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The Stereochemistry of Some New Chiral Brominated Compounds with a 2,4,8,10-Tetraoxaspiro[5.5]undecanic Skeleton

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Summary. New compounds containing the 2,4,8,10-tetraoxaspiro[5.5]undecanic skeleton, substituted with brominated groups, have been synthesized by a regioselective radicalic bromination reaction. The stereochemistry of the compounds was studied by high resolution NMR methods. The anancomericity or the flipping of the rings was inferred from the conformational analysis. The chirality of the spiranic skeleton was investigated by means of the diastereotopicity of hydrogen and carbon atoms.

Keywords. Axial and helical chirality; Conformational analysis; Diastereotopicity of protons and carbon atoms; Regioselective bromination reaction; Spiro 1,3-dioxanes.

Zur Stereochemie einiger neuer chiraler Bromverbindungen mit einem 2,4,8,10-Tetraoxaspiro[5.5]-undecan – Gerüst

Zusammenfassung. Mittels einer regioselektiven radikalischen Bromierungsreaktion wurden neue bromsubstituierte Verbindungen mit einem 2,4,8,10-Tetraoxaspiro[5.5]undecan – Gerüst synthetisiert. Die Stereochemie der Verbindungen wurde mit Hilfe hochauflösender Kernresonanzspektroskopie untersucht. Die Chiralität des Spiranskeletts wird im Zusammenhang mit der Diastereotopie von Wasserstoff- und Kohlenstoffatomen diskutiert.

Introduction

The chirality of the spiro[5.5]undecanic skeleton and its heterocyclic analogs (*e.g.* the 2,4,8,10-tetraoxaspiro[5.5]undecane) as well as the chirality of their derivatives is a problem that generates different opinions. In early works [1–6], the chirality of the spiranic compounds with six-membered rings was considered similar to the common axial chirality of allenic compounds or of spiranes with planar rings. The

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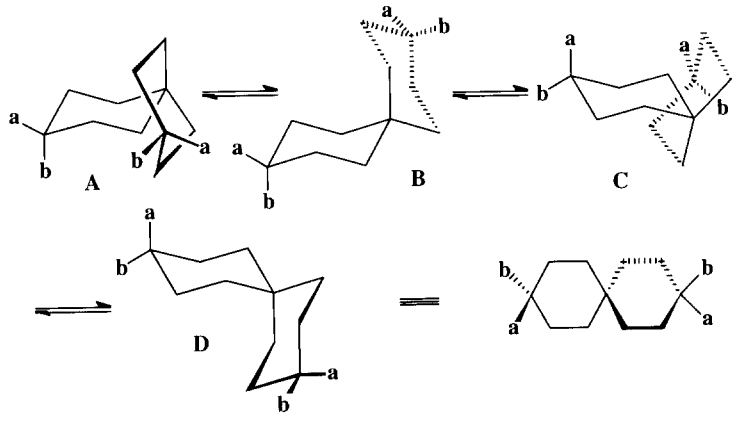
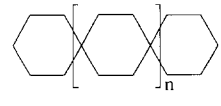
authors have suggested an average structure with planar rings for the parent skeleton of spiro[5.5]undecane as a result of fast flipping. The spiranic compounds were considered chiral only when substituted at both extremities of the spiranic skeleton by different geminal groups (a ≠ b). If one or both of the extremities of the spiranic skeleton presented identical geminal groups (a = b), *e.g.* the unsubstituted spiro[5.5]undecane, the compounds were considered achiral (Scheme 1).



Scheme 1

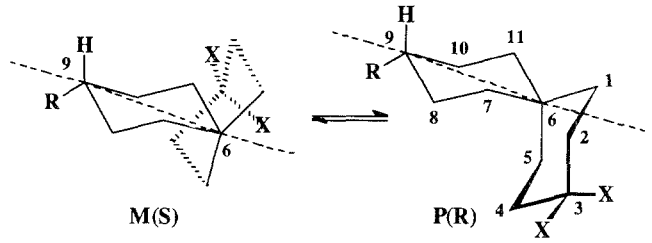
Later, *Dodziuk* has shown the chirality of the frozen spiro[5.5]undecane and its possibility to adopt enantiomeric configurations (Scheme 1 (a = b = H): conformer A is identical with C but is enantiomer with B which at the same time is identical with D) [7–10]. The chirality of the carbocyclic spirane or of its heterocyclic analogs as well as of the derivatives substituted at C(3) or/and at C(9) with identical geminal groups was considered different from the usual situations included in the *Cahn, Ingold*, and *Prelog* (*CIP*) classification of chiral elements. The presence of a $C_{a,a,a,a}$ chiral carbon atom, *i.e.* a carbon atom (the spiranic one) bearing four formally identical substituents, was considered.

