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# Synthesis and stereochemistry of some new 1,3,5-Tris(1,3-dioxan-2-yl)-benzene derivatives

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**Abstract:** The synthesis and the stereochemistry of new 1,3,5-tris(1,3-dioxan-2-yl)-benzene derivatives are reported. The anancomeric structure and the axial orientation of the aryl group with respect to all 1,3-dioxane rings, and the *cis-trans* isomerism of some of the compounds are revealed. The data are supported by NMR investigations and by the molecular structure of one compound determined by single crystal X-ray diffractometry.


*Keywords: 1,3-Dioxanes; Conformational analysis; NMR; X-ray structure,* cis-trans *isomers*

## 1 Introduction

The synthesis and the investigations on the stereochemistry of some 2-aryl-1,3-dioxane derivatives bearing two 1,3-dioxane rings connected to the same aromatic group (Scheme 1) were previously reported [1–6].

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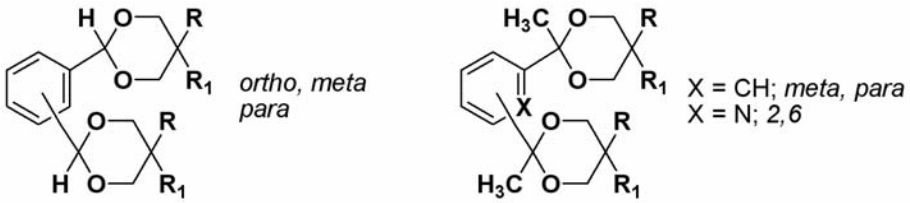
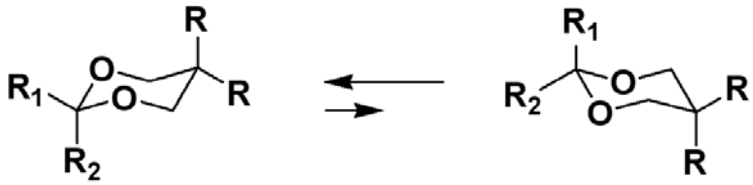



**Scheme 1** General formulae of the investigated bis(1,3-dioxan-2-yl)arene derivatives.

The NMR experiments revealed the anancomeric behaviour of the compounds. The aromatic group prefers the equatorial orientation for both saturated heterocycles if this group is the unique substituent at the position 2 of the 1,3-dioxane rings, while the aromatic group shows an axial preference for both 1,3-dioxane rings in the compounds which exhibit aryl and methyl groups at the ketal part of the heterocycles (scheme 1). These results are supported by the thermodynamic data reported for 2-aryl- and 2-aryl,2-methyl-1,3-dioxanes. The A values (A = free conformational enthalpy [7]) of aryl groups located in the acetal part of the 1,3-dioxane ring are high (*e.g.* $A_{Ph}$= 13.04 kJ/mol [8]) and 2-aryl-1,3-dioxanes are anancomeric compounds. They show high preference for the conformer presenting the aromatic group ($R^1$ = aryl, $R^2$= H, Scheme 2) in equatorial orientation [1–3, 9, 10]. At position 2 of the 1,3-dioxane ring the A-value of methyl group ($A_{Me}$ = 16.63 kJ/mol [8]) is higher than the A-value of phenyl group and the thermodynamic measurements [11] showed that the equatorial preference of methyl group in 2-methyl-2-phenyl-1,3-dioxanes is three times higher than expected by the simple addition of the A values of the two substituents ($\Delta G^o_{exp}$ = 10.11 kJ/mol; $A_{Me}$-$A_{Ph}$ = 3.63 kJ/mol) and the conformational equilibrium of the corresponding 2,2-disubstituted-1,3-dioxanes ($R^1$ = $CH_3$, $R^2$= aryl, Scheme 2) is strongly shifted towards the conformer exhibiting the aryl group in axial position [4, 6, 12].

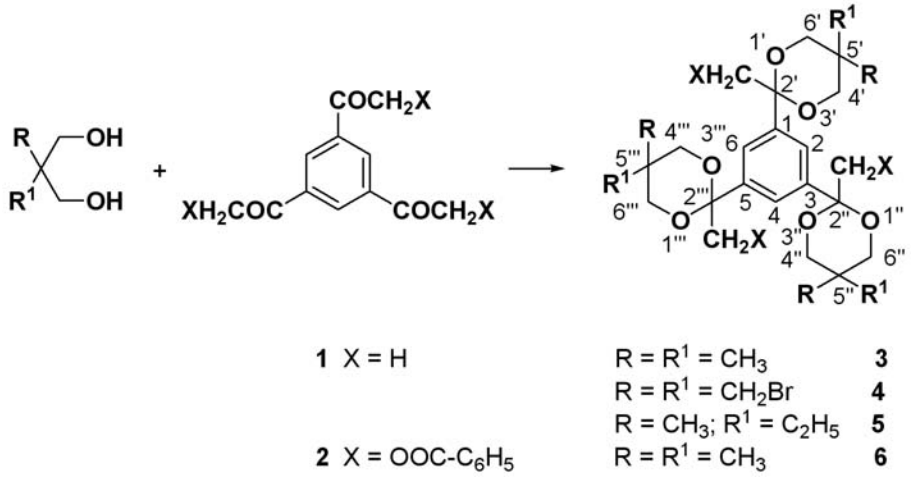


**Scheme 2** Conformational equilibria for 2-aryl-1,3-dioxane ($R^1$ = Ar, $R^2$ =H) and 2-aryl, 2-methyl-1,3-dioxane ($R^1$ = $CH_3$, $R^2$ =Ar) derivatives.

Derivatives with two 1,3-dioxane rings connected to the same aromatic ring were successfully used for the synthesis of macrocyclic cyclophanes [13, 14]. In order to obtain versatile substrates for the synthesis of new "host" molecules (1,3,5-cyclophanes) we considered it of interest to carry out the synthesis, and investigate the stereochemistry and the *preorganization* [15] for macrocyclisation of derivatives bearing three 1,3-dioxane rings connected to the same aromatic substrate.

