0.25 × 0.27	0.02 × 0.17 × 0.27	0.02 × 0.25 × 0.25	0.12 × 0.25 × 0.35	0.12 × 0.25 × 0.35	0.10 × 0.23 × 0.37	0.08 × 0.18 × 0.30	0.08 × 0.20 × 0.40	0.23 × 0.28 × 0.38	0.02 × 0.26 × 0.50
2θ range (deg)	3–114	3–114	3–114	3–114	3–114	3–114	3–114	3–114	3–114	3–114
reflctns measd	$\pm h, +k, +l$	$+h, +k, +l$	$\pm h, +k, +l$	$\pm h, +k, +l$	$\pm h, +k, +l$	$\pm h, +k, +l$	$\pm h, \pm k, +l$	$\pm h, +k, +l$	$+h, +k, +l$	$\pm h, +k, +l$
unique reflctns	3059	1738	3399	3587	3272	3383	7379	1861	3319	7132
obsd reflctns[b]	2652	1060	2058	3066	2903	3067	4854	1770	2833	4551
data-to-parameter ratio	8.64	5.86	6.00	8.94	8.93	9.44	6.11	5.16	8.72	6.00
R (R_w)	0.050 (0.054)	0.071 (0.068)	0.087 (0.084)	0.053 (0.062)	0.045 (0.051)	0.038 (0.045)	0.118 (0.130)	0.037 (0.036)	0.046 (0.050)	0.071 (0.071)
goodness of fit	1.29	1.28	1.56	1.11	1.48	1.70	2.02	0.91	1.20	1.40

[a] α = 64.45 (2)°, β = 79.00 (2)°, γ = 78.60 (2)°. [b] Reflections were considered to be observed if $|F_o| > 3\sigma(F_o)$.

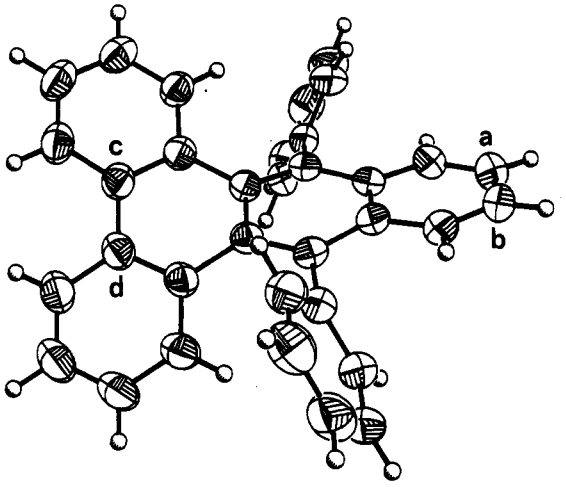
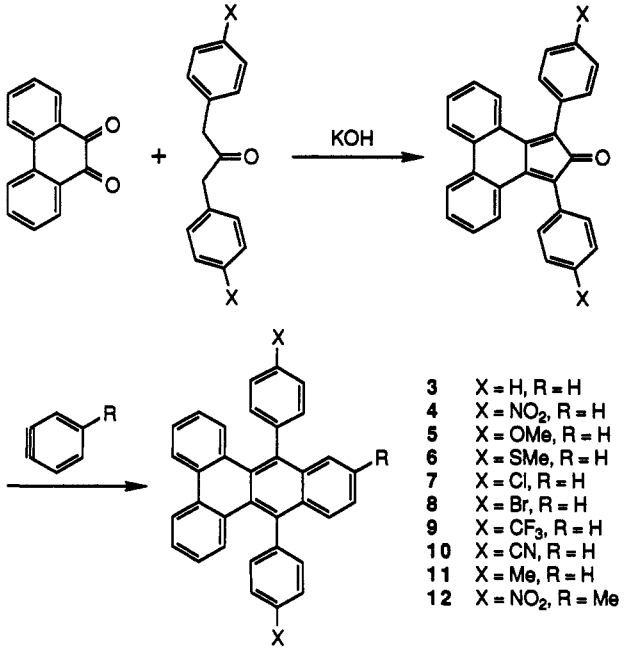


Figure 1. X-ray structure of 9,14-diphenylbenzo[*b*]triphenylene (**3**).

nonbonded repulsions. In this paper we report the syntheses and molecular structures of ten phenyl-substituted derivatives of **3** and consider the effects of substituents and crystal packing forces on the solid-state conformations of these compounds.

Results and Discussion

Syntheses. 9,14-Diphenylbenzo[*b*]triphenylene and its derivatives are synthesized most easily by aldol condensation of 9,10-phenanthrenequinone with an appropriately substituted 1,3-diphenylacetone, followed by the addition of benzyne to the resulting cyclopentadienone as illustrated below. Indeed, compounds **3**, **5**, and **11** have been prepared previously by this method,[6-8] and our syntheses of **4**, **7**, **8**, **9**, and **12** were similar. However, thioethers are incompatible with benzyne additions, so we prepared compound **6** by displacement of the bromine atoms of compound **8** with thiomethoxide. For reasons of synthetic convenience only, compound **10** also was obtained by a similar nucleophilic aromatic substitution of **8** with sodium cyanide.



