SELECTIVE BROMINATION REACTION
OF SOME BIS(1,3-DIOXAN-2-YL)ALKANES

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The bromination reaction of some bis(1,3-dioxan-2yl)alkanes was investigated in order to reveal the influence of the relative positions of the heterocycles on the stereoselectivity of the halogenation reaction. The structure of the compounds was determined using NMR investigations and the single crystal X ray molecular structure determined for one compound.

INTRODUCTION

The bromination reaction of protected carbonyl compounds (i.e. 1,3-dioxolane and 1,3-dioxane derivatives) was largely investigated.[1] The reaction occurs by the addition of Br^+ to the enol form of the protonated heterocycle.[1g-j] In many cases the bromination reaction of cyclic acetals revealed a high stereoselectivity and the property of this reaction was mainly exploited to carry out enantioselective reactions in the 1,3-dioxolane series using as chiral auxiliaries the esters of tartaric acid.[1g-i, 2]

The bromination of spiro-1,3-dioxanes was also intensively investigated (Scheme 1) and the diastereoselectivity of this reaction having as result the obtaining of only the *like* dibrominated isomers (*RR, SS*) was revealed.[1j, 3]
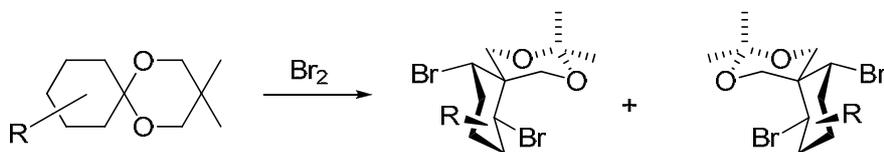
Scheme 1

The dibromination process of flexible 2,2-disubstituted-5,5-dimethyl-1,3-dioxanes **1-3** or anancomeric 2,2-disubstituted-5-methyl-1,3-dioxanes **7-9** (Scheme 2) is diastereoselective and the structure of the major isomer formed in the reaction depends on the conformational behavior of the substrate and on the bulkiness of the substituents located at position 2.[1a,4] The investigations of the bromination reaction of flexible compounds revealed the obtaining of *like* isomer (**4**, *RR, SS*) if the bromination occurs to benzyl groups ($R^1 = C_6H_5$), of the *unlike* isomer (**6**, *RS, SR*) if the substituents are propyl ($R^1 = C_2H_5$) and of a mixture of the two diastereoisomers (**5**,

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the major one being the *unlike* isomer) if the substituents of the starting 1,3-dioxane derivative are ethyl groups ($R^1 = CH_3$).[1a] The bromination of the similar anancomeric structures gave different results. In the case when $R^1 = CH_3$ a mixture of diastereoisomers of **11** was obtained, while in the cases when $R^1 = C_6H_5$ or C_2H_5 only the formation of the *unlike* (*RS, SR*) isomers (**10** and **12**) was observed.[4]

The stereochemistry for many compounds with two (or more) 1,3-dioxane units connected to the same aromatic (I, II) or aliphatic (III) unit were investigated in order to observe the influences on the stereochemistry of these compounds of the interactions between the heterocycles connected to the same skeleton (Scheme 3).[5-12]

We considered series III to be of interest for investigations on the selectivity of the bromination reaction because the reaction is carried out on substrates bearing two cyclic acetal groups and it is possible to observe the influence of the distance between the 1,3-dioxan-2-yl groups (the distance increases with the length of the polymethylene chain) on the diastereoselectivity of the halogenation reaction.
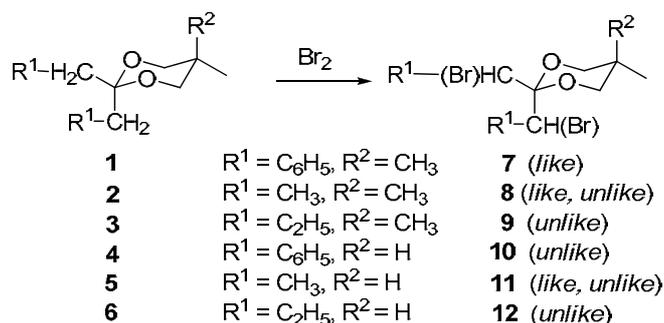
Scheme 2
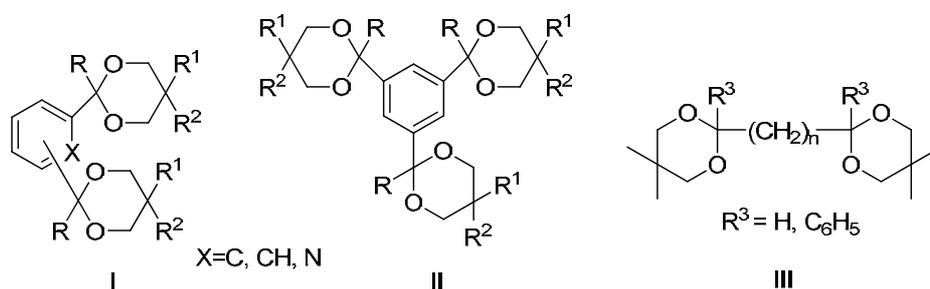
Scheme 3

