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Note

Assignment of the ^{1}H and ^{13}C NMR Spectra of 9-Deoxo-9a-aza-9a-homoerythromycin A, 9-Deoxo-9a-aza-9a-homoerythromycin A 11,12-hydrogenborate and Azithromycin 11,12-hydrogenborate

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ABSTRACT: The ^{1}H and ^{13}C NMR spectra of 9-deoxo-9a-aza-9a-homoerythromycin A, its 11,12-hydrogenborate derivative and azithromycin 11,12-hydrogenborate were unambiguously assigned using a combination of 1D and 2D H–C correlation spectra.

KEYWORDS: NMR; ^{1}H NMR; ^{13}C NMR; azaerythromycin; azithromycin; hydrogenborate

INTRODUCTION

Azithromycin (**1**) is an azalide[1] antibiotic derived from erythromycin A (**2**) by ring expansion of its oxime through Beckmann rearrangement followed by reduction of the imino ether **3** and subsequent methylation of the amine nitrogen present in azaerythromycin (**4**).[2] The 15-membered aza-macrolide of azithromycin significantly improves the biological and pharmacodynamic properties over the parent compound.[3] A notable feature of azithromycin is its high activity against Gram-negative bacteria.[4] Both antibiotics have a common mode of action starting by binding to bacterial ribosomes.[5] Interestingly, the conformation of the drugs in the bound state shows greater similarity than that of the free state.[6]

Recently, we have isolated two by-products formed during the synthesis of azithromycin when the reduction of the imino ether is carried out with sodium borohydride.[7] They have been identified as 9-deoxo-9a-aza-9a-homoerythromycin A 11,12-hydrogenborate (**5**) and azithromycin 11,12-hydrogenborate (**6**). Their structures have been confirmed by an alternative synthesis.[7] Moreover, the hydrogenborate **6** can be easily processed to pure azithromycin dihydrate[8] in excellent yields. The ^{1}H and ^{13}C NMR spectra of erythromycin,[9] azithromycin[10] and the intermediate imino ether[11] **3** have been assigned previously. Here we report the full assignment of the ^{1}H and ^{13}C NMR spectra of **4** and the hydrogenborate derivatives **5** and **6** in $CDCl_3$, based mainly on their HMQC[12] and HMBC[13] spectra. Artifact-free spectra were obtained using the gradient enhanced version of these pulse sequences.[14]

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RESULTS AND DISCUSSION

The hydrogenborate structures of **5** and **6** were deduced from the corresponding fast atom bombardment mass spectrometric and ^{11}B NMR data.[7] The binding positions of the boron atom to the molecular framework can be determined by identifying the carbon atoms whose chemical shift is significantly affected by the proximity of the boron moiety related to the non-boron-containing product. For this reason we first analysed the ^{1}H and ^{13}C spectra of 9-deoxo-9a-aza-9a-homoerythromycin A (**4**).

9-Deoxo-9a-aza-9a-homoerythromycin A (4)

The ^{13}C spectrum shows 35 of the 36 resonances expected (C-7′ and C-8′ are equivalent at 40.30 ppm). The high intensity of the resonance at 72.92 ppm suggests that it corresponds to two carbon atoms. The signal overlap is revealed by NMR editing techniques. Thus, the DEPT spectrum acquired with a 90° proton read pulse allows one to identify the resonance at 72.92 ppm as a CH, while the spin-echo experiment with a delay for echo of $1/2(^{1}J_{CH})$ indicates that a quaternary carbon appears at the same chemical shift. Two additional quaternary carbons absorbed at 73.61 and 73.76 ppm. From the DEPT spectrum it was also deduced that there are five methylene carbons at 20.94, 28.72, 34.64, 42.05 and 57.39 ppm.