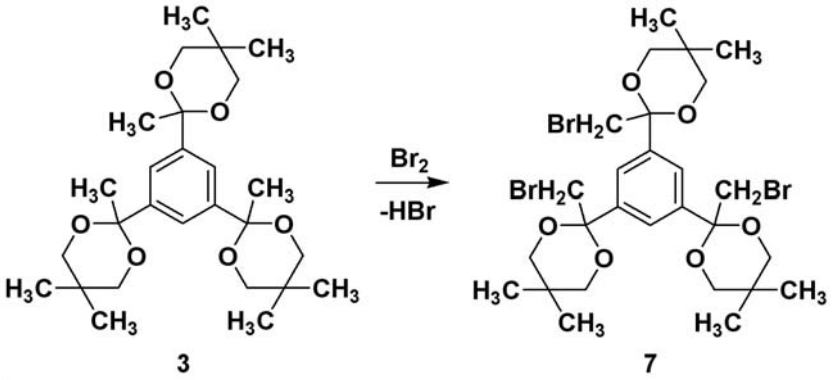
## 2 Results and discussion

New 1,3-dioxane derivatives (**3-6**) were obtained by the condensation of 1,3,5-triacetylbenzene **1** and of its $\alpha$,$\alpha$',$\alpha$"-tribenzoate derivative **2** with several 1,3-propanediols (Scheme 3).




**Scheme 3** Synthesis of compds **3-6**.

High yield of the tribrominated derivative **7** was obtained by the bromination reaction of compound **3** using the usual procedure for the bromination of cyclic acetals (Scheme 4) [16, 17].

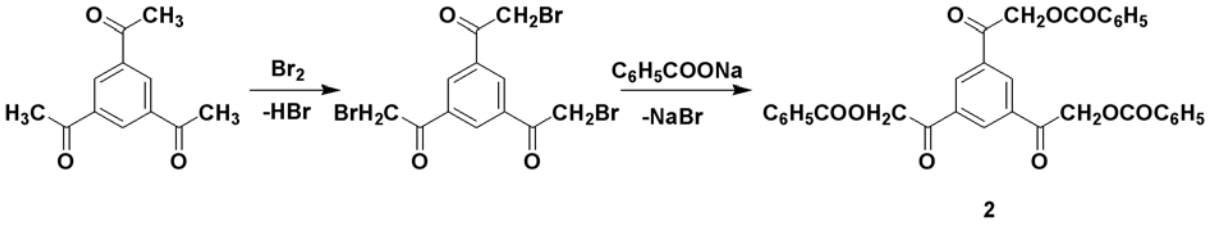



**Scheme 4** Synthesis of compd **7**.

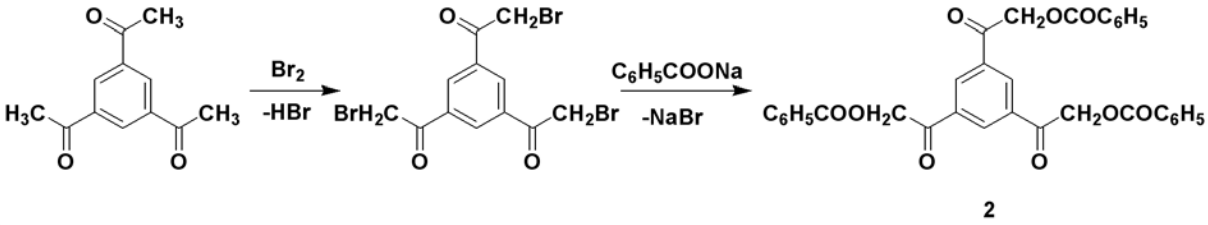
Compound **7** was reacted with $C_6H_5COONa$ in order to obtain the corresponding triester **6**. All the attempts to run this reaction failed and we believe that the substitution reaction of the bromine atoms could not be carried out because the steric hindrance in **7** is very high. In order to obtain **6** the synthesis of **2** was done starting from triacetylbenzene in a two steps sequence (Scheme 5). Then **2** was condensed with neopentylglycol to give the tri-1,3-dioxane-triester **6** (Scheme 3).

Compound **6** was deprotected in good yields to triol **8** (Scheme 6)

The structure of **3-8** was investigated by NMR methods and by the single crystal X ray molecular structure of compound **3**. The molecular structure of **3** (Figure 1) shows the




**Scheme 5** Synthesis of compd **2**.




**Scheme 6** Synthesis of compd **8**.

axial orientation of the aromatic ring for the three 1,3-dioxane rings and the orientation of the three heterocycles on the same side of the aromatic group.

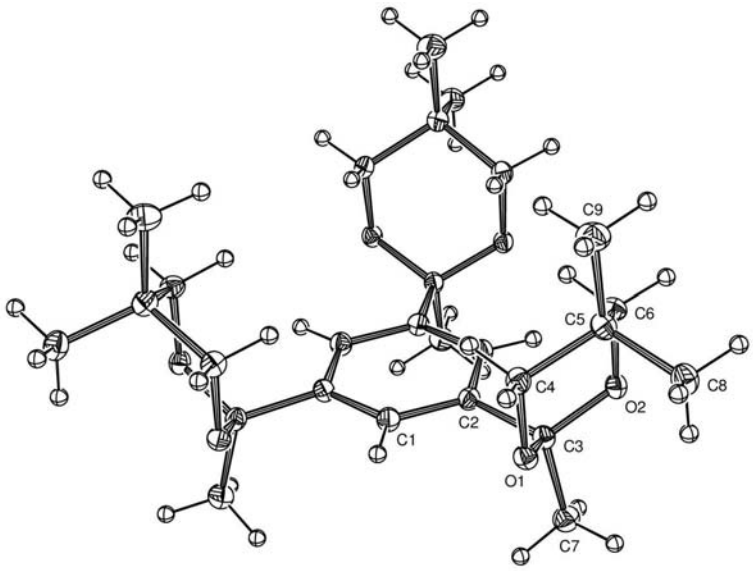



**Fig. 1** ORTEP diagram for compd **3**.

NMR investigations revealed the anancomeric structure of the heterocycles and the similar magnetic environments for the three 1,3-dioxane rings of compounds **3**,**4** and **6-8** (as a consequence their NMR spectra exhibit only one set of signals for the protons of the heterocycles). Due to the anancomeric behaviour of the compounds the $^1$H NMR spectra exhibit different signals for the axial and equatorial protons of the heterocycles and for the protons of the corresponding axial and equatorial groups located at positions 5', 5" and 5"' (Table 1). The signal corresponding to the aromatic protons is a singlet and proves the equivalence in NMR of the three 1,3-dioxane rings. The NOESY spectrum (Figure 2)