RESULTS AND DISCUSSION

Bromination of the 1,3-dioxanes prepared previously[11] was performed with bromine in conditions similar to those used by Giusti in the bromination of 1,3-dioxolane compounds[13] as the aim was to obtain the dibrominated derivatives where dibromination could take place (Scheme 4).

As in the case of the non-brominated 1,3-dioxanes, the molecules are rigid, anacomeric as the conformational equilibrium is shifted toward the conformer that bears the aliphatic (or the brominated aliphatic) part in equatorial position. This behaviour is illustrated by more complex NMR spectra.

In order to explain the ^{1}H NMR spectrum of compound **14**, some considerations must be made.
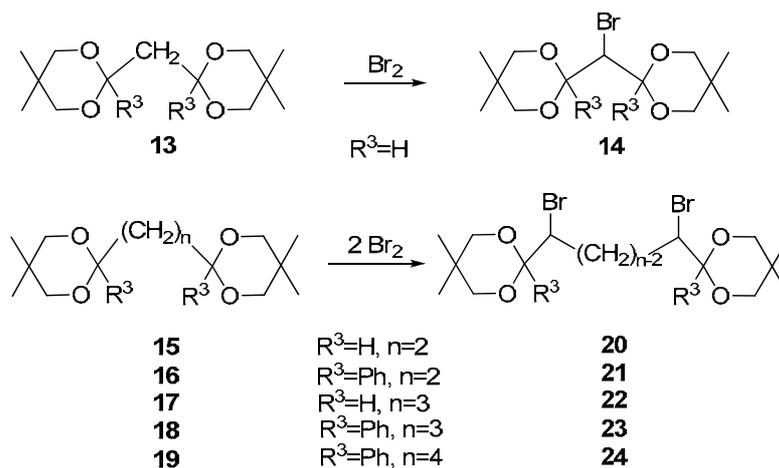
Positions 4'(4") and 6'(6") are diastereotopic even if there are no chiral centres in the molecule; a similar example has been reported for citric acid[14]. This is because the carbon atom that bears the bromine atom (C^α) is a prochiral centre.

^{1}H NMR spectrum of compound **14** in benzene-d_6 displays two distinct singlets for the methyl groups at positions 5'(5") at δ=0.24 ppm for equatorial methyl and at δ=1.18 ppm for the axial one. The signal corresponding to the axial protons at positions 4'(4") and 6'(6") of the heterocycles appears as two doublets at δ=3.13 ppm and δ=3.15 ppm, respectively with a large geminal coupling constant (^2J=10.7 Hz). The signals of the equatorial protons in the same positions are overlapped (two doublets of doublets) at δ=3.44 ppm with the large coupling constant with the axial protons (^2J=10.7

Hz) and a small coupling constant through 4 bonds (^4J=2.8 Hz) due to the W (M) disposal of the equatorial protons at positions 4 and 6.

A clear triplet for the proton of the aliphatic chain at the carbon atom that also bears the bromine atom appears at δ=4.33 ppm (^3J=4.8 Hz) while for the protons belonging to the heterocycle at position 2 (2') there is a doublet (^3J=4.8 Hz) at δ=4.82 ppm (Figure 1).

The difference of chemical shifts of the methyl groups at position 5'(5") ($\Delta\delta_{ax\text{-}eq}$ =0.94 ppm) is diminished when the solvent is changed to deuterated chloroform-d_1 ($\Delta\delta_{ax\text{-}eq}$ =0.49 ppm), as well as that for the protons at positions 4 or 6 ($\Delta\delta_{ax\text{-}eq}$ =0.30 ppm in C_6D_6 compared to $\Delta\delta_{ax\text{-}eq}$ =0.18 ppm in $CDCl_3$).