3 X = H, R = H
4 X = NO_2, R = H
5 X = OMe, R = H
6 X = SMe, R = H
7 X = Cl, R = H
8 X = Br, R = H
9 X = CF_3, R = H
10 X = CN, R = H
11 X = Me, R = H
12 X = NO_2, R = Me

Our goal at the outset of this project was to prepare about a dozen derivatives of compound **3** for crystallographic analysis. Phenyl substituents with a wide variety of electronic properties were required, but hydrogen-bond donors were excluded from the candidate structures in an attempt to minimize strong *inter*molecular interactions in the crystals. Compounds **3**–**12** fulfill our requirements for diversity, and the only derivative that we desired but were unable to synthesize was bis(dimethylamino)-**3**.

Crystal Structure Determinations. Compounds **3**–**12** are highly crystalline, and single crystals suitable for X-ray measurements were obtained without much difficulty. Interestingly, none of these materials contained solvents of crystallization, and even though most compounds were successfully crystallized from more than one solvent sys-

(6) Grein, K.; Kirste, B.; Kurreck, H. *Chem. Ber.* **1981**, *114*, 254–266.
(7) Mondal, S.; Bandyopadhyay, T. K.; Bhattacharya, A. J. *Indian J. Chem.* **1983**, *22B*, 448–452.
(8) The physical properties of our compounds **3** and **11** agree well with the literature data, but our melting point for compound **5**, 274–276 °C, is some 80° higher than the literature value.[7] Inasmuch as our data were obtained from the same batch of crystals used for the X-ray measurements, there can be no question as to the identity of our sample.

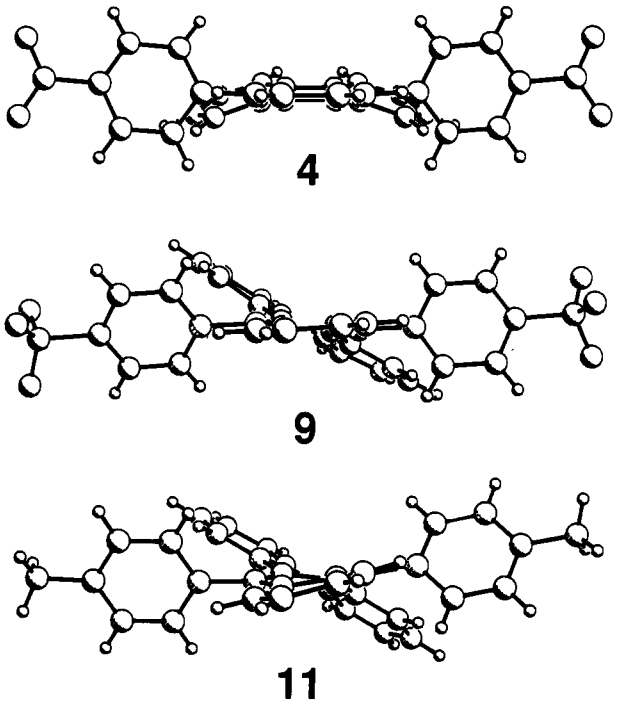


Figure 2. X-ray structures of 9,14-bis(4-nitrophenyl)benzo[*b*]-triphenylene (**4**), 9,14-bis[4-(trifluoromethyl)phenyl]benzo[*b*]-triphenylene (**9**), and 9,14-bis(4-methylphenyl)benzo[*b*]triphenylene (**11**). All views are looking down the long axis of the benzo[*b*]triphenylene nucleus.

tem, only one crystal form was obtained for each derivative.

The crystallographic data for compounds **3–12** are summarized in Table I; all data were collected at room temperature. The full details of these structural determinations are found in the supplementary material. Five of the ten compounds (**3**, **6**, **7**, **8**, and **12**) crystallized in the extremely common[9] monoclinic space group $P2_1/c$ ($P2_1/n$ is a nonstandard setting of this space group); only one compound (**10**) crystallized in a noncentrosymmetric space group ($P2_1$). Generally speaking, nine of the ten structures refined satisfactorily, and six of the ten converged with *R*s of 0.053 or less. Only compound **9** failed to meet the common criterion of $R < 0.10$; this was due primarily to rotational disorder in the trifluoromethyl groups. Compound **9** has not been excluded from the data set, but the large standard deviations of the derived parameters clearly indicate that this structure was less well determined than the others.

Solid-State Conformations and the Effects of Crystal Packing Forces. Molecular mechanics calculations [MM2(85)[10]] predict an end-to-end twist[11] of 42.2° for compound **3** in the gas phase. Before preparing any other derivatives, we determined the crystal structure of **3** (Figure 1); the observed twist in the solid state is 40.4 ± 0.4°,[11,12] in good agreement with the calculation. We then began to prepare the chosen derivatives of **3**, and the crystal structure of each compound was obtained as it became available. Imagine our surprise when the second X-ray structure determination, of the dinitro derivative **4**, showed a completely different, nontwisted (but still nonplanar) conformation! This "bent phenanthrene" geometry (see Figure 2), which possesses C_s symmetry, is estimated by MM2(85) to lie only 2 kcal/mol above the twisted ground state. With such a small difference in energy between the two conformations, it was possible that several other derivatives might prefer this novel geometry, but, as the work progressed, compounds **5–11** all proved to be twisted in the manner of **3**.

