JOC The Journal of Organic Chemistry

Article

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Cryptands with 1,3,5-Tris(1′,3′-dioxan-2′-yl)-benzene Units: Synthesis and Structural Investigations

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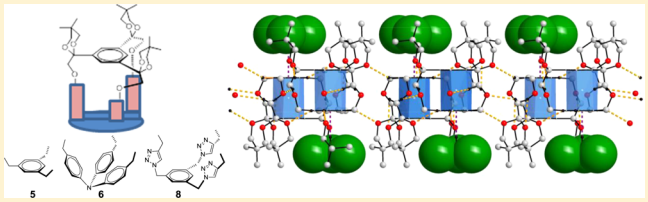
Supporting Information

ABSTRACT: Various cryptands based on 1,3-dioxane decorated 1,3,5-trisubstituted-benzene building blocks, connected by different chains (exhibiting ester, ether, or triazol groups) to several units with C_3 symmetry, are reported. The structure of the compounds was investigated by single crystal X-ray diffraction, NMR, and MS. The role of the 1,3-dioxane units was targeted to ensure the preorganization of the substrate for the macrocyclization reactions on one side, and for easier NMR assignment of the structure of the cryptands on the other side.



INTRODUCTION

Building blocks exhibiting 1,3-dioxane units were successfully used in the synthesis of macrocycles and cyclophanes.[1] Many 1,3-dioxane derivatives were extensively investigated, and the main aspects of their stereochemistry were elucidated.[2] The NMR spectra of 1,3-dioxane derivatives are very sensitive to structural alterations, and the changes in NMR spectra of the dioxacyclohexane units were successfully used to monitor the rotameric behavior of the aromatic groups in some cyclophanes with conformational equilibria suggesting the work of rudders or wringers,[1b] in the elucidation of the mechanism of a molecular "rocking chair"[1a] or of the temperature-induced flipping of the chains in a [4.4]cyclophane.[1c] The NMR data obtained for the 1,3-dioxane rings supported the determination of the stereochemistry of spiranes with six-membered rings[2d,e] and of the atropenantiomers of 2-methyl-2-aryl-1,3-dioxane derivatives.[2f]

The preorganization of the substrates with spiro-1,3-dioxanes or with bis(1,3-dioxan-2-yl)arenes facilitated the macrocyclization reactions.[1] The axial−axial orientation of the aromatic ring for both 1,3-dioxane units in I ensured the favorable disposition of the reactive groups and the good yields obtaining of [7.7]cyclophanes II or [4.4]cyclophanes III (Chart 1).[1]

Cryptands with C_3 symmetry are attractive targets for the building of host molecules, and such compounds with 1,3,5-trisubstituted benzene,[3] tertiary amines[4] or phosphines,[5] cyclotribenzylene[6] and 1,3,5-triazine[7] units were successfully obtained and investigated. Some tripodands with 1,3,5-tris(2′-*R*-1′,3′-dioxan-2′-yl)-benzene core (IV) were already reported (Chart 2),[8] and the structural investigations revealed a favorable arrangement of the substrate (the aromatic unit is axial for all 1,3-dioxane rings) for the access to cryptand like compounds (Chart 2).

The target in this work was to synthesize and investigate a series of cryptands exhibiting 1,3-dioxane moieties in the main structural unit (Chart 2, V and VI). The synthetic strategy was based on etherification, esterification, and "click" reactions using as substrates the already obtained tripodands with 1,3,5-tris(2′-*R*-1′,3′-dioxan-2′-yl)-benzene core IV (Chart 2).[8]

RESULTS AND DISCUSSION

Cryptands **4** and **5** exhibiting ether groups in the chains were obtained in good yields by reacting the tripodand **1** (IV, X = OH; Chart 2, Scheme 1) with 1,3,5-tris(bromomethyl)benzene **2** and *N*,*N*,*N*-tris(4-bromomethyl-benzen-1-yl)amine **3**, respectively (Scheme 1).

Tripodand **6** bearing propargyl groups at the extremities of the pendant arms (IV, X = O—CH_2—C≡CH; Chart 2, obtained from **1** in reaction with propargyl bromide) was submitted to a click reaction with triazide **7** (obtained from **2** in reaction with NaN_3) in order to give cryptand **8** (Scheme 2).

Despite the abundance of macrocycles,[9] there are only a reduced number of reports on the synthesis of macrocyclic compounds by click reactions.[10] The obtaining of rotaxanes (the click reaction generates the axle or attaches the stoppers),[11] of catenanes (clipping by click reaction),[12] of a rotaxane-catenane (click obtaining of the axle),[13] of knots,[14] and of a cryptand[7b] are the most spectacular encountered examples. The major difficulties in investigating in solution the cyclophanes and cryptands obtained by click reaction were caused by the poor solubility of these compounds in manifold solvents.

In the case of **8** the 1,3-dioxane units ensured a favorable preorganization of the substrate for obtaining the cryptand and also increased significantly the solubility of the final compound (**8**) in many solvents (e.g., dichloromethane, chloroform, acetone, ethylacetate).