Recently, we proposed to discuss the chirality of spiranic compounds with six-membered rings in a new way [11, 12]. Using a systematic NMR investigation combined with a detailed *Dreiding* model analysis, we observed the helical chirality of spiranic compounds of the type given below [11].



Such a polyspiranic system can adopt a helical disposal, similar to the helicity reported for helicenes, proteins, or for spiranic compounds with five-membered rings [13]. The helix can turn identical with itself after each fourth six-membered ring.

The compounds unsymmetrically substituted at least at one extremity of the spiranic skeleton exhibit axial chirality in addition to the helical chirality [11] (Scheme 2).



Scheme 2

The axis C(6)–C(9) introduces axial chirality. The reference groups are R and H at C(9) and the whole disubstituted ring at C(9) (can be situated on the left or on the right side of the chiral axis). The flipping of the symmetrically substituted ring inverts both axial and helical chiralities. The shown equilibrium represents an enantiomeric interconversion [$M(S) \rightleftharpoons P(R)$]. As a conclusion, the chirality of the spiranic compounds with six-membered rings can be discussed in the terms of helical and axial chirality.

The chirality of the derivatives of the 2,4,8,10-tetraoxaspiro[5.5]undecanic skeleton bearing different geminal groups at positions 3 and 9 is not contested in any one of the mentioned theories; however, it is incomplete to suppose that these compounds exhibit only the axial chirality characteristic for spiranic compounds with planar rings. These compounds display at the same time three chiral elements (in accordance with the *CIP* classification): helical chirality (the helix characteristic for polyspiranic skeletons with six-membered rings begins to be built) and two chiral axes, C(3)–C(6) and C(6)–C(9). Theoretically, these compounds can form 8 stereoisomers (Table 1). These types of compounds exhibit anancomeric structures: both rings prefer the conformations with the bulky groups in equatorial orientation. As can be observed (Table 1), the compounds exist as a racemic mixture being represented by structures *I* and *V*.

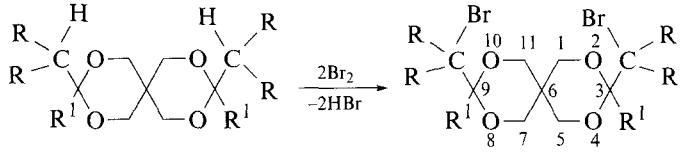
Table 1. Possible steroisomers of compounds **9–14**

Isomer	Axis C(3)–C(6)	Axis C(6)–C(9)	Helix	Position of largest group	
				C(3)	C(9)
I	S	S	M	eq.	eq.
II	R	S	M	ax.	eq.
III	S	R	M	eq.	ax.
IV	R	R	M	ax.	ax.
V	R	R	P	eq.	eq.
VI	S	R	P	ax.	eq.
VII	R	S	P	eq.	ax.
VIII	S	S	P	ax.	ax.

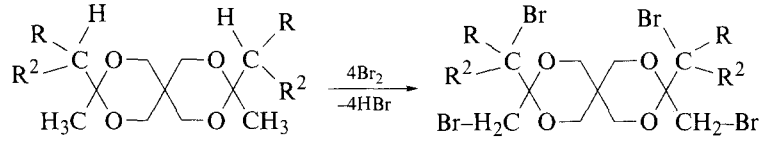
Note: Eliel proposed, as an alternative, to use the symbols a*R* and a*S* for the specification of axial chirality instead of the symbols *R* and *S* [14]

Results and Discussion

Spiranic compounds with bromoalkyl groups located at both extremities of the 2,4,8,10-tetraoxaspiro[5.5]undecanic skeleton (**9–16**) have been obtained (Scheme 3) in good yields starting from the corresponding spiranic compounds (**1–8**) by a regioselective bromination reaction. The conditions used were similar to those reported in the case of the bromination reaction of other monocyclic or spiranic 1,3-dioxolanic [15] or 1,3-dioxanic compounds [16].



