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Synthesis of New Anthracene Derivatives

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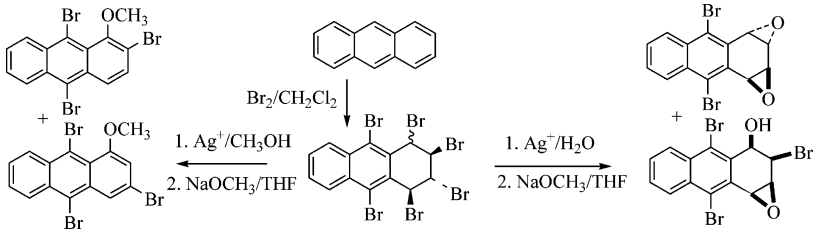
Received September 1, 2005



An efficient synthesis is described for hexabromoanthracenes **3** and **4** by direct bromination of 9,10-dibromoanthrecene **2**. Whereas base-induced elimination of hexabromide **3** with *t*-BuOK gave 2,3,9,10-tetrabromoanthracene **5**, the reaction of hexabromide **4** with DBU afforded 1,3,9,10-tetrabromoanthracene **6** as the sole product. Tetrabromide **5** was also obtained by aromatization of 1,4-dinitroxy-2,3,9,10-tetrabromo-1,2,3,4-tetrahydroanthracene **17**. Efficient and convenient synthetic routes are described for the preparation of dinotroxy **17**, dimethoxy **23**, and dihydroxides **18** and **19** with silver-induced substitution of hexabromides **3** and **4**. The hydroxy compounds **19** and **18** were converted to diepoxide **20** and monoepoxide **21**, respectively, with sodium methoxide. Base-promoted aromatization of dimethoxide **23** afforded dibromomonomethoxides **26** and **27**. Bromoanthracenes and isomeric arene oxides constitute valuable precursors for the preparation of functionalized substituted anthracene derivatives that are difficult to prepare by other routes.

Introduction

Among the polycyclic aromatic hydrocarbons, anthracene and its derivatives have been extensively investigated; this is reflected in the tens of thousands of publications dealing with anthracene since 1970 (see Chemical Abstracts). One of anthracenes' specialties is the bimolecular photochemical reaction. The ring is able to act as a light-induced electron donor or as an acceptor, a property easily tuned by substitution. Anthracenes also possess photochromic properties that can be used in the design of optical, electronic, or magnetic switches incorporated in mesophases, polymers, films, or crystals. These reversible properties are based on the photodimerization reaction.[1]

Dihydrodiols and epoxides are implicated as the active forms of carcinogenic polynuclear aromatic hydrocarbons.[2] Despite the many published studies on the biological activity of tetrahydrodiol and tetrahydro epoxides, little is known about their chemical reactivity and the mechanisms of their reactions. Many natural products also contain reduced derivatives of the anthaquinones (oxanthrones, anthranols, and anthrones). Bromoanthracenes have specialty intermediate applications for the production of amine, ether, nitrile, sulfide, silyl, and organometallic derivatives of anthracene. Studies on the bromination of anthracene are tedious and unsatisfactory**.** No reaction details or spectral data of bromoanthracenes (except for 9,10-dibromoanthracene) are available in the earliest research.[3]

We aimed to employ the exhaustive bromination of 9,10-dibromoanthracene or anthracene to obtain still higher brominated anthracenes. We recently described the selective bromination of 1-bromonaphthalene and efficient preparation methods for bromonaphthalene derivatives.[4] As an extension of this work we studied the bromination reaction of 9,10-dibromoantracene in specific reaction conditions. In this paper we describe the first isolation and identification of two arene oxides from hexabromoanthracene and other derivatives of anthracene from

† Gaziosmanpasa University.

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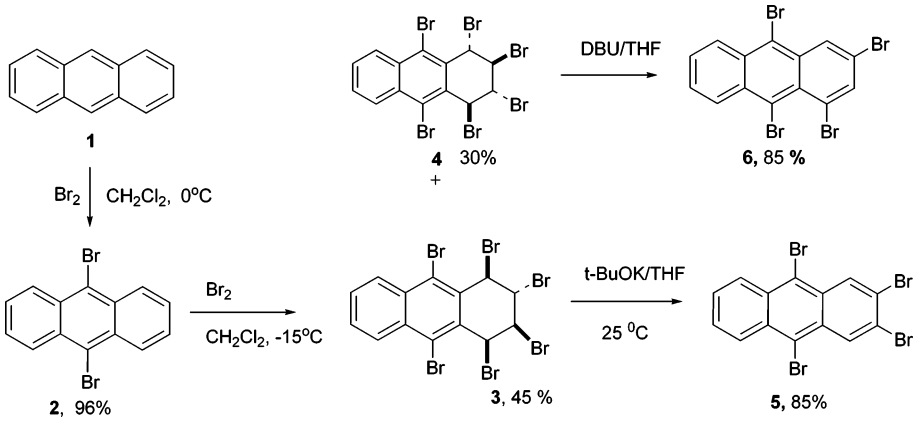
(2) (a) Wislocki, P. G.; Lu, A. Y. *Polycyclic Aromatic Hydrocarbons and Carginogenesis: Structure−Activity Relationships*; Yang, S. K., Silverman, B. D., Eds.; CRC Press: Boca Raton, FL, 1988; p 1.

(3) (a) Barry-Barnett, E. D.; Cook, J. W. *J. Chem. Soc.* **1925**, *127*, 1490. (b) Barry-Barnett, E. D.; Cook, J. W. *J. Chem. Soc.* **1925**, *127*, 204. (c) Sampey, J. R.; McCuen, A. K.; Cox, J. M. *J. Am. Chem. Soc.* **1950**, *72*, 1854.

10.1021/jo051846u CCC: $33.50
Published on Web 02/04/2006

SCHEME 1



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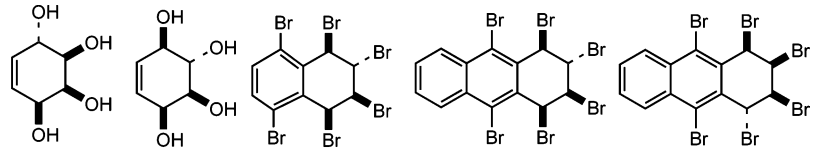


	Conduritol-C	Conduritol-F	**7**	**3**	**8**
				Dihedral Angles	
J_{12} = 8.1	8.4	4.2	3.8	128°	
J_{23} = 2.1	11.0	11.3	11.2	167°	
J_{34} = 3.0	4.4	3.0	2.8	64.5°	

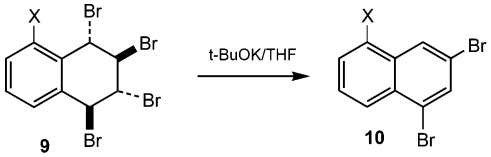
hexabromoanthracene. We also aimed to elaborate the conversions and to illustrate the potential utility of isomeric anthracene oxides for the synthesis of polysubstituted anthracene derivatives that are difficult to synthesize using other routes.