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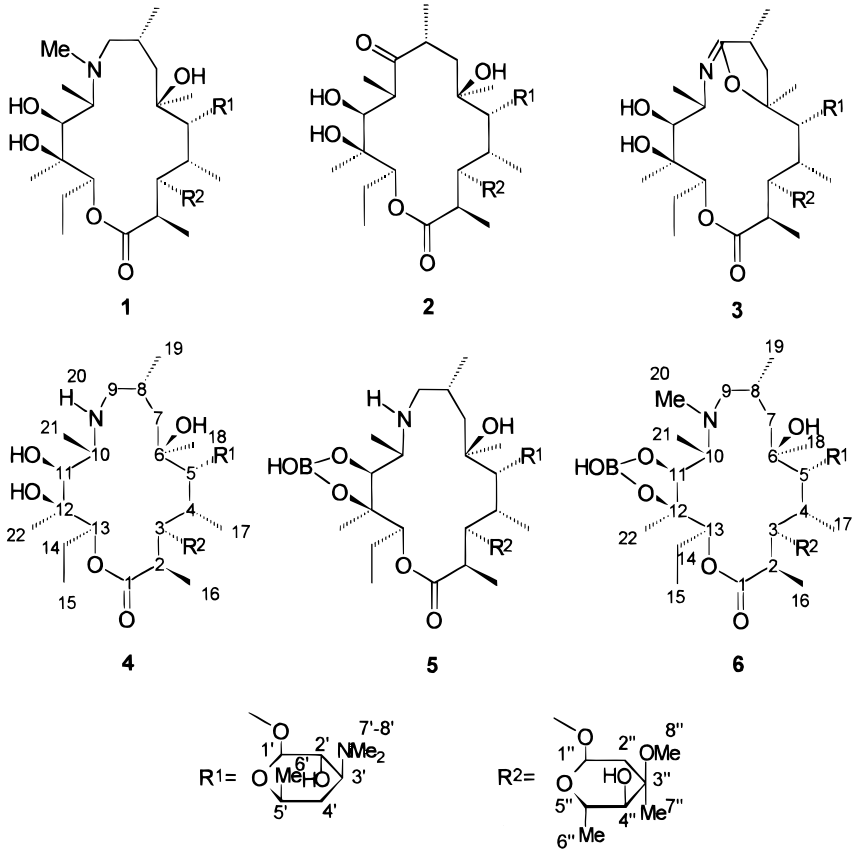

The assignment of the ^{1}H and ^{13}C spectra was based mainly on the study of the 2D HMQC and HMBC spectra. The strategy of work started by establishing the connectivity of a known carbon with the protons separated by two or three bonds in the HMBC spectrum. Then we read from the HMQC spectrum the direct response ($^{1}J_{CH}$) of these protons with the corresponding carbon nuclei. The second step of this procedure is comparatively obvious, so we shall outline only the correlations deduced from the HMBC spectrum (Fig. 1). The results are given in Table 1. Fortunately, the azamacrolide ring protons showed almost all possible long-range cross peaks ($^{n}J_{CH}$, $n = 2$, 3) with carbons. A clear entry to the analysis of the spectrum is the carbonyl group signal at 178.99 ppm. It correlates with H-2, H-3, H-13 and H_3-16. These protons are easily identified on account of their chemical shifts and multiplicities (and consequently the carbons bonded to them; see Table 1).

Using now H-3 as a departure point, we initiated the sequential assignment of all other protons and carbons of the aglycone moiety (Fig. 2, Table 1). Three criteria were applied to distinguish between correlations derived from $^{2}J_{CH}$ or $^{3}J_{CH}$ for a given proton: (i) the number of protons bonded to the carbon as deduced from the DEPT and heteronuclear spin-echo experiments, (ii) ^{13}C chemical shifts and (iii) correlations with other vicinal protons. In fact, the third point also served as self-test of the consistency of the assignments made because a correlation through $^{2}J_{CH}$ for a given proton and carbon is confirmed by an additional cross peak between the same carbon and a second proton three bonds away. This procedure is highlighted in Fig. 2. For simplicity, only the minimum number of ^{1}H, ^{13}C correlations consistent with the scheme of assignment mentioned above are included. In this way, the sequence of ring carbons and protons between C-1 and C-11 and the corresponding methyl group substituents (C-10, C-11, C-16, C-17, C-18 and C-19) are assigned.

The connectivity maps shown in Figs 1 and 2 apparently contain a discontinuity point in the macrocyclic ring between C-11 and C-12 due to the absence of a cross peak connecting H-11 with the quaternary carbon C-12. Fortunately, this discontinuity is surpassed by observing that H-11 (δ 3.41) correlates via $^{3}J_{CH}$ with C-13 (δ 78.03), and the connection with C-12 (δ 73.61) is deduced from the corresponding cross peak between this carbon and H-13 (δ 4.69). Moreover, H-13 is unambiguously assigned through its correlation with C-1, which at the same time 'closes' the cycle.

The identification of the sugars linked to the azamacrolide was achieved by taking the correlations of H-3 and H-5 in the HMBC spectrum as entries for the subsequent analysis. Thus, H-3 (δ 4.30) shows a cross peak with a carbon at 94.60 ppm corresponding to C-1″ of the L-cladinose ring, whereas H-5 (δ 3.61) correlates with C-1′ of the D-desosamine moiety, which appears at 102.89 ppm. Once C-1′ and C-1″ were known, the protons attached to them were assigned from the HMQC spectrum. Then the combined use of the HMBC and HMQC correlations in the same form as mentioned above established the identity of both structural fragments (Table 1). Starting with H-1″ one can find a cyclic route of connections for L-cladinose as