run with **4** shows important correlation between the singlet ($\delta$ = 7.42 ppm) belonging to the aromatic protons and the doublet ($\delta$ = 3.60 ppm) pertaining to the axial protons of the 1,3-dioxane rings. The other doublet ($\delta$ = 3.87 ppm) given by the equatorial protons of the heterocycles does not show correlations with the aromatic protons. The NOESY spectrum confirms the axial orientation of the aromatic ring for all the 1,3-dioxane rings in solution, too.

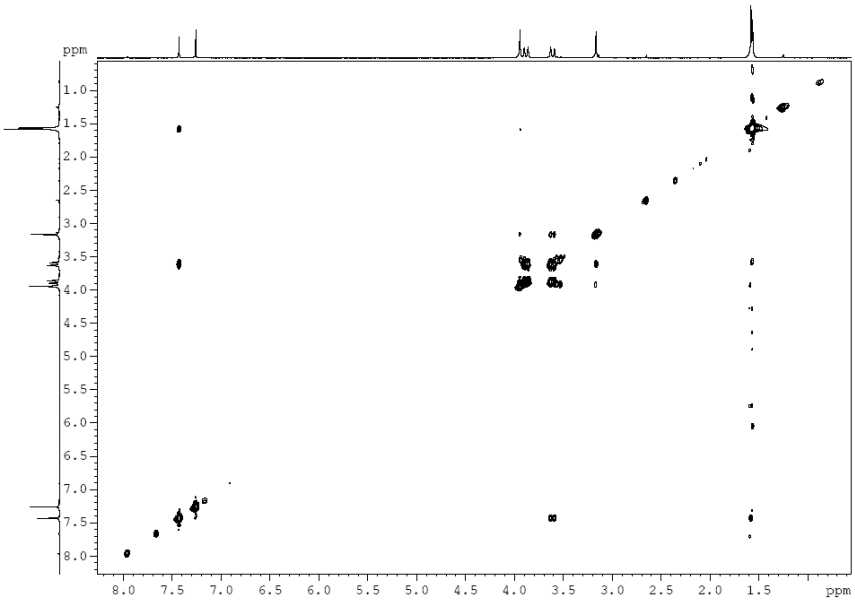


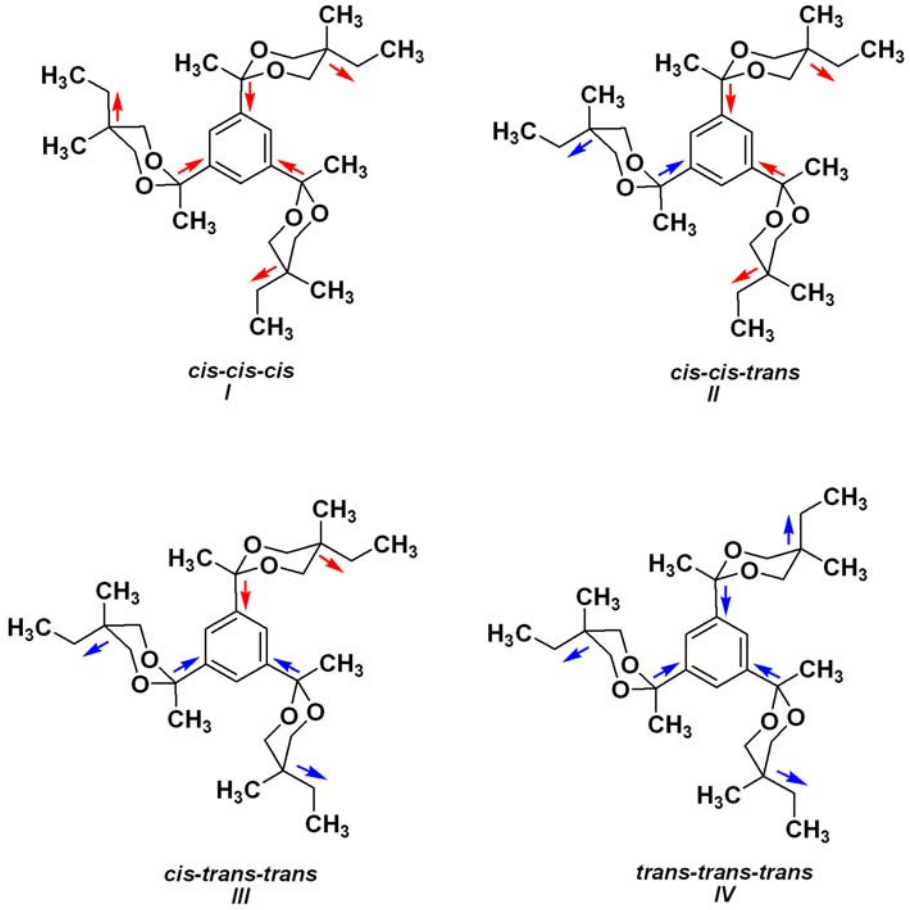

**Fig. 2** NOESY spectrum of compd **4**.

**Table 1** $^1$H-NMR data ($\delta$, ppm, $CDCl_3$) for compds **3**, **4**, **6-8**.

| Compound | 4'(4",4"')-H; 6'(6",6"')-H | | | 5'(5", 5"')-$CH_2$-X | | |
|---|---|---|---|---|---|---|
| | axial | equatorial | $\Delta$ax-eq | axial | equatorial | $\Delta$ax-eq |
| 3 | 3.36 | 3.41 | 0.05 | 1.27 | 0.60 | 0.67 |
| 4 | 3.60 | 3.87 | 0.27 | 3.94 | 3.16 | 0.78 |
| 6 | 3.30 | 3.38 | 0.08 | 1.25 | 0.47 | 0.78 |
| 7 | 3.37 | 3.51 | 0.14 | 1.33 | 0.61 | 0.72 |
| 8 | 3.40 | 3.48 | 0.08 | 1.29 | 0.62 | 0.67 |