Received: July 4, 2013
Published: August 7, 2013

Chart 1. [7.7]Cyclophanes (II) and [4.4]Cyclophanes (III) with 1,3-Dioxane Units

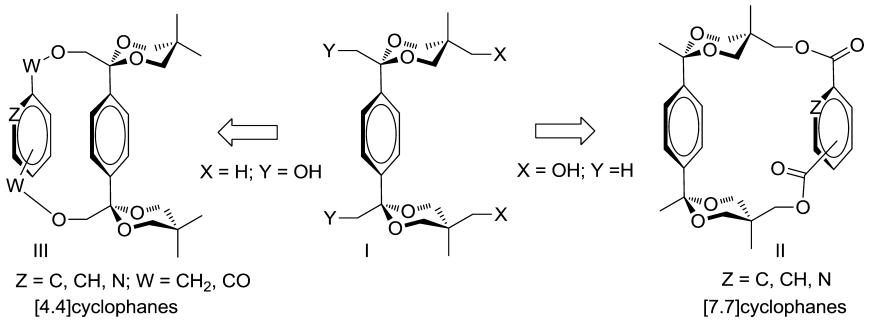
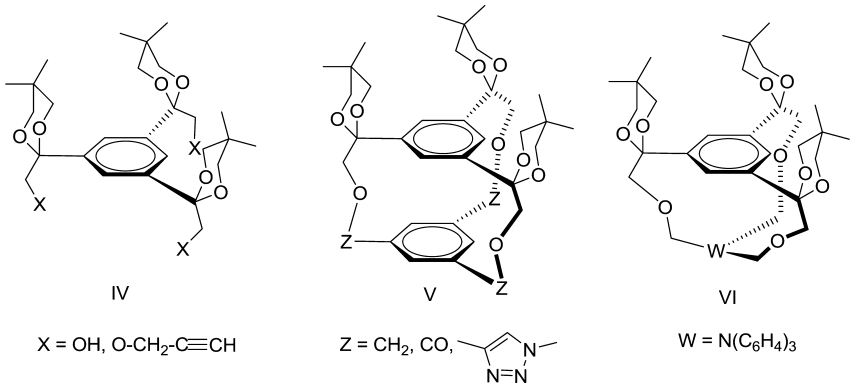
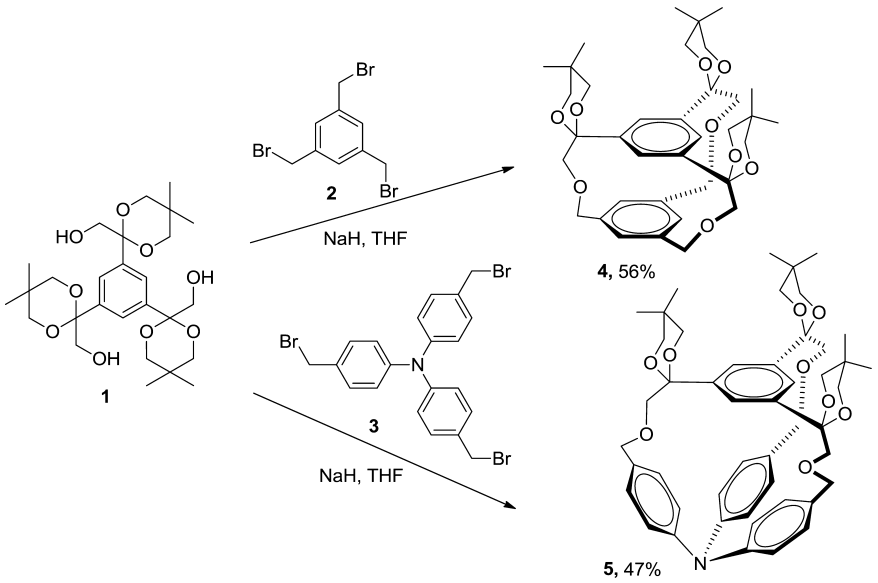


Chart 2. Tripodands with 1,3-Dioxane Units (IV) and Target Cryptands (V and VI)



Scheme 1



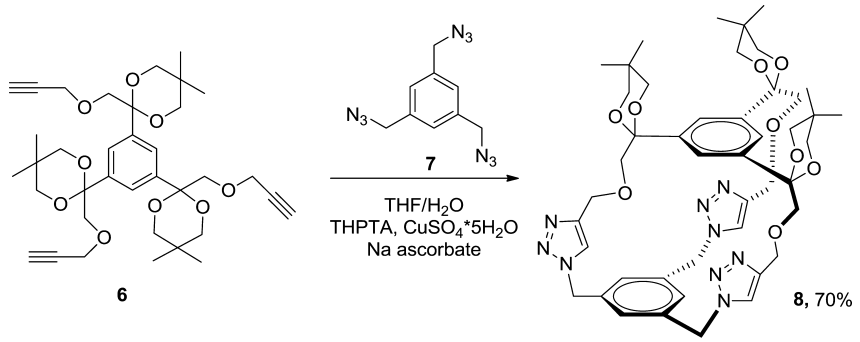
The reaction of **1** with 1,3,5-benzene tricarboxylic acid trichloride **9**, surprisingly, led to the obtaining of cryptand **10**, which corresponds to the 2 + 2 reaction (dimer, 38%, Scheme 3). MS investigations of the crude product revealed the formation of small amounts of the 3 + 3 cryptand (trimer; could not be isolated), in addition to the main compound (the dimer), but no formation of monomer (target 1 + 1 product) was observed.

In order to investigate the structure and the properties of a more simple [4.4.4]cyclophane, the deprotection of the carbonyl groups in cryptand **4** was carried out (Scheme 4). Conditions employed for the already reported similar [4.4]-cyclophane,[1d] i.e., the deprotection with cerium ammonium nitrate (CAN) and HCl, produced mixtures of mono-, di-, and tri-deprotected products, which are difficult to separate, while the deprotection reaction with trifluoroacetic acid (TFA) gave in good yields (92%) the completely deprotected product, the target cryptand **11**.

