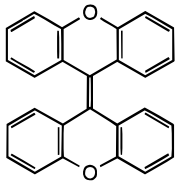
Dixanthylene Double Calix[6]arene

Oleg Aleksiuk and Silvio E. Biali*

Department of Organic Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

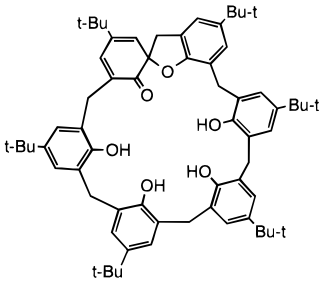
Received April 1, 1996

The calixarenes have emerged as one of the most useful building blocks for the construction of complex molecular hosts of predesigned architectures[1] and, in particular for the synthesis of molecular receptors of nanosize dimensions.[2] 9,9′-dixanthylene (**1**) belongs to the crowded bistricyclic ethylene family which possess thermochromic, photochromic, and piezochromic properties,[3−5] and its introduction to a macrocyclic host may result in systems whose photophysical properties may be modified by complexation. 9,9′-Dixanthylene adopts in the crystal and in solution an *anti*-folded ("doubly bent") conformation which partially relieves the steric interactions across the double bond.[4,6] In this Note we describe the mutual interconnection of two calix[6]arenes subunits by the formal incorporation of a dixanthylene core into a double calix[6]arene system.[7]

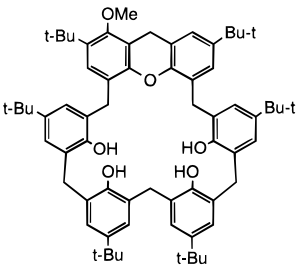


1

Acid-catalyzed rearrangement of a methanolic solution of the monospirodienone derivative of *p-tert*-butylcalix[6]arene (**2**) yields the xanthenocalix[6]arene (**3**).[8] The chemical modification of the xanthene moiety of **3** was achieved in three steps. Firstly, the phenolic groups of **2** were protected by methylation ($NaH/(MeO)_2SO_2/THF$) yielding **4**. System **4** displays in the ^1H NMR (400 MHz, $CDCl_3$, rt) a singlet and 10 well-resolved doublets in the aromatic region, and several singlets for the methylene groups in the δ 3.844−4.092 region, which indicate fast ring inversion of the calixarene macrocyclic ring on the NMR timescale.[9] Two methoxy groups are shifted upfield (δ 2.719 and 2.803), suggesting that these groups are in the shielding region of neighboring aryl rings.[9c] The xanthene methylene group was selectively oxidized to a carbonyl group by treatment with $K_2Cr_2O_7$/acetic acid, yielding **5**. The carbonyl group resonates in the ^{13}C NMR at δ 177.36, a value similar to that of the parent xanthone (δ 176.9 ppm).[10] The methylene proton pattern in the ^1H NMR is in agreement with fast ring inversion on the NMR time scale. Notably, one aromatic doublet is strongly shifted downfield (δ: 8.184) (Figure 1). We assign this signal to the aromatic proton of the xanthone group which is *ortho* to the carbonyl group since this proton should be deshielded due to the anisotropic effect of the group. As in the case of **4**, two methoxy signals are at a relatively high field (δ 2.907 and 2.910). The ^1H NMR spectrum was analyzed by 2D techniques (COSY and NOESY) which allowed us to assign almost all signals and showed that the two high-field methoxy signals correspond to the anisyl rings flanking the xanthone moiety.



2



3

The xanthone calix[6]arene **5** was reductively dimerized by treatment with Zn/HCl,[11] yielding the dixanthylene calix[6]arene **6** (CI MS *m*/*z* 2079.8) in 33% yield (Scheme 1). The strongly fluorescent product has a fluorescence maximum at λ 408 nm.[12] Molecular mechanics calculations (MM3(92) program)[13] indicate that in the substituted dixanthylene core **7** the *anti*-folded conformation is favored by 4.1 kcal mol^{-1} over a twisted[3] conformation. On the basis of the nonbonded distance of 11 Å[8] observed in the X-ray structure of **3** between the methylene carbon of the xanthene subunit (C35) and the distal methylene carbon C14 (cf. Figure 5 in ref 8) and examination of CPK models, the dimensions of **6** along the main molecular axis can be estimated as ∼2 nm. In principle two diastereomeric forms (*Z* and *E*) are possible for the systems (**6*Z*** and **6*E*** respectively). The ^1H and ^{13}C NMR spectra are in agreement with the presence of a single form, which on the basis of steric considerations, is ascribed to the *E* diastereomer. The ^1H NMR of **6** was analyzed by 2D NMR techniques (NOESY, COSY, and H−C correlation). Notably, in contrast to **4** and **5**, the

