Characterization by 2D-NMR and Chemical Properties of (20*Z*)-3-Methoxy-17-[2-(triphenylstannyl)vinyl]estra-1,3,5(10)-trien-17β-ol

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The complete solution structure and conformation of the title compound were determined by 2D proton detected ^{1}H–^{13}C HMQC-RELAY and 2D-NOESY build-up experiments. The assignment of the low field resonances of the quaternary carbon atoms was achieved by 1D–^{13}C NMR with selective decoupling of the high field protons. Proton detected ^{1}H–^{119}Sn HMBC 1D and 2D NMR spectroscopy enables the observation of a very weak coupling between the hydroxy proton of the steroid moiety and the ^{119}Sn nucleus. These proton detected experiments as well as ^{13}C and ^{119}Sn SIMPLE NMR provide evidence for a HO→Sn coordination to occur in solution.

Steroids with tin–carbon bonds are still rare.[1,2] We recently reported the synthesis, X-ray diffraction analysis[2] and full 2D-NMR characterization[3] of (20*Z*)-17-[2-(triphenylstannyl)-vinyl]estr-4-en-17β-ol (**1**), as well as the high *in vitro* antitumour activity of some of its derivatives.[4,5] We now report the structural and conformational characterization in solution of another steroid tin compound (20*Z*)-3-methoxy-17-[2-(triphenylstannyl)vinyl]estra-1,3,5(10)-trien-17β-ol (**2**).

Basically, the same assignment strategy was used as for compound **1**,[3] *i.e.* the combination of inverse detected HMQC-RELAY[6] and 2D-NOESY[7] experiments. Some new aspects are however to be emphasized. First, compound **2** exhibits three quaternary aromatic carbons in the steroid moiety the assignment of which cannot be performed by the approach used for **1**. A 1D–^{13}C spectrum with selective decoupling of the high field protons completed the missing signal assignment. Second, comparison of interproton distances of **2** with those of **1** as obtained from 2D NOESY build-up experiments and molecular mechanics calculations enables one to assess the influence of the aromatic ring A upon the conformation of the other steroid rings. Finally, we present the result of heteronuclear multiple bond correlation (HMBC)[8,9,10] experiments applied to the ^{119}Sn nucleus as a novel tool to evaluate the possible existence of an intramolecular coordinative bond between the steroidal hydroxy group and the tin atom. The existence of such a coordinative bond was confirmed by ^{13}C and ^{119}Sn Secondary Isotope Multiplet of Partially Labelled Entities[11] experiments (^{13}C and ^{119}Sn SIMPLE-NMR).

Experimental

The syntheses of compounds **2** and **3** were described previously.[4] The NMR samples were prepared by dissolving the appropriate amount of **2** in CDCl$_3$ (0.5 cm^3), *ca.* 5 mg for ^{1}H and for proton detected heteronuclear experiments (degassed and sealed sample) and 60 mg for ^{13}C, DEPT and ^{119}Sn spectra.

The HO:DO ratio for SIMPLE-NMR experiments[11] was adjusted to $\approx 30:70$ by adding the appropriate amount of the deuteriated sample to a CDCl$_3$ solution of the protonated one. The degree of deuteriation was estimated from the intensity decrease in the resonance of the hydroxy proton as well as from the ^{13}C–OH/^{13}C–OD resonances.

Selective decoupling of the high field proton resonances was achieved by reducing the decoupling power, setting the decoupler frequency in the middle of the aliphatic region, until aromatic proton decoupling was no longer observed.