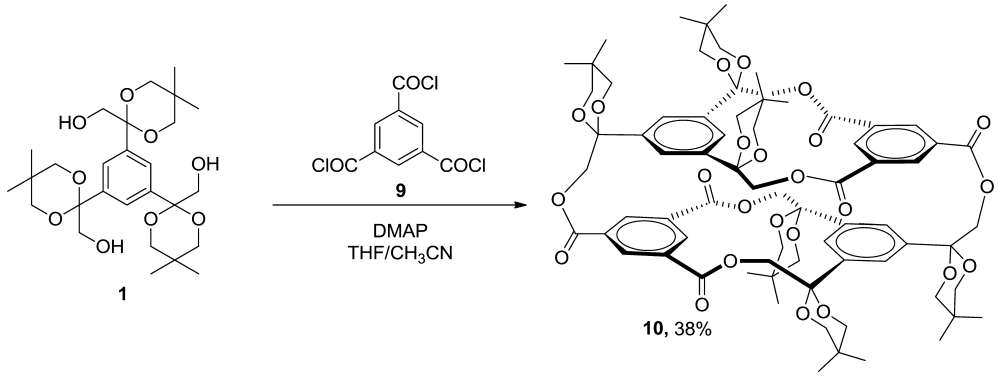
Structural Investigations in Solid State. Suitable crystals for single crystal X-ray diffractometry investigations were obtained only for **4**.

dx.doi.org/10.1021/jo401432y | J. Org. Chem. 2013, 78, 8722−8729

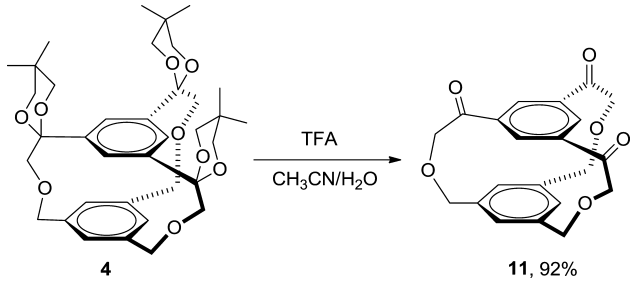
Scheme 2



Scheme 3



Scheme 4



The single crystal X-ray diffraction on compound **4** reveals that the asymmetric unit, having a 3-fold symmetry, consists of a single molecule solvate with chloroform (Figure 1). The aromatic rings of the cryptand are perfectly parallel [angle between planes defined by the rings is 0° within standard deviation].

Each cryptand molecule is associated through 12 weak hydrogen bonds with three other neighboring molecules. The H bonds involve the H(12) atom of the basal aromatic ring, H(9b) atom of the methylene bridge on one hand, and oxygen O(1) of the 1,3-dioxane ring and oxygen O(3) atom of the bridge on the other hand [C(9)−H(9b)···O(3) = 2.54 Å, C(12)−H(12)···O(1) = 2.58 Å, Σr_{vdW}(H,O) = 2.60 Å[15]], leading to a sheet-like supramolecular assembly. The orientation of molecules within these sheets is head-to-tail (Figures 2 and 3).

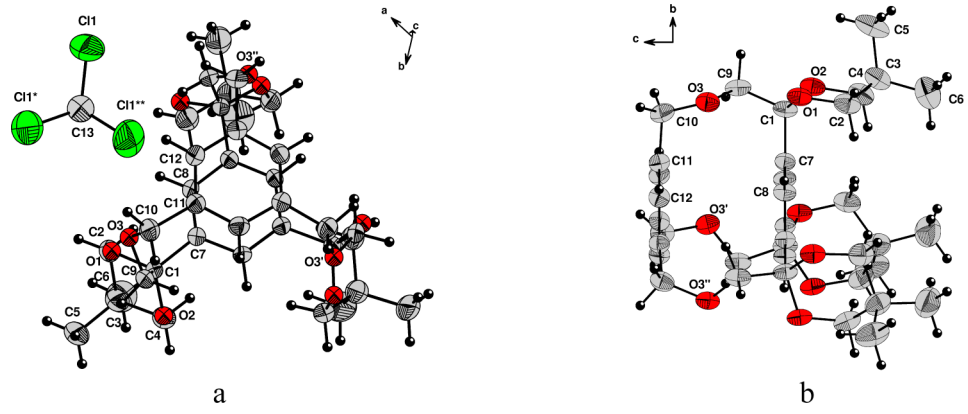


Figure 1. Views of the asymmetric unit of **4**·$CHCl_3$ solvate (a) and of the cryptand **4** (solvent was removed for clarity) along the *a* axis (b) with 40% probability ellipsoids). Symmetry equivalent atoms are given by "prime" [$-y, x - y, z$], "double prime" [$-x + y, -x, z$], "*" [$1 - y, 1 + x - y, z$] and "**" [$-x + y, 1 - x, z$].

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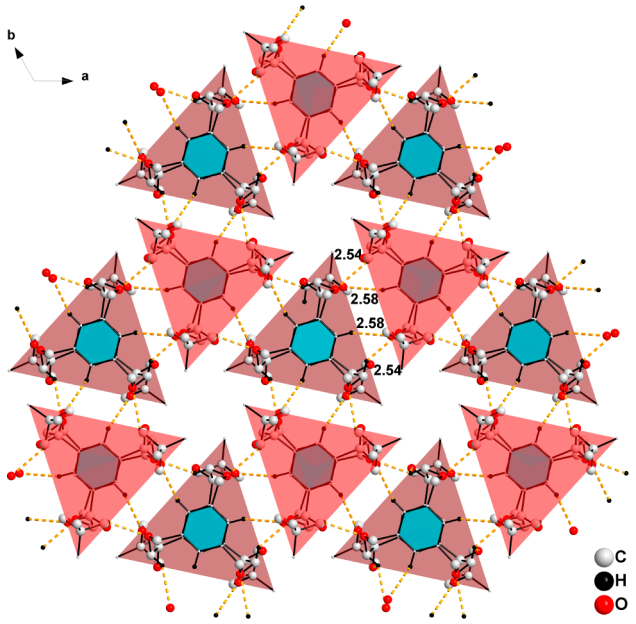


Figure 2. View along *c* axis of the supramolecular associations through H···O bonds between head-to-tail arranged molecules of **4**. Only hydrogen atoms involved in interactions are shown. Different colors were used for the representation of the differently oriented molecules.