Table II. Magnitude of Twists in Compounds 3–12

compd	phenyl substit	end-to-end twist, deg	center ring twist, deg
3	H	40.4 ± 0.4	13.2 ± 0.3
4	NO_2	C_s conformation	C_s conformation
5	OCH_3	36.8 ± 1.3	12.6 ± 1.1
6	SCH_3	40.5 ± 0.6	14.2 ± 0.5
7	Cl	39.4 ± 0.5	14.5 ± 0.4
8	Br	39.4 ● 0.8	14.7 ● 0.6
9	CF_3	36.3 ± 1.5	13.2 ± 1.4
		33.0 ± 1.5	12.3 ± 1.4
10	CN	38.2 ± 0.5	14.7 ● 0.5
11	CH_3	43.1 ● 0.4	15.2 ± 0.3
12	NO_2	40.4 ± 0.9	15.4 ± 0.8
		33.4 ± 0.9	11.0 ± 0.9

We were faced with two possibilities: either the abnormal conformation of **4** was an electronic effect of the very strongly electron-withdrawing nitro group or it was a dramatic effect of crystal packing forces in this particular crystal form. We made many attempts to obtain another crystal form of **4** by crystallization from a variety of solvents, but all conditions yielded the same material. Therefore a second dinitro derivative of **3** was synthesized, compound **12**, containing an extra methyl group at a presumably innocuous position on the benzo[*b*]triphenylene nucleus, but which ensured that the crystal packing would be different from that of **4**. The X-ray structure of **12** showed it to be twisted in the normal way, strongly indicating that the "bent phenanthrene" (C_s) geometry of **4** is the result of packing forces.[13]

The end-to-end twists[11] of compounds **3** and **5–12** are listed in Table II, and in addition the twists of the central ring[11] in each compound, which is usually the most distorted, are also listed. The end-to-end twists range from 33.0° to 43.1°, and end-on views of the most and least twisted structures are illustrated in Figure 2. Two compounds, **9** and **12**, crystallized to form lattices containing two crystallographically independent molecules in the unit cell. Each of these compounds yields two entries in Table II, but, more significantly, they provide an estimate of the variation in twist that may be expected as a result of crystal packing forces alone. The difference in the twists of the two independent molecules of **9** is 3.3°, and that of **12** is 7.0°, indicating that crystal packing forces may provide most of the observed overall 10° variation in twists.

(9) Mighell, A. D.; Himes, V. L.; Rodgers, J. R. *Acta Crystallogr., Sect. A* **1983**, *39*, 737–740.

(10) Allinger, N. L. *QCPE* MM2(85), 1986.

(11) The twists in compounds **3** and **5–12** were defined as illustrated in the following example, which refers to the labeled drawing of compound **3** in Figure 1. The centroids of carbons a and b (X1) and c and d (X2) were located, and dummy atoms were assigned to these positions, to calculate the end-to-end twist of **3**. The twist is the dihedral angle of the type a–X1–X2–c. The twists of the center rings of each compound were determined in a similar manner.

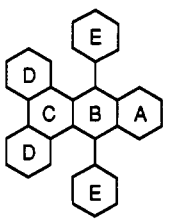
(12) The estimated standard deviations for the nuclear twist angles were calculated by the method of Stanford and Waser: Stanford, R. H.; Waser, J. *Acta Crystallogr., Sect. A* **1972**, *28*, 213–215.

(13) The crystal structure of compound **4** is most easily rationalized as a case where the minor component of an equilibrating mixture crystallizes from solution. It must be emphasized that the observed C_s conformation is not a planar structure: as with all of the compounds discussed in this paper, the benzo[*b*]triphenylene nucleus must distort from planarity to relieve the H–Ar nonbonded repulsions, but by chance there are two distorted conformations of comparable energy. In order to estimate the energy required to produce a conformation containing a truly planar benzo[*b*]triphenylene, we performed an MM2(85) calculation in which the carbon atoms of the polycyclic nucleus (but not the phenyl substituents) were constrained to be coplanar. The resulting geometry (also of C_s symmetry) is not a local minimum, and it lies 8 kcal/mol higher in energy than the twisted ground state (of approximate C_2 symmetry) and 6 kcal/mol above the C_s local minimum observed for compound **4**.

Worse, the largest (15.4°) and smallest (11.0°) central ring twists were observed in the two independent molecules of **12**. Because the X-ray structure determinations were carried out at room temperature, we were concerned that the effects of libration on the observed atomic positions might have generated errors in the derived twist parameters. However, after correction for libration by using the program THMA11,[14] no changes in the twist angles were found.

We have found no statistically significant correlation of the observed solid-state twists with any commonly used set of Hammett parameters, nor is there a correlation of the twists with the estimated dipole moments of the substituted phenyl groups. However, the distribution of observed twists does not appear to be entirely random. The average end-to-end twist of the eleven twisted molecules (recall that there are two independent molecules of **9** and **12** in their crystal structures) is 38.3°, but four of the five molecules with twists below this mean value carry strongly electron-withdrawing phenyl substituents—trifluoromethyl, nitro, or cyano groups—and only one compound with strongly electron-withdrawing groups has an end-to-end twist greater that the mean.