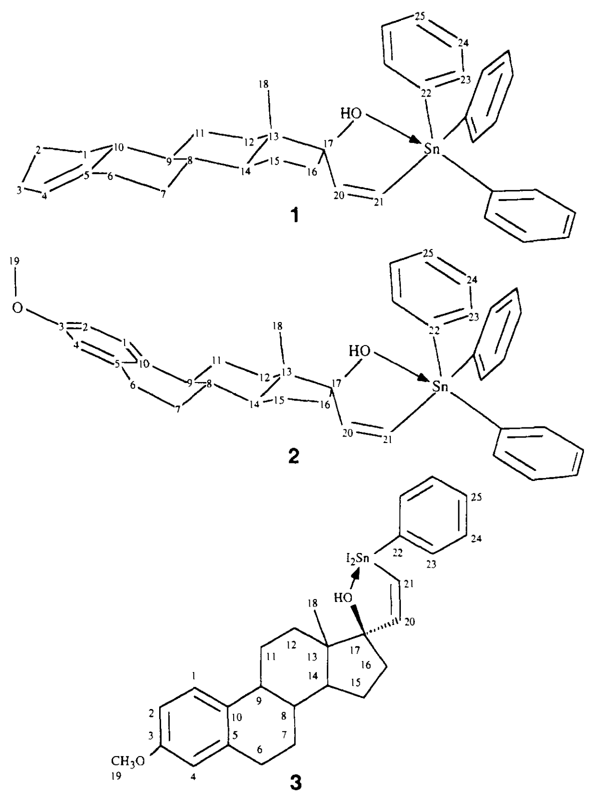

Fig. 1 Compounds **1** and **2** and the diiodophenylstannyl analogue **3** of compound **2**

The 2D ^{1}H–^{119}Sn heteronuclear multiple bond correlation (HMBC) spectra were recorded at 93.28 MHz for the ^{119}Sn and at 250.13 MHz for the ^{1}H nuclei on a Bruker AC250 NMR spectrometer equipped with a 5 mm QNP (^{1}H, ^{19}F, ^{119}Sn, ^{13}C) probe. 1D ^{1}H–^{119}Sn HMBC spectra were obtained using a 10 mm X-{^{1}H} BB probe at 186.50 MHz resonance frequency for the ^{119}Sn nucleus and at 500.13 MHz for the proton. All other spectra were recorded on a Bruker AMX500 spectrometer using standard pulse sequences from the Bruker pulse program

Table 1 Chemical shift and coupling data for compound **2**[a]

C	δ	H	δ
1	126.3	1	7.12 (d: 9)
2	111.4	2	6.65 (dd: 9, 3)
3	157.4		
4	113.8	4	6.58 (d: 3)
5	137.8		
6	29.8	6αβ	2.80
7	27.5	7α	1.31
		7β	1.85
8	39.5	8	1.41
9	43.7	9	2.11
10	132.4		
11	26.3	11α	2.19
		11β	1.31
12	32.6	12α	1.42
		12β	1.24
13	47.2		
14	49.8	14	1.61
15	23.7	15α	1.76
		15β	1.40
16	39.4	16α	2.02
		16β	1.68
17	85.6 [28][b]	17β-OH	1.40 (bs) [≈1][c]
18	14.1	18	0.68 (s)
19	55.2	19	3.69 (s)
20	152.6	20	7.03 (d: 12) [177/187]
21	121.5 [573/599]	21	6.21 (d: 12) [97/100]
22	142.6 [516/542]		
23	136.8 [37][b]	23	7.6 [50][b]
24	128.1 [50/51]	24	7.3
25	128.2 [11]	25	7.3

[a] ^{13}C Chemical shifts were obtained from a proton decoupled spectrum. ^{1}H Shifts were obtained from 1D-proton and/or inverse detected HMQC-RELAY spectra. Multiplicity and coupling values in Hz derived from the 1D proton spectrum are shown in parentheses. Multiplicity for proton resonances: a, singlet; bs, broad singlet; d, doublet; dd, doublet of doublets; all other protons exhibit complex and/or overlapping coupling patterns. $^{x}J_{^{1}H-^{117/119}Sn}$ and $^{x}J_{^{13}C-^{117/119}Sn}$ coupling constant values are given in brackets. [b] Not resolved. [c] $^{4}J_{^{1}H-^{1}H}$ Coupling only visible in the 1D ^{1}H–^{119}Sn HMBC spectrum.

library. The spectral referencing and the parameters used for the ^{1}H–^{13}C HMQC-COSY,[12] ^{1}H–^{13}C HMQC-RELAY[6] and 2D NOESY[7] experiments were similar to those used for compound **1**.[3]

The 1D proton detected ^{1}H–^{119}Sn HMBC spectra were recorded using the four pulse sequence and phase cycling proposed by Bax *et al.*[9] The delays were set to 260 ms corresponding to a $^{n}J_{^{1}H-^{119}Sn}$ value of 2 Hz. 32 K Data points with a spectral width of 10 204 Hz were sampled for each spectrum with and without ^{119}Sn decoupling.