(1) For reviews on calixarenes, see: Gutsche, C. D. *Calixarenes*; Royal Society of Chemistry: Cambridge, 1989. *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Vicens, J.; Böhmer, V.; Eds.; Kluwer: Dordrecht, 1991. Gutsche, C. D. *Aldrichimica Acta* **1995**, *28*, 1. Böhmer, V. *Angew. Chem.* **1995**, *107*, 785; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713.

(2) Timmerman, P.; Verboom, W.; van Veggel, F. C. J. M.; van Duynhoven, J. P. M.; Reinhoudt, D. N. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2345. Rudkevich, D. M.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron Lett.* **1994**, *35*, 7131.

(3) For reviews on strained and twisted olefins, see: Luef, W.; Keese, R. *Top. Stereochem.* **1991**, *20*, 231. Sandström, J. *Top. Stereochem.* **1983**, *14*, 83. Day, J. H. *Chem. Rev.* **1963**, 65.

(4) Agranat, I.; Tapuhi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 665.

(5) For a study of the thermochromic, piezochromic, and photochromic properties of dixanthylene, see: Kortüm, G.; Krieg, P. *Chem. Ber.* **1969**, *102*, 3033. See also: Korenstein, R.; Muszkat, K. A.; Slifkin, M. A.; Fischer, E. *J. Chem. Soc. Perkin Trans. 2*, **1976**, 438.

(6) Mills, J. F. D.; Nyburg, S. C. *J. Chem. Soc.* **1963**, 308.

(7) For a review on double calix[4]arene, see: Asfari, Z.; Weiss, J.; Pappalardo, S.; Vicens, J. *Pure Appl. Chem.* **1993**, *65*, 585.

(8) Aleksiuk, O.; Cohen, S.; Biali, S. E. *J. Am. Chem. Soc.* **1995**, *117*, 9645.

(9) The methyl ether derivatives of *p-tert*-butylcalix[6]arene are conformationally more flexible than the parent system. See: (a) Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *59*, 3871. (b) Janssen, R. G.; Verboom, W.; Reinhoudt, D. N.; Casnati, A.; Freriks, M.; Pochini, A.; Ugozzoli, F.; Ungaro, R.; Nieto, P. M.; Carramolino, M.; Cuevas, F.; Prados, P.; de Mendoza, J. *Synthesis* **1993**, 380. (c) Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1994**, *59*, 3871.

(10) Breitmaier, E.; Volter, W. *^{13}C NMR Spectroscopy*, 2nd ed.; Verlag Chemie, Weinheim, 1978; p 297.

(11) These reagents have been used for the synthesis of dixanthylene from xanthone: Gurgenjanz, G.; Konstanecki, S. V. *Ber. Dtsch. Chem. Ges.* **1885**, *28*, 2310. For an alternative synthesis of dixanthylene see for example: Schönberg; A.; Asker, W. *J. Chem. Soc.* **1942**, 272.

(12) For example of a calix[4]arene substituted by a fluorescent group, see: Aoki, I.; Kawabata, H.; Nakashima, K.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1991**, 1771. Jin, T.; Ichikawa, K.; Koyama, T. *J. Chem. Soc., Chem. Commun.* **1992**, 499. Perez-Jimenez, C.; Harris, S. J.; Diamond, D. *J. Chem. Soc., Chem. Commun.* **1993**, 480.

(13) Allinger, N. L. *Molecular Mechanics. Operating Instructions for the MM3 Program*. Technical Utilization Corporation.