Results and Discussion

The bromination of anthracene with 2 equiv of molecular bromine was carried out at 0 °C in the dark in CH_2Cl_2. A fast bromination occurred to form 9,10-dibromoanthracene in a yield of 96%. In the same manner, bromination of 9,10-dibromoanthracene in CH_2CI_2 at −15 °C gave 1,2,3,4,9,10-hexabromotetrahydroanthracene **3** and **4** in a ratio of 60:40. Careful fractional crystallization in the dark afforded hexabromides **3** and **4** in yields of 45% and 30%, respectively (Scheme 1).

Proton and carbon NMR studies indicate that hexabromide **3** has asymmetry in its structure. There are two possible isomeric structures, **3** and **8**, for unsymmetrical hexabromide. The vicinal coupling constant value (11.2 Hz) for hexabromide **3** indicates the *trans*-configuration of the bromine atoms at C_2 and C_3 carbon atoms, which is only in agreement with the proposed structure **3**. Similar signal systems and the coupling constants with those of naphthalene hexabromide **7**[5] confirm the suggested structure. Analysis of the first-order ^{1}H NMR spectrum indicated a large coupling constant (11.2 Hz) for the protons bonded to C_2 and C_3 atoms, which strongly supports axial−axial alignment of the protons. In other words, bromine atoms prefer equatorial positions. Abraham et al.[6] performed ^{1}H NMR analysis of all possible conduritol derivatives and found similar coupling (J = 11.0 Hz) for conduritol-F. In the case of the *cis* configuration (conduritol-C) of hydroxy groups (axial−equatorial), the measured coupling constant is 2.1 Hz. This comparison indicates clearly that the isolated hexabromide **3** has the *trans*,*trans*,*cis* configuration (Scheme 2).

SCHEME 3



X=H, 1,3-dibromonaphthalene
X= Br ,1,3,5-tribromonapthalene

^{1}H NMR spectra exhibited two AA′BB′ for symmetrical hexabromide **4**. Seven lines in the ^{13}C NMR spectra also agreed with the symmetrical hexabromide. Four symmetrical stereoisomers can be formed in the reaction. Attempts to X-ray hexabromide **4** failed because we could not obtain suitable single crystal; it readily aromatizes and configuration isomerization occurs in solvent even in daylight. Although base-induced aromatization of the hexabromide **4** can lead to three tetrabromides, **5**, **6**, and **16**, we obtained only tetrabromide **6**. It is interesting that dehydrobromination of *trans*,*trans*,*trans*-bromotetralines (**9**,[4a,d] Scheme 3) exhibited the same selectivity, which may be evidence for the suggested *trans*,*trans*,*trans* configuration.

(4) (a) Cakmak, O. *J. Chem. Res. (S)* **1999**, 366−367. (b) Cakmak, O.; Kahveci, I.; Demirtas, I.; Hokelek, T.; Smith, K. *Collect. Czech. Chem. Commun*. **2000**, *65*, 1791−1804. (c) Tutar, A.; Cakmak, O.; Balcı, M. *Tetrahedron* **2001**, *57*, 9759−9763. (d) Cakmak, O.; Demirtas, I.; Balaydin, H. T. *Tetrahedron* **2002,** *58*, 5603. (e) Adam, W.; Çakmak, O.; Saha-Möller, C. R.; Tutar, A. *Synlett* **2002**, 49−52, (f) Tutar, A.; Çakmak, O.; Karakaş, M.; Onal, A.; Die, S. *J. Chem. Res.* **2004**, 545−549. (g) Erenler, R. Çakmak, O. *J. Chem. Res*. **2004**, 545−549.

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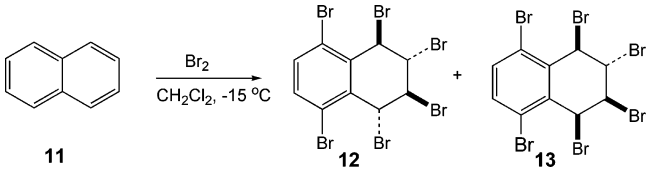
(6) Abraham, R. J.; Gottschalck, H.; Paulsen, H.; Thomas, W. A. *J. Chem. Soc.* **1965**, 6268−6275.

SCHEME 4



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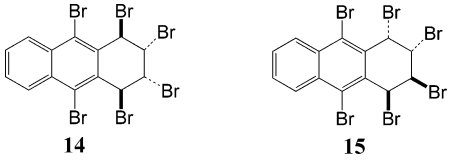


Further evidence for the stereochemistry of hexabromides **3** and **4** is the fact that bromination of naphthalene (or 1,4-dibromonaphthalene) in the same conditions gives two hexabromides, **12** and **13**, with the same stereochemistry as that of hexabromides **3** and **4** (Scheme 4). Last, because of the existence of X-ray analyses of two other symmetrical hexabromides **14**[7] and **15** (Scheme 5; unpublished results), the symmetrical product must be in the *trans* configuration of all bromo substituents (i.e., hexabromide **4**)

After the successful isolation of the hexabromides **3** and **4**, which have the requisite skeletal arrangement and functionality to permit the easy introduction of two double bonds to form anthracene derivatives, we submitted both hexabromides **3** and **4** to dehydrobromination. Whereas aromatization of hexabromide **3** with 2 mol of potassium *tert*-butoxide gave tetrabromide **5**, dehydrobromination of hexabromide **4** with 2 mol of DBU afforded 1,3,9,10-tetrabromide **6** in high yields as the sole products.

NMR spectra indicate symmetry in its structure. Dehydrobromination of the hexabromides **3** and **4** can lead to two symmetrical tetrabromoantracene isomers: 1,4,9,10- (**16**) and 2,3,9,10-tetrabromoanthracenes. ^{1}H NMR is in accord with only symmetrical 2,3,9,10-tetrabromoanhtacene structure **5** as a result of the fact that the shifts downfield (8.8 ppm) of the singlet resonance of H_1 and H_4 can only be interpreted for structure **5**, which has a van der Waals interaction between the protons (H_1/H_4) and the bromine atoms (Br_9/Br_{10}). Simple characteristic ^{1}H NMR spectra exhibited a singlet for H_1 and H_4 and AA′BB′ for aryl protons. The obtaining of tetrabromide **5** instead of tetrabromide **16** may be attributed to the enormous increase in strain energy (26.10 kJ/mol)[8] in the case of structure **16** due to steric compression of bromo groups in γ-gauche positions (Scheme 6).

Proton and carbon NMR of tetrabromide **6** is in accord with the suggested unsymmetrical structure. Resonance of H_4 is a doublet (J = 1.84 Hz) at 8.89 ppm. A meta coupling doublet of H_2 appears at 8.15. The other protons are multiplets due to the asymmetry. Fourteen ^{13}C NMR signals of four carbons bonded, bromine atoms are in accord with the suggested structure.