Scheme 4

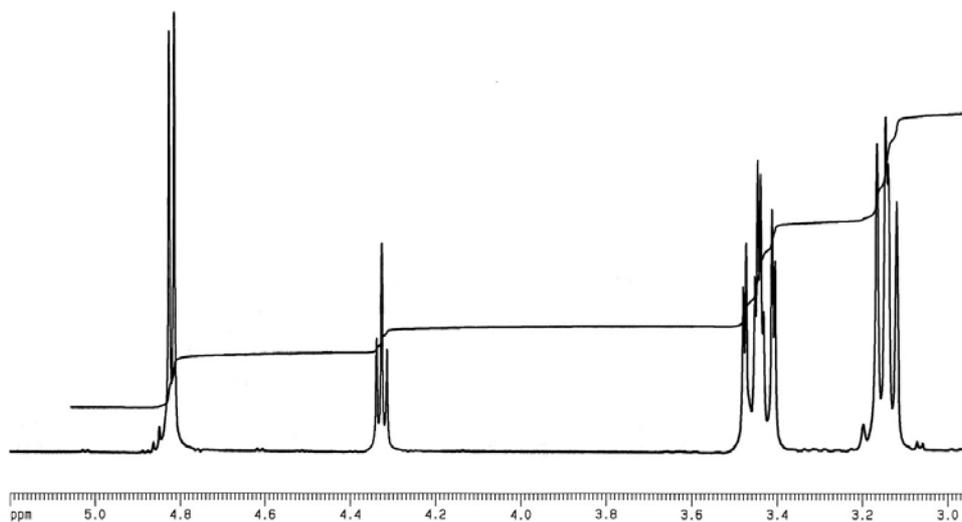|		
13	R^3=H	14
15	R^3=H, n=2	20
16	R^3=Ph, n=2	21
17	R^3=H, n=3	22
18	R^3=Ph, n=3	23
19	R^3=Ph, n=4	24

Fig. 1 – ^{1}H NMR spectrum of **14** (400 MHz, C_6D_6, detail).

From the ^{13}C NMR spectrum it is confirmed that positions 4'(4") and 6'(6") are not identical, there are two signals at 71.37 ppm and 71.55 ppm, respectively, but the difference of chemical shifts is low (only 0.18 ppm).

When dibromination takes place, two new chiral centres are formed and therefore two diastereoisomers are possible: an *unlike* isomer (*RS* or *SR* configurations for the chiral carbon atoms) and a racemic *like* isomer (*RR* or *SS* configurations). In some cases, the two isomers can be differentiated in NMR spectra as some of the carbon atoms or protons are diastereotopic (*i.e.* distinguishable in NMR spectrum) in one isomer and enantiotopic or homotopic (*i.e.* not distinguishable in NMR spectrum) in the other.

One of the situations that do not fit to the above recognition algorithm is compound **20**. Both

possible isomers would have the same pattern in NMR spectra. In the reaction mass both isomers are present in a quasi equal amount as determined from the NMR spectra. The diastereoisomers were separated by column chromatography (cyclohexane:diethylether = 12:1).

The ^{1}H NMR spectra of the first eluted isomer shows one singlet for the equatorial methyl groups at positions 5'(5") and one singlet for the axial ones at δ=0.73 ppm and δ=1.17 ppm, respectively. Positions 4 and 6 of the 1,3-dioxane ring are diastereotopic and the axial protons at positions 4'(4") and 6'(6") appear overlapped at δ=3.48 ppm as a dublet (^2J=11 Hz). The equatorial protons of the heterocycles are overlapped in a multiplet at 3.63-3.72 ppm (Figure 2a). For the protons at the chiral centres bearing bromine there is a dublet at δ=4.38 ppm, while the protons at position 2'(2") appear as dublet (^3J=7 Hz) at δ=4.62 ppm.

The other isomer's ^{1}H NMR spectrum does not differ much. The pattern for the protons at positions 4'(4") and 6'(6") of the 1,3-dioxane part is similar, while for the –CHBr groups a singlet appears at δ=4.33 ppm and another singlet is present at δ=4.90 ppm for the protons at position 2'(2") (Figure 2b). The fact that singlets appear for these last groups instead of dublets is most probably due to some spatial arrangement of the atoms that would lead to a ^3J=0 Hz coupling constant for these protons. Therefore, the NMR spectra would be of no help in identifying the diastereoisomers.

