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Note

NMR spectral analysis of some spirostanoids†

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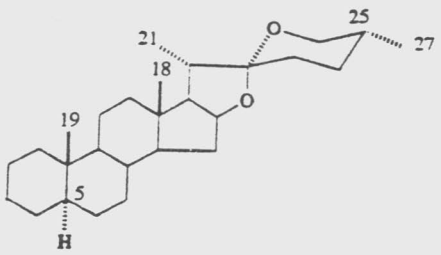
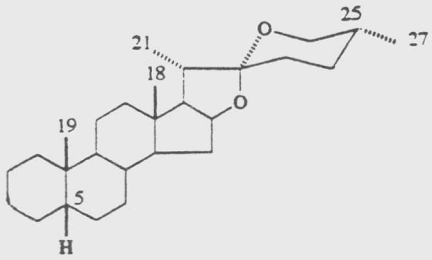
An approach based upon NOE between H_3-19 and H-5 has been proposed for the establishment of 5β- and 5α- stereochemistry at A/B ring junction in spirostanoids and the recently reported ^{13}C NMR shielding data for several steroidal enones has been analyzed.

As a part of our continuing effort to understand the ^{13}C NMR spectral behaviour of steroidal sapogenins and steroidal saponins[1-9], we have earlier suggested that the ^{13}C NMR chemical shift of the C-22 resonance acts as a reporter for the identification of the parent skeletal type[10-12]. The variation in parent skeleton generally arises from the configuration at C-5, i.e. the A/B ring junction and the configuration of the methyl group at C-25 as naturally occurring spirostanoids characterized so far, possess B/C *trans*, C/D *trans* and D/E *cis* ring junctions. Depending upon the *trans* and *cis* relationship between H_3-19 and H-5, the spirostanoids have been grouped into 5α (**A**) and 5β (**B**) types respectively (Figure 1). Recently, we proposed a correlationship between the ^1H and ^{13}C NMR chemical shifts of ring F resonances and orientation of the 27-methyl group for the discrimination of *25R/25S* stereochemistry[13]. Despite the fact that ^{13}C NMR chemical shifts of C-5, C-7, C-9 and C-19 are quite distinctive for the identification of stereochemistry at A/B ring junction[11,12], we are involved in determining additional NMR approaches applicable for ascertaining 5α- and 5β-stereochemistry. In the present communication, we wish to report the significance of ^1H-^1H NOE (NOESY) spectroscopy for the determination of stereochemistry at ring junctions as well as analysis of recently reported ^{13}C NMR data for several functionalized spirostanoids[14].



A



B

In view of our homo- and heteronuclear NMR studies on *25R/25S* epimeric pair of 5β spirostanoids (smilagenin and sarsasapogenin)[15] together with the literature reports[16-20] led us to deduce several conclusions: (i) NOE cross peaks are usually observed for equatorial-axial vicinal and 1,3- *syn*-diaxial proton pair, (ii) NOE is absent between vicinal *trans* diaxial protons, (iii) NOE connectivity between H-8/H_3-18, H_3-19; H-9/H-14, H-17; and H_3-18/H-20 are common for B/C *trans*, C/D *trans*, and D/E *cis* ring junctions respectively, (iv) NOE between H_3-19/H-2a, H-4a; and for H_3-19/H-5 are characteristic for A/B *trans* (5α) and *cis* (5β) respectively. Thus, once the ^1H NMR assignments are evident, presence and absence of NOESY cross peak between H_3-19 and H-5 could be utilized for identifying 5β(**B**) and 5α(**A**) subgroups of spirostanoids.

In a recent publication[14], DeNinno and McCarthy have reported ^{13}C NMR chemical shift

† Part 47 in the series, 'NMR Spectral Investigations', for part 46 see ref. 13.