S0022-3263(96)00599-3 CCC: $12.00

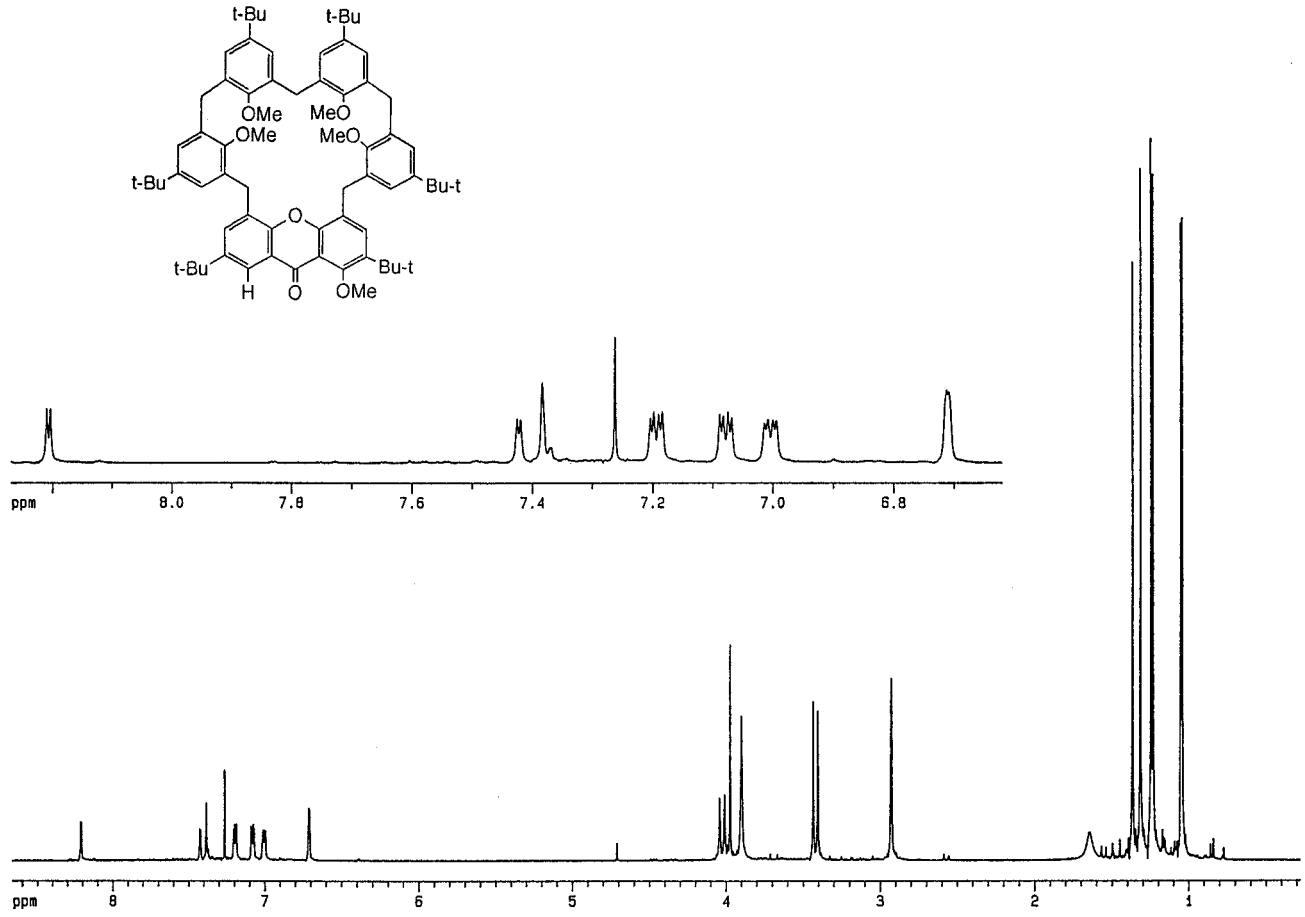
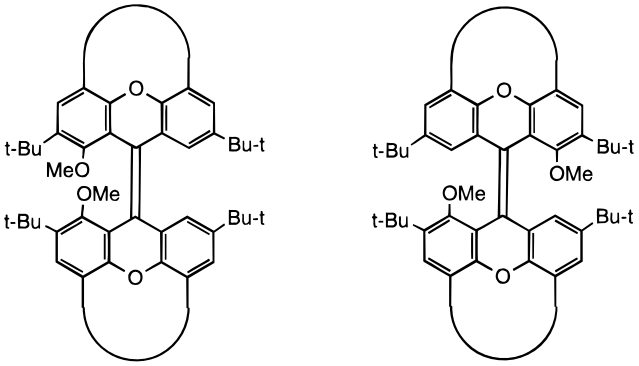