In view of this consideration, we wondered if there might still be significant correlations within subsets of crystal structures with similar packing, so we carefully surveyed the lattices for each compound and cataloged the various types of intermolecular interactions. The lattices are remarkably diverse, and we found only three nearly ubiquitous structural features. (a) In all but one of the lattices, there are pairs of enantiomeric molecules stacked in a head-to-tail fashion, usually at an inversion center. This is most clearly illustrated in the stereoview of the unit cell of compound **9** (Figure 3, part A). The lone structure not possessing this feature is the noncentrosymmetric lattice of compound **10**. In this case the crystals contain only a single enantiomer,[15] so no such stacking is possible. (b) All of the twisted structures except for **10** and **12** exhibit herringbone interactions (although with quite variable orientations) between the A and D rings of the benzo[*b*]triphenylene nuclei. This phenomenon is well illustrated



in the stereoview of the unit cell of compound **6** (Figure 3, part B). (c) In all of the lattices except for that of compound **9**, there is stacking, either herringbone or parallel, of the E rings (and their substituents) of two adjacent molecules, although not all E rings are involved. Both types of E ring stacking are evident in the stereoview of the unit cell of compound **12** (Figure 3, part C). One other common feature is the partial parallel stacking of the phenanthrene moieties of the benzo[*b*]triphenylene systems. Compounds **3**, **5**, **6**, and **12** exhibit such stacking, which typically involves only one of the rings D of the benzo[*b*]triphenylenes and which is well illustrated in the stereoviews of the unit cells of **6** and **12** (Figure 3, parts B and C).

Unfortunately, no significant correlations arise from the segregation of various lattice types according to the types of packing interactions observed, and in general the effects of particular interactions on molecular conformations are not unambiguously discernible. It does not seem possible to rationalize even the extraordinarily different structures of the dinitro compound **4** and the methyl dinitro compound **12**—the lattices could hardly be more dissimilar given the slight structural modification. The lattice of **12** (Figure 3, part C) is a layered structure consisting of antiparallel sheets of molecules with extensive stacking interactions between the sheets. In contrast, the principle interactions in the lattice of **4** (Figue 3, part D) are between molecules whose mean planes are strictly perpendicular to one another!

Conclusion. It is apparent that the electronic effects of phenyl substituents on the conformations of compounds **3**–**12** in the solid state, if any, are small in comparison to crystal packing forces. From our limited data set, we tentatively conclude that strongly electron-withdrawing substituents on the phenyl rings favor smaller end-to-end twists, consistent with the idea that H–Ar repulsions are diminished when electron density is reduced. However, in the absence of a much more extensive data set, any rigorous correlation of electronic substituent effects with the observed distortions in these molecules will require either a method to force different compounds to crystallize in similar lattices or a method to obtain accurate geometries of relatively large molecules in solution or the gas phase.

Experimental Section

Phencyclone (1,3-diphenylcyclopenta[*l*]phenanthren-2-one), 1,3-bis(4-chlorophenyl)cyclopenta[*l*]phenanthren-2-one, and 1,3-bis[4-(trifluoromethyl)phenyl]cyclopenta[*l*]phenanthren-2-one were prepared as described previously.[1c,16]

1,3-Bis(4-nitrophenyl)acetone (13). Triethylamine (30 mL) was added dropwise to a stirred solution of 4-nitrophenylacetic acid (18.1 g, 0.1 mmol) in acetic anhydride (90 mL). After 1 h, the mixture was poured into cold 15% HCl. The orange-yellow solid was collected and washed with water. This material was refluxed for 17 h in a mixture of THF (50 mL) and 9 M H_2SO_4 (100 mL). After cooling, water was added, and the mixture was extracted with methylene chloride. The organic extract was dried over anhydrous Na_2SO_4. Evaporation of solvent left compound **13** as a yellow solid (11.4 g), mp 178–180 °C (recrystallized from ethanol; lit.[17] mp 140–141 °C). ^1H NMR ($CDCl_3$, 270 MHz): δ 8.20 and 7.34 (AA'BB' system, 8 H), 3.93 (s, 4 H).

1,3-Bis(4-methylphenyl)acetone (14). A solution of 4-methylphenylacetic acid (25 g, 166 mmol), acetic anhydride (100 mL), and pyridine (100 mL) was heated at reflux for 6 h. The excess acetic anhydride and pyridine were removed on a rotary evaporator. The residue was taken up in benzene, washed with two 100-mL portions of 12% NaOH and one 100-mL portion of brine, dried, and concentrated to yield a dark oil. Vacuum distillation yielded 0.6 g of compound **14** at 110–150 °C (0.25 mmHg). ^1H NMR ($CDCl_3$, 270 MHz): δ 7.12 and 7.04 (AA'BB' system, 8 H), 3.66 (s, 4 H), 2.33 (s, 6 H).

1,3-Bis(4-methoxyphenyl)acetone (15). To a solution of LDA [from 22.2 mL (97 mmol) of 2.5 M *n*-butyllithium in hexane and 9.8 g (97 mmol) of diisopropylamine] in ether (60 mL) was added a solution of methyl 4-methoxyphenylacetate (10 g, 55 mmol) in ether (30 mL) at 0 °C under argon. After 15 min, the ice bath was removed, and the mixture was stirred for 20 h. The reaction mixture was poured into 100 mL water and acidified to pH 1 with

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(15) The barrier to enantiomerization in compound **10** is far to low to permit the isolation of a single enantiomer in *solution* at room temperature. This is true even for the much more twisted polycycle 9,18-diphenyltetrabenz[*a,c,h,j*]anthracene and its derivatives.[1c]