Compound **5** exhibits a peculiar stereochemistry. The different substituents located at positions 5' (5" and 5"') generate *cis* and *trans* isomers. The reference groups are the aromatic substituent at positions 2' (2" and 2"') and the ethyl groups at positions 5', 5" and 5"'. Four configuration isomers are possible: *cis-cis-cis* (I); *cis-cis-trans* (II); *cis-trans-trans* (III) and *trans-trans-trans* (IV) (Scheme 7). The A-values of methyl and ethyl substituents at position 5 of the 1,3-dioxane ring are very close ($A_{Me}$ = 3.7 kJ/mol [10]; $A_{Et}$ = 3.3 kJ/mol [10]), while the aromatic substituent in the ketal part (positions 2', 2", 2"') strongly prefers the axial orientation. The isomers of **5** exhibit anancomeric

structures (as the NMR spectrum of the row product shows) with axial orientation of the aromatic group and with statistically equal axial and equatorial orientations of the methyl and ethyl groups at positions 5', 5" and 5"'. Thus, the four isomers are obtained statistically and *cis-cis-trans* (II) and *cis-trans-trans* (III) isomers are the major ones (approximate ratios I/II/III/IV = 1/3/3/1). After repeated crystallization from methanol the *cis-trans-trans* isomer could be isolated as single compound.




**Scheme 7** Configurational isomers for compd **5**.

The NMR spectrum of compound **5** confirms its structure. The aromatic protons give a triplet and a doublet (1/2; overlapped; $\delta_a = 7.44$, $\delta_{b,c} = 7.45$ ppm; Figure 3). The 1,3-dioxane rings are differentiated by the axial (ring A, major) or equatorial (ring B, minor) orientations of the ethyl groups at positions 5', 5" and 5"'. The axial and equatorial protons of each type of 1,3-dioxane ring produce two doublets (A: $\delta = 3.53$, 3.32 ppm; B: $\delta = 3.44$, 3.38 ppm) in the $^1$H NMR spectrum while the signals of the methyl groups at positions 2', 2" and 2"' are very close singlets (A: $\delta = 1.54$ ppm; B: $\delta = 1.56$ ppm).

The major differentiations are observed for the signals of the substituents at positions 5', 5" and 5"'. At these positions, the protons of the axial groups are considerably more deshielded than those of the similar groups with equatorial orientation. Thus, the protons of the axial methyl group (ring B; $\delta = 1.24$ ppm) are more deshielded with 0.74 ppm than the protons of the similar equatorial group (ring A; $\delta = 0.50$ ppm). The differences

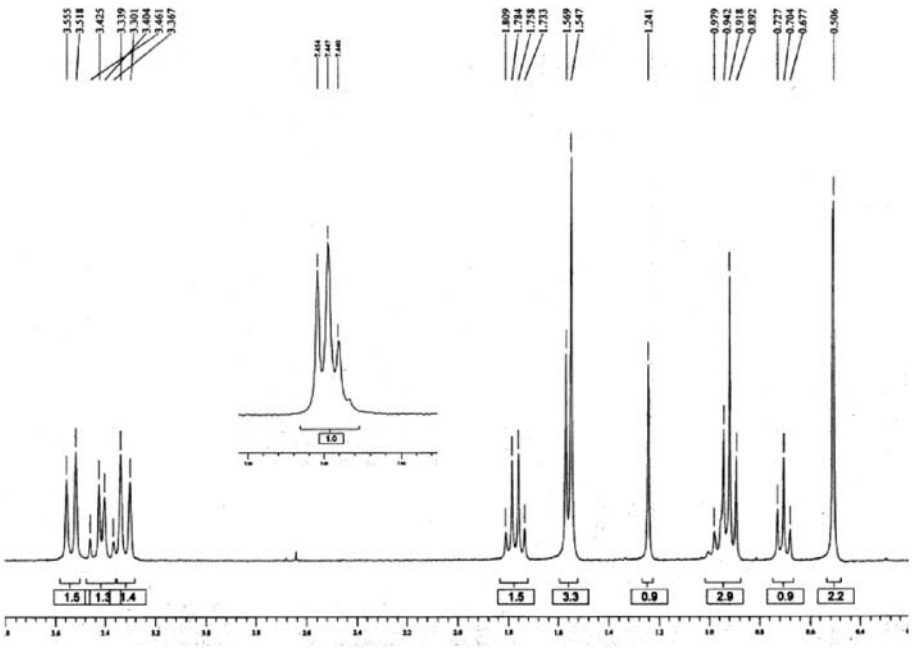


**Fig. 3** $^{1}$H-NMR spectrum (300 MHz, $CDCl_3$) of the *cis-trans-trans* isomer of **5**.

measured for the deshielding of the protons of ethyl groups are higher for the methylene protons [$\delta$ (A) = 1.77 ppm; $\delta$ (B) = 0.93 ppm; $\Delta\delta$ = 0.84 ppm] than for the methyl groups [$\delta$ (A) = 0.91 ppm; $\delta$ (B) = 0.70 ppm; $\Delta\delta$ = 0.21 ppm].