Fortunately, the second eluted isomers provided single crystals that were analysed by X-Ray crystallography and proved to be the *unlike* diastereoisomer (Figure 3).
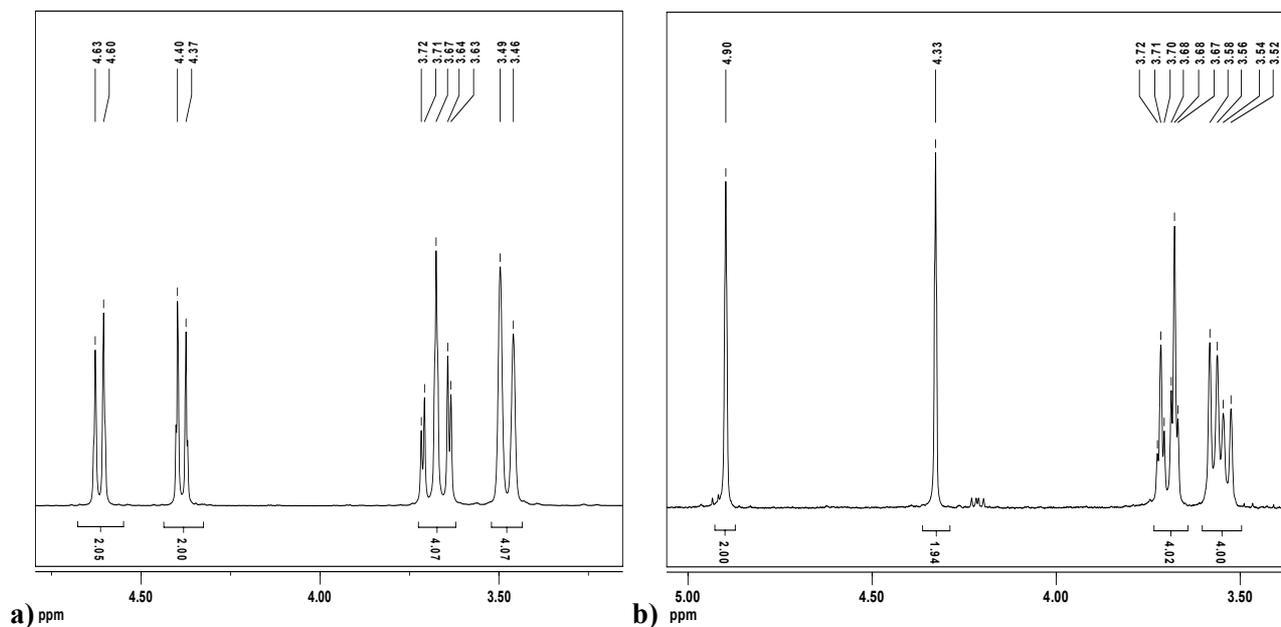

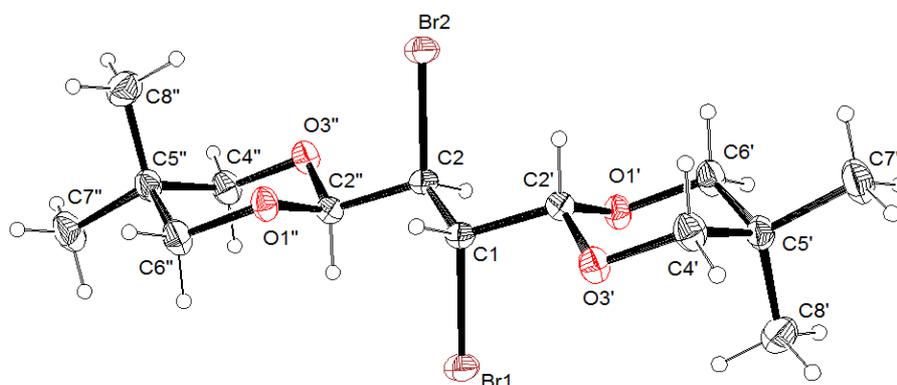Fig. 2 – ^{1}H NMR spectra of **20** (300MHz, CDCl₃, detail): a) *like* isomer; b) *unlike* isomer.

Fig. 3 – ORTEP diagram for the *unlike* isomer of **20.**

The situation is similar for compound **21** bearing phenyl rings at positions 2'(2"). From the reaction only one isomer is obtained. In the ^{1}H NMR spectrum of this compound there are two singlets for the equatorial methyl groups at positions 5'(5") at δ=0.53 ppm and at δ=1.28 ppm for the axial ones. Positions 4 and 6 are diastereotopic and the equatorial protons at positions 4'(4") appear at δ=3.49 ppm as a dublet of dublets (^2J=11 Hz, ^3J=2.5 Hz). All the other protons of the heterocycles are overlapped in a multiplet at 3.45-3.50 ppm - dublet of dublets for the equatorial protons at positions 6'(6") at δ=3.41 ppm (^2J=11 Hz, ^3J=2.5 Hz) and the axial protons are displayed as dublets at $δ_{4'(4")-Hax}$=3.38 ppm and $δ_{6'(6")-Hax}$=3.34 ppm with the same geminal constant (^2J=11 Hz). For the protons at the chiral centres there is a singlet at δ=4.38 ppm.

When we build Fischer projections for the two isomers and perform the substitution test for the protons on the carbon atoms bearing the bromine atoms, the result is that the two protons would be isochronous (they would give only one signal in the ^{1}H NMR spectrum) in both cases, as they are enantiotopic in the *meso* isomer and homotopic in the chiral *d,l*, isomer. As the compound could not be suitably crystallized for X-Ray diffractometry, we are not able to decide at this point which diastereoisomer of **21** was obtained.