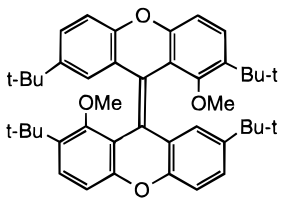
Figure 1. ^{1}H NMR (400 MHz) of the xanthonecalix[6]arene **5** ($CDCl_3$, RT) and (top) expansion of the aromatic region.



6*Z* **6*E***

methylene protons of **6** appear in the ^{1}H NMR (400 MHz, $CDCl_3$, RT) as 10 pairs of somewhat broad doublets.[14] Heating a sample of **6** in $CDCl_2CDCl_2$ up to 400 K did not result in any appreciable coalescence of the signals, but rather in sharpening of the methylene doublets. The methylene pattern *is not* the result of a high barrier for the ring inversion process, since calix[6]arene methyl ether derivatives usually have low ring inversion barriers[9] and since it is rather unlikely that the barrier for **6** will be substantially higher than the corresponding barriers for **4** and **5**. The nonequivalence of the methylene protons must be the result of the nonplanarity of the dixanthylene moiety which renders the protons within each methylene group diastereotopic, even if the ring inversion is fast on the NMR time scale.

A 2D NOESY NMR spectrum showed that a single methoxy signal (δ 3.50 ppm) displays a NOE cross peak with a *t*-Bu signal (δ 1.02 ppm). This assigns the first signal to the methoxy groups at the dixanthylene moiety since these are the only methoxy groups which are vicinal (*ortho*) to a *t*-Bu group. This methoxy signal displays a NOE cross peak with the aromatic signal at δ 6.94 which was independently assigned to the two dixanthylene aromatic protons pointing toward the double bond. According to the calculated geometry for the model **7**, this NOE is due to interactions of protons within the same calix[6]arene subunit rather than due to interactions across the double bond (i.e., those involving the protons of the two calixarene subunits).

