^{13}C and ^{1}H NMR Spectra of Synthetic (25*R*)-5α-Spirostanes†

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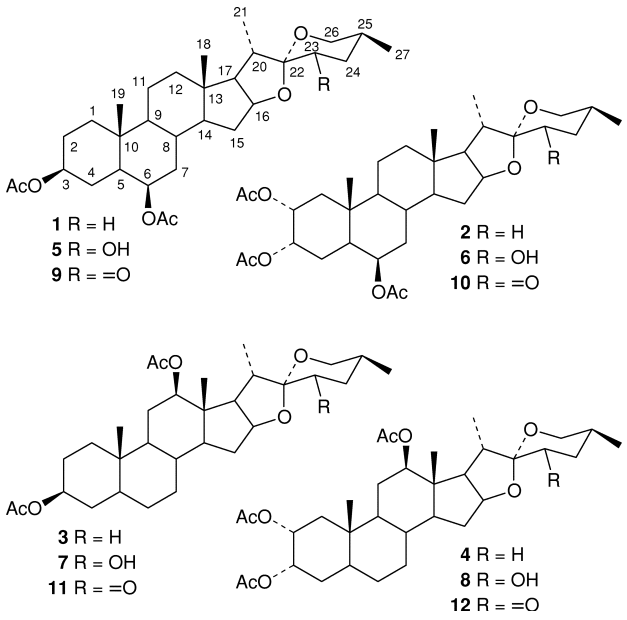
The assignment of ^{13}C and ^{1}H NMR signals of synthetic (25*R*)-5α-spirostanes is presented; the main effects on chemical shifts due to substitution at C-23 are briefly discussed.

In connection with our studies of different bioactive spirostanic compounds we required the detailed NMR spectra of a number of synthetic compounds being extensively used as materials in our program. Several reports have dealt with the ^{13}C NMR spectra of a number of naturally occurring spirostanic sapogenins.[1–3] The assignment of all ^{1}H chemical shifts for hecogenin acetate has also been reported.[4] We now report on the assignments of all ^{13}C signals of the synthetic 23-oxygenated (25*R*)-5α-spirostanes **5**–**12** and the corresponding C-23 non-substituted compounds **1**–**4** (Scheme 1).[5] Additionally, assignments for all the ^{1}H chemical shifts for compounds **1**, **5** and **9** are provided.‡



Scheme 1 Synthetic compounds studied

Results and Discussion

^{1}H and ^{13}C NMR chemical shifts of the nuclei on rings A, B and C are in good agreement with the shielding data available for equivalent substitution patterns.[4,6,7] As expected, substitution in the steroid nucleus only produces minor modifications of the shieldings of ^{1}H and ^{13}C nuclei placed on the spiroketal moiety. Table 1 shows the ^{1}H chemical shifts§ for compounds **1**, **5** and **9**.

Substitution at C-23 exerts different effects on neighbouring ^{1}H nuclei. The presence of a carbonyl function at C-23 strongly deshields H-20, H-24 and H-25. Deshielding and inversion of the relative positions of the signals of axial and equatorial H-26 due to magnetic anisotropy also characterizes the presence of the carbonyl function at C-23. Minor deshieldings are observed on the signals of H-16 and the CH_3-27. Substitution by an equatorial hydroxy group at C-23 affects the signal of H-23 axial (3.47 ppm, dd *J* 11.6/4.9) and only exerts moderate effects on the remaining protons placed on the spiroketal side chain. Only H-20 signals show a large downfield shift. Deshielding of H-20 in the C-23 substituted compounds may be rationalized on the basis of spatial proximity, van der Waals compression[4] for the hydroxy compounds (*see* Fig. 1) and a combination of such effects and carbonyl magnetic anisotropy in the ketocompounds.