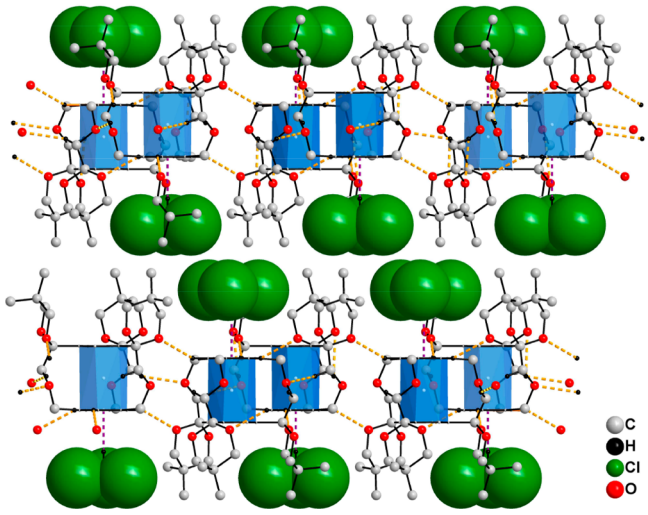


Figure 4. View along *b* axis showing H···π interactions between solvent $CHCl_3$ molecules and aromatic rings, leading to the three-dimensional structure. Solvent molecules are displayed with van der Waals radii. The aromatic parts of the cryptand are shown as blue hexagonal prisms.

Strong H−π interactions are observed between the basal aromatic ring of each cryptand and a chloroform molecule [centroid(C_6H_3)···H(13) = 2.374(1) Å, Σr_{vdW}(H,C) = 3.00 Å[15]]. The chloroform molecule is placed exactly above the centroid of the aromatic ring [the angle between the C(13)−H(13) bond vector and the normal of the plane is 180° (0°) within standard deviation]. These values are at the extremity of the range for the reported data for the highest H−π interactions involving chloroform and aromatic rings (the already reported distances and angles are in the domains 2.53 ± 0.17 Å and 169 ± 11°, respectively)[16] and suggest the high strength of the H−π interactions in our case. Overall, the contacts between adjacent layers are made by the hydrophobic interactions between the methyl groups located at position 5 of the 1,3-dioxane rings (Figure 4).

Structural Investigations in Solution. All cryptands obtained by 1 + 1 reactions exhibit simple NMR spectra, which suggest not only the equivalence of the chains, but also their flexible behavior. For **4**, **5**, and **8**, the ^{1}H NMR spectra (Figure 5) reveals an AB system for the protons of the 1′,5′-dioxacyclohexane rings (Table 1) and singlets for the other types of protons [Figure 5, Table 1; excepting the protons of the triphenylamino unit in **5**, which give (formally) doublets (AA′XX′ system)].

In the case of the 2 + 2 reaction product **10** (a cartoon representation is given in Chart 3), similar building blocks become different because of their belonging to either the formal macrocycles or to the bridges that connect the macrocyclic units.

Thus, the 1,5-dioxaalkylidene units (formally 1,3-dioxane rings) belonging to the macrocycles (noted with D) are different of those of the chains (noted with C). Similarly the CH_2 groups are different if they are incorporated in the macrocycles or if they belong to the chains. The ^{1}H NMR spectrum of **10** (Figure 5e) exhibits two signals (intensities ratio 1/2; "inside" and "outside" macrocycle aromatic protons) for each type of aromatic rings (A and B). The CH_2 groups of the chains, the equatorial and axial methyl groups located at the positions 3′ of the 1′,5′-dioxaalkylidene groups, as well as the protons located at positions 2′ and 4′ of the 1′,5′-dioxaalkylidene groups (saturated heterocycles) show two sets of signals, one set belonging to the protons of the macrocycles

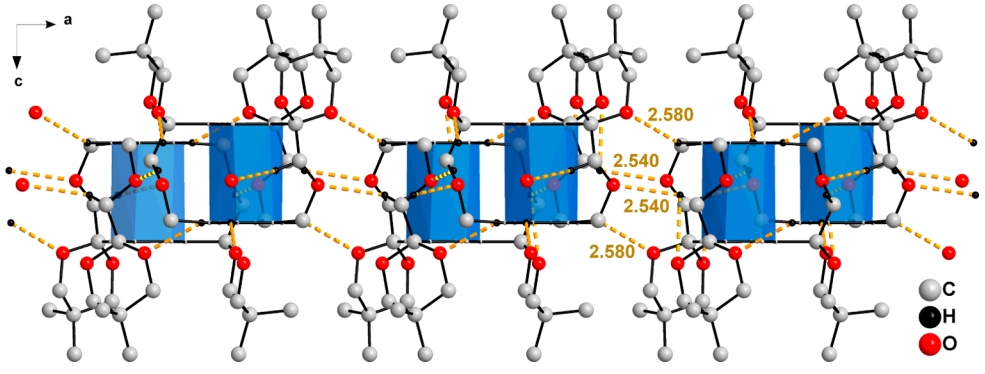


Figure 3. View along *b* axis of the supramolecular associations through H···O bonds between head-to-tail arranged molecules of **4**. Only hydrogen atoms involved in interactions are shown. The aromatic parts of the cryptand are shown as blue hexagonal prisms.