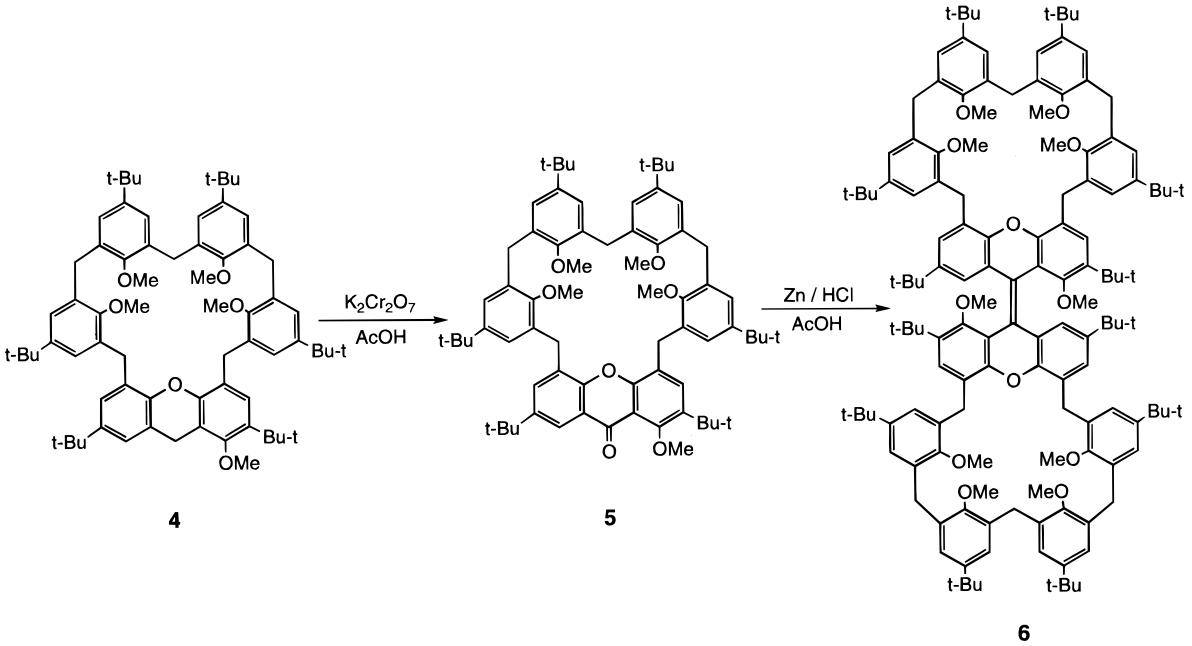


7

If the dixanthylene moiety of **6** adopts an *anti*-folded conformation, the system should exist in an achiral conformation of C_i symmetry in which the two calix[6]-arene subunits are related by an inversion symmetry operation and are therefore enantiotopic. Addition of 40 mg of the chiral solvating agent (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol[15] to 20 mg of **6** resulted in resonance

(14) Cooling down a $CDCl_3$ solution of **6** to 220 K resulted in an extensively broadened spectra, indicating that a dynamic process is operating, which can be ascribed to aryl and/or methoxy group rotations.

Scheme 1



4 **5** **6**

doubling of most of the signals in the ^{1}H NMR (Figure 2), in agreement with the presence of pairs of groups which are enantiotopic.[16]

Heating a sample of **6** in boiling mesitylene did not result in any appreciable "naked eye" thermochromism, as reported for other substituted dixanthylenes which, when substituted at the 1 position, do not display thermochromism.[17]

Experimental Section

Tetramethoxyxanthene 4. To a solution of **3**[8] (200 mg, 0.2 mmol) in 15 mL dry THF was added NaH (24 mg, 1 mmol). The mixture was heated to reflux, and a solution of dimethyl sulfate (0.1 mL, 1 mmol) in 2 mL dry THF was added, and the reflux was continued for 45 min. The excess of NaH was neutralized with EtOH. CH_2Cl_2 (100 ml) was added, and the mixture was washed with water. After phase separation, the organic phase was evaporated and the product purified by column chromatography (silica, eluent CH_2Cl_2), yielding 170 mg (82%) **4**: mp 163 °C dec; ^{1}H NMR (400 MHz, $CDCl_3$, rt) 1.023 (s, 9H, *t*-Bu), 1.063 (s, 9H, *t*-Bu), 1.211 (s, 9H, *t*-Bu), 1.217 (s, 9H, *t*-Bu), 1.238 (s, 9H, *t*-Bu), 1.287 (s, 9H, *t*-Bu), 2.719 (s, 3H, OMe), 2.803 (s, 3H, OMe), 3.483 (s, 3H, OMe), 3.501 (s, 3H, OMe), 3.844 (s, 2H, CH_2), 3.866 (br s, 9H, 1 OMe + 3 CH_2), 3.906 (s, 2H, CH_2), 4.092 (s, 2H, CH_2), 6.705 (d, J = 2.5 Hz, 1H, Ar−H), 6.731 (d, J = 2.4 Hz, 1H, Ar−H), 6.851 (s, 1H, Ar−H), 6.885 (d, J = 2.3 Hz, 1H, Ar−H), 6.980 (d, J = 2.5 Hz, 1H, Ar−H), 7.012 (d, J = 2.5 Hz, 1H, Ar−H), 7.037 (d, J = 2.5 Hz, 1H, Ar−H), 7.072 (d, J = 2.5 Hz, 1H, Ar−H), 7.097 (d, J = 2.3 Hz, 1H, Ar−H), 7.162 (d, J = 2.5 Hz, 1H, Ar−H), 7.190 (d, J = 2.5 Hz, 1H, Ar−H); ^{13}C NMR 25.15, 29.043, 29.067, 31.15, 31.31, 31.37, 31.44, 31.47, 32.12, 32.18, 34.06, 34.08, 34.09, 34.18, 59.55, 59.61, 60.24, 60.35, 61.12, 115.81, 119.69, 122.13, 123.31, 124.66, 124.72, 125.43, 125.55, 126.03, 126.13, 126.16, 126.28, 126.34, 126.83, 126.92, 132.00, 132.13, 133.52, 133.61, 133.62, 133.66, 133.75, 133.89, 136.24, 145.24, 145.35, 145.42, 145.46, 145.47, 148.50, 149.96, 154.03, 154.10, 154.20, 154.21, 155.65; CI MS m/z 1041.8 (MH^+). Anal. Calcd for $C_{71}H_{92}O_6$ C: 81.88, H: 8.90. Found C: 81.59, H: 8.77.