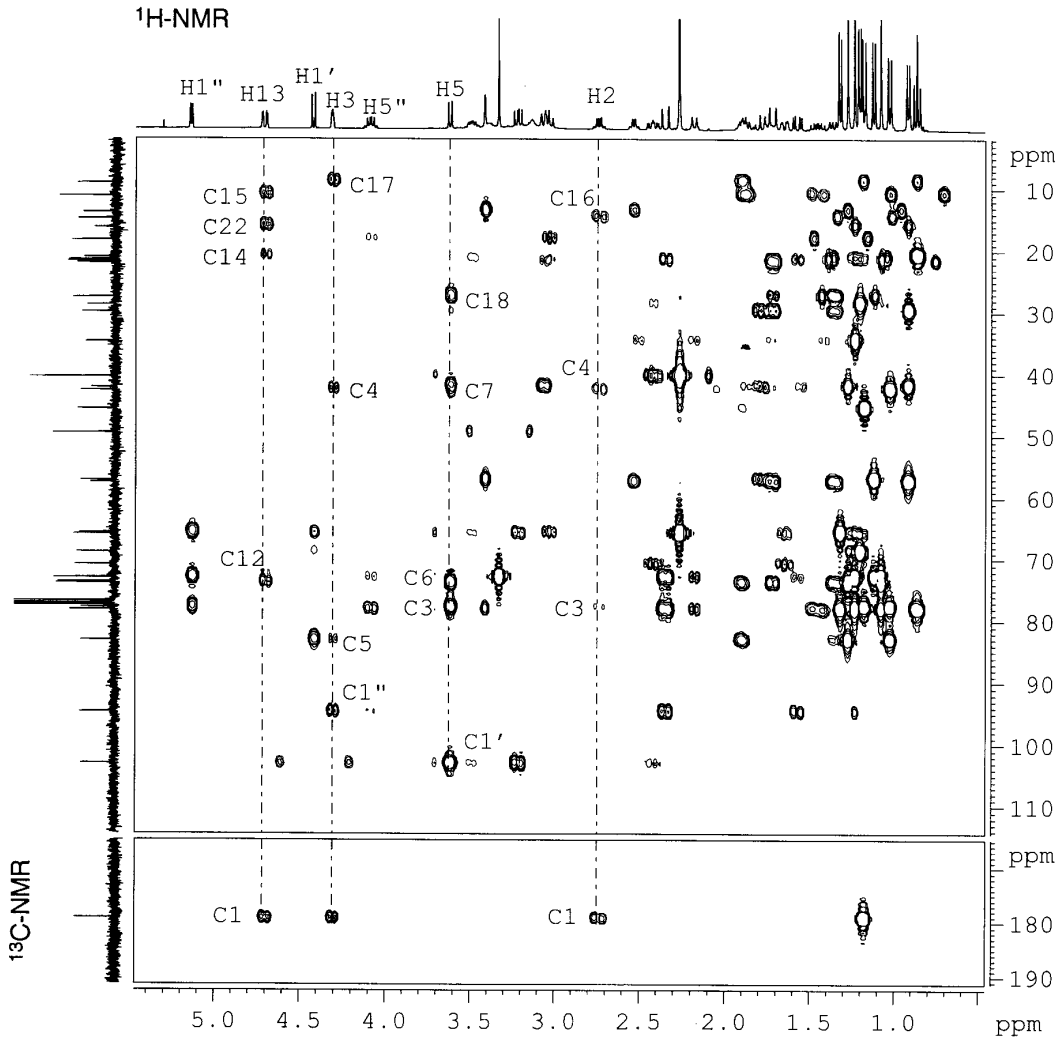

Figure 1. 400.13 MHz g-HMBC spectrum of 9-deoxo-9a-aza-9a-homoerythromycin A (**4**) in $CDCl_3$. The ^{1}H and ^{13}C spectra are given on the F_2 and F_1 axes, respectively.

described in Fig. 2. However, H-1′ in D-desosamine shows only two cross peaks. The carbon at 83.05 ppm has been previously assigned to C-5. The second correlation at 65.76 ppm arises from the coupling with C-3′ because this carbon also correlates with H_3-7′/H_3-8′. Once C-3′ is fixed, it is easy to identify H-3′ as the double doublet of doublets at 2.42 ppm in the HMQC spectrum. Focusing now on H-3′, the HMBC spectrum reveals that this proton is coupled to three carbon atoms. One cross peaks corresponds to the pair of isochronous carbons C-7′/C-8′ (δ 40.30), and the other two are C-2′ (δ 70.82) and C-4′ (δ 28.72). The possibility of confusing C-2′ with C-5′ (δ 68.70) is eliminated simply by observing the multiplicity of the protons bonded to them. The remaining links of the desosamine sugar are deduced from the two cross peaks of H_3-6′ (δ 1.20) with C-5′ and C-4′ (δ 28.72) (Table 1).