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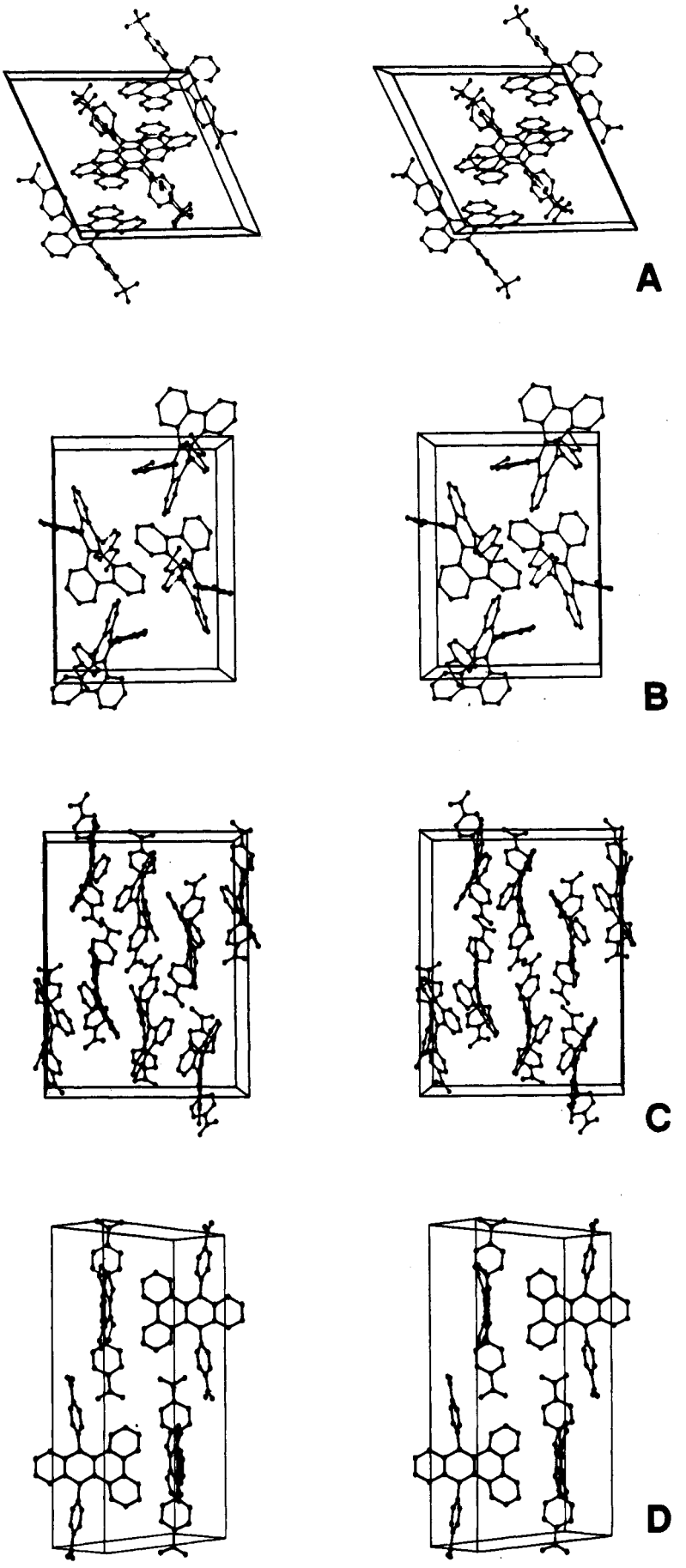

Figure 3. Stereoviews of the unit cells of (A) 9,14-bis[4-(trifluoromethyl)phenyl]benzo[*b*]triphenylene (**9**), (B) 9,14-bis[4-(methylthio)phenyl]benzo[*b*]triphenylene (**6**), (C) 9,14-bis(4-nitrophenyl)-11-methylbenzo[*b*]triphenylene (**12**), and (D) 9,14-bis(4-nitrophenyl)benzo[*b*]triphenylene (**4**).

concentrated HCl. The layers were separated and the aqueous phase was extracted with ether. The combined organic extracts were dried and the solvent was removed to leave a yellow oil (7.85 g). This material was refluxed for 5 h in a mixture of glacial acetic acid (100 mL) and 6 N HCl (14 mL). After cooling, the mixture was concentrated, and water was added. The mixture was extracted with ether, and the organic extract was washed with 12% NaOH, dried, and concentrated to give 4.7 g (63%) of compound **15** as an orange solid, mp 85–87 °C (recrystallized from hexanes; lit.[18] mp 80–82 °C). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.06 and 6.84 (AA′BB′ system, 8 H), 3.78 (s, 6 H), 3.64 (s, 4 H).

1,3-Bis(4-bromophenyl)acetone (16). This material was prepared as described above for compound **15**. From 13.8 g (60 mmol) of methyl 4-bromophenylacetate, compound **16** (2 g, 18%) was obtained as a tan solid after recrystallization from ethanol, mp 118–120 °C (lit.[19] mp 116–118 °C). ^{1}H NMR ($CDCl_3$, 270 MHz): δ 7.45 and 7.02 (AA′BB′ system, 8 H), 3.68 (s, 4 H).

General Procedure for the Synthesis of 9,14-Bis(aryl)benzo[*b*]triphenylenes. 1,3-Bis(aryl)cyclopenta[*l*]-phenanthren-2-ones, if not already available from prior studies, were prepared as described for the synthesis of phencyclone[16] by aldol condensations of phenanthrenequinone with the appropriate 1,3-bis(aryl)acetone. The characteristically green-black solids thus obtained were invariably contaminated to some extent with the corresponding hydrates, but they were used without further purification. For preparation of the desired 9,14-bis(aryl)benzo-[*b*]triphenylenes, a solution of the appropriate 1,3-bis(aryl)-cyclopenta[*l*]phenanthren-2-one, benzenediazonium-2-carboxylate hydrochloride, and propylene oxide in 1,2-dichloroethane (or 3-pentanone) was refluxed under an argon atmosphere for 5 h. After cooling, the solution was diluted with an equal volume of chloroform, washed with saturated $NaHCO_3$, dried, and concentrated to give a brown oil. This material was purified either by silica gel column chromatography or by preparative thin layer chromatography.