On the other hand, the high synthetic potential of benzylic bromides as precursors of anthracene prompted us to investigate the silver-induced substitution reaction. The bromides in benzylic positions (i.e. 1,4-positions) in the hexabromides are expected to be reactive for substitution. Therefore, the silver-induced nucleophilic substitution of hexabromides **3** or **4** in benzylic positions followed by base-induced aromatization would be a prime tool for producing some difficult to obtain anthracene derivatives.

A solution of hexabromide **3** in dry diethyl ether was combined with 2 equiv of silver nitrate, followed by stirring for 3 days at room temperature in dry THF in the dark. After crystallization and column chromatography, 1,4-dinitrate-2,3,9,10-tetrabromo-1,2,3,4-tetrahydroanthracene **17** was obtained in a yield of 59%.

Spectra of ^{1}H NMR of dinitroxy **17** consist of two AA′BB′ signal systems indicating a symmetry structure. As a result of the strong inductive effect of the nitroxy group, the resonance of H_1 and H_4 shifts to quite a lower field (6.93 ppm) in comparison to those of the hexabromides. The mass and elemental analysis results showed a good agreement with the proposed structure. Surprisingly, base-induced elimination of dinitroxy **17** with sodium methoxide resulted in the elimination of HNO_3 instead of HBr to give 2,3,9,10-tetrabromoanthracene **5** (Scheme 7). Our findings from the benzylic nitration[9] are of special interest due to the group leaving more easily than bromo atoms. It is clear from models that the steric interactions of the bromo atoms have an enormous effect, and presumably smaller steric requirements can cause the reaction to take place preferentially from the *trans* direction.

We also investigated the silver-induced hydrolysis of hexabromides **3** and **4**. This procedure in aqueous THF resulted in the replacement of benzylic bromides to give 1,4-dihydroxyanthracenes. After careful chromatography, followed by fractional crystallization, two dihydroxides, **18** and **19**, were isolated in 40% and 35% yields, respectively (Scheme 9).

The structures were determined by mass analysis and ^{1}H and ^{13}C NMR spectroscopy, including a comparison with literature values of analogous compounds. Seven lines in the ^{13}C NMR spectra and the ^{1}H NMR spectrum consisting of two AA′BB′ system, including hydroxyl groups (5.20 ppm), are in good agreement with the proposed symmetrical structure **19**. The symmetry at dihydroxide **19** can adopt two different configurations, *trans*,*trans*,*trans* or *cis*,*trans*,*cis*. Comparison of this **19** molecule with the Conduritol-E (J_{12} = 4.3 Hz) and Conduritol-B (J_{12} = 8.3 Hz) indicate clearly that the isolated symmetry dihydroxyl **19** has the *trans*,*trans*,*trans* (J_{12} = 7.1 Hz) configuration (Scheme 9).[6] Further confirmation of the stereochemistry of compound **19** was achieved by cyclization of the *trans*-halohydrin **19** to diepoxide **20** (Scheme 9).

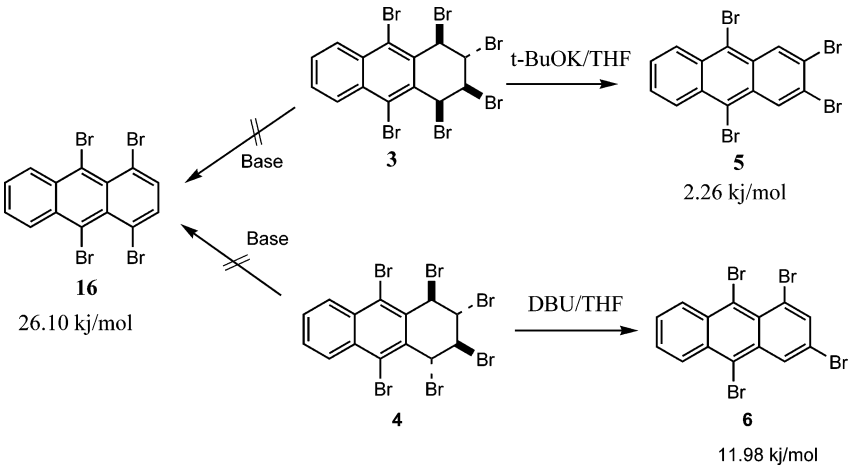
^{1}H and ^{13}C NMR spectral studies on the other dihydroxide **18** indicate its asymmetry. It is obvious that there is only one possible asymmetrical isomeric structure of **18** due to the configuration retention of bromine-bonded C_2 and C_3 atoms. The ^{1}H NMR spectrum of the *cis*-1,4-diol **18** has a *cis* coupling constant (J = 1.9 Hz) for the H_1 and H_2 protons and a *trans* diaxial coupling constant (J = 3.2 Hz) for the H_3 and H_4 protons. H_1 and H_4 protons are also coupled with the hydroxyl groups (J_{1-OH} = 10.0 Hz; J_{4-OH} = 4.0 Hz). Resonances of H_2 and H_4 are a doublet of doublets at δ 4.88 and δ 4.41, respectively. A doublet of hydroxyl groups appears at 4.38 and 3.59 ppm. The 10 sp^2 (six quaternary and four methine carbons) and four sp^3 carbons in ^{13}C NMR spectra are consistent with the proposed structure **18**.

(7) Hokelek, T.; Tutar, A.; Cakmak, O. *Acta Crystallogr.* **2002**, *E58*, 10−12,

(8) ChemOffice 6.0 (ChemBats3D Ultra 6.0, ChemDraw Ultra Version 6.0.) CS ChemBats3D Ultra, 2000; CambridgeSoft.com, 100Cambridge Park, Dr. Cambridge, MA 02140-2317 U.S.A.

(9) Demirtas, I.; Erenler, R.; Buyukkidan, B.; Çakmak, O. Submitted for publication.