The 2D proton detected ^{1}H–^{119}Sn HMBC was recorded using the pulse sequence and phase cycling proposed by Bax and Summers.[8] The experiment was optimized to an average $^{n}J_{^{1}H-^{119}Sn}$ value of 8 Hz (delay = 62 ms). No lowpass *J*-filter and no ^{119}Sn decoupling were used. 24 FIDs were recorded and zero-filled to 64 in the F_1 dimension with a spectral width of 800 Hz. 4 K Data points, no zero-filling, a spectral width of 2500 Hz (acquisition time 82 ms), 128 scans, and a relaxation delay of 2 s, were used in the F_2 dimension.

NMR spectral simulations were carried out on an Apple Macintosh II computer using NMR″ software.[13] Molecular mechanics calculations were carried out on an Apple Macintosh II computer using Chem3D[14] software.

Results and Discussion

Complete ^{1}H *and* ^{13}C *Resonance Assignment of Compound* **2**.—The proton NMR spectrum of **2** exhibits as expected two characteristic ethylenic proton doublets at 7.03 and 6.21 ppm, with $^{3}J_{H-C=C-H}$ = 12.3 Hz, respectively featuring $^{3}J_{H-C=C-^{117/119}Sn}$ = 177/187 and $^{2}J_{H-C-^{117/119}Sn}$ = 97/100 Hz coupling satellites. These olefinic ^{1}H resonances can be easily assigned to H(20) and H(21) respectively on the basis of their tin–proton ^{3}J coupling constant being usually larger than the ^{2}J one.[15] According to data[3] obtained for **1** and the value of the $^{3}J_{H-C=C-H}$ coupling constant[16] of the present compound **2** the latter is identified as the *Z*-isomer.

The final ^{1}H and ^{13}C resonance assignments obtained for compound **2** are given in Table 1. As for the olefinic protons, the phenyl *ortho* proton H(23) is easily identified by its proton–tin coupling satellites.

The aromatic protons H(4), H(2) and H(1) of the steroid moiety induce a well resolved AMX spectrum. The phenyl *meta* and *para* protons H(24) and H(25) exhibit the usual complex pattern around 7.3 ppm. Starting from this proton identification, an inverse detected hetero-shift ^{1}H–^{13}C correlation spectrum (HMQC-COSY) allowed the assignment of all low field ^{1}H–^{13}C resonance pairs. The assignment of the C(21) and C(23) resonances is reinforced by the presence of ^{13}C–$^{117/119}$Sn coupling satellites. The carbon atom C(20) is resonating at very low field (152.6 ppm) without any visible $^{2}J_{^{13}C-^{117/119}Sn}$ coupling. The absence of such $^{2}J_{^{13}C-^{117/119}Sn}$ couplings in olefinic compounds is well established.[15,17] However, the HMQC-COSY spectrum displays an unambiguous correlation peak C(20)–H(20) and this proton exhibits the characteristic $^{3}J_{^{1}H-^{117/119}Sn}$ coupling satellites. The quaternary carbon atoms C(22) and C(17) are also identified by their $^{n}J_{^{13}C-^{117/119}Sn}$ coupling satellites.

The resonance assignment of the quaternary carbons of the steroid moiety in the low field region was more cumbersome. The carbon atom C(3) is resonating at lower field, as predicted from aromatic chemical shift increment calculations.[17] The unambiguous assignment of the C(5) and the C(10) resonances required an additional 1D–^{13}C spectrum with selective decoupling of the aliphatic protons. Thus, C(5) exhibits a doublet while C(10) displays a doublet of doublets appearing as a pseudo-triplet due to two identical *meta* $^{3}J_{^{13}C-^{1}H}$ couplings, the *ortho* $^{2}J_{^{13}C-^{1}H}$ coupling in the aromatic ring being much smaller. This simple 1D–^{13}C experiment makes a 2D heteronuclear long range correlation experiment of only limited need for this type of steroidal compound. Therefore an additional inverse detected ^{1}H–^{13}C heteronuclear multiple bond correlation experiment (HMBC) spectrum, was recorded only for the sake of confirming the above assignment.