9,14-Diphenylbenzo[*b*]triphenylene (3) was obtained from phencyclone (0.5 g, 1.3 mmol), benzenediazonium-2-carboxylate hydrochloride (0.24 g, 1.3 mmol), and propylene oxide (0.28 g, 4.8 mmol) in 10 mL of 1,2-dichloroethane in 27% yield (0.15 g) after purification on a silica gel column (9:1 hexane–benzene). Single crystals, mp 280–282 °C (lit.[6] mp 282–283 °C), were grown from solutions of **3** in CH_2Cl_2–acetone. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.27 (d, 2 H, J = 8 Hz), 7.94 and 7.45 (AA′BB′ system, 4 H), 7.53 (m, 10 H), 7.34 (dd, 2 H, J = 8, 8 Hz), 6.98 (dd, 2 H, J = 8, 8 Hz). MS: m/z 430 (M^+, 100), 352 (25), 350 (27). Exact mass 430.1739, calcd for $C_{34}H_{22}$ 430.1721.

9,14-Bis(4-nitrophenyl)benzo[*b*]triphenylene (4). 1,3-Bis(4-nitrophenyl)cyclopenta[*l*]phenanthren-2-one (**17**) was obtained from phenanthrenequinone (6 g, 20 mmol), 1,3-bis(4-nitrophenyl)acetone (4.16 g, 20 mmol), and KOH (0.98 g, 17 mmol) in ethanol (100 mL) in 49% yield (4.7 g). Compound **4** was then obtained from **17** (2.5 g, 5.3 mmol), benzenediazonium-2-carboxylate hydrochloride (1.95 g, 10.6 mmol), and propylene oxide (1.23 g, 21.2 mmol) in 150 mL of 3-pentanone in 2% yield (55 mg) after purification on a silica gel column (3:1 hexane–toluene). Single crystals, mp 380–381 °C, were grown from solutions of **4** in toluene. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.42 and 7.77 (AA′BB′ system, 8 H), 8.32 (d, 2 H, J = 8 Hz), 7.79 and 7.53 (AA′BB′ system, 4 H), 7.42 (dd, 2 H, J = 8,8 Hz), 7.32 (d, 2 H, J = 8 Hz), 7.03 (dd, 2 H, J = 8, 8 Hz). MS: m/z 520 (M^+, 100), 490 (22), 352 (21), 350 (17). Exact mass 520.1429, calcd for $C_{34}H_{20}N_2O_4$ 520.1423.

9,14-Bis(4-methoxyphenyl)benzo[*b*]triphenylene (5). 1,3-Bis(4-methoxyphenyl)cyclopenta[*l*]phenanthren-2-one (**18**) was obtained from phenanthrenequinone (2.12 g, 10.2 mmol), 1,3-bis(4-methoxyphenyl)acetone (2.5 g, 9.2 mmol), and KOH (1.0 g, 18.4 mmol) in ethanol (84 mL) in 58% yield (2.4 g). Exact mass 442.1588, calcd for $C_{31}H_{22}O_3$ 442.1569. Compound **5** was then obtained from **18** (1.2 g, 2.7 mmol), benzenediazonium-2-carboxylate hydrochloride (1.02 g, 5.5 mmol), and propylene oxide (0.9 g, 15.5 mmol) in 30 mL of dichloroethane in 8% yield (111 mg) after purification on a silica gel column (1:1 hexane–benzene). Single crystals, mp 274–276 °C (lit.[7] mp 195 °C), were grown from solutions of **5** in CH_2Cl_2–MeOH. ^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.26 (dd, 2 H, J = 8, 1 Hz), 7.96 and 7.45 (AA′BB′ system, 4 H), 7.55 (dd, 2 H, J = 8, 1 Hz), 7.45 and 7.06 (AA′BB′ system, 8 H), 7.34 (ddd, 2 H, J = 8, 8, 1 Hz), 7.01 (ddd, 2 H, J = 8, 8, 1 Hz), 3.92 (s, 6 H). MS: m/z 490 (M^+, 100), 458 (25), 395 (14), 339 (12). Exact mass 490.1938, calcd for $C_{36}H_{26}O_2$ 490.1933.

9,14-Bis(4-chlorophenyl)benzo[*b*]triphenylene (7) was obtained from 1,3-bis(4-chlorophenyl)cyclopenta[*l*]-phenanthren-2-one (0.72 g, 1.71 mmol), benzenediazonium-2-carboxylate hydrochloride (1.27 g, 6.9 mmol), and propylene oxide (0.38 g, 6.9 mmol) in 30 mL of dichloroethane in 1% yield (7.5 mg) after purification by preparative TLC (9:1 hexane–benzene). Single crystals, mp 314–315 °C, were grown from solutions of **7** in CH_2Cl_2–MeOH. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.28 (d, 2 H, J = 8 Hz), 7.87 (m, 2 H), 7.50 (m, 12 H), 7.38 (ddd, 2 H, J = 8, 7, 1 Hz), 7.04 (ddd, 2 H, J = 8, 7, 1 Hz). MS: m/z 498 (M^+, 100), 352 (21), 199 (23). Exact mass 498.0958, calcd for $C_{34}H_{20}{}^{35}Cl_2$ 498.0942.