## 3 Experimental part

### 3.1 General

$^{1}$H and $^{13}$C-NMR spectra were recorded at room temperature using $CDCl_3$ as solvent in 5 mm tubes on Bruker AM 300 spectrometer operating at 300 MHz for protons and 75 MHz for carbon atoms. Melting points were determined with a Kleinfeld apparatus and are uncorrected. Elemental analyses were obtained at the University of Rouen. Thin-layer chromatography was performed on Merck 60F 254 silicagel sheets. Merck silicagel (40-63 $\mu$m) was used for flash chromatography. FAB spectra were obtained on a JEOL JMS AX-500 spectrometer under usual conditions. CI-MS spectra were recorded on a Shimadzu GC-MS QP-2010 spectrometer.

### 3.2 X-Ray Crystallographic Study

Crystal data and data-collection information for compound **3** are summarized in Table 2.

The sample ($0.52_{*}0.45_{*}0.45$ mm) is studied on a NONIUS Kappa CCD with graphite monochromatized MoK$\alpha$ radiation. The cell parameters are obtained with Denzo and Scalepack (Otwinowski & Minor, 1997)[18] with 10 frames ($\psi$ rotation: 1°per frame).

The data collection (Nonius, 1999)[19] ($2\theta_{max}$ = 54°, 125 frames via 2.0°$\omega$ rotation and 10s per frame, range HKL : H 0,20 K -17,0 L -11,11) gives 20308 reflections. The data reduction with Denzo and Scalepack (Otwinowski & Minor, 1997) leads to 1017 independent reflections from which 556 with I>2.0$\sigma$ (I). The structure was solved with SIR-97 (Altomare & al., 1998)[20] which reveals the non hydrogen atoms of the molecule. After anisotropic refinement, many hydrogen atoms may be found. The whole structure was refined with SHELXL97 (Sheldrick, 1997)[21] by the full-matrix least-square techniques (use of F square magnitude; x , y, z, $\beta_{ij}$ for C and O atoms, x, y, z in riding mode for H atoms; 62 variables and 556 observations with I>2.0$\sigma$ (I); calc w=1/[$\sigma^2$(Fo$^2$) +(0.18P)$^2$+1.97P] where P=(Fo$^2$+2Fc$^2$)/3 with the resulting R = 0.037, $R_w$ = 0.096 and $S_w$= 1.137, $\Delta\rho < 0.2$ eÅ$^{-3}$. Atomic scattering factors from International Tables for X-ray Crystallography (1992)[22] were used and the Ortep view was realized with PLATON98 (Spek, 1998)[23].

The structural data were deposited at the Cambridge Crystallographic Data Center with the number CCDC 600990

### 1,3,5-tris(2'-benzoyloxy-acetyl)benzene (2)

1,3,5-tris(2'-bromoacetyl)benzene (2.26 mmol, 1g) in acetone (50 ml) was added to sodium benzoate (7.48 mmol, 1.07 g) in 100 ml acetone. The mixture was stirred and heated to reflux for 7 h. The product formation was monitored by TLC. The solvent was distilled off, and the residue was extracted with dichloromethane. The dichloromethane layer was washed three times with water (50 ml). The organic layer was dried over $MgSO_4$ and the solvent was removed to obtain the crude product. The crude product was purified by crystallization from petroleum ether. Solid, white crystals, m.p. 188-189 °C yield 72%. Found: C: 70.04, H: 4.46%; Calc. for $C_{33}H_{24}O_9$ C:70.21, H:4.25%

$^1$H NMR (300 MHz, $CDCl_3$)$\delta_H$ppm: 5.61 (s, 6H, 2'-H, 2"-H, 2"'-H), 7.48 (t, 6H, *m*-H, *J*=7.8Hz, *J*=1.5Hz), 7.61 (tt, 3H, p-H, *J*=7.5Hz, *J*=1.8Hz, *J*=1.2Hz), 8.12 (dd, 6H, *o*-H, *J*=7.8Hz, *J*=1.5Hz), 8.76 (s, 3H, 2-H, 4-H, 6-H)

$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_C$ ppm:66.7 (2'-C, 2"-C, 2"'-C), 128.7 (*m*-C), 129.1 (1-C, 3-C, 5-C), 130.1 (2-C, 4-C, 6-C), 131.5 (*o*-C), 133.7(*p*-C), 135.7 (quaternary aromatic carbon atoms), 166.1 (-$CH_2$-OO<u>C</u>-Ph), 191,1 (-<u>C</u>O-$CH_2$-OOC-)

MS (CI, $CH_4$, 150 eV), m/z (rel. int., %): 565 ([M+H]$^+$, 100)

General procedure for synthesis of compounds 3-6

30 mmol of 1,3-diol and 5 mmol of 1,3,5-triacetylbenzene together with catalytic amounts of *p*-toluenesulfonic acid (0.1 g) were dissolved in 100 ml toluene. The mixture was refluxed and the water that was formed was removed using a Dean-Stark trap. When 80% of the theoretical amount of water had been separated, the catalyst was neutralized with $CH_3COONa$ powder in excess (0.2 g) by stirring over 0.5 h. The reaction mixture was washed twice with 50 ml water. The organic layer was dried over $Na_2SO_4$ then the toluene was removed under reduced pressure and the 1,3-dioxane derivatives were purified by crystallization.

**Table 2** Parameters of the crystalographic determination for **3**.

| Compound | **3** |
|---|---|
| Empirical formula | $C_{13.50}H_{21}\ O_3$ |
| Formula weight | 231.30 |
| Temperature (K) | 293(2) K |
| Wavelength, Å | 0.71069 |
| Crystal system | Trigonal |
| Space group | R3m |
| a, Å | 15.8078(4) |
| b, Å | 15.8078(4) |
| c, Å | 9.2047(3) |
| $\alpha^\circ$ | 90 |
| $\beta^\circ$ | 90 |
| $\gamma^\circ$ | 120 |
| Volume, $Å^3$ | 1991.97(10) |
| Z | 6 |
| Density (calculated) $mg/m^3$ | 1.157 |
| Absorption coefficient, $mm^{-1}$ | 0.080 |
| F(000) | 756 |
| Crystal size/mm | 0.55 x 0.45 x 0.45 |
| Theta range for data collection/ (°) | 2.58 to 27.50 |
| Index ranges | 0<=h<=20; -17<=k<=0; -11<=l<=11 |
| Reflections collected | 1017 |
| Independent reflections | 567 [R(int) = 0.0084] |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data/restraints/parameters | 567 / 1 / 62 |
| Goodness-of-fit on $F^2$ | 1.137 |
| Final R indices [I>2$\sigma$(I)] | R∼1 = 0.0379 wR∼2 = 0.0967 |
| R indices (all data) | R∼1 = 0.0385 wR∼2 = 0.0973 |
| Largest diff. peack on hole, $eA^3$ | 0.238 and -0.246 |