As for most steroids, the high field region of the proton spectrum is overcrowded. Standard and DEPT ^{13}C as well as HMQC-COSY spectra do not enable the direct assignment of the ^{1}H and/or ^{13}C resonances of the methine and especially of the methylene groups. Proton detected ^{1}H–^{13}C heteronuclear relayed coherence transfer spectroscopy (HMQC-RELAY)[3,6] provided the additional data needed (Fig. 2). One bond ^{1}H–^{13}C correlations are easily identified in the HMQC-RELAY spectrum (Fig. 2) from the higher intensity of their cross-peaks, provided a sufficiently small initial evolution delay is chosen. Despite the overlapping of some one-bond correlation peaks with relay cross-peaks the complete assignment of the aliphatic ^{1}H and ^{13}C resonances could be achieved in this way from the HMQC-RELAY spectrum. The resonance assignment in the HMQC-RELAY spectrum was started from the 2D-NOESY cross-peak H(4)–H(6αβ) identifying the resonance of both H(6) which appear to be isochronous. From this starting point all the aliphatic ^{13}C and ^{1}H resonances were assigned straightforwardly, since each ^{1}H–^{13}C pair appears to be correlated to its neighbour by at least one well visible relay cross-peak. Alternative starting points from the 2D-NOESY cross-peaks H(1)–H(9) or H(20)–H(14) confirmed these assignments.

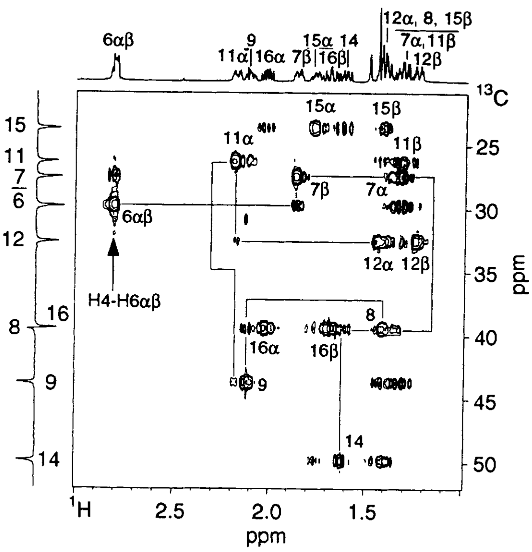

Fig. 2 2D Proton detected HMQC-RELAY spectrum of compound **2** recorded at 500.13 MHz. A 1D proton and a ^{13}C DEPT spectrum are plotted along the horizontal and the vertical axes, respectively. The resonance assignment for the A, B and C rings starting from the 2D-NOESY cross-peak H(4)–H(6αβ) identifying the resonance of both H(6), is outlined by solid lines. The assignment of the D ring is omitted for clarity.

Table 2 Selected 2D-NOESY cross-peaks and distances calculated from the 2D-NOESY build-up experiment for **2**[a]

Proton pair	Distance/Å
α-Face	
1–9	3.15[b] (3.07)
1–11α	2.07 (1.88)
7α–9	2.55[b] (2.31) [2.29]
7α–14	2.78 (2.66) [2.49]
9–12α	2.67 (2.57) [2.45]
9–14	2.32 (2.42) [2.30]
12α–20	2.77 (2.48) [2.45]
14–15α	2.63 (2.39)
14–20	2.14 (2.48) [2.03]
16α–20	2.72 (2.79) [2.62]
β-Face	
11β–18	2.54
12β–18	2.55 [2.26]
16β–18	2.57 [2.92]
Other distances	
1–2	2.45[c] (2.45)
7α–7β	1.93 (1.82) [1.76]
11α–11β	1.89 (1.82) [1.76]
11α–12α	2.37 (2.46)
11α–12β	2.08 (2.45) [2.53]
15α–15β	2.03 (1.82)
15α–16α	1.98 (2.27)
15β–16β	2.02 (2.25)
16α–16β	1.82 (1.83)

[a] The distances given within parentheses are the distances determined from molecular mechanics calculations using MM2. The distances given within brackets are the distances obtained[3] for compound **1**. [b] Poor correlation coefficients are found for the build-up straight lines of these proton pairs. The 2D-NOESY build-up data were analysed using method 3 of Andersen *et al.*[21] [c] Used as reference distance.