dx.doi.org/10.1021/jo401432y | J. Org. Chem. 2013, 78, 8722−8729

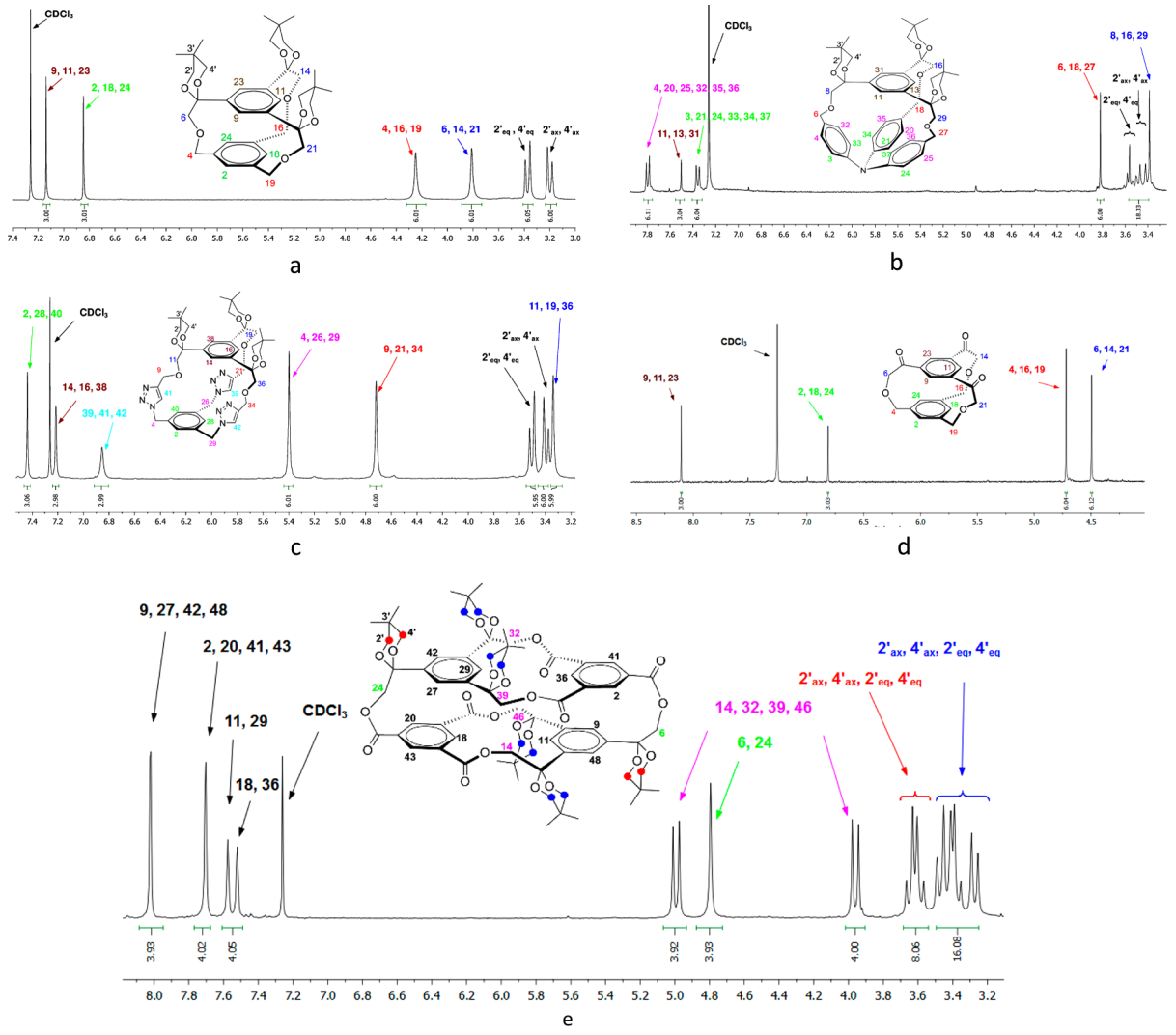
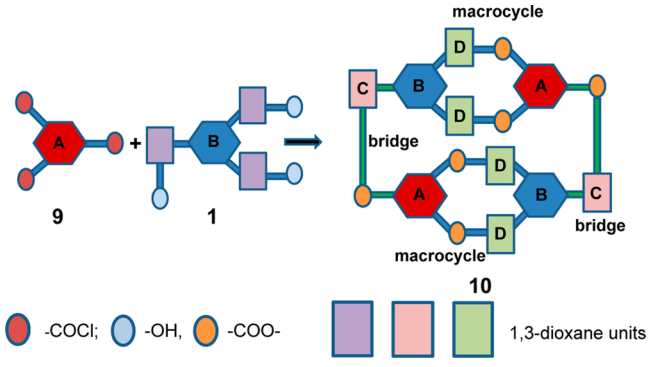


Figure 5. ^{1}H NMR spectra (fragments) of compounds **4** (a), **5** (b), **8** (c), **10** (e), and **11** (d).

Table 1. NMR Data (Selected) for Compounds 4, 5, 8, and 11

	chains (CH_2 groups) (ppm)			dioxacyclohexane units		
compd	C–CH_2–O	–CH_2–Ar	N–CH_2–O	2′a,4′a; 2′e,4′e	3′-CH_3 (e)	3′-CH_3 (a)
4	3.81	4.25	–	3.20; 3.37	0.50	1.24
5	3.39	3.82	–	3.44; 3.53	0.62	1.30
8	3.34	5.40	4.72	3.39; 3.50	0.64	1.29
11	4.49	4.72	–	–	–	–

Chart 3. Cartoon Representation of the Formal Synthesis of 10 Revealing the Differences among Similar Building Blocks



and the other set is given by the similar protons of the chains (ratio of signals intensities 2/1). The signal belonging to the CH_2 groups of the chains appears as one singlet, while the protons of the CH_2 groups of the macrocycles give an AB system (the protons of the same CH_2 group are diastereotopic).

Similarly, positions 2′ and 4′ of the dioxacyclohexane rings belonging to the bridges (type C) are equivalent in NMR and give one AB system, while the protons of the similar positions (2′ and 4′) of the dioxacyclohexane rings of the macrocycles (type D) are diastereotopic and give different signals in the NMR spectrum (two AB systems, Figure 5e). Hence, a comparison can be made between compound **10** and a [4.4]cyclophane in which the aromatic units were replaced by the "rigid" macrocycles. The NMR differences between the signals of the chains and of the similar units included in the macrocycles can be explained by the flexibility of the chains (usual flipping of the chains in [4.4]cyclophanes)[1d,17] and the hindrance of this equilibrium in the macrocycles. The flipping of the chains render equivalent positions 2′ and 4′ of the 1′,5′-

dx.doi.org/10.1021/jo401432y | J. Org. Chem. 2013, 78, 8722–8729

dioxaalkylidene units on one side and the H atoms of the CH_2 groups on the other side.