As the aliphatic chain becomes longer, the differences in the NMR spectra of the two possible isomers should be more obvious. This is the case of the dibrominated compound **22** for which the chiral (*d,l*) and *meso* stereoisomers may be distinguished.

The methylene protons are homotopic and isochronous in the *like* isomer because of a C_2 axis, while protons H_a and H_b in the *unlike* form are diastereotopic and therefore anisochronous.

In the ^{1}H NMR spectrum of **22** (Figure 4a), the axial protons at positions 4'(4") and 6'(6") appear, as mentioned above, as two overlapped dublets at δ=3.48 and 3.50 ppm, respectively, while the equatorial protons at the same positions are displayed as a multiplet (two overlapped dublets of dublets) at δ=3.69 ppm (^2J=10 Hz, ^3J=2.8 Hz). A long-range coupling due to the W disposition of the bonds between the axial protons of the heterocycle with the axial methyl at positions 5'(5") may be observed in the COSY spectrum (Figure 4b). The protons at positions 2'(2") appear as a dublet (^3J=2.8 Hz) at δ=4.56 ppm.

In the ^{1}H NMR spectrum there is also an AA'XX' system for the diastereotopic methylene protons ($δ_{A(A')}$=2.45 ppm) and for the –CHBr protons ($δ_{X(X')}$=4.30 ppm) as for the *unlike* isomer.

When at position 2'(2") of the 1,3-dioxane rings there are phenyl groups instead of the hydrogen atoms as in the case of compound **23**, again an AA'XX' system appear for the –CHBr protons ($δ_{A(A')}$= 4.30 ppm) and for the –CH$_2$— protons ($δ_{X(X')}$= 2.46 ppm) as in the case of the already discussed compound **22**. All the protons of the 1,3-dioxane moieties are overlapped in a multiplet at δ = 3.31-3.63 ppm and the methyl groups at positions 5'(5") appear at δ=0.54 ppm the equatorial ones and at δ=1.28 ppm the axial ones. So, in this case again the *unlike* isomer is obtained.

As the aliphatic chain between the two newly formed chiral centres grows longer, the first introduced bromine atom will be too far to influence the introduction of the second one. As a result, the bromination reaction of **19** leads to formation of both *like* and *unlike* isomers of **24** in almost equal amounts as it can be seen from the NMR spectra.
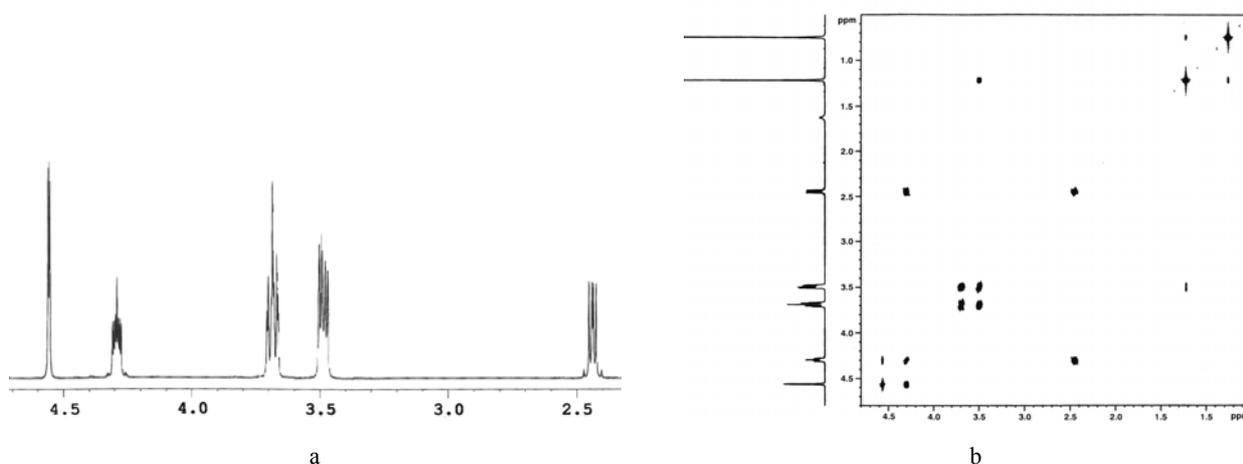

a

b

Fig. 4 – NMR spectra of compound **22** (600 MHz, CD$_2$Cl$_2$, a: ^{1}H NMR spectrum (detail); b: COSY spectrum).