SCHEME 6



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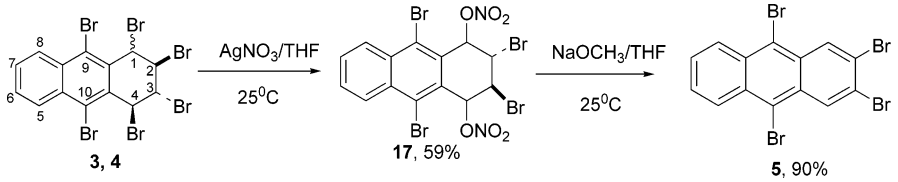
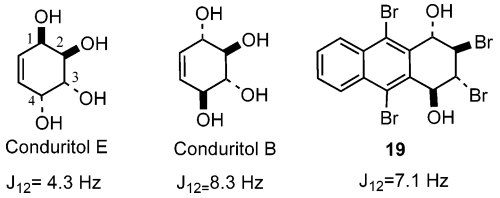
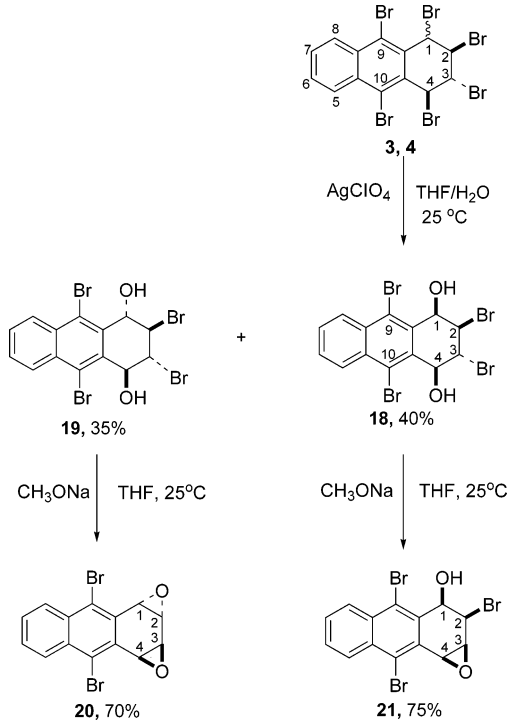


SCHEME 8



SCHEME 9



Because the halohydrines **18** and **19** are good precursors for corresponding arene oxides, we treated them with 2 equiv of sodium methoxide. Elimination of 2 mol of HBr with dry sodium methoxide in tetrahydrofuran cyclized the bromohydrins to the oxiranes in a good yield and high purity, whereas dihydroxy **19** gave *anti*-diepoxide **20** as a consequence of *trans* alignment of the hydroxyls and bromines. It is expected that compound **18** afforded monoepoxide **21** due to the existence of only one *trans* orientation of hydroxyl and bromine in the same conditions.

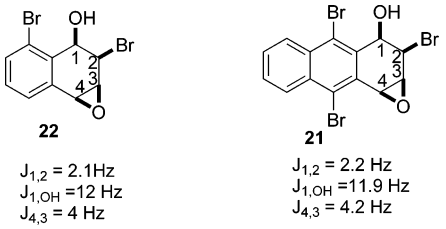
The ^{1}H NMR spectrum of diepoxide **20** exhibits two AA′BB′ splitting patterns of aromatic and aliphatic protons. The A part of the aliphatic protons resonates at δ 4.46 and the B part of the system resonates at δ 4.0. Seven lines in the ^{13}C NMR spectra are also in accord with the proposed symmetrical diepoxide structure **20**. The ^{1}H NMR spectrum of monoepoxide **21** displays a characteristic signal splitting pattern. The H_1, coupled with OH and vicinal proton H_2, resonates at 5.41 as a doublet of doublets ($J_{1-OH} = 11.9$ Hz, $J_{12} = 2.2$ Hz). The OH signal is observed at δ 4.10 as a doublet. H_4 and H_3 resonate at δ 5.06 and 4.44, respectively, as a doublet ($J_{43} = 4.2$ Hz). In the ^{13}C NMR spectrum, 10 lines in the aromatic region and five lines in the aliphatic region support the proposed structure. The similarity between the NMR signal system of **21** with that of tetralin oxide[9] **22** that we elucidated by X-ray analysis[10] is also consistent with the proposed structure **21** (Scheme 10).

Silver-induced methanolysis followed by aromatization can lead to methoxy derivatives of anthracene. For this reason, a solution of hexabromides **3** and **4** in dry methanol was combined with 2 equiv of silver sulfate at room temperature. After crystallization and column chromatography of the solvolysis mixture, 1,4-dimethoxy-2,3,9,10-tetrabromo-1,2,3,4-tetrahydroanthracene **23** was selectively obtained in a yield of 75% (Scheme 11).

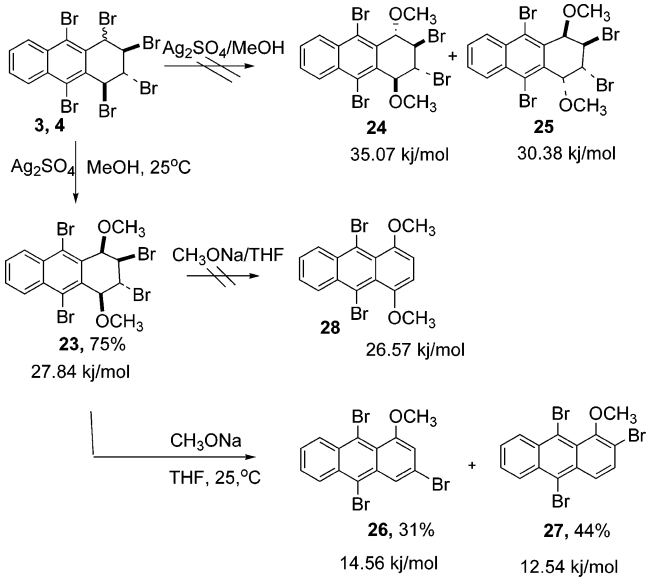
Proton and carbon NMR studies indicate that dimethoxide **23** has asymmetry in its structure. The vicinal coupling constant

(10) Celik, I.; Demirtas, I.; Akkurt, M.; Erenler, R.; Guven, K.; Cakmak, O. *Cryst. Res. Technol.* **2003**, *38*, 193−196.

SCHEME 10



SCHEME 11



value for the H_1 and H_2 protons (J_{12} = 2.3 Hz) indicates that the methoxy and the bromine groups have a *cis* orientation (see Scheme 2). The downfield shift of the resonance of H_5 and H_8 protons (8.44 ppm, m) is attributable to a van der Waals interaction (steric compression) between the related protons and bromines. The reaction can afford three stereisomeric dimethoxides (**23**, **24**, and **25**); only structure **23** is unsymmetrical and its strain energy (SE)[8] is the lowest (SE = 27.84 kJ/mol total strain energy, Scheme 11) among the possible stereoisomers, which may explain why compound **23** is selectively formed.

After the successful isolation of the methoxide **23**, which has the requisite skeletal arrangement and functionality to permit the easy introduction of two double bonds to form anthracene derivatives, compound **23** was subjected to base-induced elimination with sodium methoxide in dry THF at room temperature. The reaction afforded 1-methoxy-3-bromide **26** and 1-methoxy-2-bromide **27**, which were easily separated by column chromatography in high yields due to convenient R_f values and ready crystallizable materials (Scheme 11). It is noteworthy that MeOH elimination occurs as well as 2 mol HBr elimination dehydrohalogenation; otherwise, in the case of forming compound **28**, strain energy increases enormously (26.57 kJ/mol) due to the bulky groups in γ-gauche positions (Scheme 11).