Tetramethoxyxanthone 5. To a solution of 5.7 g **4** in 0.25 L acetic acid was added 15 g of $K_2Cr_2O_7$, and the mixture was stirred overnight at room temperature. Water (1 L) was added until the the excess of $K_2Cr_2O_7$ was dissolved completely. A white precipitate formed which was filtered and washed with water. Further purification of the compound was achieved by column chromatography (silica, eluent CH_2Cl_2), yielding 4.1 g (71%) **5**: mp 165 °C dec; ^{1}H NMR (400 MHz, $CDCl_3$, rt) 1.022 (s, 9H, *t*-Bu), 1.032 (s, 9H, *t*-Bu), 1.213 (s, 9H, *t*-Bu), 1.226 (s, 9H, *t*-Bu), 1.294 (s, 9H, *t*-Bu), 1.346 (s, 9H, *t*-Bu), 2.907 (s, 3H, OMe), 2.910 (s, 3H, OMe), 3.382 (s, 3H, OMe), 3.412 (s, 3H, OMe), 3.878 (s, 6H, CH_2), 3.951 (s, 3H, 1 OMe), 3.988 (s, 2H, CH_2), 4.020 (s, 2H, CH_2), 6.689 (overlapping d, 2H, Ar−H), 6.976 (d, J = 2.2 Hz, 1H, Ar−H), 6.990 (d, J = 2.3 Hz, 1H, Ar−H), 7.049 (d, J = 2.5 Hz, 1H, Ar−H), 7.063 (d, J = 2.4 Hz, 1H, Ar−H), 7.165 (d, J = 2.5 Hz, 1H, Ar−H), 7.178 (d, J = 2.5 Hz, 1H, Ar−H), 7.361 (s, 1H, Ar−H), 7.400 (d, J = 2.4 Hz, 1H, Ar−H), 8.184 (d, J = 2.5 Hz, 1H, Ar−H); ^{13}C NMR δ 29.31, 29.57, 31.03, 31.17, 31.34, 31.46, 32.53, 32.59, 34.07, 34.09, 34.10, 34.69, 35.15, 59.63, 59.65, 60.31, 60.36, 62.80, 62.82, 115.50, 120.62, 121.88, 122.88, 124.33, 126.13, 128.27, 130.99, 131.09, 133.17, 133.24, 133.38, 133.43, 133.90, 133.95, 134.09, 134.52, 134.57, 137.28, 145.48, 145.51, 145.77, 145.84, 146.27, 151.38, 154.07, 154.13, 154.16, 154.19, 158.33, 177.36; CI MS m/z 1055.8 (MH^+). Anal. Calcd for $C_{71}H_{90}O_7$ C: 80.79, H: 8.59. Found C: 81.09, H: 8.85.