### 1,3,5-tris(2,5,5-trimethyl-1,3-dioxan-2-yl)-benzene (3)

Solid, white crystals, m.p. 228 °C, yield 64%, crystallized from methanol, Found: C 69.87, H 9.09% Calc. for $C_{27}H_{42}O_6$ C 70.10, H 9.15%

$^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$ppm: 0.60 (s, 9H, 5'-$CH_{3eq}$, 5"- $CH_{3eq}$,5"'-$CH_{3eq}$), 1.27 (s, 9H, 5'-$CH_{3ax}$, 5"-$CH_{3ax}$,5"'-$CH_{3ax}$), 1.56 (s, 9H, 2'-$CH_3$, 2"-$CH_3$, 2"'-$CH_3$), 3.36 (d, 6H, 4'-$H_{ax}$, 6'-$H_{ax}$, 4"-$H_{ax}$, 6"-$H_{ax}$, 4"'-$H_{ax}$, 6"'-$H_{ax}$, $J$=10.9Hz), 3.41 (d, 6H, 4'-$H_{eq}$, 6'-$H_{eq}$, 4"-$H_{eq}$, 6"-$H_{eq}$, 4"'-$H_{eq}$, 6"'-$H_{eq}$ , $J$=10.9Hz), 7.44 (s, 3H, 2-H, 4-H, 6-H)

$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_C$ ppm: 22.4 (5'-$CH_{3eq}$, 5"-$CH_{3eq}$, 5"'-$CH_{3eq}$), 23.3 (5'-$CH_{3ax}$, 5"-$CH_{3ax}$, 5"'-$CH_{3ax}$), 30.4 (5'-C, 5"-C, 5"'-C), 32.3 (2'-$CH_3$, 2"-$CH_3$, 2"-$CH_3$), 72.0 (4'-C, 6'-C, 4"-C, 6"-C, 4"'-C, 6"'-C), 100.6 (2'-C, 2"-C, 2"'-C), 125.0 (tertiary aromatic carbon atoms), 142.3 (quaternary aromatic carbon atoms).

MS (CI, $CH_4$, 150 eV) m/z (rel. int., %): 463 ($[M+H]^+$, 100), 447 ($[M-15]^+$, 95)

**1,3,5-tris[5,5-di(bromomethyl)-2-methyl-1,3-dioxan-2-yl]-benzene (4)**

Solid, white crystals, p.t. = 168-169 °C , yield 59%, crystallized from methanol, Found: C 34.72, H 3.83, Br 51.35%; Calc. for $C_{27}H_{36}O_6Br_6$ C 34.65, H 3.87, Br 51.28%
$^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$ppm: 1.57 (s, 9H, 2'-$CH_3$, 2"-$CH_3$, 2"'-$CH_3$), 3.16 (s, 6H, 5'-$CH_{2eq}$, 5"-$CH_{2eq}$, 5""-$CH_{2eq}$), 3.60 (d, 6H, 4'-$H_{ax}$, 6'-$H_{ax}$, 4"-$H_{ax}$, 6"-$H_{ax}$, 4"'-$H_{ax}$, 6"'-$H_{ax}$, $J$=11.4Hz), 3.87 (d, 6H, 4'-$H_{eq}$, 6'-$H_{eq}$, 4"-$H_{eq}$, 6"-$H_{eq}$, 4"'-$H_{eq}$, 6"'-$H_{eq}$, $J$=11.4Hz), 3.94 (s, 6H, 5'-$CH_{2ax}$, 5"-$CH_{2ax}$, 5"-$CH_{2ax}$), 7.42 (s, 3H, 2-H, 4-H, 6-H)
$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_C$ ppm: 31.6 (2'-$CH_3$, 2"-$CH_3$, 2"'-$CH_3$), 35.4 (5'-(Br-$CH_2$)$_{eq}$, 5"-(Br-$CH_2$)$_{eq}$, 5"'-(Br- $CH_2$)$_{eq}$), 36.5 (5'-(Br-$CH_2$)$_{ax}$, 5"-(Br-$CH_2$)$_{eq}$, 5"'-(Br-$CH_2$)$_{eq}$), 37.8 (5'-C, 5"-C, 5"'-C), 66.3 (4'-C, 6'-C, 4"-C, 6"-C, 4"'-C, 6"'-C), 101.4 (2'-C, 2"-C, 2"'-C), 124.9 (tertiary aromatic carbon atoms), 142.0 (quaternary aromatic carbon atoms)
MS (CI, $CH_4$, 150 eV) m/z (rel. int.): 931 ($[M+H]^+$, 1), 933 ($[M+H]^+$, 5), 935 ($[M+H]^+$, 10), 937 ($[M+H]^+$, 14), 939 ($[M+H]^+$, 10), 941 ($[M+H]^+$, 5), 943 ($[M+H]^+$, 1), 285 (50), 287 (100), 289 (50).