The ^{1}H NMR spectra of **26** and **27** consist of three characteristic signals, indicating one methoxy group in each compound and showing the position of the bromine group. The observed *meta* coupling in the ^{1}H NMR spectrum of **26** (J_{24} = 1.7 Hz) is consistent with the 1-methoxy and 3-bromo constitution. While H_4 (δ 8.30) resonates at quite an upper field due to the steric compression of Br_{10}, H_2 (δ 6.83) appears at a lower field due to the electron donor OMe group bonded to C1. The observed AB system (8.27 and 7.60 ppm; J_{43} = 9.5 Hz) is in good agreement with the proposed structure **27**. ^{13}C NMR spectra of the compounds' eight quaternary and six methine carbons and one sp^3 carbon atom (methoxyl group) are in accord with both compounds **26** and **27**.

Conclusion

A convenient and effective procedure for the synthesis of hexabromoanthracenes **3** and **4** has been developed, whose base-mediated elimination affords the synthetically valuable 2,3,9,10-tetrabromoanthracene **5** and 1,3,9,10-tetrabromoanthracene **6** as the sole products in high yield. The synthesis employs readily available anthracene as a starting material and is applicable to the large-scale preparation of compounds that constitute excellent precursors for substituted anthracenes.

Silver-induced substitution of a mixture of hexabromides **3** and **4** with various nucleophiles, followed by aromatization, opened up a new route to various anthracene derivatives important in terms of the synthesis of pharmaceutical chemicals,[11] natural products,[12] and donor properties.[13] For example, tribromo methoxides **26** and **27** are very useful precursors for the synthesis of many other substituted anthracenes as a result of the easy substitution of the bromo groups. The chemistry of *anti*-9,10-dibromo-1,2;3,4-anthracene dioxide **20** and monoepoxide **21** is not important for the polyfunctionalization of anthracene nor is the chemistry of non K-region arene oxide.

Experimental Section

Preparation of 9,10-Dibromoanthracene (2). A magnetically stirred solution of anthracene (1.78 g, 10 mmol) in CH_2Cl_2 (110 mL) was cooled to 0 °C. The device for absorbing the evolved hydrogen bromide was attached to the reaction flask. [CARE!! The reaction evolves HBr and is best connected to a HBr gas trap (bubbler containing 1 M NaOH solution) preferably in a fumehood.] To the solution which is protected from light was added dropwise Br_2 (3.45 g, 22 mmol) in CH_2Cl_2 (10 mL) over 5 min and the mixture was stirred for 1 h. Reaction progress was checked by ^{1}H NMR and TLC. After removing the solvent, the precipitated material was filtered and purified in a short Al_2O_3 column (10 g). The residue was dissolved in hot chloroform (120 mL) and allowed to stand at room temperature for 1 day, 9,10-Dibromoanthracene (**1**) was collected as pure yellow needles (3.22 g, 96%), mp 218−220 °C (lit.[14] 220−222 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60 (AA′ part of AA′BB′ system, 4H, H_1, H_4, H_5, H_8), 7.66 (BB′ part of AA′BB′ system, 4H, H_2, H_3, H_6, H_7). Anal. Calcd for $C_{14}H_8Br_2$ (336.0): C 50.04, H 2.40. Found: C 50.10, H 2.35.

Bromination of 9,10-Dibromoanthrecene (2). The solution of 9,10-dibromoanthracene (**2**) (3.76 g, 11.22 mmol) in CH_2Cl_2 (150 mL) was cooled to −15 °C. To the solution which is protected from light was added Br_2 (5.27 g, 1.7 mL, 33 mmol) in one portion. The mixture was allowed to stand in a frezeer at −15 °C. Reaction progress was monitored by TLC and ^{1}H NMR. ^{1}H NMR control of reaction mixture after 1 week showed that conversion is 50%. After completing the reaction in 20 day, excess bromine and the

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solvent were removed. ^{1}H NMR investigation of the rest showed formation of two hexabromide **3** and **4** in a ratio of 60:40, respectively. It was seen that hexabromide **4** is quite sensitive to daylight and aromatizes, with configuration isomerization occuring in ca. 0.5 h. Chromatographic separation failed due to nearly same R_f values (R_f = 0.4, hexane) of compound **3** and **4**. Moreover, during column chromatography, aromatization of compound **4** and configuration isomerizations of both hexabromides occurred. Crude product (7.08 g) was applied to fractionally crystallize (THF) in benzene (170 mL) in the dark at room temperature (or refrigerator). The crystallized materials were taken as several fractions. Unseparated fractions were combined, and further recrystallization was applied. Hexabromide **4** (2.2 g 30%) and hexabromide **3** (3.3 g, 45%) were separated in pure form, and the products were saved in dark in freezer.

***trans,trans,cis*-1,2,3,4,9,10-Hexabromo-1,2,3,4-tetrahydroanthracene (3).** Crystallized from benzene, mp 160−170 °C (dec). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.41 (m, 2H, H_5, H_8), 7.69 (m, 2H, H_6 and H_7), 6.31 (d, J_{12} 3.8, 1H, H_1), 6.02 (d, J_{43} = 2.8, 1H, H_4), 5.36 (dd, J_{21} = 3.8, J_{23} = 11.2, 1H, H_2), 4.33 (dd, J_{32} = 11.2, J_{34} 2.8, 1H, H_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 135.6, 135.3, 134.6, 133.8, 131.9, 131.8, 130.7, 129.8, 126.9, 113.9, 59.6, 59.4, 56.7, 54.9; MS (CI) *m*/*z* 652/654/656/658/660 (M^+) 571/573/575/577/579/581/582 (M^+, −Br), 490/492/494/496/498/500 (M^+-2Br); 410/412/414/416/418(M^+-3Br); 333/334/336/338/339 (M^+, −4Br); 254/256/257/259 (M^+, −5Br); 174/176/177. (M^+ −6Br), 149/150, 98/99, 87/88, 74, 62, 39; IR (KBr) ν_{max} 2990, 1480, 1220, 1220, 1120, 1020, 910, 830, 820. Anal. Calcd for $C_{14}H_8Br_6$ (655.6): C, 25.65; H, 1.23. Found: C, 25.55; H, 1.27. Anal. Calcd for $C_{14}H_8Br_6$ (655.6): C, 25.65; H, 1.23. Found: C, 25.52; H, 1.26.

***cis,trans,cis*-1,2,3,4,9,10-Hexabromo-1,2,3,4-tetrahydroanthracene (4).** Crystallized from benzene, mp 146−150 °C (dec). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (m, AA′ part of AA′BB′ system, 2H, H_5, H_8), 7.73 (m, BB′ part of AA′BB′ system, 2H, H_6,H_7), 6.52 (AA′ part of AA′BB′ system, 2H, H_1, H_4), 5.55 (BB′ part of AA′BB′ system, 2H, H_2, H_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 133.2, 126.4, 125.8, 122.5, 54.0, 44.3; IR (KBr) ν_{max} 2996, 1398, 1330, 1251, 1160, 1135 1037, 914, 759. Anal. Calcd for $C_{14}H_8Br_6$ (655.6): C, 25.65; H, 1.23. Found: C, 25.57; H, 1.28.