Dixanthylene 6. **5** (0.2 g) was dissolved in 100 mL of acetic acid, and then 6 g of Zn (dust) were added. The solution was heated to 80 °C, and 20 mL of concentrated HCl were added during a 2 h period. After stirring overnight at 80 °C, the solid was filtered, 200 mL of $CHCl_3$ was added to the filtrate, and the resulting solution was washed several times with water. The organic phase was evaporated and the residue purified by column chromatography (silica, eluent CH_2Cl_2), yielding 65 mg (33.0%) of **6**: mp 220 °C dec; the compound displayed a single spot in TLC (silica, eluent CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, rt) 0.93 (s, 9H, *t*-Bu), 1.00 (s, 9H, *t*-Bu), 1.02 (s, 9H, *t*-Bu), 1.14 (s, 9H, *t*-Bu), 1.19 (s, 9H, *t*-Bu), 1.29 (s, 9H, *t*-Bu), 2.64 (s, 3H, OMe), 3.13 (s, 3H, OMe), 3.36 (s, 3H, OMe), 3.51 (s, 3H, OMe), 3.62 (d, J = 14.0 Hz, 1H, CH_2), 3.63 (s, 3H, OMe), 3.67 (d (overlap), 1H, CH_2), 3.68 (d (overlap), 1H, CH_2), 3.80 (d, J = 14.2 Hz, 1H, CH_2), 3.94 (d, J = 13.9 Hz, 1H, CH_2), 3.96 (d, J = 16.8 Hz, 1H, CH_2), 4.07 (d, J = 16.5 Hz, 1H, CH_2), 4.13 (d, J =

(15) Pirkle, W.; Hoekstra, M. S. *J. Am. Chem. Soc.* **1976**, *98*, 1832. See also Agranat, I.; Tapuhi, Y.; Lallemand, J. Y. *Nouv. J. Chim.* **1979**, *3*, 59.

(16) A chiral solvating agent can discriminate between groups which are enantiotopic by either internal (i.e., enantiotopic groups on the same molecule) or external comparison (enantiotopic groups on enantiomeric molecules). An alternative explanation of the observed resonance doubling is that **6** exists as a racemic mixture of chiral dixanthylenes of C_2 symmetry which are rendered anisochronous by the chiral solvating agent. For this symmetry to exist, the central dixanthylene moiety must adopt a either twisted conformation or an *anti* folded conformation with a *Z* arrangement of the methoxy substituents. However, since the calculations predict for **7** an *anti* folded conformation and since on the basis of steric arguments the *E* form should be preferred over the *Z*, the NMR data is interpreted in terms of an *anti* folded *E* form.

(17) Mustafa, A.; Sobhy, M. E. E. *J. Am. Chem. Soc.* **1955**, *77*, 5124.