1	$R = R^1 = H$	**9**
2	$R = H; R^1 = C(CH_3)_3$	**10**
3	$R = CH_3; R^1 = H$	**11**
4	$R = H; R^1 = C_6H_5$	**12**
5	$R = H; R^1 = p\text{-}O_2N\text{-}C_6H_4$	**13**

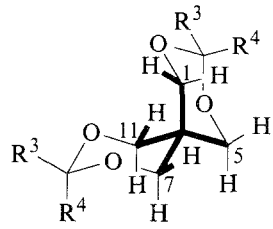


6	$R = R^2 = CH_3$	**14**
7	$R = H; R^2 = CH_3$	**15**
8	$R = R^2 = H$	**16**

Scheme 3

As shown in Scheme 4, compounds **9** and **11**, bearing only one substituent at C(3) and C(9) atoms, as well as the geminal disubstituted compounds **12–13**, have equatorially oriented brominated groups. The preference of the aromatic groups for the axial position (compounds **12** and **13**) is considered taking into account literature data [17] concerning the conformational equilibria in geminal disubstituted compounds with alkyl (or haloalkyl) and aryl groups in the acetalic part of the 1,3-dioxanic ring. These data predict a considerable higher preference of the aromatic groups for the axial position in the geminal disubstituted compounds than that resulting from calculations based on the conformational free enthalpies of the involved groups [18]. The CH_2Br groups in compounds **10** and **14** prefer the axial orientation, being less bulky than the other geminal substituent.

The influence of the chirality of the spiranic skeleton was investigated by means of the diastereotopicity of hydrogen and carbon atoms. The ^1H and ^{13}CNMR spectra exhibit different signals for the protons and for the carbon atoms at the diastereotopic positions 1 (11) and 5 (7). The anancomericity of the spiranic system entails, at the same time, the recording of different signals for the protons of the equatorial and of the axial positions. The pattern for the ring protons shows two



		9	10	11	12	13	14
R^3	eq	CH_2Br	$C(CH_3)_3$	$C(CH_3)_2Br$	CH_2Br	CH_2Br	$C(CH_3)_2Br$
R^4	ax	H	CH_2Br	H	C_6H_5	p-O_2N-C_6H_4	CH_2Br

Scheme 4

AB systems. The signals corresponding to the equatorial protons are further splitted due to the W disposal of the involved bonds (Table 2, Scheme 4).

For example, in the ^1H NMR spectrum of compound **12** recorded in C_6D_6 (Fig. 1), significant values of the diastereotopicity of the equatorial ($\Delta\delta_{[1(11)-5(7)]eq} = 2.34$ ppm) and of the axial ($\Delta\delta_{[1(11)-5(7)]ax} = 0.64$ ppm) protons are observed. The long range coupling constant between the diastereotopic equatorial protons, due to the W disposal of the involved bonds H_{eq}–$C^{1(5)}$–C^6–$C^{7(11)}$–H_{eq} (Scheme 4, Fig. 1),

Table 2. NMR data (δ, ppm) for the spiranic skeleton of compounds **9**–**14**

Compound	^1H				^{13}C	
	1(11)eq	5(7)eq	1(11)ax	5(11)ax	1(11)	5(7)
9	4.52	2.92	3.00	2.53	70.31	69.41
10	4.40	2.82	3.39	2.96	64.11	63.85
11	4.55	3.01	3.06	2.61	70.39	69.47
12	4.95	2.61	3.50	2.86	65.40	64.55
13	4.69	2.70	3.18	2.62	65.84	65.35
14	4.41	2.75	3.31	2.83	64.70	64.04

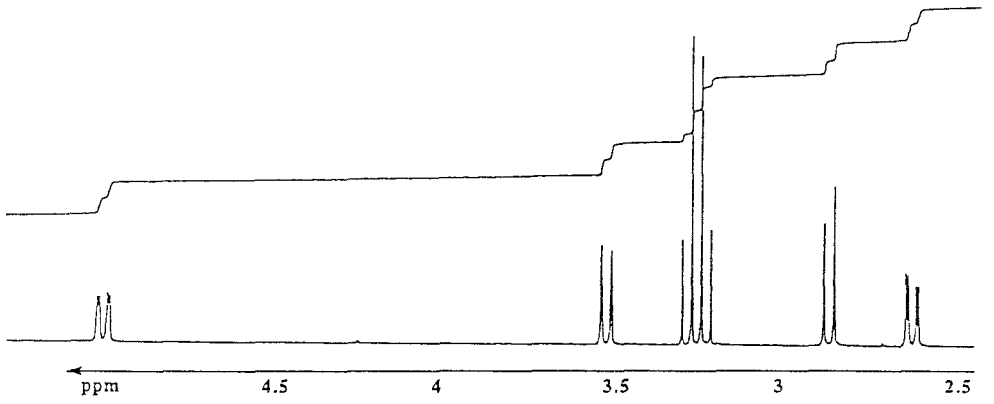


Fig. 1. ^1H NMR spectrum of compound **12** (section)

could be measured. Its magnitude ($J = 2.5$ Hz) is in accordance with literature data [19] and similar to the values obtained in all the investigated compounds (**9–14**; $J = 2.5$–2.7 Hz).