Synthesis of 1,3,9,10-Tetrabromoanthracene (6). To a stirred solution of hexabromide **4** (1.0 g, 1.52 mmol) in dry and freshly distilled THF (60 mL) was added dropwise 1,5-diazabicyclo[5.4.0]-undec-5-ene (DBU, 0.532 g, 3.5 mmol) in THF (20 mL) over 30 min. The reaction mixture was protected from light and stirred at room temperature for 4 h. After the reaction was complete (TLC control), the precipitated material was filtered and the reaction material was diluted with methylene chloride (100 mL). The organic layer was washed with H_2O (3 × 25 mL) and dilute KOH and dried over K_2CO_3. After removal of the solvent, the precipitated material was recrystallized from chloroform. 1,3,9,10-Tetrabromoanthracene was obtained in a yield of 85% (0.65 g) as yellow needles, mp 161−162 °C (from hexane, R_f 0.59). ^{1}H NMR spectra of the rest after crystallization showed a product mixture; chromatography gave no pure products because of their similar R_f values. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, J_{42} = 1.84, H_4), 8.77 (m, H_8), 8.56 (m, H_5), 8.15 (d, J_{24} = 1.84, H_2), 7. 69 (m, H_6 and H_7); ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO) δ 140.6, 139.2, 134.5, 133.5, 131.5, 130.9, 130.6, 129.9, 129.1, 128.9, 123.8, 122.9, 121.9, 121.4; IR (KBr) ν_{max} 3079, 3027, 2923, 1585, 1506, 1284,1250, 1178, 1238, 1178, 954,750. Anal. Calcd for $C_{14}H_6Br_4$ (493.8): C, 34.05; H, 1.22. Found: C, 34.17; H, 1.19.

Synthesis of 2,3,9,10-Tetrabromoanthracene (5). To a solution of hexabromide **3** (4.2. g, 6.4 mmol) in dry and freshly distilled THF (150 mL) was added 1.44 g (12.8 mmol) of potassium *tert*-butoxide solution in dry and freshly THF (40 mL). The resulting reaction mixture was magnetically stirred for 12 h at 20 °C in dark. Reaction progress was monitored by TLC (R_f = 0.64 eluted with petroleum ether). The reaction mixture was diluted with water (100 mL) and extracted with ether (2 × 100 mL), and the combined organic layers were washed with water (2 × 50 mL) and dried over $CaCl_2$. After evaporation of the solvent (20 °C, 10 Torr), the residue was placed on a short silica gel (15 g) column and eluted with hexane. Recrystallization from hot benzene afforded 2.69 g (85%) of pure tetrabromoanthracene **5** as yellow needles from benzene, mp 273−274 °C from benzene. ^{1}H NMR spectra of the rest after crystallization showed a product mixture. Chromatography gave no pure products because of similar R_f values (the rest consist of possible other bromoisomers along with 9,10-dibromoanthracene). It was not possible to measure ^{13}C NMR for tetrabromide **5** due to unsolubility of the tetrabromide **5** (ca. 35 mg of tetrabromide **5** is solved in 10 mL of benzene. Solubility of tetrabromide **5** is lower in other solvents such as acetone, THF, DMF, and $CHCl_3$). ^{1}H NMR (200 MHz, DMSO-d_6) δ 8.8 (s, 2H, H_1/H_4), 8.5 (AA′ part of AA′BB′ sys. 2H, H_5/H_8), 7.9 (BB′ part of AA′BB′ sys. H_6/H_7); MS (CI) *(m/z)* 489.63/491.63/493.63/495.63/497.63 (M^+), 411.75/413.75/415.75/417.75 (M^+, −Br), 331.87/333.87/335.87), 251.99/253.99/255.99, 173.07/174.07/176.07, 149.06, 135, 122.07, 97, 81, 69. Anal. Calcd for $C_{14}H_6Br_4$ (493.8): C, 34.05; H,1.22. Found: C, 34.15; H, 1.25.

Preparation of 2,4-Dinitroxy-2,3,9,10-tetrabromo-1,2,3,4-hydroanthracene (17). To a solution of a mixture of hexabromides **3** and **4** (3.0 g, 4.57 mmol) (obtained from bromination of 9,10-dibromoanthracene) in dry diethyl ether (150 mL) was added silver nitrate (2.33 g, 13.7 mmol.). The reaction mixture was magnetically stirred under nitrogen gas atmosphere in the dark for 3 days. Reaction progress was monitored TLC. After the reaction was complete, precipitated solid material was filtered and the solvent was removed by vacuo. The residue was passed through a short silica gel (10 g) column by elution with a dichloromethane−hexane mixture. After separation of the crystallizing material (dinitroxy **17**, 150 mg), the mother liquor (2.85 g) was applied to a silica gel column (190 g) eluting with hexanes−ethyl asetate (9:1). Dinitroxy **17** was recrystallized from dichloromethane−hexane; isolated yield 1.56 g (total yield 59%). Other fractions from the column chromatography, which was unable to isolate purely, were mixtures consisting of probable other dinitoxy stereoisomers, mp 176−177 °C (dec). ^{1}H NMR (400 MHz, $CDCI_3$) δ 8.46 (m, 2H, H_5, H_8), 7.82(m, 2H, H_6, H_7), 6.93 (brs, 2H, H_1,H_4), 5.25 (brs,2H, H_2, H_3); ^{13}C NMR (400 MHz, $CDCI_3$) δ 133.7, 130.6, 130.2, 128.5, 124.5, 80.0, 77.9; MS (CI) *m*/*z* 620 (M^+), 575, 528, 512, 495, 368, 336, 176, 125, 98, 74, 63; IR (KBr) υ_{max} 3564, 3269, 2999, 2978, 2902, 2538, 2337, 1973, 1946, 1846, 1817, 1718, 1651, 1566, 1483, 1414, 1375, 1356, 1275, 1184, 1155, 1120, 1039, 1018, 952. Anal. Calcd for $C_{14}H_8Br_4N_2O_6$ (619,84): C, 27,13; H, 1,30. Found: C, 26.95; H, 1.25.

Preparation of 2,3,9,10-Tetrabromoanthracene 5 from Dinitroxy 17. 1,4-Dinitrate-2,3,9,10-tetrabromo-1,2,3,4-tetrahydroanthracene 1**7** (1.24 g, 2 mmol) in dry THF (30 mL) was treated with sodium methoxide (0.27 g, 2.5 equiv) in dry THF (10 mL). The mixture was stirred at room temperature overnight. After being worked up (3 × 20 mL diethyl ether), dried (Na_2SO_4), and evaporated, the residue was filtered by using a short silica gel (10 g) column eluting with hexane−chloroform. The precipitated product was recrystallized from hot benzene, and 2,3,9,10-tetrabromide **5** was isolated in a yield of 691 mg (70%). Other fractions from the column chromatography could not be isolated purely.