CONCLUSIONS

The good yields synthesis by various procedures (etherification, esterification, and click reactions) of several cryptands exhibiting 1,3,5-tris(2′-*R*-1′,3′-dioxan-2′-yl)-benzene units was reported. The reactions led to the target cryptands in etherification and click procedures, while the macrocyclization based on esterification reactions determined the formation of the 2 + 2 reaction product (dimer). The small cryptand **11** obtained by the deprotection of **4** exhibits three reactive carbonyl groups, and it is an interesting building block for further developments. The molecular structure of **4** revealed the formation of a solvate, with strong CH−π contact between the chloroform and the cryptand.

EXPERIMENTAL SECTION

General Experimental Data. ^{1}H NMR (300, 400 MHz) and ^{13}C NMR (75, 100 MHz) spectra, COSY, HSQC, and HMBC were recorded in $CDCl_3$ at rt on 300 and 400 MHz spectrometers using the solvent line as reference. Atmospheric pressure chemical ionization (APCI, positive ions mode) high-resolution mass spectra were recorded on LTQ ORBITRAP XL spectrometer using external mass calibration. Melting points were measured with a routine melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was conducted on silica gel 60 F254 TLC plates, while preparative column chromatography was performed using 40−63 μm silica gel. Solvents were dried and distilled under argon using standard procedures. Chemicals of commercial grade were used without further purification. X-ray diffraction data were collected at room temperature on a diffractometer using graphite monochromated Mo Kα radiation (λ = 0.71073 Å). For this purpose the crystal was mounted on a cryo-loop with Paraton oil. The structure was solved by direct methods (SHELXS-97)[18] and refined by full matrix least-squares procedures based on F^2 with all measured reflections (SHELXL-97).[18] All non-hydrogen atoms were refined anisotropically. H atoms were introduced in their idealized positions and refined as riding. Further details on the data collection and refinement methods can be found in Table 1 in the Supporting Information. The drawings were created with the Diamond program.[19]

These data can be also obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax, (+44) 1223-336-033; or e-mail, deposit@ccdc.cam.ac.uk). The deposition number is CCDC 904025 (**4**).

Compound **1** was already reported in a previous work;[20] compounds **2**,[21] **3**,[22] and **7**[21] were obtained according with published procedures.

Procedure for the Synthesis of 4 and 5. A solution of triol **1** [0.98 mmol (**4**)/0.39 mmol (**5**)] in THF (10/5 mL) was added to a suspension of NaH (5.88/2.35 mmol) in anhydrous THF (300/150 mL), under inert atmosphere (Ar). The mixture was refluxed for 1 h, followed by the addition of the tribrominated derivative **2** (0.98 mmol) or **3** (0.39 mmol) in THF (10 mL) with a push-syringe for 72 h. The reaction mixture was refluxed for another 24 h and cooled to room temperature, the solvent was removed in vacuo, and the residue was dissolved in CH_2Cl_2 and washed with water; the organic layer was separated, dried over anhydrous $MgSO_4$, filtered and purified by flash chromatography [ethylacetate:pentane = 2:3 (**4**) or 1:4 (**5**)].

7,7,13,13,22,22-Tris(3′,3′-dimethyl-1′,5′-dioxapentan-1′,5′-diyl)-5,15,20-trioxatetracyclo[8.8.4.1^{3,17}.1^{8,12}]tetracosa-1,3-(24),8(23),9,11,17-hexaene 4. White solid (347 mg, 56%, R_f = 0.54): mp = 279−280 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.50 (s, 9H, 3′-CH_{3eq}), 1.24 (s, 9H, 3′-CH_{3ax}), 3.20 (d, J = 12 Hz, 6H, 2′-H_{ax}, 4′-H_{ax}), 3.37 (d, J = 12 Hz, 6H, 2′-H_{eq}, 4′-H_{eq}), 3.81 (s, 6H, 6-H, 14-H, 21-H), 4.25 (s, 6H, 4-H, 16-H, 19-H), 6.85 (s, 3H, 2-H, 18-H, 24-H), 7.14 (s, 3H, 9-H, 11-H, 23-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 22.1 (3′-CH_{3eq}), 22.9 (3′-CH_{3ax}), 30.2 (3′-C), 70.9 (2′-C, 4′-C), 73.0 (6-C, 14-C, 21-C), 75.3 (4-C, 16-C, 19-C), 99.5 (7-C, 13-C, 22-C), 128.0 (9-C, 11-C, 23-C), 130.9 (2-C, 18-C, 24-C), 136.4 (8-C, 10-C, 12-C), 137.00 (1-C, 3-C, 17-C); HRMS (APCI+) m/z calcd for $C_{36}H_{49}O_9$ $[M + H]^+$ 625.3371, found 625.3370.

9,9,15,15,30,30-Tris(3′,3′-dimethyl-1′,5′-dioxapentan-1′,5′-diyl)-1-aza-7,17,28-trioxahexacyclo-[10.10.8.2^{2,5}.2^{19,22}.2^{24,26}.1^{10,14}]heptatricosa-2,4,10-(31),11,13,19,21,23,25,32,34,36-dodecaene 5. Light yellow solid (144 mg, 0.18 mmol, 47%, R_f = 0.47): mp = 63 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.62 (s, 9H, 3′-CH_{3eq}), 1.30 (s, 9H, 3′-CH_{3ax}), 3.39 (s, 6H, 8-H, 16-H, 29-H), 3.44 (d, J = 12 Hz, 6H, 2′-H_{ax}, 4′-H_{ax}), 3.53 (d, J = 12 Hz, 6H, 2′-H_{eq}, 4′-H_{eq}), 3.82 (s, 6H, 6-H, 18-H, 27-H), 7.35 (d, 6H, J = 9 Hz, 3-H, 21-H, 24-H, 33-H, 34-H, 37-H), 7.50 (s, 3H, 11-H, 13-H, 31-H), 7.79 (d, 6H, J = 9 Hz, 4-H, 20-H, 25-H, 32-H, 35-H, 36-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.9 (3′-CH_{3eq}), 22.7 (3′-CH_{3ax}), 30.2 (3′-C), 53.4 (8-C, 16-C, 29-C), 66.0 (6-C, 18-C, 27-C), 71.2 (2′-C, 4′-C), 100.8 (9-C, 15-C, 30-C), 120.9 (11-C, 13-C, 31-C), 127.3 (3-C, 21-C, 24-C, 33-C, 34-C, 37-C), 129.4 (4-C, 20-C, 25-C, 32-C, 35-C, 36-C), 136.9 (5-C, 19-C, 26-C), 137.9 (10-C, 12-C, 14-C), 146.5 (2-C, 22-C, 23-C); HRMS (APCI+) m/z calcd for $C_{48}H_{58}NO_9$ $[M + H]^+$ 792.4106, found 792.4110.