The protons at positions 1(11) are more deshielded than the protons at positions 5(7) as a result of the influence of the oxygen atoms of the spiranic skeleton. In positions 1(11), the equatorial protons are more deshielded than the axial ones. In the compounds bearing only one substituent at C(3) and C(9), *i.e.* **9** and **11**, the equatorial protons of the positions 5(7) are also more deshielded than the axial ones. In compounds bearing two geminal groups at C(3) and at C(9), *i.e.* **10** and **12–14**, the axial protons of the positions 5(7) can become more deshielded than the equatorial ones as a consequence of the influence of the axial groups located in these positions (Table 2).

The diastereotopicity of the equatorial protons is about $1.54\text{ ppm} < \Delta\delta < 2.34\text{ ppm}$, whereas that of the axial ones is about $0.43\text{ ppm} < \Delta\delta < 0.64\text{ ppm}$. The diastereotopicity of the equatorial protons belonging to the 1,3-dioxanic ring (compounds **9–14**) is significantly higher than the diastereotopicity reported for the same kind of protons in other anancomeric 1,3-dioxanic compounds with chiral carbon atoms located in position 5 ($\Delta\delta_{eq} < 0.95$ ppm) [20] or in position 2 ($\Delta\delta_{eq} < 0.05$ ppm) [16] or having chiral sulfur atoms in the aliphatic part of the heterocycle ($\Delta\delta_{eq} < 0.60$ ppm) [21]. The diastereotopicity of the axial protons gives rise to similar values as found in the other chiral compounds mentioned above ($\Delta\delta_{ax} < 0.60$ ppm [20]; < 0.25 ppm [21]). The diastereotopicity of the axial and of the equatorial protons in compounds **9–14** is also higher than that reported for other rigid spiranic compounds with a 1,5-dioxaspiro[5.5]undecanic skeleton exhibiting axial and helical chirality ($\Delta\delta_{eq} < 0.09$ ppm; $\Delta\delta_{ax} < 0.22$ ppm) [12].

The possibility was taken into account that the differences between the chemical shifts of the equatorial and axial protons and of the carbon atoms of the positions 1(11) and 5(7) could be due to a frozen structure of the groups located at positions 3 and 9 with a preference for a specific rotamer. With compounds **10** and **14**, ^{1}H NMR experiments at high temperature (in $C_6D_5CD_3$) were performed. Comparing the spectra obtained at room temperature and at 90 °C, we did not observe significant differences. The groups located at positions 3 and 9 exhibit free rotation at room temperature as well as at 90 °C. The differences between the chemical shifts of the formally identical protons of the heterocycle are therefore due to the chirality of the spiranic skeleton and not to a frozen rotation of the groups located on the spiranic skeleton.

The ^{13}C NMR spectra display also different signals for the diastereotopic methylenic carbon atoms of the 1,3-dioxanic rings (Table 2). The diastereotopicity measured for the carbon atoms is about $0.45\text{ ppm} < \Delta\delta < 0.90\text{ ppm}$. These values are similar to the majority of the data reported for other chiral 1,3-dioxanic compounds [12, 16, 20], but they are significantly smaller than the values reported for the compounds bearing a chiral sulfur atom in position 5 of the 1,3-dioxanic ring [21].

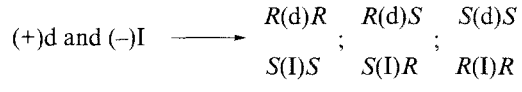
A significant feature that proves the chirality of the spiranic skeleton is the diastereotopicity of the protons and of the carbon atoms of the substituents ($-CH(H)Br$ or $-CCH_3(CH_3)Br$) located at the spiranic skeleton. In the ^{1}H NMR spectra, the protons of the CH_2Br group display an AB system and the two diastereotopic CH_3 groups of the substituent $-CCH_3(CH_3)Br$ show also two

Table 3. NMR data (δ, ppm) of the groups located on the spiranic skeleton of compounds **9–14**

Compound	^{1}H				^{13}C	
	CH(H)Br		$CBr(CH_3)CH_3$		$CBr(CH_3)CH_3$	
9	3.03	3.03	–	–	–	–
10	3.39	3.37	–	–	–	–
11	–	–	1.66	1.65	–	–
12	3.27	3.21	–	–	–	–
13	3.09	3.03	–	–	–	–
14	3.71	3.64	1.82	1.78	30.08	29.98

singlets. A similar diastereotopicity was reported for the protons of the groups located on the 1,3-dioxanic ring of other chiral 1,3-dioxanic compounds [16, 20, 22]. The ^{13}C NMR spectra show also two signals for the diastereotopic methyl groups of the substituent $-CCH_3(CH_3)Br$ (Table 3).

