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In memoriam Professor Emil Chifu

SYNTHESIS AND STEREOCHEMISTRY OF SOME NEW 2,4,8,10-TETRAOXASPIRO[5.5]UNDECANE DERIVATIVES

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ABSTRACT. The synthesis and the stereochemistry of some new 2,4,8,10-tetraoxaspiro[5.5]undecane derivatives are reported. The structural analysis carried out using NMR investigations revealed the anancomeric structure of the compounds and the influence of the chirality of the spirane skeleton.

INTRODUCTION

Many spiro and polispiro compounds with saturated six-membered rings were studied in connection with their structural behavior.[1-10] The investigations of these compounds revealed the helical chirality of the spirane skeleton and the anancomeric or flipping conformational behavior of the compounds in correlation with the nature of the substituents located at the extremity of the spirane skeleton.[1-4,10] In polyspirane the helix turns identical with itself after each fourth six-membered ring. Many spiro 1,3-dioxane compounds, derivatives of pentaerythritol were synthesized for various applications in material sciences,[11] as chiral reagents,[12] and drugs[13].

We considered of interest to obtain new derivatives with larger aromatic moieties and to investigate the influence of the aromatic part on the stereochemistry of the heterocyclic compounds.

RESULTS AND DISCUSSIONS

New 2,4,8,10-tetraoxaspiro[5.5]undecane derivatives were obtained by the condensation reaction of pentaerythritol with appropriate aromatic aldehydes (Scheme 1).

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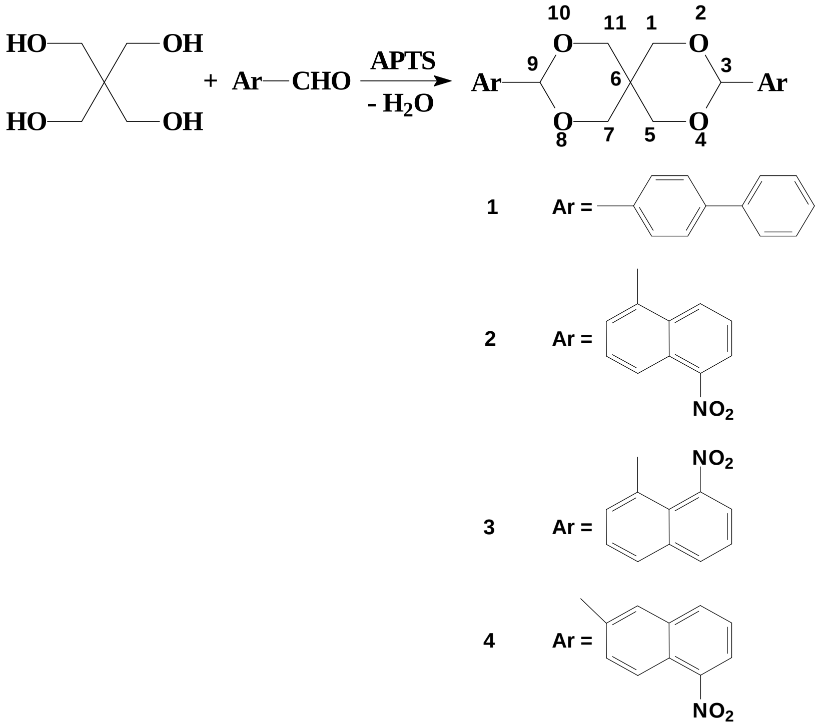
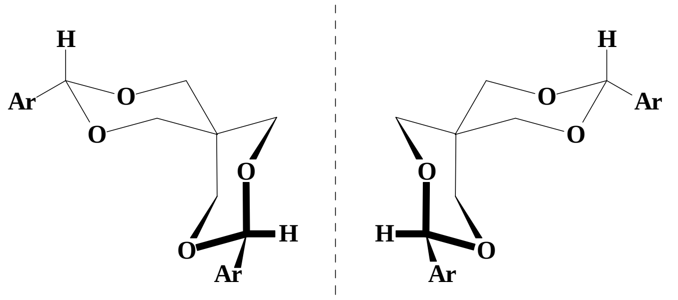


Scheme 1

The structural analysis was carried out using NMR investigations. The spectra of compounds **1-4** exhibit different signals for the axial and equatorial protons of the 1,3-dioxane rings (Table 2) and prove the anancomeric structure of these compounds. On the other side positions 1(11) and 5(7) are diastereotopic as a consequence of the chirality of the spirane skeleton.

The conformational equilibrium involving the heterocycles is shifted toward the conformer exhibiting the aryl group in equatorial orientation and the stable enantiomers of the compound are shown in Scheme 2.



Scheme 2

The equatorial preference of the naphthyl groups is in agreement with the high conformational enthalpy of the aromatic substituents located at the position 2 of the 1,3-dioxane rings[14-16].

Table 2.