^{13}C signals of the spiroketal side chain are also affected by substitution at C-23. Besides the new functional carbon signals related to the ketone (201.5 ppm) or the alcohol

Table 1 ^{1}H NMR chemical shifts (ppm) for compounds **1**, **5** and **9**

H	1	5	9	H	1	5	9	H	1	5	9
1α	1.01	1.02	1.02	9α	0.73	0.74	0.73	20	1.86	2.54	2.89
1β	1.70	1.69	1.71	11β	1.45[a]	1.41[a]	1.40[a]	21	0.96	0.95	0.93
2β	1.53	1.54	1.54	11α	1.62[a]	1.57[a]	1.55[a]	23ax	1.62	3.47	
2α	1.83	1.80	1.84	12α	1.16	1.17	1.15	23eq	1.62		
3α	4.71	4.71	4.72	12β	1.73	1.77	1.78	24ax	1.41	1.25	2.44
4β	1.31	1.30	1.32	14α	1.09	1.14	1.11	24eq	1.61	1.96	2.44
4α	1.64	1.60	1.64	15α	1.92	1.95	1.96	25ax	1.62	1.79	2.29
5α	1.33	1.33	1.33	15β	1.28	1.35	1.29	26ax	3.36	3.25	3.79
6α	4.96	4.95	4.94	16α	4.38	4.45	4.58	26eq	3.46	3.41	3.57
7α	1.15	1.16	1.15	17α	1.76	1.81	1.76	27	0.79	0.82	0.94
7β	1.82	1.82	1.81	18	0.81	0.85	0.80				
8β	1.80	1.79	1.78	19	1.03	1.03	1.03				

[a]Strongly coupled protons, approximate values.

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‡The assignments were obtained with the information given by HHCOSY and HETCOR spectra. Complementary ^{1}H spectral data are available on request from the authors.

§Spectra were recorded on a Bruker ACF 250 NMR Spectrometer using $CDCl_3$ as solvent with Me_4Si (^{1}H) or the solvent signal at 77.0 ppm (^{13}C) as references. The working temperature was 300 K and the concentrations of the samples were 10 and 30 mg ml^{-1} for ^{1}H and ^{13}C NMR spectra respectively.

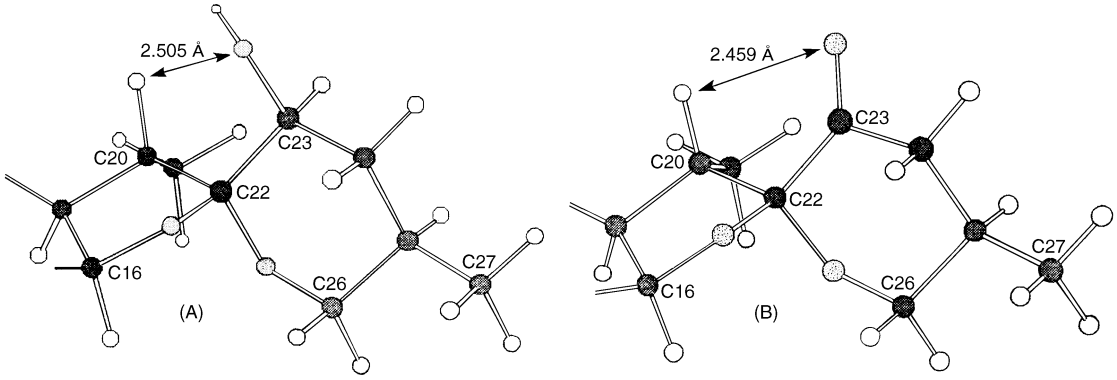

Fig. 1 Fragment of the molecular graphics[8] corresponding to the side chains of (A) (25*R*)-23-hydroxyspirostan and (B) (25*R*)-23-ketospirostan