***cis*-1,*trans*-3,*trans*-5-tris[5(r)-ethyl-2,5-dimethyl-1,3-dioxan-2-yl]benzene (5)**

Solid, white crystals, m.p. 123$^o$C yield 13%, crystallized from methanol, Found: C 71.24, H 9.66%; Calc. for $C_{30}H_{48}O_6$ C:71.42, H:9.52%
$^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$ppm: 0.50 (s, 6H, 5"-$CH_{3eq}$, 5"'-$CH_{3eq}$), 0.70 (t, 3H, 5'-($CH_2$-C$\underline{H}_3$)$_{eq}$, $J$=7.5Hz), 0.89-0.97 (overlapped peaks, 8H, 5"-($CH_2$-C$\underline{H}_3$)$_{ax}$, 5"'-($CH_2$-C$\underline{H}_3$)$_{ax}$, 5'-(C$\underline{H}_2$-$CH_3$)$_{eq}$), 1.24 (s, 3H, 5'-$CH_{3ax}$), 1.54 (s, 9H, 2'-$CH_3$, 2"-$CH_3$, 2"'-$CH_3$), 1.77 (q, 4H, 5"-(C$\underline{H}_2$-$CH_3$)$_{ax}$, 5"'-(C$\underline{H}_2$-$CH_3$)$_{ax}$, $J$=7.5Hz), 3.32 (d, 4H, 4"-$H_{ax}$, 6"-$H_{ax}$, 4"'-$H_{ax}$, 6"'-$H_{ax}$, $J$=11.1Hz), 3.38 (d, 2H, 4'-$H_{ax}$, 6'-$H_{ax,}$ $J$=10.8Hz), 3.44 (d, 2H, 4'-$H_{eq}$, 6'-$H_{eq,}$ $J$=10.8Hz), 3.53 (d, 4H, 4"-$H_{eq}$, 6"-$H_{eq}$, 4"'-$H_{eq}$, 6"'-$H_{eq}$, $J$=11.1Hz), 7.44-7.45 (overlapped peaks, 3H, 2-H, 4-H, 6-H)
$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_C$ ppm: 6.9 (5"-$CH_{3eq}$, 5"'-$CH_{3eq}$), 8.1 (5'-($CH_2$-C$\underline{H}_3$)$_{eq}$), 18.5 (5"-($CH_2$-C$\underline{H}_3$)$_{ax}$, 5"'-($CH_2$-C$\underline{H}_3$)$_{ax}$), 19.7 (5'-$CH_{3ax}$), 26.7 (5'-(C$\underline{H}_2$-$CH_3$)$_{eq}$), 28.8 (5"-(C$\underline{H}_2$-$CH_3$)$_{ax}$, 5"'-(C$\underline{H}_2$-$CH_3$)$_{ax}$), 32.1 (2'-$CH_3$, 2"-$CH_3$, 2"'-$CH_3$), 32.5 (5"-C, 5"'-C), 32.6 (5'-C), 69.8 (4"-C, 6"-C, 4"'-C, 6"'-C), 70.8 (4'-C, 6'-C), 100.4, 100.5 (2'-C, 2"-C, 2"'-C), 124.7, 124.7 (tertiary aromatic carbon atoms), 142.12, 142.16, 142.19 (quaternary aromatic carbon atoms).
MS (FAB/NOBA) m/z=505 ($[M+H]^+$)

**1,3,5-Tris (5,5-dimethyl-2-benzoyloxymethyl-1,3-dioxan-2-yl)-benzene (6)**

Solid white crystals, m.p. 169.5-170 °C, crystallized from methanol at a yield of 40% with the following compostion: C 70.11, H 6.67%; Calc. for $C_{48}H_{54}O_{12}$: C 70.06; H 6.56%
$^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$ ppm 0.47 (s, 9H, 5'-$CH_{3eq,}$ 5"- $CH_{3eq,}$5"'-$CH_{3eq}$), 1.25 (s, 9H, 5'-$CH_{3ax,}$ 5"-$CH_{3ax,}$5"'-$CH_{3ax}$), 3.30 (d, 6H, 4'-$H_{ax}$, 6'-$H_{ax}$, 4"-$H_{ax}$, 6"-$H_{ax}$, 4"'-$H_{ax}$, 6"'-$H_{ax}$, $J$=10.9Hz), 3.38 (d, 6H, 4'-$H_{eq}$, 6'-$H_{eq}$, 4"-$H_{eq}$, 6"-$H_{eq}$, 4"'-$H_{eq}$, 6"'-$H_{eq}$ ,

$J$=10.9Hz), 4.33 (s, 6H, 2'-C$\underline{H}_2$-O, 2"-C$\underline{H}_2$-O, 2"'-C$\underline{H}_2$-O), 7.39 (t, 6H, $m$-H, $J$=7.5Hz), 7.51 (tt, 3H, $p$-H, $J$=7.5Hz, $J$=2.4Hz, $J$=1,2Hz), 7.67 (s, 3H, 2-H, 4-H, 6-H), 7.99 (dd, 6H, $o$-H, $J$=1.2Hz)
$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_C$ ppm: 21.9 (5'-$CH_{3eq}$, 5"-$CH_{3eq}$, 5"'-$CH_{3eq}$), 22.9 (5'-$CH_{3ax}$, 5"-$CH_{3ax}$, 5"'-$CH_{3ax}$), 30.2 (5'-C, 5"-C, 5"'-C), 70.0 (2'-$\underline{C}H_2$-O, 2"-$\underline{C}H_2$-O, 2"'-$\underline{C}H_2$-O), 71.6 (4'-C, 6'-C, 4"-C, 6"-C, 4"'-C, 6"'-C), 99.5 (2'-C, 2"-C, 2"'-C), 128.3 ($m$-C), 128.5 (2-C, 4-C, 6-C), 129.8 ($o$-C), 130.0 (1-C, 3-C, 5-C), 133,2 ($p$-C), 138.0 (quaternary aromatic carbon atoms), 165.8 (-$\underline{C}$OO-)
MS (CI, $CH_4$, 150 eV), m/z :823 $[M+H]^+$