Compound **15** displays, in addition to the chiral elements of the spiranic skeleton, two chiral carbon atoms introduced in the system by the bromination reaction. The compound was obtained as a mixture of 3 diastereomers (Scheme 5).



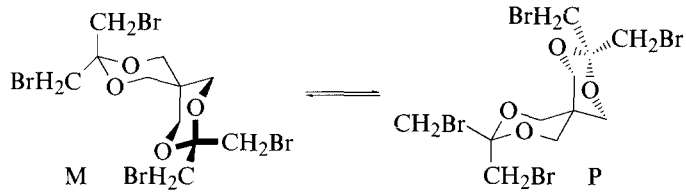
Compound **7** Compound **15**

Scheme 5

The ^{1}H NMR spectrum shows three series of signals corresponding to the diastereomers of the compound. The ratio of the isomers was evaluated from the integrals of the corresponding signals: 47% (**15A**); 33% (**15B**), and 20% (**15C**).

The differences between the chemical shifts are small both in ^{1}H and ^{13}C spectra, and therefore no the correlation between the signals of the carbon atoms and of the protons of each isomer can be performed (the 2D heteronuclear spectrum permits only correlations within the groups of signals). The structural differences between the diastereomers are not significant, and an assignment of the series of signals to each isomer is hazardous. Despite these limits in the investigation of the stereochemistry of compound **15**, the three diastereomers identified by the NMR spectra prove the chirality of the spiranic skeleton.

In the case of compound **16**, the conditions for the axial chirality are not fulfilled because both extremities of the spiranic skeleton bear identical substituents. The compound displays helical chirality (the helix begins to be built), but the rapid flipping of the rings at room temperature results in an interconversion of enantiomers ($P \rightleftharpoons M$, Scheme 6). The diastereotopicity of the protons and of the carbon atoms cannot be observed; in the NMR time-scale, mean values of the chemical shifts are recorded. The fast flipping of the rings also entails the recording of unique signals (with mean values) for the axial and for the equatorial positions.



Scheme 6

The ^{1}H NMR spectrum is a very simple one showing only two singlets: $\delta_{1,5,7,11}$ = 3.28 ppm; $\delta_{CH(H)Br}$ = 3.12 ppm.

To freeze the ring flipping, a variable temperature experiment was performed in acetone-d_6 at 300 MHz. A limit of −92 °C was imposed by the melting point of the available solvent. The separation of the signals could not be obtained; even at −92 °C, only the coalescence of the signals was recorded. The literature data [10] reported for compound **8** (with a stereochemistry similar to compound **16**) and for several symmetrically substituted spiranes with a 1,5-dioxaspiro[5.5]undecanic skeleton [11, 12, 23] show the separation of the signals corresponding to the axial and to the equatorial protons at lower temperatures than −90 °C. The activation energy for the ring flipping process (compound **16**) can be considered unsignificantly modified (as expected for an inertia effect) by the four bulky brominated group located on the spiranic structure.

Experimental

^{1}H and ^{13}C NMR spectra were recorded at room temperature in 5 mm tubes on a Bruker AM 400 (compounds **9–12**, **14–16**) or Varian VXR-300S* (compound **13**) NMR spectrometer equipped with a dual ^{13}C-^{1}H (multinuclear)* probe operating at 400 (300)* MHz for protons and 100 (75.4)* MHz for carbon atoms (solvent: C_6D_6). δ values are given in ppm relative to internal *TMS*. M.p.s were measured with a Fisher Johns melting point apparatus and are uncorrected. The synthesis and the stereochemistry of starting compounds **1–8** has already been reported [24].