Table 2 ^{13}C chemical shifts (ppm) for compounds **1**–**12**

C	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
C-1	37.9	39.2	36.5	37.9	38.0	39.4	36.5	37.9	37.9	39.2	36.5	37.7
C-2	27.2	69.2	27.3	69.8	27.3	69.4	27.3	69.8	27.2	69.2	27.2	69.5
C-3	73.2	68.5	73.4	69.1	73.3	68.8	73.4	69.1	73.3	68.6	73.3	68.8
C-4	30.8	29.2	33.8	32.2	30.9	29.4	33.8	32.2	30.8	29.2	33.8	32.0
C-5	46.0	41.0	44.5	39.3	46.2	41.2	44.5	39.4	46.1	41.0	44.4	39.1
C-6	72.9	71.9	28.3	27.2	73.1	72.3	28.3	27.2	73.0	72.0	28.3	27.0
C-7	36.4	36.0	31.1	31.1	36.5	36.3	31.1	31.1	36.3	36.0	31.1	31.2
C-8	30.5	29.7	34.1	33.4	30.4	29.8	33.9	33.3	30.5	29.7	34.0	33.1
C-9	53.7	53.4	52.6	52.6	53.8	53.8	52.6	52.6	53.7	53.4	52.6	52.4
C-10	35.5	36.7	35.6	37.0	35.6	37.0	35.6	37.0	35.5	36.8	35.6	36.8
C-11	20.6	20.3	26.7	26.5	20.7	20.4	26.7	26.4	20.6	20.2	26.7	27.0
C-12	39.7	39.4	81.6	81.6	39.9	39.7	81.6	81.6	39.5	39.2	81.3	81.1
C-13	40.5	40.3	44.6	44.5	41.0	41.0	45.0	45.0	41.0	40.8	45.0	44.7
C-14	55.7	55.5	54.7	54.7	55.7	55.6	54.6	54.6	55.8	55.6	54.8	54.6
C-15	31.6	31.4	31.6	31.5	31.7	31.6	31.6	31.5	31.6	31.4	31.6	31.7
C-16	80.5	80.3	80.5	80.4	81.4	81.3	81.2	81.2	83.0	82.8	82.9	82.7
C-17	62.0	61.9	61.2	61.2	61.5	61.5	60.6	60.7	61.6	61.5	60.7	60.5
C-18	16.4	16.2	11.6	11.6	16.6	16.5	11.8	11.8	16.2	16.0	11.4	11.3
C-19	15.0	15.2	12.1	12.4	15.1	15.5	12.1	12.4	15.1	15.3	12.1	12.2
C-20	41.5	41.3	42.1	42.1	35.6	35.5	36.0	36.1	34.7	34.5	35.7	35.1
C-21	14.4	14.2	13.6	13.7	14.1	14.0	13.2	13.2	14.3	14.1	13.5	13.3
C-22	109.0	108.8	109.2	109.3	110.5	110.6	110.6	110.7	109.7	109.5	109.8	109.6
C-23	31.3	31.1	31.4	31.4	67.0	67.0	67.0	67.0	201.7	201.2	201.6	201.4
C-24	28.7	28.5	28.8	28.8	38.5	38.4	38.4	38.4	45.1	44.9	45.2	45.0
C-25	30.2	30.0	30.2	30.2	30.8	30.7	30.8	30.8	35.8	35.6	35.3	35.5
C-26	66.6	66.5	66.8	66.8	65.9	65.9	65.9	65.9	65.5	65.3	65.6	65.4
C-27	17.0	16.9	17.1	17.1	16.7	16.6	16.6	16.5	17.0	16.8	17.0	16.9

group (67.0 ppm) present at C-23 and the corresponding β effects at C-24, a significant deshielding of C-25 is observed in the 23-keto compounds, which is attributable to the loss of the 1,3 diaxial interaction between H-23 and H-25. Substitution at C-23 also produces shielding at C-20 which be attributed to a γ-*gauche* interaction, which is in agreement with the corresponding H-20 shifts (*see* Fig. 1). A minor deshielding effect at C-16 is also observed. Table 2 shows the ^{13}C chemical shifts for compounds **1**–**12**.

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