### 1,3,5-tris(5,5-dimethyl-2-bromomethyl -1,3-dioxan-2-yl)-benzene (7)

1,3-Dioxane derivative 3 (2.1 mmol, 1 g) and dry dichloromethane (40 ml) were introduced into a three-necked flask equipped with a reflux condenser, a thermometer and a dropping funnel and the mixture was cooled into an ice bath at 0-5 °C. Bromine (13 mmol, 2.08 g) in 10 ml dry dichloromethane was added dropwise, under magnetically stirring, the ensuing reaction being monitored initially by the fading of the solution color. After the addition of bromine, the ice bath was removed and stirring was continued for 1h, the contents of the flask being allowed to reach room temperature (20-25 °C) slowly. The mixture was evaporated *in vacuo* and the residue was crystallized from methanol. Solid white crystals with a m.p. 165 °C , which were obtained at a yield of 25% were found to have the following composition : C 46.52, H 5.47, Br 34.48%. Calc for $C_{27}H_{39}O_6Br_3$: C 46.35, H 5.57, Br 34.33%.
$^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$ ppm: 0.61 (s, 9H, 5'-$CH_{3eq}$, 5"- $CH_{3eq}$,5"'-$CH_{3eq}$), 1.33 (s, 9H, 5'-$CH_{3ax}$, 5"-$CH_{3ax}$,5"'-$CH_{3ax}$), 1.57 (s, 6H, 2'-C$\underline{H}_2$-Br, 2"-C$\underline{H}_2$-Br, 2"'-C$\underline{H}_2$-Br), 3.37 (d, 6H, 4'-$H_{ax}$, 6'-$H_{ax}$, 4"-$H_{ax}$, 6"-$H_{ax}$, 4"'-$H_{ax}$, 6"'-$H_{ax}$, $J$=10.9Hz), 3.51 (d, 6H, 4'-$H_{eq}$, 6'-$H_{eq}$, 4"-$H_{eq}$, 6"-$H_{eq}$, 4"'-$H_{eq}$, 6"'-$H_{eq}$, $J$=10.9Hz), 7.59 (s, 3H, 2-H, 4-H, 6-H)
$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_C$ ppm: 21.9 (5'-$CH_{3eq}$, 5"-$CH_{3eq}$, 5"'-$CH_{3eq}$), 23.0 (5'-$CH_{3ax}$, 5"-$CH_{3ax}$, 5"'-$CH_{3ax}$), 30.2 5'-C, 5"-C, 5"'-C), 40.5 (2'-$\underline{C}H_2$-Br, 2"-$\underline{C}H_2$-Br, 2"'-$\underline{C}H_2$-Br), 72.3 (4'-C, 6'-C, 4"-C, 6"-C, 4"'-C, 6"'-C), 98.5 (2'-C, 2"-C, 2"'-C), 129.0 (tertiary aromatic carbon atoms), 138.9 (quaternary aromatic carbon atoms).
MS (CI, $CH_4$, 150 eV) m/z (rel. int.): 697 ($[M+H]^+$, 1), 699 ($[M+H]^+$, 3), 701 ($[M+H]^+$, 3), 703 ($[M+H]^+$, 1), 517 (50), 519 (100), 521 (50)

### 1,3,5-tris(5,5-dimethyl-2-hydroxymethyl-1,3-dioxan-2-yl)-benzene (8)

LiOH (10 mg, 0.43 mmol) was added to a solution of 6 (0.06 g, 0.07 mmol) in THF (15 ml), MeOH (3 ml) and water (1 ml) at 0 °C, the mixture having been stirred at this temperature for 2 days. After adding water (50 ml) and diethyl ether (150 ml), the organic layer was separated and the aqueous phase was extracted with diethyl ether (2 X 50 ml). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo*. The crude product was purified by crystallisation from acetone. Solid, white crystals, m.p. 196.5-197 °C, yield 89%. Found: C 63.57; H 8.39%, Calc. for $C_{27}H_{42}O_9$ : C 63.52; H 8.23%

$^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$ ppm 0.62 (s, 9H, 5'-$CH_{3eq}$, 5"- $CH_{3eq}$,5"'-$CH_{3eq}$), 1.29 (s, 9H, 5'-$CH_{3ax}$, 5"-$CH_{3ax}$,5"'-$CH_{3ax}$), 3.40 (d, 6H, 4'-$H_{ax}$, 6'-$H_{ax}$, 4"-$H_{ax}$, 6"-$H_{ax}$, 4"'-$H_{ax}$, 6"'-$H_{ax}$, $J$=10.6Hz), 3.48 (d, 6H, 4'-$H_{eq}$, 6'-$H_{eq}$, 4"-$H_{eq}$, 6"-$H_{eq}$, 4"'-$H_{eq}$, 6"'-$H_{eq}$ , $J$=10.6Hz), 3.56 (s, 6H, 2'-C$\underline{H}_2$-OH, 2"-C$\underline{H}_2$-OH, 2"'-C$\underline{H}_2$-OH), 7.50 (s, 3H, 2-H, 4-H, 6-H)
$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta_C$ ppm: 22.0 (5'-$CH_{3eq}$, 5"-$CH_{3eq}$, 5"'-$CH_{3eq}$), 23.0 (5'-$CH_{3ax}$, 5"-$CH_{3ax}$, 5"'-$CH_{3ax}$), 30.3 (5'-C, 5"-C, 5"'-C), 70.9 (2'-$\underline{C}H_2$-OH, 2"-$\underline{C}H_2$-OH, 2"'-$\underline{C}H_2$-OH), 71.6 (4'-C, 6'-C, 4"-C, 6"-C, 4"'-C, 6"'-C), 100.6 (2'-C, 2"-C, 2"'-C), 127.4 (tertiary aromatic carbon atoms), 138.5 (quaternary aromatic carbon atoms)
MS (CI, $CH_4$, 150 eV), m/z :511 $[M+H]^+$

## 4 Conclusions

The synthesis of several 1,3,5-tris(1,3-dioxan-2-yl)benzene derivatives were performed by the ketalization reactions or by further transformations of the derivatives with this skeleton. The compounds exhibit anancomeric structures with axial orientation of the aromatic substituent for all 1,3-dioxane rings. Importantly, the tribrominated derivative **6** showed resistance to nucleophilic substitution, while the triol **8** was transformed into an efficient nucleophilic reagent useful for the synthesis of 1,3,5-cyclophanes.

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