1,3,5-Tris[1′,1′-(3″,3″-dimethyl-1″,5″-dioxapentan-1″,5″-diyl)-3′-oxahexan-5′-yn-1′-yl]benzene 6. 1,3,5-Tris(5,5-dimethyl-2-hydroxymethyl-1,3-dioxan-2-yl)-benzene **1** (1.37 mmol, 700 mg, 1 equiv) was dissolved in dichloromethane (20 mL); a saturated aqueous solution of NaOH and *tert*-butyl ammonium bromide (0.25 equiv) were added and then stirred together for 30 min at 10 °C. After adding propargyl bromide (0.734 mL sol. 80% in toluene, 6.594 mmol, 4.8 equiv), the reaction mixture was stirred overnight at room temperature. At the end the final solution was diluted with 60 mL of dichloromethane, and the organic layer was washed with water, dried over anhydrous $MgSO_4$, and filtered. After the evaporation (in vacuo) of the solvent, the pure compound was obtained by column chromatography separation (ethylacetate:pentane = 1:4). White solid (444 mg, 0.71 mmol, 52%, R_f = 0.53): mp = 126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.59 (s, 9H, 3″-CH_{3eq}), 1.28 (s, 9H, 3″-CH_{3ax}), 2.28 (t, 3H, J = 2.1 Hz, 6′-H), 3.44 (s, 12H, 4″-H, 6″-H), 3.62 (s, 6H, 2′-H), 4.16 (d, 6H, J = 2.1 Hz, 4′-H), 7.53 (s, 3H, 2-H, 4-H, 6-H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 21.9 (3″-CH_{3eq}), 22.9 (3″-CH_{3ax}), 30.2 (3″-C), 58.9 (4′-C), 71.3 (2″-C, 4″-C), 74.3 (6′-C), 76.4 (2′-C), 79.6 (5′-C), 100.5 (1′-C), 127.8 (2-C, 4-C, 6-C), 137.6 (1-C, 3-C, 5-C). ESI-MS m/z = 647.3 $[M + Na]^+$, 663.4 $[M + K]^+$. Calculated for $C_{36}H_{48}O_9$: C, 69.21; H, 7.74. Found: C, 69.39; H, 7.58.

12,12,18,18,37,37-Tris(3′,3′-dimethyl-1′,5′-dioxapentan-1′,5′-diyl)-5,6,7,23,24,25,30,31,32-nonaaza-10,20,35-trioxaheptacyclo[9.3.3.1^{5,8}.1^{13,17}.1^{22,25}.1^{3,27}.1^{30,33}]dotetraconta-1,3(40),6,8(41),13(38),14,16,22(39),23,27,31,33(42)-dodecaene 8. Compound **6** (250 mg, 0.4 mmol) was dissolved in a 1:1 mixture of H_2O:THF (40 mL). After degassing the reaction mixture, $CuSO_4 \cdot 5H_2O$ (200 mg, 0.8 mmol) and sodium ascorbate (31 mg, 0.16 mmol) were added at room temperature, followed by the addition of 1,3,5-tris(azidomethyl)benzene **7** (97 mg, 0.4 mmol) and TBTA {tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine; 17 mg, 0.033 mmol}. The new mixture was stirred at room temperature for 3 h and then extracted with dichloromethane and washed with brine. The layers were separated, and the organic phase was dried on anhydrous $MgSO_4$, filtered, and evaporated in order to obtain the crude product. Purification was achieved on column chromatography (CH_2Cl_2:MeOH = 95:5, R_f = 0.24) to give compound **8** (243 mg, 0.28 mmol, 70%) as a white solid: mp = 175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.64 (s, 9H, 3′-CH_{3eq}), 1.29 (s, 9H, 3′-CH_{3ax}), 3.34 (s, 6H, 11-H, 19-H, 36-H), 3.39 (d, 6H, J = 11 Hz, 2′-H_{ax}, 4′-H_{ax}), 3.50 (d, 6H, J = 11 Hz, 2′-H_{eq}, 4′-H_{eq}), 4.72 (s, 6H, 9-H, 21-H, 34-H), 5.40 (s, 6H, 4-H, 26-H, 29-H), 6.85 (s, 3H, 39-H, 41-H, 42-H), 7.21 (s, 3H, 14-H, 16-H, 38-H), 7.44 (s, 3H, 2-H, 28-H, 40-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 22.1 (3′-CH_{3eq}), 22.7 (3′-CH_{3ax}), 30.2 (3′-C), 53.4 (4-C, 26-C, 29-C), 66.2 (9-C, 21-C, 34-C), 71.3 (2′-C, 4′-C), 77.2 (11-C, 19-C, 36-C), 100.8 (12-C, 18-C, 37-C), 120.9 (39-C, 41-C, 42-C), 127.1 (14-C, 16-C, 38-C), 129.2 (2-C, 28-C, 40-C), 136.9 (13-C, 15-C, 17-C), 137.72 (1-C, 3-C, 27-C), 146.3 (8-C, 22-C, 33-

dx.doi.org/10.1021/jo401432y | J. Org. Chem. 2013, 78, 8722−8729

C); HRMS (APCI+) m/z calcd for $C_{45}H_{58}N_9O_9$ $[M + H]^+$ 868.4352, found 868.4357.