Hydrolysis of Hexabromides 3 and 4. To a stirred solution of a mixture of hexabromides **3** and **4** (obtained from bromination of 9,10-dibromoanthracene) (3.0 g, 4.57 mmol) in acetone (50 mL) was added a solution of $AgClO_4 \cdot H_2O$ (3.1 g, 13.7 mmol) in aqueous acetone (7 mL acetone−3 mL H_2O) in the dark. The resulting mixture was stirred at room temperature for 2 days in dark. The precipitated AgBr was removed by filtration. After removal of the solvent, the residue was chromatographed on silica gel (200 g), eluted with ethyl acetate−hexane (4:1) to give 1,4-dihidroxy-2,3,9,10-tetrabromoanthracenes **18** and **19**.

[2*R*(*S*),3*R*(*S*]-9,10-Tetrabromo-1,2,3,4-tetrahydroanthracene-[1*S*(*R*),4*S*(*R*)]-diol (18). The compound was recrystallized from

dichloromethane−hexane as colorless needles, yield 0.97 g (40%), mp 160−161 °C, R_f = 0.58 (hexanes−EtOAc, 7:3). ^{1}H NMR (400 MHz, *d*-DMSO) δ 8.42−7.72 (4H, m, aryl H), 5.92 (1H, dd, J_{1-OH} = 10.0, J_{12} 1.9, H_1), 5.77 (1H, dd, J_{4-OH} = 4.0, J_{43} = 3.2, H_4), 4.88 (1H, dd, J_{23} = 7.4, H_2), 4.41 (1H, dd, H_3), 4.38 (1H, d, J_{1-OH} = 10.0, C_1−OH), 3.59 (1H, d, J_{4-OH} = 4.0, C_4−OH); ^{13}C NMR (100 MHz, d-DMSO) δ 135.4, 133.8, 132.8, 132.3, 128.7, 128.2, 125.6, 123.8, 119.5, 118.9, 76.5, 73.1, 57.9, 56.7; IR (KBr) ν_{max} 3192, 2997, 1707, 1583, 1551, 1481, 1390, 1348, 1325, 1296, 1244, 1189, 1160, 1122, 1095, 1053, 1022, 970. Anal. Calcd for $C_{14}H_{10}Br_4O_2$ (529.84): C, 31.74; H, 1.90. Found: C, 31.45; H, 1.95.

[2*R*(*S*),3*R*(*S*)]-9,10-Tetrabromo-1,2,3,4-tetrahydroanthracene-[1*S*(*R*),4*S*(*R*)]-diol (19). The compound was recyrstallized from acetone−hexane as colorless needles, yield 0.85 g (35%), mp 208−209 °C, R_f = 0.52 (hexanes−EtOAc, 3:1). ^{1}H NMR (400 MHz, *d*-DMSO) δ 8.48 (2H, AA′ part of AA′BB′ system, H_5, H_8), 7.90 (2H, BB′ part of AA′BB′ system, H_6, H_7), 6.32 (2H, d, J_{12} J_{34} 7.15, H_1, H_4), 5.48 (2H, d, H_2, H_3), 5.20 (2H, brs, 2-OH); ^{13}C NMR (100 MHz, *d*-DMSO) δ 136.08 (C_{11}−C_{12}), 133.7 (C_{13}−C_{14}), 130.20 (C_6−C_7), 127.1 (C_9−C_{10}), 123.2 (C_5−C_8), 72.9 (C1−C4), 57.3 (C_2−C_3); IR (KBr) ν_{max} 3855, 3839, 3677, 3529, 2916, 1701, 1655, 1560, 1477, 1439, 1373, 1331, 1288, 1245, 1159, 1072, 956, 901, 862. Anal. Calcd for $C_{14}H_{10}Br_4O_2$ (529.84): C, 31.74; H, 1.90. Found: C, 31.37; H, 1.95.

Synthesis of *anti*-1,2:3,4-Dioxide-9,10-dibromo-1,2,3,4-tetrahydroanthracene (20). To a solution of dihydroxide **19** (1.2 g, 2.28 mmol) in freshly distilled THF (40 mL) was added a solution of sodium methoxide (0.384 g, 5.68 mmol) in THF (30 mL). The mixture was stirred at ambient temperature under a nitrogen gas atmosphere for 8 h. After consumption of the starting material (monitoring TLC), to the reaction mixture were added diethyl ether (70 mL) and H_2O (50 mL), and precipitated material was removed by filtration. The organic layer was washed with H_2O (3 × 40 mL) and dried over $CaCl_2$. After removing the solvent at reduced pressure, crude product was chromatographed using an aluminum oxide (30 g, neutral) column, eluted with hexane. The product which was recrytallised from chloroform/hexane as colorless needles, yield 0.58 g (70%), mp 214−220 °C (dec), R_f = 0.59 (hexane/chloroform, 4:1). ^{1}H NMR (400 MHz, $CDCI_3$ δ 8.32 (AA′ part of AA′BB′ system, 2H, H_5/H_8), 7.63 (BB′ part of AA′BB′ system, 2H, H_6/H_7), 4.46 (AA′ part of AA′BB′ system, 2H, H_1/H_4), 4.00 (B part of AA′BB′ system, 2H, H_2/H_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 134.7, 134.3, 133,8, 133.4, 59.6, 57.54; IR (KBr) ν_{max} 2923, 1629, 1484, 1253, 1174, 927, 860, 756, 507. Anal. Calcd for $C_{14}H_8Br_2O_2$ (368.02): C, 45.69; H, 2.19. Found: C, 45.80; H, 2.10.

Synthesis of 1-Hydroxy-2-bromo-3,4-oxide-1,2,3,4-tetrahydroanthracene (21). To a solution of dihydroxide **18** (1.5 g, 2.85 mmol) in freshly distilled THF (40 mL) was added a solution of sodium methoxide (0.45 g, 8.4 mmol) in dried THF (30 mL). The mixture was stirred at ambient temperature under a nitrogen gas atmosphere for 6 h in the dark. Reaction progress was monitored by TLC for consumption of the starting material. Diethyl ether (60 mL) and H_2O (50 mL) were added to the reaction mixture and the resulting precipitate was removed by filtration. The organic layer was washed with H_2O (3 × 25 mL), dried over $CaCl_2$, and concentrated at reduced pressure. After the crude product was purified by column chromatography (Al_2O_3, 100 g), monoepoxide **21** was recrystallized from hexane−chloroform, yield 0.95 g (75%), mp 182−184 °C (dec), R_f = 1.67 (hexane−chloroform, 4:1). ^{1}H NMR (400 MHz, $CDCI_3$) δ 8.34 (2H, m, H_5/H_8), 7.63 (2H, m, H_6/H_7), 5.41 (1H, dd, J_{1-OH} = 11.9, J_{12} = 2.2, H_1), 5.06 (1H, d, J_{43} = 4.2, H_4), 4.44 (1H, d, J_{34} = 4.2, H_3), 4.10 (1H, d, J_{21} = 2.2 H_2), 3.12 (d, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6, 133.8, 133.3, 129.7, 129.6, 129.3, 128.7, 128.6, 127.7, 127.4, 71.8, 60.6, 58.7, 48.7; IR (KBr) ν_{max} 3500, 2932, 1568, 1483, 1306, 1254, 1163, 1043, 962, 889, 804, 760, 669, 648, 607, 573, 544, 459. Anal. Calcd for $C_{14}H_9Br_3O_2$ (448.93): C, 37.46; H, 2.0. Found: C, 37.10; H, 2.07.