2D-NOESY spectra were used to assign the α or β position of the methylene protons. Furthermore, the NOESY cross-peaks H(18)–OH(17β) and H(23)–OH(17β) characterize clearly the singlet at 1.40 ppm in the 1D-proton spectrum as arising from the OH(17β) group. This was further confirmed by the addition of CD_3OD to the solution causing this singlet to collapse. However, the H(23)–OH(17β) cross-peak is not really any evidence to the existence of a coordination of this hydroxy group to the tin atom. Because rotation around the C(17)–C(20) bond is likely to be hindered the hydroxy group could be forced into a position close to H(23) even without coordination to the tin atom. Secondary isotopic effects observed in the ^{13}C and the ^{119}Sn NMR spectra (^{13}C and ^{119}Sn SIMPLE-NMR)[11] as well as 1D ^{1}H–^{119}Sn HMBC experiments[10] provide evidence for the existence of the latter (see below).

Proton–Proton Distances.—The important cross-peaks and proton–proton distances derived from the 2D-NOESY build-up experiment are shown in Table 2. The distances are given together with those obtained from molecular mechanics calculations (MM2) as well as with the corresponding distances of **1** when comparison is possible.

The NOESY cross-peak between the H(1) and H(9) atoms being observed, ring B can only exhibit a (6β,7α)-diaxial conformation. This is further confirmed by the presence of the cross-peaks 7α-14, 7α-9, 6β-8 and the absence of any cross-peak between H(6α) and H(9). Despite their isochrony, the origin of the cross-peaks associated with H(6) can be assigned to the α or β side from geometrical arguments. However the isochrony of the 6α and 6β resonances prevents any normalization of such cross-peaks to the auto-peak 6αβ–6αβ. Therefore no distance evaluation can be done with reference to the H6αβ auto-peak. For ring C the (11β–12α)-diaxial chair conformation is observed. For ring D the conformation is somewhat more uncertain. Indeed, the protons H(15β) and H(8) are isochronous and no distances involving these protons could be determined. However, the distances of 2.63 and 2.57 Å for the proton pairs 14–15α and 16β–18 indicate an envelope conformation with 15β in a pseudo-axial position.

The conformational data obtained from the NOESY build-up experiment was complemented for the D ring by those from the DQF-COSY spectrum. The coupling values obtained were checked by spectral simulation of the 1D multiplets using the Bruker PANIC software in the iterative mode. The same set of coupling values was obtained from the simulation when the initial coupling values used were calculated from the torsional angles of the MM2 model using a Karplus relationship.[18] The rather large coupling values of 9.7 and 11.2 Hz found for the proton pairs 15α–16α and 15β–16β respectively indicate a small torsional angle between these protons, confirming our findings from the 2D NOESY build-up experiment. No useful set of ^{1}H–^{1}H couplings were obtained for the B and C rings of the steroid moiety because of the numerous overlaps of several proton resonances as well as the rather large ($\geqslant 1$ Hz) line width of the resonances resulting in DQF-COSY signal cancellation[19] and/or noninterpretable multiplet patterns. The other coupling constants found for the pairs 8–14, 14–15α, 14–15β, 15α–15β, 15α–16β, 15β–16α and 16α–16β with values of 12.1, 6.4, 10.7, 12.3, 2.7, 6.4 and 14.1 Hz respectively, are consistent with the conformation proposed as well as with literature data.[18]

All the calculated distances (Table 2) differ only slightly from the experimental ones, the maximal deviation being 0.37 Å. However, the rings B and C seem to be more flattened in compound **2** than in **1**. Indeed, the distances 7α–9, 7α–14, 12α–20 and 12β–18 appear to be longer in **2** while the distances 16β–18 and 11α–12β are shorter as would be expected for the substitution of the sp^3 carbon of **1** at position 10 by a sp^2 one.

^{1}H–^{119}Sn *HMBC Spectroscopy.*—The standard 1D ^{119}Sn spectrum of **2** exhibits a singlet at −157.5 ppm. This chemical shift value is nearly identical to the one observed[3] for compound **1**. We introduced recently 1D and 2D HMBC