7,7,13,13,25,25,31,31,40,40,47,47-Hexakis(3′,3′-dimethyl-1′,5′-dioxapentan-1′,5′-diyl)-5,15,23,33,48,45-hexaoxaheptacyclo[26.8.4.4^{10,19}.1^{3,35}.1^{8,12}.1^{17,21}.1$^{26.30}$]-octatetraconta-1,3(41),8(48),9,11,17(43),18,20,26(42),27,29,35-dodecaene 10. 1,3,5-Benzenetricarbonyl trichloride **9** (1.47 mmol) in anhydrous THF (10 mL) was added via a push-syringe over 24 h to a solution of compound **1** (0.98 mmol) in a mixture of dry THF (50 mL), acetonitrile (200 mL), and DMAP (1.96 mmol). The reaction mixture was stirred overnight at room temperature, and then the mixture of solvents was removed in vacuo, and the residue dissolved in diethylether and washed with water. The organic layer was separated, dried over anhydrous $MgSO_4$, and filtered, the solvents were removed in vacuo, and the crude product was purified by column chromatography (ethyl acetate:pentane = 1:3; R_f = 0.50) giving a white solid (496 mg, 0.372 mmol, 38%): mp = 360 °C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.62 (s, 12 H, 3′-$CH_{3eq"D"}$), 0.79 (s, 6H, 3′-$CH_{3eq"C"}$), 1.18 (s, 12H, 3′-$CH_{3ax"D"}$), 1.27 (s, 6H, 3′-$CH_{3ax"C"}$), 3.27, 3.37, 3.43, 3.47 [four d (rings D), J = 12 Hz, 16H, 2′-H_{ax}, 4′-H_{ax}, 2′-H_{eq}, 4′-H_{eq}], 3.58, 3.65 [two d (rings C), J = 12 Hz, 8H, 2′-H_{ax}, 4′-H_{ax}, 2′-H_{eq}, 4′-H_{eq}], 3.96, 4.49 [two d, J = 12 Hz, 8H, 14-H, 32-H, 39-H, 46-H), 4.79 (s, 4H, 6-H, 24-H), 7.52 (s, 2H, 18-H, 36-H), 7.58 (s, 2H, 11-H, 29-H), 7.70 (s, 4H, 2-H, 20-H, 41-H, 43-H), 8.02 (s, 4H, 9-H, 27-H, 42-H, 48-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 22.3 (3′-$CH_{3eq"D"}$), 22.5 (3′-$CH_{3eq"C"}$), 22.8 (3′-$CH_{3ax"C"}$), 22.9 (3′-$CH_{3ax"D"}$), 30.2 (3′-$C_{"C"}$), 30.4 (3′-$C_{"D"}$), 69.2 (6-C, 24-C), 69.4 (14-C, 32-C, 39-C, 46-C), 71.0, 71.5, 71.9 [(2′-$C_{"C"}$, 4′-$C_{"C"}$), 2′-$C_{"D"}$, 4′-$C_{"D"}$], 99.6 (13-C, 31-C, 40-C, 47-C), 100.6 (7-C, 25-C), 127.5 (2-C, 20-C, 41-C, 43-C), 129.77 (3-C, 21-C), 130.10 (18-C, 36-C), 130.33 (1-C, 17-C, 19-C, 35-C), 132.6 (9-C, 27-C, 42-C, 48-C), 137.3 (8-C, 26-C), 137.7 (11-C, 29-C), 138.7 (10-C, 12-C, 28-C, 30-C), 162.3 (4-C, 16-C, 22-C, 34-C), 163.8 (37-C, 44-C); HRMS (APCI+) m/z calcd for $C_{72}H_{85}O_{24}$ $[M + H]^+$ 1333.5425, found 1333.5429.

5,15,20-Trioxatetracyclo[8.8.4.1^{3,17}.1^{8,12}]tetracosa-1,3(23),8-(24),9,11,17-hexaene-7,13,22-trione 11. Trifluoroacetic acid (TFA, 0.25 mL) and a drop of water were added to a stirred solution of compound **4** (24 mg, 0.038 mmol) in MeCN (1 mL). The solution was refluxed for 48 h. After cooling to room temperature, TFA was evaporated in vacuo, and then water (5 mL) was added, and the mixture was extracted with dichloromethane and washed with saturated $NaHCO_3$ solution (3 × 10 mL). The organic layers were dried with $MgSO_4$ and filtered, and the solvent was evaporated in vacuo. The crude product was further purified by washing with pentane and recrystallization in diethyl ether giving **11** (13 mg, 0.035 mmol, 92%, R_f = 0.41 (pentane:ethyl acetate = 20:1) as a white solid: mp = 154−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 4.50 (s, 6 H, 6-H, 14-H, 21-H), 4.72 (s, 6H, 4-H, 16-H, 19-H), 6.81 (s, 3H, 2-H, 18-H, 24-H), 8.11 (s, 3H,9-H, 11-H, 23-H);. ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 76.3 (4-C, 16-C, 19-C), 79.3 (6-C, 14-C, 21-C), 130.6 (2-C, 18-C, 24-C), 135.2 (9-C, 11-C, 23-C), 137.0 (1-C, 3-C, 17-C), 139.0 (8-C, 10-C, 12-C), 201.5 (7-C, 13-C, 22-C); HRMS (APCI+) m/z calcd for $C_{21}H_{19}O_6$ $[M + H]^+$ 367.1176, found 367.1175.

■ ASSOCIATED CONTENT

Supporting Information

General data regarding the X-ray diffractometry measurement, the table of the parameters for the crystallographic determinations, CIF file, and the copies of ^{1}H and ^{13}C NMR spectra for **4**−**6**, **8**, **10**, and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to CNCS−UEFISCDI for the financial support of this work, Project PN-II-ID-PCCE-2011-2-0050

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