NMR data for compounds 1-4

Compound/Solvent	1(11)-H		5(7)-H	
	ax.	eq.	ax.	eq.
1/ $CDCl_3$	3,91	4,93	3,71	3,88
2/ $(CD_3)_2SO$	3,80	4,18	3,65	3,80
3/ $(CD_3)_2SO$	4,25	4,80	3,98	3,98
4/ $(CD_3)_2SO$	3,96	4,88	3,80	3,96

CONCLUSIONS

Spiranes with aromatic substituents at the extremities of the spirane skeleton exhibit anancomeric structures. The aromatic groups prefer the equatorial orientation. Despite the size of the naphtalene ring and of the substituents located on it, the rotation of the naphtalene unit is not hindered.

EXPERIMENTAL

^{1}H-NMR (300 MHz) spectra were recorded at *rt* in $CDCl_3$ or in $(CD_3)_2SO$ on a Bruker 300 MHz / 400MHz spectrometer, using the solvent line as reference.

Melting points were measured with a Kleinfeld melting point apparatus and are uncorrected. Chemicals were purchased from Aldrich or Acros and were used without further purification.

General procedure for the synthesis of compounds 1-4

(25 mmol) pentaerythritol and (50 mmol) aromatic aldehyde with catalytic amounts of *p*-toluenesulphonic acid (0.1 g) were solved in 150 mL benzene. The mixture was refluxed and the water produced in the reaction removed using a Dean-Stark trap. When 80 % of the water had been separated, the mixture was cooled to room temperature and the catalyst was neutralized (under stirring 0.5 h) with Na_2CO_3 powder in excess (1 g). After filtration, the solvent was removed and the crude products were purified by crystallization from ethanol or methanol.

3,9-Bis-(biphenyl)-2,4,8,10-tetraoxaspiro[5.5]undecane 1

White solid, m.p.=217-219°C, yield 47.3%. $C_{31}H_{28}O_4$ (464.56), calc. 80.15 C, 6.08 H, found 80.04 C, 6.27 H. **^{1}H-NMR** (300 MHz,$CDCl_3$, δ ppm): 3.71 (2H, d, J = 11.5 Hz, 5,7-H_{ax}), 3.88 (2H, dd, J = 11.5 Hz, J = 2.4 Hz, 5,7-H_{eq}), 3.91 (2H, d, J = 10.4 Hz, 1,11-H_{ax}), 4.93 (2H, dd, J = 10.4 Hz, J = 2.4 Hz, 1,11-H_{eq}), 5.55 (2H, s, 3,9-H), 7.20-7.80 (18 aromatic H, overlapped peaks)

3,9-Bis-(5-nitro-1-naphthyl)-2,4,8,10-tetraoxaspiro[5.5]undecane 2

Yellow solid, m.p.=255-258℃, yield 55.2%. $C_{29}H_{30}N_2O_8$ (534.56), calc. 65.16 C, 5.66 H, 5.24 N, found 64.70 C, 5.90 H, 4.90 N. **^{1}H-NMR** (300 MHz, $(CD_3)_2SO$, δ ppm): 3.65 (2H, d, J = 11.0 Hz, 5,7-H_{ax}), 3.80 (4H, overlapped peaks, 1,11-H_{ax}, 5,7-H_{eq}), 4.80 (2H, d, J = 11.0 Hz, 1,11-H_{eq}), 5.60 (2H, s, 3,9-H), 7.50-8.40 (12 aromatic H, overlapped peaks)

3,9-Bis-(8-nitro-1-naphthyl)-2,4,8,10-tetraoxaspiro[5.5]undecane 3

Yellow solid, m.p.=178-180℃, yield 60.8%. $C_{29}H_{30}N_2O_8$ (534.56), calc. 65.16 C, 5.66 H, 5.24 N, found 65.30 C, 5.70 H, 5.10 N. **^{1}H-NMR** (300 MHz, $(CD_3)_2SO$, δ ppm): 3.98 (4H, overlapped peaks, 5,7-H_{ax}, 5,7-H_{eq}), 4.25 (2H, d, J = 10.4 Hz, 1,11-H_{ax}), 4.80 (2H, d, J = 10,4 Hz, 1,11-H_{eq}), 6.25 (2H, s, 3,9-H), 7.70-7.80 (12 aromatic H, overlapped peaks).

3,9-Bis-(5-nitro-2-naphthyl)-2,4,8,10-tetraoxaspiro[5.5]undecane 4

White-yellow solid, m.p.=210-212℃, yield 48.8%. $C_{29}H_{30}N_2O_8$ (534.56), calc. 65.16 C, 5.66 H, 5.24 N, found 65.20 C, 5.50 H, 5.10 N. **^{1}H-NMR** (400 MHz, $(CD_3)_2SO$, δ ppm): 3.80 (2H, d, J = 11.2 Hz, 5,7-H_{ax}), 3.96 (4H, overlapped peaks, 1,11-H_{ax}, 5,7-H_{eq}), 4.88 (2H, d, J = 11.4 Hz, 1,11-H_{eq}), 5.71 (2H, s, 3,9-H), 7.75 – 8.78 (12 H, overlapped peaks).

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