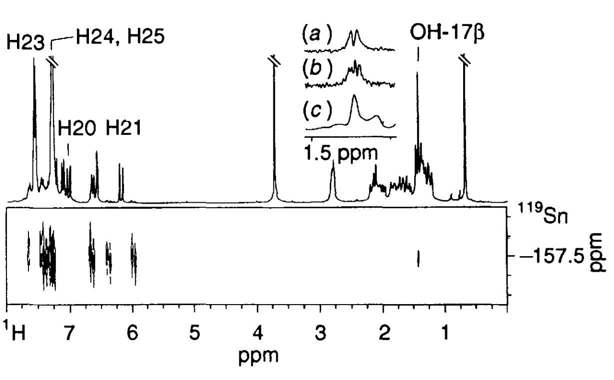

Fig. 3 2D Proton detected ^{1}H–^{119}Sn HMBC spectrum at 250.13 MHz of compound **2** optimized for $1/(2J_{H\text{-}Sn}) = 62$ ms exhibiting a cross-peak between the hydroxy proton H(17β) and the tin resonance with the corresponding 1D spectrum on top. Insert: 1D HMBC spectra at 500.13 MHz of compound **2** optimized for $1/(2J_{H\text{-}Sn}) = 260$ ms [hydroxy proton H(17β)] showing the effect of the pulse sequences applied with (*a*) and without (*b*) ^{119}Sn decoupling. The corresponding standard 1D proton spectrum is given for comparison (*c*).

spectroscopy applied to the ^{119}Sn nucleus[10] in order to assess the existence of intramolecular coordinations from a hydroxy group to a tin atom in organotin derivatives. For compound **2** the results of such experiments can be summarized as follows.

The 2D ^{1}H–^{119}Sn HMBC spectrum at 250.13 MHz of **2** (Fig. 3) exhibits an unambiguous cross-peak between the OH–17β proton and the ^{119}Sn nucleus. 1D HMBC spectra at 500.13 MHz with and without ^{119}Sn decoupling, shown in the insert of Fig. 3, together with the corresponding standard 1D spectrum, allows a more accurate analysis of the spectral pattern of the hydroxy proton. The doublet of 1.9 Hz observed in the presence of ^{119}Sn decoupling (insert *a*) can be assigned to a $^{4}J_{^{1}HO\text{-}^{1}H}$ of the hydroxy group with H(20) as confirmed by a long-range ^{1}H–^{1}H COSY spectrum. The existence of this coupling can be explained by the presence of an intramolecular HO → Sn bond which forces the moiety H(17)–O–C–C–H into a 'W conformation',[16] giving such long-range couplings. In the absence of such a coordination, this 'W-conformation' would be a single one among a distribution of conformations which would make the long range coupling unlikely to be observed.

Accordingly, the resonance observed in the 1D ^{1}H–^{119}Sn HMBC experiment without ^{119}Sn decoupling (insert *b*) is a doublet ($^{4}J_{HO\text{-}H}$) of doublets, the additional splitting arising from a ^{1}H–^{119}Sn coupling of about 1 Hz. The latter arises from either a $^{2}J_{HO\rightarrow Sn}$ coupling due to the intramolecular HO→Sn coordination, a $^{5}J_{H\text{-}O\text{-}C\text{-}C=C\text{-}Sn}$ long range coupling or a combination of both. No unambiguous discrimination between these coupling pathways is possible. However, the standard 1D spectrum (insert *c*) shows no $^{4}J_{HO\text{-}H}$ coupling but only a broad singlet. We suggest the latter singlet to be broadened because it arises from the averaging of the hydroxy resonances of the distribution of conformations mentioned above. This makes the small $^{4}J_{HO\text{-}H}$ coupling splitting and also the small ^{1}H–^{119}Sn satellites invisible. In contrast, the HMBC spectra specifically edit only those protons coupled to a tin-119 nucleus. The spectral pattern of the ^{1}H–^{119}Sn HMBC spectrum indicates that this occurs in a conformation where the $^{4}J_{HO\text{-}H}$ coupling is visible simultaneously to the $^{n}J_{HO\text{-}Sn}$ coupling, that is precisely in the W-like conformation where the HO→Sn coordination can be achieved. Obviously the pattern of the 1D HMBC spectrum is not in agreement with conformations where the $^{n}J_{HO\text{-}Sn}$ coupling exists and the $^{4}J_{HO\text{-}H}$ one does not. This observation provides strong evidence for the existence of the HO→Sn coordination.