Synthesis of (2*R*(*S*),3*R*(*S*))-9,10-Tetrabromo-(1*R*(*S*),4*S*(*R*))-dimethoxy-1,2,3,4-tetrahydroanthracene (23). To a solution of a mixture of hexabromides **3** and **4** (obtained from bromination of 9,10-dibromoanthracene) (3.0 g, 4.59 mmol) in dry methanol (40 mL) was added Ag_2SO_4 (2.85 g, 9.15 mmol) under a nitrogen atmosphere in the dark. The resulting reaction mixture was stirred magnetically at room temperature for 3 days. Reaction progress was monitored by TLC for consumption of the starting material. After removal of the residual by filtration and then removal of the solvent, the crude product was passed through a short column packed with silica gel (10 g). Recrytallization from chloroform−hexane in the refrigerator gave the clear yellow crystals of methoxide **23**, yield 0.91 g, (75%), mp 144−145 °C (from chloroform−hexane), R_f = 0.59 (hexanes−EtOAc, 6:1). ^{1}H NMR (400 MHz, $CDCI_3$) δ 8.42 (m, 1H, H_5/H_8), 8.47 (m, 1H, H_5/H_8), 7.70 (2H, m, H_6, H_7), 5.62 (1H, d, J_{43} = 2.3, H_4), 5.52 (1H, d, J_{12} =1.8, H_1), 4.97 (1H, dd, J_{32} = 10.7, H_3), 4.26 (1H, dd, J_{32} = 10.7, J_{12} =1.8, H_2), 3.72 (3H, s, C_1−OMe), 3.53 (3H, s, C_4−OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.7, 133.4, 132.7, 132.6, 129.3, 129.1, 129.0, 128.8, 128.6, 125.3, 86.5, 80.9, 58.2, 58.2, 57.2, 54.9; MS (CI) *m*/*z* 576 (M^++18), 558 (M^+ +1), 544, 527, 510, 496, 479, 464, 445; IR (KBr) ν_{max} 2994, 2929, 2825, 2023, 1832, 1801, 1706, 1612, 1572, 1481, 1458, 1400, 1371, 1325, 1288, 1250, 1205, 1184, 1163, 1082, 1043, 997. Anal. Calcd for $C_{16}H_{14}Br_4O_2$ (557.9): C, 34.45; H, 2.53. Found: C, 34.42; H, 2.17.

Aromatization of dimethoxide 23. To a solution of dimethoxide **23** (1.72 g, 3.08 mmol) in freshly distilled THF (50 mL) was added a solution of sodium methoxide (0.5 g, 9.2 mmol) in dried THF (20 mL). The mixture was stirred at ambient temperature for 8 h. Reaction progress was monitored by TLC for consumption of the starting material. Diethyl ether (60 mL) and H_2O (50 mL) were added to the reaction mixture and the resulting precipitate was removed by filtration. The organic layer was separated, washed with H_2O (3 × 35 mL), and dried over $CaCl_2$. The filtrate was concentrated in vacuo to give crude product, which was chromatographed using a SiO_2 (140 g) column eluted with hexane (3.5 L) to give the two methoxides **26** and **27**.

1-methoxy-3,9,10-tribromoanthracene (26). The product was recrystallized from chloroform−hexane, yield 0.42 g (31%), mp 159−160 °C, R_f = 0.41 (hexane). ^{1}H NMR (400 MHz, $CDCI_3$) δ 8.66 (1H, m, H_5), 8.39 (1H, m, H_8), 8.30 (1H, d, J_{42} 1.7, H_4), 7.50 (2H, m, H_6, H_7), 6.83 (1H, d, J_{24} 1.7, H_2), 3.93 (3H, s, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9 (C_1), 109.9 (C_2), 122.8 (C_3), 123.3(C_4), 129.8 (C_5), 127.9(C_6), 128.5 (C_7), 128.7 (C_8), 119.7 (C_9), 121.9 (C_{10}), 131.9 (C_{11}), 123.4 (C_{12}), 132.5 (C_{13}), 133.4 (C_{14}), 56.2 (OMe); MS (EI^+): *m*/*z* 442(M^+), 427, 403, 399, 394, 368, 366, 351, 349, 325, 323, 321, 319, 287; IR (KBr) ν_{max} 2956, 2925, 2831, 1618, 1597, 1541, 1524, 1458, 1439, 1427, 1402, 1373, 1350, 1304, 1248, 1230, 1155, 1115, 1095, 984. Anal. Calcd for $C_{15}H_9Br_3O$ (444.94): C, 40.49; H, 2.04. Found: C, 40.34; H, 2.10.

1-Methoxy-2,9,10-tribromoanthracene (27). The product was recrystallized from chloroform−hexane, yield 0.60 g (44%), mp 164−165 °C (chloroform−hexane); R_f = 0.24 (hexane). ^{1}H NMR (400 MHz, $CDCI_3$) δ 8.76 (1H, m, H_5), 8.46 (1H, m, H_8), 8.27 (1H, d, J_{43} = 9.5, H_4), 7.60 (1H, d, J_{34} = 9.5, H_3), 7.57 (2H, m, H_1, H_7), 3.84 (3H, s, OMe). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 117.1, 131.7, 126.4, 129.4, 128.5, 128.6, 128.8, 117.7, 125.1, 127.1, 132.2, 131.6, 133.1, 62.2; MS (CI) *m*/*z* 442 (M^+), 427, 403, 387, 386, 384, 382, 370, 369, 367, 366, 365, 364, 363, 351; IR (KBr) ν_{max} 2935, 1618, 1591, 1537, 1512, 1446, 1427, 1379, 1333, 1290, 1250, 1209, 1155, 1059, 1033, 964. Anal. Calcd for $C_{15}H_9Br_3O$ (444.94): C, 40.49; H, 2.04. Found: C, 40.37; H, 2.06.

Acknowledgment. The authors thank the Gaziosmanpasa University Research Foundation (Grants 2003/43 and 2000/26) and The Scientific and Technical Research Council of Turkey (TUBITAK, Grant TBAG-1322) for financial support.

JO051846U