9,14-Bis(4-bromophenyl)benzo[*b*]triphenylene (8). 1,3-Bis(4-bromophenyl)cyclopenta[*l*]phenanthrene-2-one (**19**) was obtained from phenanthrenequinone (0.56 g, 2.7 mmol), 1,3-bis(4-bromophenyl)acetone (1.0 gm 2.7 mmol), and KOH (0.3 g, 5.4 mmol) in ethanol (32 mL) in 18% yield (0.27 g). Exact mass 537.9567, calcd for $C_{29}H_{16}{}^{79}Br_2O$ 537.9568. Compound **8** was then obtained from **19** (0.30 g, 0.55 mmol), benzenediazonium-2-carboxylate hydrochloride (0.31 g, 1.7 mmol), and propylene oxide (0.98 g, 1.7 mmol) in 5 mL of dichloroethane in 22% yield (59 mg) after purification on a silica gel column (9:1 hexane–benzene). Single crystals, mp 310–311 °C, were grown from solutions of **8** in CH_2Cl_2–MeOH. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.28 (d, 2 H, J = 8 Hz), 7.87 and 7.47 (AA′BB′ system, 4 H), 7.67 and 7.43 (AA′BB′ system, 8 H), 7.50 (d, 2 H, J = 8 Hz), 7.38 (dd, 2 H, J = 8, 7 Hz), 7.04 (dd, 2 H, J = 8, 7 Hz). MS: m/z 588 (M^+ [$^{79}Br^{81}Br$], 100), 508 (13), 426 (21), 352 (27), 350 (27). Exact mass 585.9919, calcd for $C_{34}H_{20}{}^{79}Br_2$ 585.9932.

9,14-Bis[4-(trifluoromethyl)phenyl]benzo[*b*]triphenylene (9) was obtained from 1,3-bis[4-(trifluoromethyl)phenyl]cyclopenta[*l*]phenanthrene-2-one (30 mg, 0.06 mmol), benzenediazonium-2-carboxylate hydrochloride (49 mg 0.27 mmol), and propylene oxide (15 mg 4.8 mmol) in 5 mL of dichloroethane in 17% yield (5.7 mg) after purification by preparative TLC (3:1 hexane–benzene). Single crystals, mp 307–308 °C, were grown from solutions of **9** in CH_2Cl_2–acetone. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.30 (d, 2 H, J = 8 Hz), 7.83 and 7.50 (AA′BB′ system, 4 H), 7.81 and 7.70 (AA′BB′ system, 8 H), 7.40 (m, 4 H), 7.01 (ddd, 2 H, J = 8, 7, 1 Hz). MS: m/z 566 (M^+, 100), 420 (20), 352 (12), 350 (14). Exact mass 566.1475, calcd for $C_{36}H_{20}F_6$ 566.1469.

9,14-Bis(4-methylphenyl)benzo[*b*]triphenylene (11). 1,3-Bis(4-methylphenyl)cyclopenta[*l*]phenanthren-2-one (**20**) was obtained from phenanthrenequinone (0.52 g, 2.5 mmol), 1,3-bis(4-methylphenyl)acetone (0.6 g, 2.5 mmol), and KOH (0.28 g, 5 mmol) in ethanol (10 mL) in 25% yield (0.26 g). Exact mass 410.1672, calcd for $C_{31}H_{22}O$ 410.1671. Compound **11** was then obtained from **20** (0.2 g, 0.49 mmol), benzenediazonium-2-carboxylate hydrochloride (0.36 g, 1.95 mmol), and propylene oxide (0.46 g, 8.2 mmol) in 10 mL of dichloroethane in 30% yield (66 mg) after purification on a silica gel column (19:1 hexane–benzene). Single crystals, mp 275–276 °C (lit.[7] mp 268 °C), were grown from solutions of **11** in CH_2Cl_2–acetone. ^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.26 (dd, 2 H, J = 8, 1 Hz), 7.96 (m, 2 H), 7.57 (dd, 2 H, J = 8, 1 Hz), 7.43 (m, 6 H), 7.34 (m, 6 H), 6.99 (ddd, 2 H, J = 8, 8, 1 Hz), 2.50 (s, 6 H). MS: m/z 458 (M^+, 52), 94 (100). Exact mass 458.2050, calcd for $C_{36}H_{26}$ 458.2035.

9,14-Bis(4-nitrophenyl)-11-methylbenzo[*b*]triphenylene (12) was obtained from 1,3-bis(4-nitrophenyl)cyclopenta[*l*]-phenanthren-2-one (**17** [see preparation of compound **4**], 3.8 g, 8.0 mmol), 5-methylbenzenediazonium-2-carboxylate hydrochloride (6.4 g, 32.2 mmol), and propylene oxide (2.0 g, 34.5 mmol) in 3-pentanone (200 mL) in 0.6% yield (28 mg) after purification on a silica gel column (1:1 hexane–toluene) followed by preparative TLC. Single crystals, mp 274–275 °C, were grown from solutions of **12** in ethyl acetate. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.42 and 7.75 (AA′BB′ system, 8 H), 8.31 (d, 2 H, J = 8 Hz), 7.68 (d, 1 H, J = 9 Hz), 7.52 (s, 1 H), 7.41 (dd, 2 H, J = 8, 7 Hz), 7.35 (m, 3

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H), 7.02 (dd, 2 H, J = 8, 7 Hz), 2.48 (s, 3 H). MS: m/z 534 (M^+, 100), 504 (35), 366 (16), 203 (24). Exact mass 534.1581, calcd for $C_{35}H_{22}N_2O_4$ 534.1579.