Further evidence to the existence of this coordinative bond in solution was also gained from ^{13}C and ^{119}Sn SIMPLE-NMR[11] experiments. Secondary isotopic effects on the ^{13}C chemical shift ($\delta_{^{13}C^{2}H} - \delta_{^{13}C^{1}H}$) of −0.01, −0.07, −0.10, −0.01 and −0.01 ppm, resulting from the deuteriation of the hydroxy group, were observed for the carbon atoms C(13), C(16), C(17), C(20) and C(22) respectively. The isotope shift for the ipso carbon [C(22)] can reasonably only result from a three bond effect through the pathway: D–O→Sn–C(22). This is further confirmed by the secondary isotopic effect on the ^{119}Sn chemical shift ($\delta_{^{119}Sn^{2}H} - \delta_{^{119}Sn^{1}H}$) of +0.02 ppm observed in a ^{119}Sn SIMPLE-NMR experiment.

Proton NMR Study of the Iododemetallation of **2**.—The iododemetallation of compound **2** to its diiodo derivative **3** was studied by ^{1}H NMR. Roughly its spectral features are in agreement with our previous results[2,4] on compound **1**. The two olefinic protons of compound **3** are shifted to 6.72 and 6.48 ppm. The resonance of H(20) overlaps with that of the aromatic H(2) while that of H(21) is a doublet with a coupling constant $^{3}J_{H\text{-}C=C\text{-}H}$ of 10.5 Hz. H(20) Appears as an incompletely resolved doublet of doublets likely to be due to a small additional $^{4}J_{H\text{-}H}$ coupling between H(20) and the OH-17β. No resonances for a vinyl iodide moiety are observed. This indicates a high regiospecificity of the iododemetallation reaction toward the phenyl group. This observation is additional chemical evidence for the existence of the intramolecular HO→Sn coordination[2] in **2**.

The spectral pattern of the ^{1}H–^{119}Sn satellites in compound **3** is worth outlining. The vinylic tin–proton couplings are not easily recognized (Fig. 4) because they obey a non-first order spectral pattern. In addition the low-field tin satellite of H(20) is hidden by resonances of iodobenzene. A spectral simulation, shown in Fig. 4, establishes that this rather unusual tin–proton coupling pattern observed at 270 MHz can be understood in terms of a superposition of non-first-order ABX and ABZ systems (A = H(20); B = H(21); X = ^{119}Sn; Z = ^{117}Sn). Spectrum (*b*) represents the best fit to the experimental spectrum (*a*) (omitting the aromatic resonances above 7 ppm). It was obtained with values of $^{3}J_{^{1}H\text{-}C=C\text{-}^{117/119}Sn} = 315/330$ and $^{2}J_{^{1}H\text{-}^{117/119}Sn} = 194/203$ Hz. The value of the ^{2}J constant was obtained from the simulations shown in spectra (*c*)–(*n*). Thus the spectra (*c*)–(*f*) are simulations of the ^{1}H–$^{117/119}Sn$ coupling satellites with the value of $^{3}J_{^{1}H\text{-}C=C\text{-}^{117/119}Sn}$ fixed at 315/330 Hz and the value of $^{2}J_{^{1}H\text{-}^{117/119}Sn}$ being varied. For simplicity, the pattern arising from the aromatic H(2) and H(4) were omitted. The spectra (*c*)–(*f*) are superpositions of respectively the spectra (*g*)–(*j*) resulting from the ABX system consisting of H(20) (A), H(21) B and ^{119}Sn (X) and the spectra (*k*)–(*n*) resulting from the ABZ system consisting of H(20) (A), H(21) (B) and ^{117}Sn (Z). The best fit to the experimental satellite pattern of spectrum (*a*) was that obtained with the parameters used in simultation (*e*), the superposition of the simulations (*i*) and (*m*). A proton spectrum recorded at 500 MHz exhibits as expected first order $^{117/119}Sn$ satellites confirming the coupling values obtained from the spectral simulations. These simulations illustrate that the proton–tin satellites can be nonsymmetric[20] and may exhibit local non-first-order behaviour.

Conclusions

We suggest that the combination of ^{1}H–^{13}C HMQC-RELAY with a semi-selectively decoupled 1D–^{13}C experiment might be a superior approach to the NMR characterization of this type of steroid compounds than using ^{1}H–^{13}C HMBC spectroscopy. As did Lerner and Bax,[6] we observed a better sensitivity and suppression of ^{1}H–^{12}C resonances in the HMQC-RELAY than in the HMBC spectrum. Furthermore, interpreting a ^{1}H–^{13}C HMQC-RELAY spectrum is obviously less tedious than a HMBC spectrum.