New compounds (**9–16**) *general procedure*

0.1 mol (a) ketal and 100 ml dried diethyl ether were introduced in a four necked flask equipped with a reflux condenser, a mechanic stirring system, a thermometer, and a dropping funnel. To this mixture, cooled in an ice bath at 0–5 °C, the corresponding quantity (0.2–0.4 mol) of bromine was added dropwise under stirring, monitoring at the beginning the fading of the solution colour. When the addition of the bromine was finished, the ice bath was removed and the stirring was continued for an hour, the temperature in the flask reaching slowly the room value (20–25 °C). The organic solvent and the formed HBr were removed under vacuum. The products were purified by crystallization from ethanol.

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

Yield 73%; m.p. 104–105 °C; $C_9H_{14}Br_2O_4$ (346.01); calc.: 31.24 C, 4.07 H, 66.18 Br; found: 31.42 C, 4.22 H, 66.01 Br; ^{1}H NMR: 2.52 (d, 2 H J = 11.6 Hz, 5,7-H_{ax}), 2.92 (dd, 2H, J = 11.6 Hz, J = 2.6 Hz, 5,7-H_{eq}), 3.00 (d, 2H, J = 11.5 Hz, 1,11-H_{ax}), 3.03 (d, 4H, J = 4.4 Hz, 3,9-CH_2Br); 4.11 (t, 2H, J = 4.4 Hz, 3,9-H_{ax}), 4.52 (dd, 2H, J = 11.5 Hz, J = 2.6 Hz, 1,11-H_{eq}); ^{13}C NMR: 31.94 (C^6), 33.66 (3,9-CH_2Br), 69.41 ($C^{5,7}$), 70.31 ($C^{1,11}$), 100.18 ($C^{3,9}$).

3,9-Bis(bromomethyl)-3,9-di-tert-butyl-2,4,8,10-tetraoxaspiro[5.5]undecane (**10**)

Yield 62%; m.p. 210–212 °C; $C_{17}H_{30}Br_2O_4$ (458.22); calc.: 44.55 C, 6.59 H, 34.87 Br; found: 44.78 C, 6.72 H, 34.61 Br; ^{1}H NMR: 1.08 (s, 18 H, 3,9-C(CH$_3$)$_3$), 2.82 (dd, 2H, J = 12.2 Hz, J = 2.6 Hz, 5,7-H$_{eq}$), 2.96 (d, 2H, J = 12.2 Hz, 5,7-H$_{ax}$), 3.37 (d, 2H, J = 12.8 Hz, 3,9-CH(*H*)Br), 3.39 (d, 2H, J = 12.8 Hz, 3,9-CH(*H*)Br), 3.39 (d, 2H J = 11.7 Hz, 1,11-H$_{ax}$), 4.40 (dd, 2H, J = 11.7 Hz, J = 2.6 Hz, 1,11-H$_{eq}$); ^{13}C NMR: 24.53 (3,9-CH$_2$Br), 25.59 (3,9-C(*C*H$_3$)$_3$, 30.96 (C^6), 41.16 (3,9-*C*(CH$_3$)$_3$), 63.85 (C^{5,7}), 64.11 (C^{1,11}), 100.01 (C^{3,9}).

3,9-Bis(1-bromo,1-methyl-ethyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (**11**)

Yield 79%; m.p. 222–224 °C; $C_{13}H_{22}Br_2O_4$ (402.12); calc.: 38.83 C, 5.51 H, 39.74 Br; found: 38.68 C, 5.67 H, 39.98 Br; ^{1}H NMR: 1.65 (s, 6H, 3,9-C*CH*$_3$(CH$_3$)Br), 1.66 (s, 6H, 3,9-CCH$_3$(*CH*$_3$)Br), 2.61 (d, 2H, J = 11.5 Hz, 5.7-H$_{ax}$), 3.01 (dd, 2H, J = 11.5 Hz, J = 2.6 Hz, 5,7-H$_{eq}$), 3.06 (d, 2H, J = 11.5 Hz, 1,11-H$_{ax}$), 4.04 (s, 2H, 3,9-H$_{ax}$), 4.55 (dd, 2H, J = 11.5 Hz, J = 2.6 Hz, 1,11-H$_{eq}$): ^{13}C NMR: 28.28 (3,9-C*CH*$_3$(*CH*$_3$)Br), 28.91 (3,9-CCH$_3$(*CH*$_3$)Br), 32.04 (C^6), 62.73 (3,9-*C*CH$_3$(CH$_3$)Br), 69.47 (C^{5,7}), 70.39 (C^{1,11}), 105.21 (C^{3,9}).