9,14-Bis[4-(methylthio)phenyl]benzo[*b*]triphenylene (6). $NaSCH_3$ (51 mg, 0.73 mmol) was added to an argon-purged solution of compound 8 (72 mg, 0.12 mmol) in HMPA (5 mL), and the solution was heated at 80 °C for 13 h under an argon atmosphere. After cooling to room temperature, brine (15 mL) was added, and the mixture was extracted with ether (3 × 15 mL). The combined organic extracts were dried and concentrated to leave a brown oil. Purification by preparative TLC (1:1 hexane–benzene) gave 8.4 mg (13%) of the desired compound 6. Single crystals, mp 260–261 °C, were grown from solutions of 6 in CH_2Cl_2–MeOH. ^1H NMR ($CDCl_3$, 270 MHz): δ 8.27 (dd, 2 H, J = 8, 1 Hz), 7.95 (m, 2 H), 7.56 (dd, 2 H, J = 8, 1 Hz), 7.44 (m, 12 H), 7.02 (ddd, 2 H, J = 8, 8, 1 Hz), 2.59 (s, 6 H). MS: m/z 522 (M^+, 100), 474 (6), 426 (9), 352 (6), 350 (7). Exact mass 522.1480, calcd for $C_{36}H_{26}S_2$ 522.1476.

9,14-Bis(4-cyanophenyl)benzo[*b*]triphenylene (10). A solution of compound 8 (39 mg, 0.07 mmol) and cuprous cyanide (12 mg, 0.13 mmol) in DMF (15 mL) was refluxed under argon overnight. After cooling to room temperature, chloroform was added, and the solution was filtered and concentrated. The residue was purified by preparative TLC (benzene) to give 15 mg (47%) of the desired compound 10. Single crystals, mp >400 °C, were grown from solutions of 10 in CH_2Cl_2–acetone. ^1H NMR ($CDCl_3$, 270 MHz): δ 8.31 (dd, 2 H, J = 8, 1 Hz), 7.84 and 7.70 (AA'BB' system, 8 H), 7.78 and 7.52 (AA'BB' system, 4 H), 7.42 (ddd, 2 H, J = 8, 7, 1 Hz), 7.35 (dd, 2 H, J = 8, 1 Hz), 7.03 (ddd, 2 H, J = 8, 7, 1 Hz). MS: m/z 480 (M^+, 100), 377 (15). Exact mass 480.1626, calcd for $C_{28}H_{20}N_2$ 480.1635.

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Supplementary Material Available: Full details for the determination of the X-ray structures of compounds 3–12 and ^1H NMR spectra of compounds 3–16 (148 pages). Ordering information is given on any current masthead page.

Structure of a New Oligomer of Glutaraldehyde Produced by Aldol Condensation Reaction

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Glutaraldehyde (GA) was found to yield a new dimer when treated in an aqueous alkaline solution. This dimer was identified as a substance that had previously been known to be responsible for the high activity of certain immobilized enzymes prepared by using alkali-treated GA solution as a coupling agent. The dimer was isolated, and its structure was investigated by the various spectrometries. UV and IR spectra suggested the existence of an α,β-unsaturated formyl group and a hydroxyl group in its molecule, and GC-MS analysis indicated the molecular formula $C_{10}H_{14}O_3$ (MW 182). The existence of two formyl groups and one hydroxyl group was confirmed by GC-MS of the dimer derived to *O*-(pentafluorobenzyl) oxime (*O*-PFB oxime) and further to its TMS derivative, respectively. The structure of the *O*-PFB derivative was determined by two-dimensional NMR ^1H–^1H and ^1H–^{13}C spin-coupling networks in homonuclear shift correlation spectra and in proton detected heteronuclear multiple-bond connectivity spectra. Taking these results into account, we proposed the structure of the GA dimer.

Glutaraldehyde (GA) has been widely used for tanning of leather, fixation of tissues for electron microscopy, immobilization of bioactive materials such as proteins, enzymes, and microorganisms, preservation of connective tissues for bioprostheses, chemical sterilization, and so on.[1-5] In these applications GA is often dissolved in an aqueous medium and exposed to the physiological pH for a relatively long period of time, during which GA tends to undergo a polymerization reaction. The polymers thus produced include α,β-unsaturated formyl groups in their molecules exhibiting strong UV absorption with maximum absorption at 235 nm, while GA itself shows only a weak absorption maximum at 280 nm.[6] The ratio of absorption at 235 nm to that at 280 nm, therefore, has been used as a purification index.[7] Margel and Rembaum[8] investigated aldol condensation of GA and found that high polymers (poly-GA) were precipitated from the aqueous solutions of pH 7–13.5. The poly-GA included hydroxyl and carboxyl groups in addition to α,β-unsaturated formyl groups in their molecules,[8] but the exact structure could not be determined. On the other hand, the formation of water-soluble GA oligomers has been left obscure because of difficulty in the precise separation and purification. These oligomers as well as the GA monomer, however, seem to play a significant role in the above-mentioned utilities of GA. It has been known that GA solutions including such types of oligomers show higher efficiency than pure GA solution in fixation of tissues[6] and immobilization of enzyme.[9] For instance, we found that certain enzymes im-

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