Table I—^{13}C NMR chemical shifts for steroidal sapogenins 1-6

Position	*25R* 3, 11 (oxo)$_2$ **1**	*25R* 3-oxo Δ^1 **2**	*25R* 3,11 (oxo)$_2$ Δ^1 **3**	*25R* 3β-OH-3-Me Δ^1 **4**	*25R* 3β-OH 3-Me 11-oxo Δ^1 **5**	*25R* 1β, 2 β, 3 β -(OH)$_3$ 3-Me 11-oxo **6**
C-1	37.0	158.3	159.3	136.2	136.6	75.2
C-2	37.9	127.4	127.5	132.4	132.4	73.6
C-3	211.4	200.2	199.4	70.6	70.6	74.6
C-4	44.3	39.8	38.0	44.0	43.5	41.3
C-5	46.9	44.3	44.2	39.9	41.8	36.0
C-6	28.2	27.5	27.0	28.0	27.5	27.4
C-7	32.4	31.7	36.9	32.1	32.6	36.7
C-8	35.2	39.0	40.6	35.2	36.9	39.9
C-9	60.7	50.0	59.8	51.1	60.7	67.0
C-10	36.9	35.3	59.7	29.4	37.3	57.3
C-11	209.7	21.0	209.4	21.0	209.8	211.0
C-12	57.6	40.9	57.3	42.1	57.4	57.6
C-13	44.2	40.6	44.3	40.3	44.4	44.3
C-14	55.5	56.2	55.3	56.2	55.7	55.5
C-15	31.2	31.5	32.1	31.7	31.2	32.2
C-16	80.5	80.7	80.4	80.3	80.6	80.6
C-17	63.9	62.2	60.7	62.2	61.4	60.8
C-18	17.2	16.2	17.3	16.7	17.2	17.2
C-19	11.1	13.1	13.7	15.0	15.4	12.7
C-20	41.8	41.6	41.8	41.6	41.5	41.9
C-21	14.2	14.2	14.2	14.3	14.2	14.1
C-22	109.2	109.4	109.2	109.6	109.2	109.2
C-23	31.3	31.4	31.2	31.4	31.2	31.4
C-24	28.7	28.8	28.7	28.8	28.7	28.7
C-25	30.2	30.3	30.2	30.4	30.2	30.2
C-26	66.9	66.9	66.9	66.8	66.9	66.9
C-27	17.1	17.0	17.1	17.3	17.1	17.1

data for several spirostane derivatives, (5α , 25*R*)-spirostan-3,11-dione **1**, (5α, 25*R*)-spirostan-1-en-3-one **2**, (5α, 25*R*)-spirostan-1-en-3,11-dione **3**, (3*R*, 5α, 25*R*)-3-hydroxy-3-methyl-spirost-1-ene **4**, (3*R*, 5α, 25*R*)-3-hydroxy-3-methyl-spirost-1-en-11-one **5**, and (3*R*, 5α, 25*R*) 1,2,3-trihydroxy-3-methyl-spirostan-11-one **6**. The analysis of the ^{13}C NMR data of these compounds, was considered worthwhile in view of the reported cholesterol absorption inhibiting activity of diglycoside derived from 11-ketotigogenin[21]. Our earlier studies on steroidal sapogenins[10-12], facilitated the analysis and ^{13}C NMR assignments are presented in Table I. The analysis of the ^{13}C NMR data led to the several inferences: (i) substituents such as oxo, hydroxyl and olefinic bond, consistent with our studies on steroidal alkaloids[21] and steroidal sapogenins[10-12], suggest that these modifies the chemical shifts of carbons occupying α, β, and γ position respectively, (ii) Δ′ olefinic bond causes, (a) an upfield shift (12 ppm) of C-3 (**1** vs. **3**), (b) downfield shift of C-19 by about 2 ppm, (c) marginal effect (0.3 ppm) on the chemical shift of C-11; (iii) appearance of ring F resonances at almost identical position ±0.1 ppm in all the compounds (**1-6**) reflects absence of any kind of long-range interactions with 11-oxo group as well as existence of chair conformation of ring-F.

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