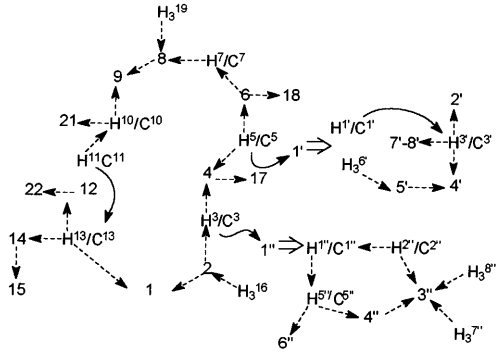

Figure 2. Sequential assignment of protons and carbons in **4**. The figures correspond to the carbon atoms that correlate with the indicated protons in the 2D g-HMBC spectrum. The protons bonded to a given carbon are assigned from the cross peaks observed in the 2D g-HMQC spectrum. For simplicity, only the minimum correlations consistent with the assignment made are shown.

The analysis mentioned allows the unequivocal assignment of practically all ^{13}C and ^{1}H atoms in **4**. An uncertainty remained for C-13/C-4″ because the resolution attainable in the F_1 dimension of the HMBC and HMQC spectra is lower than their chemical shift difference of 0.05 ppm. The problem could be solved by performing the $^1J_{CH}$ correlation in the direct mode, i.e. by detecting ^{13}C in a ^{13}C, ^{1}H HETCOR[15] experiment. In this case the ^{13}C spectrum is obtained in the F_2 dimension and it is possible to achieve a reasonable resolution without a penalty in the measuring time.

Table 1. ^{1}H and ^{13}C NMR spectra of 9-deoxo-9a-aza-homoerythromycin A (**4**) in $CDCl_3$

Site	δ_{13C} (ppm)	δ_{1H} (ppm)	Multiplicity	J(H,H) (Hz)
1	178.99	—		
2	45.52	2.73	dq	7.5, 3.7
3	77.73	4.30	dd	3.7, 2.1
4	42.48	1.91	ddq	7.6, 7.4, 2.1
5	83.05	3.61	d	7.4
6	73.76	—		
7(*proR*)	42.05	1.72	d	14.7
7(*proS*)		1.36	dd	14.7, 7.2
8	29.79	1.73	m[a]	
9(*proS*)	57.39	3.05	m	
9(*proR*)		1.79	t	11.2
10	57.01	2.53	dq	6.5, 1.7
11	72.92[b]	3.41	d	1.7
12	73.61	—		
13	78.03	4.69	dd	10.2, 2.4
14(*proR*)	20.94	1.88	m	
14(*proS*)		1.46	ddq	14.3, 10.2, 7.4
15	11.04	0.87	t	7.4
16	14.69	1.18	d	7.5
17	8.96	1.03	d	7.6
18	27.40	1.28	s	
19	21.84	0.92	d	6.7
21	13.68	1.12	d	6.5
22	16.12	1.08	s	
1′	102.89	4.41	d	7.3
2′	70.82	3.21	dd	10.2, 7.3
3′	65.76	2.42	ddd	14.1. 10.2, 3.9
4′(*proS*)	28.72	1.65	ddd	12.7, 3.9, 2.0
4′(*proR*)		1.23[c]	m	
5′	68.70	3.49	ddq	10.8, 6.1, 2.0
6′	21.32	1.20	d	6.1
7′, 8′	40.30	2.26	s	
1″	94.60	5.12	d	4.8
2″(*proR*)	34.64	2.34	d	15.2
2″(*proS*)		1.57	dd	15.2, 4.8
3″	72.92[b]	—		
4″	78.08	3.04	dd	10.1, 9.5
4″-OH	—	2.18	d	10.1
5″	65.58	4.08	dq	9.5, 6.3
6″	18.15	1.32	d	6.3
7″	21.53	1.23[c]	s	
8″	49.42	3.33	s	

[a] m, Multiplicity obscured by overlap.
[b] ^{13}C resonances coincident.
[c] ^{1}H resonances coincident.

Accordingly, the previous assignments of H-13 and H-4″ (δ 3.04) allowed one to identify the respective carbons at 78.03 and 78.08 ppm. The HETCOR spectrum also contributed to clarifying the chemical shift assignment of H-8 at 1.73 ppm and one of the diasterotopic protons H-4′ at 1.23 ppm whose resonances were buried in a crowded region of the ^{1}H spectrum.