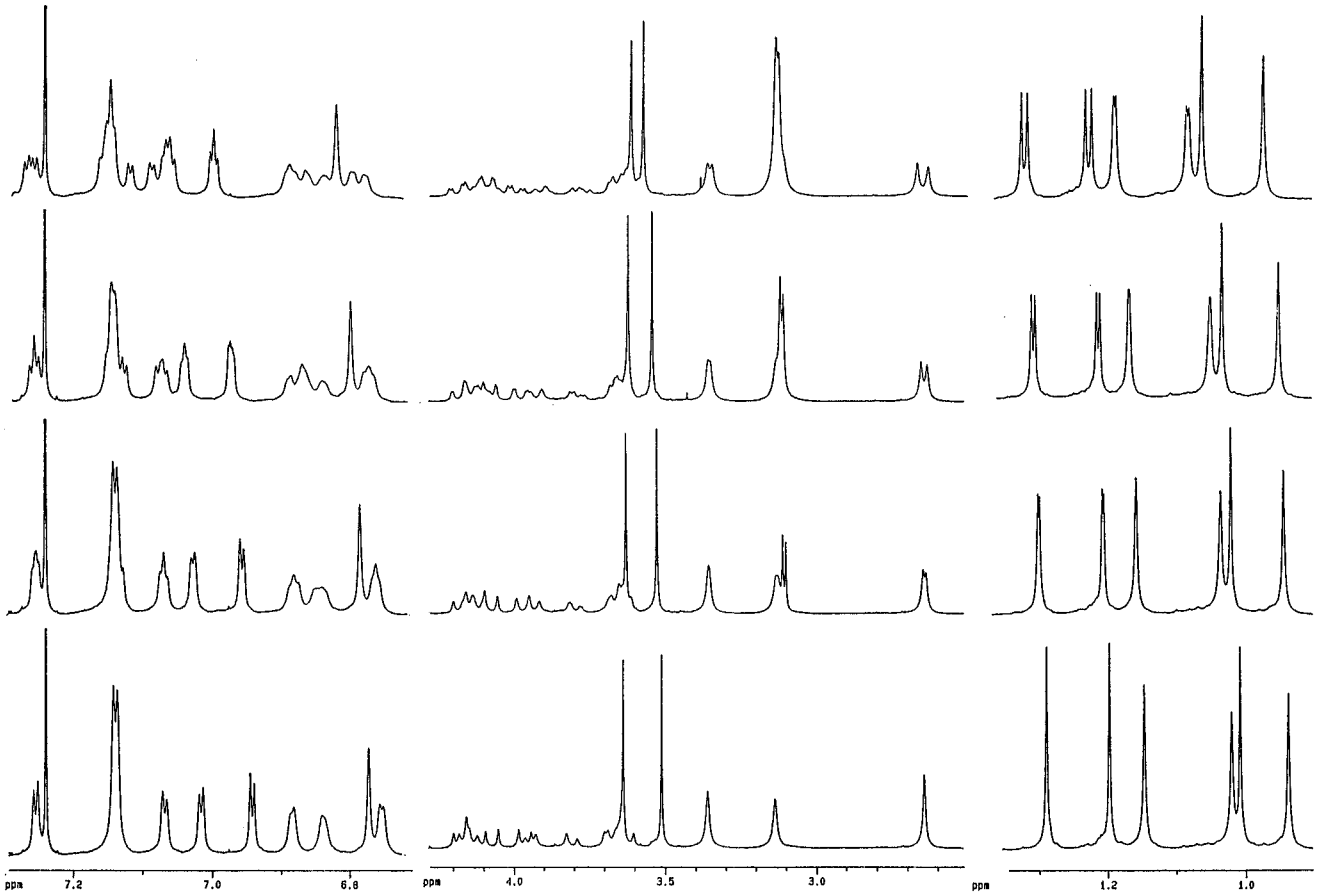


Figure 2. ^{1}H NMR (400 MHz) of the dixanthylene **6** (20 mg **6** in 0.5 mL $CDCl_3$, RT) (bottom) and spectra obtained in the presence of (*R*)-(−)2,2,2-trifluoro-1-(9-anthryl)ethanol (from bottom to top: 0, 10, 20 and 40 mg): left spectra, aromatic region; middle spectra, methylene and methoxy region; right spectra, *tert*-butyl region. Most resonances are doubled and/or shifted by the reagent. The doublet at δ 3.12 belongs to the chiral additive.

14.2 Hz, 1H, CH_2), 4.16 (d (overlap), 1H, CH_2), 4.17 (d, J = 16.7 Hz, 1H, CH_2), 6.75 (broad d, 1H, Ar−H), 6.77 (s, 1H, Ar−H), 6.83 (br s, 1H, Ar−H), 6.88 (br s, 1H, Ar−H), 6.94 (d, J = 2.3 Hz, 1H, Ar−H), 7.01 (d, J = 2.3 Hz, 1H, Ar−H), 7.06 (d, J = 2.3 Hz, 1H, Ar−H), 7.13 (d, J = 2.2 Hz, 3H, Ar−H), 7.25 (d, J = 2.4 Hz, 1H, Ar−H); ^{13}C NMR δ 28.50, 30.49, 31.14, 31.15, 31.34, 31.43, 31.52, 31.54, 32.14, 32.44, 34.03, 34.04, 34.07, 34.135, 34.14, 34.45, 59.50, 59.71, 60.34, 60.39, 60.43, 120.38, 121.08, 121.74, 123.32, 124.10, 124.73, 125.08, 125.67, 125.77, 125.91, 126.65, 126.68, 126.75, 127.03, 127.26, 127.57, 132.03, 132.73, 133.49, 133.56, 133.60, 133.69, 133.73, 134.20, 137.08, 145.28, 145.37, 145.44, 145.46, 152.46, 153.23, 153.61, 153.99, 154.40, 154.46, 154.66; UV λ_{max} 349 nm; CI MS m/z 2079.8. Anal. Calcd for $C_{142}H_{180}O_{12}$ C: 82.09, H: 8.73. Found C: 82.18, H: 8.74.

Acknowledgment. This work was supported by the German-Israeli Foundation.

JO960599E