EXPERIMENTAL

General Remarks: ^{1}H and ^{13}C NMR spectra were recorded at room temperature using CD$_2$Cl$_2$, C$_6$D$_6$ (CDCl$_3$) as solvents in 5 mm tubes on a Bruker AM 400, 600 (Varian Gemini 300) NMR spectrometer equipped with a dual ^{13}C-^{1}H (multinuclear) head operating at 400, 600 (300) MHz for protons and 100, 150 (75) MHz for carbon atoms at University of Rouen, France ("Babes-Bolyai" University Cluj-Napoca, Romania, respectively). Melting points were measured with an APOTEC melting point apparatus and are uncorrected. Elemental analyses were obtained at the University of Medicine and Pharmaceutics, Cluj-Napoca. Their results agreed favourably with the calculated values. Thin-layer chromatography was performed on Merck silica gel 60 F 254. Silica gel Merck (40-63 μm) was used for flash chromatography.

X-ray Crystal Structure Determination: The sample was studied on a Bruker AXS X8-APEX II with graphite monochromatized MoKα radiation for **20**. The structure was solved with SIR-97 which reveals the non hydrogen atoms of the molecule. After anisotropic refinement, many hydrogen atoms may be found with a Fourier Difference. The whole structure was refined with SHELXL97 by the full-matrix least-square techniques. Atomic scattering factors from International Tables for Xray Crystallography (1992). Ortep views were realized with PLATON98.

Crystal data for **20**: C$_{14}$H$_{24}$Br$_2$O$_4$, M_r = 416.15, space group $P2_1/c$, a = 14.482(2), b = 5.6204(8), c = 11.2371(15) Å; β = 112.183(2)°; V = 847.0(2) Å^3; Z = 2; T = 297(2) K; μ = 4.795 mm^{-1}. Of 5791 reflections, 1493 were independent (R_{int} = 0.0408). Final $R1$ = 0.0371, $wR2$ = 0.1257 (all data).

General Procedure for the Synthesis of Compounds

Compounds 14, 20-24: 5 mmol of the acetal in 20 ml dry dichloromethane were introduced in a 50 ml three-necked round bottom flask equipped with a condenser, a thermometer and a dropping funnel under magnetical stirring. The reaction mixture was cooled on an ice-bath at 0-5°C and the required quantity of bromine (5 or 10 mmol) was added slowly, checking the decolouring of the solution after the first drop. When all the bromine was added, the ice-bath was removed and the stirring was continued for 1 h while the temperature in the flask reached slowly room temperature. The dichloromethane and the resulted hydrogen bromide were removed under reduced pressure. The resulted product was purified by crystallisation from the appropriate solvent.

1-bromo-1,1-bis(5,5-dimethyl-1,3-dioxane-2-yl)-methane **(14)**

White crystals, crystallisation from methanol, mp=107-108°C. Yield 33% (0.53 g). ^{1}H RMN (400 MHz, C$_6$D$_6$): 0.24 (6H, s, 5'(5")-CH$_{3eq}$), 1.18 (6H, s, 5'(5")-CH$_{3ax}$), 3.14 (4H, 2d, 4'(4"), 6'(6")-H$_{ax}$, ^2J=10.7 Hz), 3.44 (4H, 2dd, 4'(4"), 6'(6")-H$_{eq}$, ^2J=10.7 Hz, ^4J=2.7 Hz), 4.33 (1H, t, 1-CHBr, ^3J=4.8 Hz), 4.82 (2H, d, 2'(2")-H$_{ax}$, ^3J=4.8 Hz). ^{13}C RMN (100 MHz, C$_6$D$_6$): 21.77 (5'(5")-CH$_{3eq}$), 23.56 (5'(5")-CH$_{3ax}$), 30.57 (C-5'(5")), 54.52 (C-1), 77.37, 77.55 (C-4'(4"), C-6'(6")), 99.71 (C-2'(2")). Anal. Calcd for C$_{13}$H$_{23}$O$_4$Br (323.22): C, 48.31; H, 7.17; Br, 24.72. Found: C, 48.25; H, 7.10; Br, 24.95.