Hence the heteronuclear correlation experiments afforded the chemical shifts of all the carbons in addition to the hydrogens attached to carbons of **4**. Additionally, the HMBC spectrum showed two cross peaks for a broad doublet at 2.18 ppm with C-3″ and C-4″ which must correspond to OH-4″. Four other OH hydrogens were found as two broad signals at 3.11 and 3.35 ppm in the ^{1}H NMR spectrum. Proton–proton scalar couplings could be obtained from the high-resolution ^{1}H spectrum except for partially overlapped multiplets. In some of these cases it was possible to measure an approximate J value in the 2D J-resolved spectrum[16] (Table 1). For CH_2 groups, the *proR* and *proS* protons are assigned according to their $^{3}J_{HH}$ values by comparison with the corresponding known data for azithromycin.[10] A similar conformation has

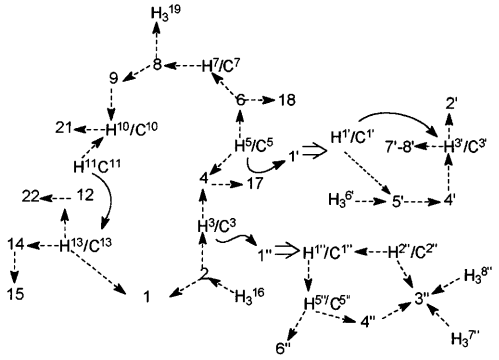

Figure 3. Sequential assignment of protons and carbons in **5**. Legend as in Fig. 2.

been assumed. *ProR*-H-4′ could not be resolved owing to the coincidence of this multiplet with the signal of the methyl group H_3-7″ (δ 1.23).

9-Deoxo-9a-aza-9a-homoerythromycin A Hydrogenborate (5)

As expected, the title compound shows ^{1}H and ^{13}C NMR spectra very similar to that of **4**, indicating that both products have a common skeleton. There are also two overlapped signals in the ^{13}C NMR spectrum of **5** because only 35 of the 36 possible signals are resolved.

Table 2. ^{1}H and ^{13}C NMR spectra of **5** in $CDCl_3$

Site	δ(^{13}C) (ppm)	δ(^{1}H) (ppm)	Multiplicity	J(H,H) (Hz)
1	180.12	—		
2	45.54	2.72	dq	7.5, 3.4
3	77.45[a]	4.59	dd	3.4, 2.0
4	42.44	1.86	ddq	7.6, 7.6, 2.0
5	82.99	3.61	d	7.6
6	73.58	—		
7(*proR*)	41.68	1.65	d	14.5
7(*proS*)		1.39	dd	14.5, 6.4
8	29.46	1.71[b]	m[c]	
9(*proS*)	57.12	3.02	d	8.7
9(*proR*)		1.71[b]	m	
10	58.65	2.25	dq	6.4, 1.1
11	80.60	3.27	d	1.1
12	77.45[a]	—		
13	79.66	4.89	dd	10.3, 2.1
14(*proR*)	21.32	1.94	ddq	14.4, 7.4, 2.1
14(*proS*)		1.45	ddq	14.4, 10.3, 7.4
15	11.53	0.88	t	7.4
16	14.70	1.18	d	7.5
17	8.90	1.02	d	7.6
18	27.38	1.27	s	
19	21.82	0.91	d	6.4
21	14.45	1.16	d	6.4
22	15.43	1.05	s	
1′	103.01	4.40	d	7.3
2′	70.77	3.22	dd	10.2, 7.3
2′-OH	—	3.35	bs	
3′	65.85	2.42	ddd	12.4, 10.2, 4.0
4′(*proS*)	28.75	1.65	dd	4.0, 2.0
4′(*proR*)		1.24	m	
5′	68.78	3.48	ddq	10.6, 6.2, 2.0
6′	21.36	1.22	d	6.2
7′, 8′	40.34	2.28	s	
1″	94.47	5.15	d	4.9
2″(*proR*)	34.55	2.33	d	15.2
2″(*proS*)		1.57	dd	15.2, 4.9
3″	72.86	—		
4″	78.14	3.00	dd	10.5, 9.7
4″-OH	—	2.20	d	10.5
5″	65.68	4.11	dq	9.7, 6.3
6″	18.20	1.36	d	6.3
7″	21.53	1.25	s	
8″	49.51	3.34	s	

[a] ^{13}C resonances coincident.
[b] ^{1}H resonances coincident.
[c] m, Multiplicity obscured by overlap.