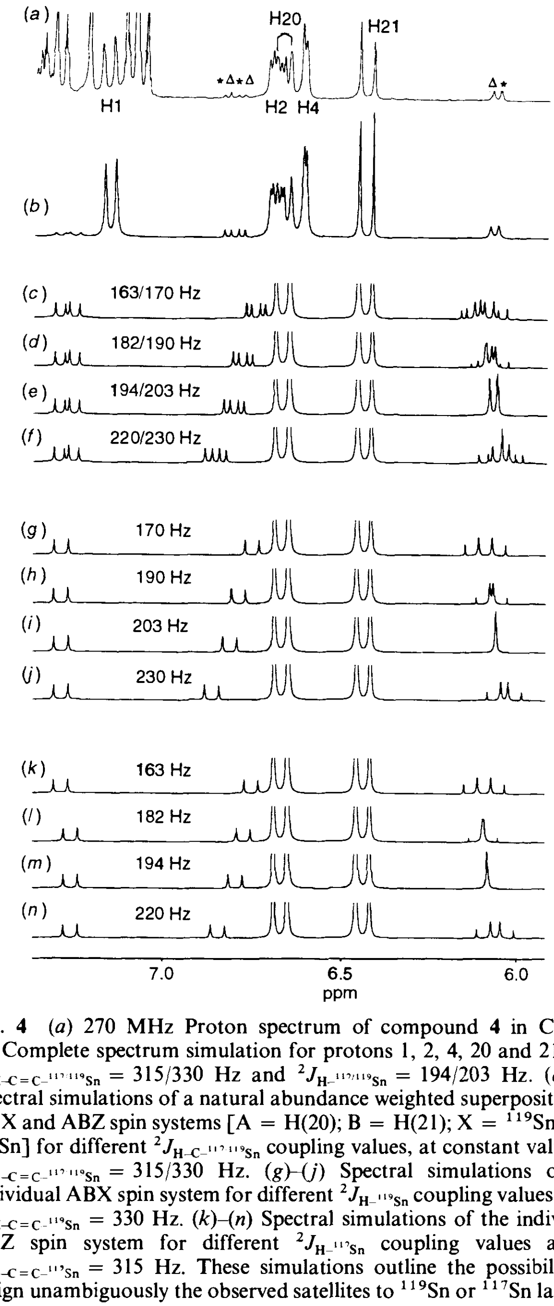

Fig. 4 (*a*) 270 MHz Proton spectrum of compound **4** in $CDCl_3$. (*b*) Complete spectrum simulation for protons 1, 2, 4, 20 and 21 with $^3J_{H\text{-}C=C\text{-}^{117/119}Sn}$ = 315/330 Hz and $^2J_{H\text{-}^{117/119}Sn}$ = 194/203 Hz. (*c*)–(*f*) Spectral simulations of a natural abundance weighted superposition of ABX and ABZ spin systems [A = H(20); B = H(21); X = ^{119}Sn; Z = ^{117}Sn] for different $^2J_{H\text{-}C\text{-}^{117/119}Sn}$ coupling values, at constant values of $^3J_{H\text{-}C=C\text{-}^{117/119}Sn}$ = 315/330 Hz. (*g*)–(*j*) Spectral simulations of the individual ABX spin system for different $^2J_{H\text{-}^{119}Sn}$ coupling values and a $^3J_{H\text{-}C=C\text{-}^{119}Sn}$ = 330 Hz. (*k*)–(*n*) Spectral simulations of the individual ABZ spin system for different $^2J_{H\text{-}^{117}Sn}$ coupling values and a $^3J_{H\text{-}C=C\text{-}^{117}Sn}$ = 315 Hz. These simulations outline the possibility to assign unambiguously the observed satellites to ^{119}Sn or ^{117}Sn labelled by asterisks and triangles respectively.

Proton detected 1D and 2D ^1H–^{119}Sn HMBC spectroscopy, on the other hand, turns out to be a powerful tool for the specific spectral editing of conformations where long range ^1H–^{119}Sn couplings exist, leading to an efficient suppression of the conformations where such couplings do not exist.

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