1,2-dibromo-1,2-bis(5,5-dimethyl-1,3-dioxane-2-yl)-ethane **(20)**

like Isomer: White crystals, crystallisation from ethanol, mp=167-167.5°C. Yield 41% (0.85 g). ^{1}H RMN (300 MHz, CDCl$_3$): 0.73 (6H, s, 5'(5")-CH$_{3eq}$), 1.17 (6H, s, 5'(5")-CH$_{3ax}$), 3.48 (4H, d, 4'(4")-H$_{ax}$, 6'(6")-H$_{ax}$, ^2J=11 Hz), 3.67 (4H, m, 4'(4")-H$_{eq}$, 6'(6")-H$_{eq}$), 4.38 (2H, d, 1,2-CHBr, ^3J=7 Hz), 4.62 (2H, d, 2'(2")-H$_{ax}$, ^3J=7 Hz). ^{13}C RMN (100 MHz, CDCl$_3$): 21.57 (5'(5")-CH$_{3eq}$), 22.99 (5'(5")-CH$_{3ax}$), 30.28 (C-5'(5")), 52.51 (C-1,2), 77.44, 77.50 (C-4'(4"), 6'(6")), 101.51 (C-2'(2")). Anal. Calcd for C$_{14}$H$_{24}$O$_4$Br$_2$ (416.15): C, 40.41; H, 5.81; Br, 38.40. Found: C, 40.27; H, 5.66; Br, 38.63.

unlike Isomer: White crystals, crystallisation from ethanol, mp=203.5-205°C. Yield 34% (0.71 g). ^{1}H RMN (300 MHz, CDCl$_3$): 0.74 (6H, s, 5'(5")-CH$_{3eq}$), 1.25 (6H, s, 5'(5")-CH$_{3ax}$), 3.53 (2H, d, 6'(6")-H$_{ax}$, ^2J=11.2 Hz), 3.57 (2H, d, 4'(4")-H$_{ax}$, ^2J=11.2 Hz), 3.68 (2H, dd, 6'(6")-H$_{eq}$, ^2J=11.2 Hz, ^4J=2.7 Hz), 3.71 (2H, dd, 4'(4")-H$_{eq}$, ^2J=11.2 Hz, ^4J=2.7 Hz), 4.33 (2H, s, 1,2-CHBr), 4.90 (2H, s, 2'(2")-H$_{ax}$). ^{13}C RMN (100 MHz, CDCl$_3$): 21.47 (5'(5")-CH$_{3eq}$), 23.03 (5'(5")-CH$_{3ax}$), 30.39 (C-5'(5")), 52.06 (C-1,2), 77.06, 77.15 (C-4'(4"), 6'(6")), 98.99 (C-2'(2")). Anal. Calcd for C$_{14}$H$_{24}$O$_4$Br$_2$ (416.15): C, 40.41; H, 5.81; Br, 38.40. Found: C, 40.47; H, 5.69; Br, 38.44.

1,2-dibromo-1,2-bis(2-phenyl-5,5-dimethyl-1,3-dioxane-2-yl)-ethane **(21)**

White crystals, crystallisation from ethanol, mp=134-135°C. Yield 56% (1.59 g). ^{1}H RMN (500 MHz, CDCl$_3$): 0.53 (6H, s, 5'(5")-CH$_{3eq}$), 1.28 (6H, s, 5'(5")-CH$_{3ax}$), 3.34 (2H, d, 6'(6")-H$_{ax}$, ^2J=11 Hz), 3.38 (2H, d, 4'(4")-H$_{ax}$, ^2J=11 Hz), 3.41 (2H, dd, 6'(6")-H$_{eq}$, ^2J=11 Hz, ^4J=2.5 Hz), 3.49 (2H, dd, 4'(4")-H$_{eq}$, ^2J=11 Hz, ^4J=2.5 Hz), 4.38 (2H, s, 1,2-CHBr), 7.33 (10H, m, aromatic protons). ^{13}C RMN (125 MHz, CDCl$_3$): 22.05 (5'(5")-CH$_{3eq}$), 23.31 (5'(5")-CH$_{3ax}$), 30.12 (C-5'(5")), 57.95 (C-1,2), 72.00, 72.25 (C-4'(4"), 6'(6")), 101.38 (C-2'(2")), 125.84, 128.85, 128.90, 135.95 (aromatic carbon atoms). Anal. Calcd for C$_{26}$H$_{32}$O$_4$Br$_2$ (568.34): C, 54.95; H, 5.68; Br, 28.12. Found: C, 55.07; H, 5.66; Br, 27.83.

1,3-dibromo-1,3-bis(5,5-dimethyl-1,3-dioxane-2-yl)-propane **(22)**

White crystals, crystallisation from ethanol, mp=133-134°C. Yield 43% (0.92 g). ^{1}H RMN (500 MHz, CDCl$_3$): 0.75 (6H, s, 5'(5")-CH$_{3eq}$), 1.21 (6H, s, 5'(5")-CH$_{3ax}$), 2.44 (2H, m, 2-H$_2$), 3.48, 3.50 (4H, 2d, 4'(4"), 6'(6")-H$_{ax}$, ^2J=10 Hz), 3.69 (4H, 2dd, 4'(4"), 6'(6")-H$_{eq}$, ^2J=10 Hz, ^4J=2.8 Hz), 4.30 (2H, m, 1,3-CHBr). 4.56 (2H, d, 2'(2")-H$_{ax}$, ^3J=2.8 Hz). ^{13}C RMN (125 MHz, CDCl$_3$): 21.77 (5'(5")-CH$_{3eq}$), 23.11 (5'(5")-CH$_{3ax}$), 30.46 (C-5'(5")), 35.53 (C-2), 52.67 (C-1,3), 77.36, 77.42 (C-4'(4"), 6'(6")), 101.50 (C-2'(2")). Anal. Calcd for C$_{15}$H$_{26}$O$_4$Br$_2$ (430.17): C, 41.88; H, 6.09; Br, 37.15. Found: C, 42.07; H, 6.12; Br, 36.94.