Table 3. ^{1}H and ^{13}C NMR spectra of **6** in $CDCl_3$

Site	$\delta(^{13}C)$ (ppm)	$\delta(^{1}H)$ (ppm)	Multiplicity	J(H,H) (Hz)
1	180.16	—		
2	45.56	2.72	dq	7.6, 3.2
3	77.33	4.53	dd	3.2, 1.6
4	42.52	1.91	ddq	7.8, 7.6, 1.6
5	83.37	3.58	d	7.8
6	73.52	—		
6-OH	—	10.31	s	
7(*proR*)	41.75	1.70	d	14.6
7(*proS*)		1.29	m[a]	
8	26.44	1.98	m	
9(*proS*)	69.05	2.46	d	9.4
9(*proR*)		1.97	m	
10	64.31	2.36	dq	6.7, 1.7
11	80.40	3.54	bs	
12	78.07	—		
13	78.34	4.91	dd	10.8, 1.6
14(*proR*)	21.36	1.95	ddq	14.4, 7.3, 1.6
14(*proS*)		1.48	ddq	14.4, 10.8, 7.3
15	11.01	0.75	t	7.3
16	14.65	1.18	d	7.6
17	8.75	1.02	d	7.6
18	27.69	1.30	s	
19	21.98	0.87	d	5.9
20	35.85	2.31	s	
21	7.09	1.13	d	6.7
22	15.59	1.07	s	
1′	103.10	4.41	d	7.3
2′	70.74	3.23	dd	10.2, 7.3
3′	65.92	2.46	ddd	12.2, 10.2, 3.9
4′(*proS*)	28.75	1.66	ddd	12.6, 3.9, 1.8
4′(*proR*)		1.26	ddd	12.6, 12.2, 10.6
5′	68.83	3.49	ddq	10.6, 6.0, 1.8
6′	21.37	1.23	d	6.0
7′, 8′	40.37	2.29	s	
1″	94.26	5.23	d	4.9
2″(*proR*)	34.58	2.30	d	15.3
2″(*proS*)		1.57	dd	15.3, 4.9
3″	72.86	—		
4″	78.26	2.99	dd	10.3, 9.4
4″-OH	—	2.15	d	10.3
5″	65.57	4.11	dq	9.4, 6.2
6″	18.45	1.37	d	6.2
7″	21.60	1.25	s	
8″	49.55	3.35	s	

[a] m, Multiplicity obscured by overlap.

The overlap occurs for the peak at 77.45 ppm. Again (see above), the combined use of DEPT and heteronuclear spin-echo spectra confirmed that this peak arises from the superposition of a methine and a quaternary carbon atom.

The assignments of the ^{1}H and ^{13}C spectra were carried out following the same procedure as described above (Fig. 3, Table 2). This analysis shows that on this occasion the overlapped carbons at 77.45 ppm are the methine C-3 and the quaternary carbon C-12. Also the methylene C-14 (δ 21.32) and the methyl group C-6′ (δ 21.36) absorbed very close to one another ($\Delta\delta$ 0.04 ppm). ^{13}C editing techniques (DEPT and heteronuclear spin-echo) allowed us to label each carbon according to the number of hydrogens attached. Interestingly, all four carbons were distinguished when the ^{13}C NMR spectrum was acquired at 333 K: 21.20 (C-6′), 21.36 (C-14), 77.41 (C-12) and 77.50 ppm (C-3).

There are only some minor differences from the sequence of assignments made for **4** (Fig. 3). Thus, it is now the multiplet at 1.71 ppm corresponding to *proR* H-9 which establishes the connection with C-10 through the nitrogen of the macrolide, whereas for **4** the opposite is observed, i.e. H-10 is scalarly coupled to