3,9-Bis(bromomethyl)-3,9-diphenyl-2,4,8,10-tetraoxaspiro[5.5]undecane (**12**)

Yield 82%; m.p. 210–212 °C; $C_{21}H_{22}Br_2O_4$ (498.20); calc.: 50.62 C, 4.45 H, 32.07 Br; found: 50.81 C, 4.63 H, 31.85 Br; ^{1}H NMR: 2.61 (dd, 2H, J = 11.5 Hz, J = 2.5 Hz, 5,7-H$_{eq}$), 2.86 (d, 2H, J = 11.5 Hz, 5,7-H$_{ax}$), 3.21 (d, 2*H*, J = 11.0 Hz, 3,9-C*H*(H)Br), 3.27 (d, 2H, J = 11.0 Hz, 3,9-CH(*H*)Br), 3.50 (d, 2H, J = 11.5 Hz, 1,11-H$_{ax}$), 4.95 (dd, 2H, J = 11.5 Hz, J = 2.5 Hz, 1,11-H$_{eq}$), 7.04–7.12 (m, 6 aromatic H), 7.21–7.24 (m, 4 aromatic H); ^{13}C NMR: 32.03 (C^6), 40.54 (3,9-CH$_2$Br), 64.55 (C^{5,7}), 65.40 (C^{1,11}), 96.46 (C^{3,9}), 127.57 (3,9-C$_6$H$_5$ (*para*)), 127.62 (3,9-C$_6$H$_5$ (*meta*)), 129.00 (3,9-C$_6$H$_5$ (*ortho*)), 135.00 (3,9-C$_6$H$_5$ (*ipso*)).

3,9-Bis(bromomethyl)-3,9-di-p-nitrophenyl-2,4,8,10-tetraoxaspiro[5.5]undecane (**13**)

Yield 78%; m.p. 260–262 °C; $C_{21}H_{20}Br_2N_2O_8$ (588.19); calc.: 42.88 C, 3.42 H, 4.76 N, 27.16 Br; found: 42.65 C, 3.22 H, 4.69 N, 27.43 Br; ^{1}H NMR: 2.62 (d, 2H, J = 11.7 Hz, 5,7-H$_{ax}$), 2.70 (dd, 2H, J = 11.7 Hz, J = 2.5 Hz, 5,7-H$_{eq}$), 3.03 (d, 2H, J = 11.0 Hz, 3,9-C*H*(H)Br), 3.09 (d, 2H, J = 11.0 Hz, 3,9-CH(*H*)Br), 3.18 (d, 2H, J = 11.7 Hz, 1,11-H$_{ax}$), 4.69 (dd, 2H, J = 11.7 Hz, J = 2.5 Hz, 1,11-H$_{eq}$), 6.94 (d, 4 aromatic H, J = 8.1 Hz), 7.81 (d, 4 aromatic H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$): 32.81 (C^6), 39.79 (3,9-CH$_2$Br), 65.35 (C^{5,7}), 65.84 (C^{1,11}), 99.53 (C^{3,9}), 124.56, 129.47 (3,9-C$_6$H$_4$–NO$_2$, tertiary carbon atoms), 143.78, 149.21 (3,9-C$_6$H$_4$NO$_1$, quaternary carbon atoms).

3,9-Bis(bromomethyl)-3,9-bis(1-bromo,1-methyl-ethyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (**14**)

Yield 72%; m.p. 174–175 °C; $C_{15}H_{24}Br_4O_4$ (587.95); calc.: 30.64 C, 4.11 H, 54.35 Br; found: 30.58 C, 4.07 H, 54.22 Br; ^{1}H NMR: 1.78 (s, 6H, 3,9-C*CH*$_3$(CH$_3$)Br), 1.82 (s, 6H, 3,9-CCH$_3$(*CH*$_3$)Br), 2.75 (dd, 2H, J = 12.3 Hz, J = 2.5 Hz, 5,7-H$_{eq}$), 3.01 (d, 2H, J = 12.3 Hz, 5,7-H$_{ax}$), 3.31 (d, 2H, J = 12.2 Hz, 1,11-H$_{ax}$), 3.64 (d, 2H, J = 13.0 Hz, 3,9-C*H*(H)Br), 3.71 (d, 2H, J = 13.0 Hz, 3,9-CH(*H*)Br), 4.41 (dd, 2H, J = 12.2 Hz, J = 2.5 Hz, 1,11-H$_{eq}$); ^{13}C NMR: 25.36 (3,9-CH$_2$Br), 29.98 (3,9-C*CH*$_3$(CH$_3$)Br), 30.08 (3,9-CCH$_3$(*CH*$_3$)Br), 30.82 (C^6), 64.04 (C^{5,7}), 64.70 (C^{1,11}), 70.55 (3,9-*C*CH$_3$(CH$_3$)Br), 98.51 (C^{3,9}).