1,3-dibromo-1,3-bis(2-phenyl-5,5-dimethyl-1,3-dioxane-2-yl)-propane **(23)**

White crystals, crystallisation from dichloromethane, mp=182-183°C. Yield 44% (1.28 g). ^{1}H RMN (300 MHz, CDCl$_3$): 0.57 (6H, s, 5'(5")-CH$_{3eq}$), 1.29 (6H, s, 5'(5")-CH$_{3ax}$), 2.46 (2H, m, 2-H$_2$), 3.36-3.50 (8H, overlapped peaks, 4'(4"), 6'(6")-H$_{ax}$, 4'(4"), 6'(6")-H$_{eq}$), 4.28 (2H, m, 1,3-CHBr), 7.40 (10H, m, aromatic protons). ^{13}C RMN (75 MHz, CDCl$_3$): 21.82 (5'(5")-CH$_{3eq}$), 23.13 (5'(5")-CH$_{3ax}$), 30.06 (C-5'(5")), 35.08 (C-2), 61.69 (C-1,3), 71.91, 72.05 (C-4'(4"), C-6'(6")), 100.67 (C-2'(2")), 128.24, 128.64, 128.97, 135.79 (aromatic carbon atoms)

Anal. Calcd for C$_{27}$H$_{34}$O$_4$Br$_2$ (582.36): C, 55.68; H, 5.88; Br, 27.44. Found: C, 55.67; H, 5.96; Br, 27.26.

1,4-dibromo-1,4-bis(2-phenyl-5,5-dimethyl-1,3-dioxane-2-yl)-buthane **(24)**

White crystals, crystallisation from dichloromethane, mp=173-178°C. Yield 49% (1.46 g; 1/1 mixture of *like* and *unlike* isomers). ^{1}H RMN (400 MHz, CDCl$_3$): 0.55 (6H, s, 5'(5")-CH$_{3eq}$), 1.29 (6H, s, 5'(5")-CH$_{3ax}$), 1.46 (2H, m, 2-H$_2$ isomer 1), 1.94 (4H, m, 2,3-H$_2$ isomer 2), 2.32 (2H, m, 2-H$_2$ isomer 1), 3.36-3.44 (8H, overlapped peaks, 4'(4"), 6'(6")-

H_{ax}, 4'(4"), 6'(6")-H_{eq}), 3.85 (2H, m, 1,4-CHBr), 7.38 (10H, m, aromatic protons). ^{13}C RMN (100 MHz, CDCl$_3$): 21.78 (5'(5")-CH$_{3eq}$), 23.08, 23.11 (5'(5")-CH$_{3ax}$, isomers 1 and 2), 30.04, 30.42 (C-5'(5"), isomers 1 and 2), 31.22 (C-2,3), 61.85, 62.97 (C-1,4, isomers 1 and 2), 71.85, 71.91, 71.95 (C-4'(4"), C-6'(6"), isomers 1 and 2), 100.71 (C-2'(2")), 128.26, 128.29, 128.55, 128.58, 128.9, 128.97 (aromatic carbon atoms, isomers 1 and 2). Anal. Calcd for C$_{28}$H$_{36}$O$_4$Br$_2$ (596.39): C, 56.39; H, 6.08; Br, 26.80. Found: C, 55.67; H, 5.96; Br, 27.26.

CONCLUSIONS

The bromination reaction of some bis(1,3-dioxan-2-yl)alkanes bearing a different number of methylene groups (from one to four) between the two heterocycles was carried out in good yields. On the basis of the NMR investigations and the molecular structure of the *unlike* isomer of compound **20** a correlation between the diastereoselectivity of the dibromination reaction of compounds **15-19** and the length of the polymethylene chain separating the two heterocycles could be observed. For the shorter (two methylene groups) and longer (four methylene groups) chains no diastereoselectivity of the dibromination reaction was observed. For the compounds exhibiting three CH$_2$ groups the dibromination reaction is totally diastereoselective with the formation of the *unlike* isomer. All investigated compounds were found to be anancomeric with the bromoalkyl chains in equatorial orientation.

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