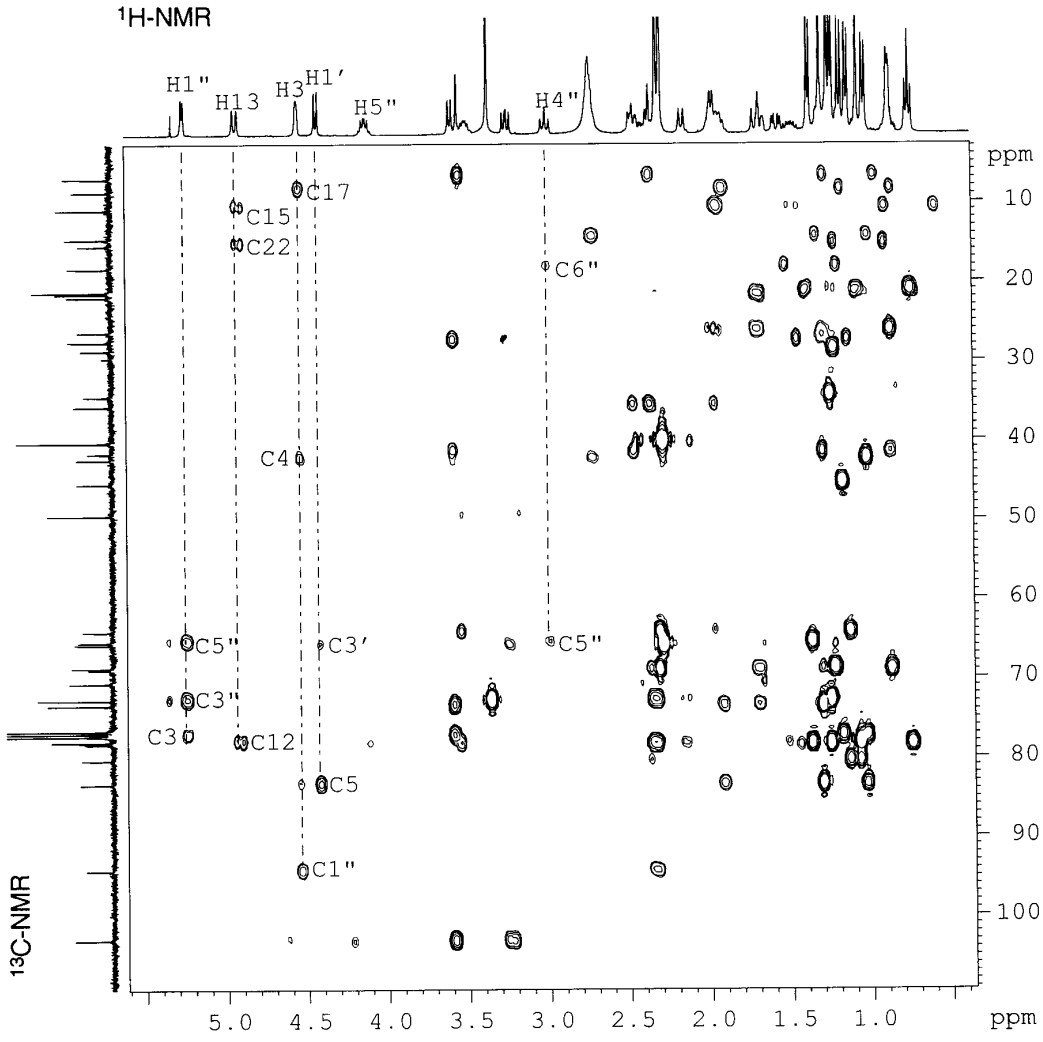

Figure 4. Expansion of the 400.13 MHz g-HMBC spectrum of azithromycin 11,12-hydrogenborate (**6**) in $CDCl_3$. The ^{1}H and ^{13}C spectra are given on the F_2 and F_1 axes, respectively.

C-9. The presence of boron in this compound has also some small effects on the D-desosamine moiety. For example, H-1′ (δ 4.40) shows a cross peak with C-5′ (δ 68.78), which was absent in the HMBC spectrum of **4**, and the connection between C-3′ (δ 65.85) and C-4′ (δ 28.74) is based on the cross peak observed for *proS* H-4′ (δ 1.65) with C-3′ because no correlation between H-3′ and C-4′ was detected. In fact, H-1′ (δ 4.40) and H-5′ (δ 3.48) experience the largest shifts within the desosamine ring by the incorporation of boron into the structure of **5**. They are deshielded by 0.04 ppm relative to **4**, while the chemical shift variations for all other protons are not higher than 0.02 ppm. However, it is assumed that both compounds have a conformation similar to that of azithromycin, which allows one to label the diastereotopic protons of the methylene groups according to the values of their vicinal coupling constants.[6]

As already mentioned, the assignments made allow one to identify the link of the boron atom to the oxygen atoms bonded to C-11 (δ 80.60) and C-12 (δ 77.45). These two carbons show the largest ^{13}C chemical shifts variations relative to **4**. They are deshielded by 7.68 and 3.84 ppm, respectively, and both signals are slightly broadened. The chemical shift differences for all other carbons of **4** and **5** are <1.63 ppm. β-Deshielding effects are well known in ^{13}C NMR spectroscopy[17] and deshieldings of the same magnitude have been found for azaerythromycin A 11,12-cyclic carbonate[2] and erythromycin A 11,12-methylene acetal[18] relative to the compounds with the free OH at C-11 and C-12.

The HMBC spectrum also allows one to identify OH-2′ and OH-4″. The proton of OH-2′ appears as a broad singlet at 3.35 ppm which shows a cross peak with C-2′ (δ 70.77), while OH-4″ is a doublet at 2.20 ppm ($^3J_{HH}$ 10.5 Hz) correlating with C-3″ (δ 72.86) and C-4″ (δ 78.14). The coupling constants of the protons were obtained from the analysis of the multiplets observed in the ^{1}H NMR and 2D *J*-resolved spectra (Table 2).

Azithromycin 11,12-hydrogenborate (6)

The structural determination of **6** was achieved in an analogous way to that of **5**. Here, the NMR data have to be compared with those of azithromycin **1**. The ^{1}H

and ^{13}C NMR spectra of **1** have been previously assigned in $CDCl_3$ and also in buffered D_2O and DMSO-d_6.[10] The study in $CDCl_3$ was based on the analysis of the 2D INADEQUATE spectrum of a saturated sample. Our assignment strategy takes advantage of the great sensitivity gain of the reverse detection experiments so that dilute samples could be used instead (see Experimental). The chemical shift differences between both studies can be considered marginal (<0.5 ppm for ^{13}C). However, it is worth mentioning that in our case it was possible to identify the five OH signals according to the cross peaks observed in the HMBC spectrum of **1**. These correlations were as follows: the singlet at 9.73 ppm (OH-6) with C-5 (δ 83.88) and C-7 (δ 42.93); the doublet at 5.37 ppm (OH-11, $^3J_{HH}$ = 6.6 Hz) with C-10 (δ 63.06), C-11 (δ 74.18) and C-12 (δ 74.79); the singlet at 3.08 ppm (OH-12) with C-11 and C-12; the singlet at 3.40 ppm (OH-2′) with C-1′ (δ 103.49), C-2′ (δ 71.45) and C-3′ (δ 66.42); and the doublet at 2.14 ppm (OH-4″, $^3J_{HH}$ = 10.1 Hz) with C-3″ (δ 73.55) and C-4″ (δ 78.75).