3,9-Bis(1-bromoethyl)-3,9-bis(bromomethyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (**15**)

Yield 78%; m.p. 161–162 °C; $C_{13}H_{18}Br_4O_4$ (559.9); calc.: 27.88 C, 3.60 h, 57.08 Br; found: 27.61 C, 3.42 H, 57.29 Br; ^{1}H NMR: **15A**: 1.442 (d, 6H, J = 6.8 Hz, 3,9-CH(Br)-CH$_3$), 2.793 (d, 2H, J = 12.2 Hz, 5,7-H$_{ax}$), 2.938 (dd, 2H, J = 12.2 Hz, J = 2.0 Hz, 5,7-H$_{eq}$), 3.187 (d, 2H, J = 12.1 Hz, 1,11-H$_{ax}$), 3.311 (d, 2H, J = 11.8 Hz, 3,9-C*H*(H)Br), 3.634 (d, 2H, J = 11.8 Hz, 3,9-CH(*H*)Br, 3.949 (dd, 2H, J = 12.1 Hz,

$J = 2.5$ Hz, 1,11-H_{eq}), 4.390 (q, 2H, $J = 6.8$ Hz, 3,9-CH(Br)CH_3); **15B**: 1.449 (d, 6H, $J = 6.8$ Hz, 3,9-CH(Br)-CH_3), 2.833 (d, 2H, $J = 12.2$ Hz, 5,7-H_{ax}), 3.013 (dd, 1H, $J = 12.2$ Hz, $J = 2.0$ Hz, 5-H_{eq}), 3.026 (dd, 1H, $J = 12.2$ Hz, $J = 2.0$ Hz, 7-H_{eq}), 3.187 (d, 2H, $J = 12.1$ Hz, 1,11-H_{ax}), 3.316 (d, 1H, $J = 11.8$ Hz, 3-C*H*(H)Br), 3.354 (d, 1H, $J = 11.8$ Hz, 3-C*H*(H)Br), 3.629 (d, 1H, $J = 11.8$ Hz, 9-CH(*H*)Br), 3.661 (d, 1H, $J = 11.8$ Hz, 9-CH(*H*)Br), 3.805 (dd, 1H, $J = 12.1$ Hz, $J = 2.5$ Hz, 1-H_{eq}), 3.875 (dd, 1H, $J = 12.1$ Hz, $J = 2.5$ Hz, 11-H_{eq}), 4.379 (q, 2H, $J = 6.8$ Hz, 3,9-CH(Br)CH_3); **15C** 1.456 (d, 6H, $J = 6.8$ Hz, 3,9-CH(Br)-CH_3), 2.788 (d, 2H, $J = 12.0$ Hz, 5,7-H_{ax}), 3.115 (dd, 2H, $J = 12.0$ Hz, $J = 2.0$ Hz, 5,7-H_{eq}), 3.187 (d, 2H, $J = 12.1$ Hz, 1,11-H_{ax}), 3.334 (d, 2H, $J = 11.8$ Hz, 3,9-C*H*(H)Br), 3.655 (d, 2H, $J = 11.8$ Hz, 3,9-CH(*H*)Br), 3.706 (dd, 2H, $J = 12.1$ Hz, $J = 2.5$ Hz, 1,11-H_{eq}), 4.371 (q, 2H, $J = 6.8$ Hz, 3,9-CH(Br)CH_3); ^{13}C NMR (**15A**, **B**, **C**): 19.26 (3,9-CH(Br)CH_3), 28.51, 28.82 (3,9-CH_2Br), 30.95 (C^6), 49.24, 49.53 (3,9-*C*H(Br)CH_3), 63.39, 63.48, 63.53, 63.75, 63.92 ($C^{1,5,7,11}$), 97.90 ($C^{3,9}$).

3,3,9,9-Tetrakis(bromomethyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (**16**)

Yield 83%; m.p. 182–183 °C; $C_{11}H_{16}Br_4O_2$ (531.84); calc.: 24.84 C, 3.03 H, 60.09 Br; found: 24.75 C, 3.08 H, 60.26 Br, ^{1}H NMR: 3.12 (s, 8H, 3,9-CH_2Br), 3.28 (s, 8H, $C^{1,5,7,11}$); ^{13}C NMR: 30.86 (3,9-CH_2Br), 31.35 (C^6), 63.37 ($C^{1,5,7,11}$), 96.46 ($C^{3,9}$).

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