The full assignment of the ^1H and ^{13}C NMR spectra of **6** was obtained from the 2D HETCOR, HMBC and *J*-resolved experiments and the results are given in Table 3. An expansion of the HMBC correlation map is depicted in Fig. 4 and the sequential assignment followed is given in Fig. 5. The DEPT spectrum shows that C-3 (δ 77.33) is accidentally buried in the $CDCl_3$ triplet signal and that the methyl group C-6′ (δ 21.37) is virtually superimposed on the methylene carbon C-14 (δ 21.36) ($\Delta\delta$ 0.01 ppm).

The sequential assignment of protons and carbons indicated in Fig. 5 is very similar to that of the previous compounds. Two points are worthy of mention regarding the HMBC spectrum. First, the new methyl group H_3-20/C-20 (δ 2.31/35.85) bonded to nitrogen is readily identified through the two cross peaks with C-9 (δ 69.05) and C-10 (δ 64.31). Second, the quaternary carbon C-12 (δ 78.07) is best assigned in this occasion from the correlation obtained with the methyl protons of H_3-22, which are also coupled to C-13 (δ 78.34). On the other hand, C-13 and C-4″ (δ 78.26) are too close together to be accurately assigned on the basis of the HMBC results. This is best accomplished from the direct response for $^1J_{CH}$ observed in the HETCOR spectrum. The resolution obtained in F_2 for the ^{13}C spectrum is high enough to assign both methine carbons unequivocally, whose proton atoms are almost 2 ppm apart.

As expected, the carbon atoms C-11 (δ 80.40) and C-12 (δ 78.07) in **6** are deshielded relative to those of **1** by 6.2 and 3.3 ppm, respectively. This allows one to establish unambiguously the link of the boron atom in **6** to the oxygens O-11 and O-12 of the macrocycle.

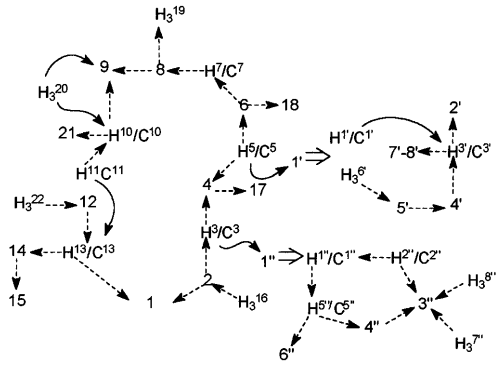

Figure 5. Sequential assignment of protons and carbons in **6**. Legend as in Fig. 2.

EXPERIMENTAL

Compound **4** was prepared according to literature methods.[2] The synthesis of hydrogenborates **5** and **6** has been reported previously.[7]

NMR spectra were recorded on a Bruker AMX 400 spectrometer operating at 400.13 and 100.61 MHz for ^1H and ^{13}C, respectively, using a 5 mm QXI $^1H/^{13}C/^{15}N/^{31}P$ reverse probe including a *z*-gradient coil. $CDCl_3$ was used as solvent and chemical shifts were referenced internally to TMS. Sample amounts ranged between 0.07 and 0.09 mmol. Pulse widths were 8.5 and 13.7 μs for ^1H and ^{13}C, respectively, at an attenuation level of 3 dB on both channels. A 5% sine truncated shaped pulse gradient of 1 ms was used with values of 5:3:4 for both g-HMQC and g-HMBC.[14] Standard Bruker software was used to acquire and process the ^{13}C DEPT, 2D, *J*-resolved, HETCOR, g-HMQC and g-HMBC spectra. Selected parameters for the homonuclear 2D *J*-resolved spectra were sweep width 2400 Hz in F_2 and 70 Hz in F_1; repetition delay 2 s; final matrix after zero filling in both dimensions 4096 × 512; and number of scans 16. Selected parameters for ^1H, ^{13}C 2D correlations were sweep width 2400 Hz for ^1H and 19 000 Hz for ^{13}C, 2048 × 512 data set, repetition delay 2 s, number of scans 40–160, with the larger values used for the HETCOR experiment, magnitude mode, data processing using zero filling in the F_1 domain and shifted sine-bell apodization of factor 0 in both dimensions. For HETCOR proton decoupling was achieved through WALTZ16 and for HMQC GARP decoupling of ^{13}C was used during acquisition.

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