$c = 18.031(3)$ Å, $\beta = 106.295(14)^\circ$, $V = 3316.1(9)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.270$ Mg m^{-3}, $F(000) = 1312$, $\mu(Mo_{K\alpha}) = 0.972$ mm^{-1}. A total of 7932 reflections were measured in the range $7.02 \leq 2\theta \leq 50.04^\circ$, of which 5847 were unique. Final R indices: $R_1 = 0.0389$ ($I > 2\sigma(I)$), w$R_2 = 0.0991$ (all data); max./min. residual electron density 1006/ -694 e nm^{-3}. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-145888 (**2**), CCDC-145889 (**3**), CCDC-145981 (**4**), and CCDC-145982 (**5**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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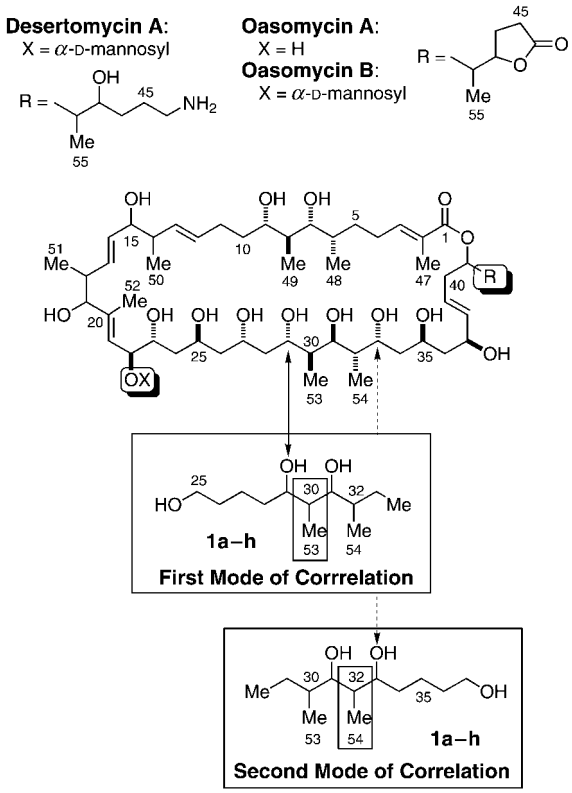
Stereochemical Assignment of the C21–C38 Portion of the Desertomycin/Oasomycin Class of Natural Products by Using Universal NMR Databases: Prediction**

Yoshihisa Kobayashi, Choon-Hong Tan, and Yoshito Kishi*

We recently reported our first step toward the creation of a universal NMR database through analysis of a typical structural motif often found in polypropionate natural products.[1] We then demonstrated the reliability and usefulness of such an NMR database by using the C5–C10 portion of the desertomycin/oasomycin class of natural products.[2] In this and the following paper,[3] we report a further development of this approach by predicting, and proving, the stereochemistry of the C21–C38 portion of the desertomycin/oasomycin class of natural products.[4]

The C29–C33 portion of desertomycins/oasomycins is viewed as a contiguous dipropionate unit so that our propionate database[1] could be applied to predict its stereochemistry. There are apparently two modes of correlation of the NMR database with this portion of desertomycins/oasomycins (see the lower half of Scheme 1). By following



Scheme 1. Structures of desertomycin A and oasomycins A and B, as well as two modes of structural correlation with the contiguous dipropionate NMR database **1a–h**.

the same procedure described previously,[2] we have compared the ^{13}C NMR characteristics of the C29–C32 (first mode of correlation) and C30–C33 (second mode of correlation) portions of the natural products with those of each of the eight diastereomers.[5] As seen from the graphs (Figures 1 and 2), none of the eight diastereomers match the corresponding structural portion of the natural products at a satisfactory level.[6] However, this outcome is not totally surprising when one takes into account the fact that the natural products have additional hydroxyl groups at C27 and C35. As these hydroxyl groups are attached on the contiguous dipropionate unit and linked through a bridge consisting of one methylene group,[7] a significant steric and/or stereoelectronic effect would be expected from them on the basis of NMR characteristics of the structural portion in question. Hence, we chose to focus only on the ^{13}C NMR characteristics of the C30 and C53 (see the smaller box in the first mode of correlation in Scheme 1) and of the C32 and C54 (see the smaller box in the second mode of correlation) portions of the natural products. From these comparisons (Figure 3) one (**1h** = $\alpha\beta\beta\alpha$) and three (**1a** = $\beta\beta\alpha\alpha$, **1f** = $\alpha\alpha\alpha\beta$, and **1h** = $\beta\alpha\alpha\beta$) candidates emerge from the first and second modes of correlation, respectively.

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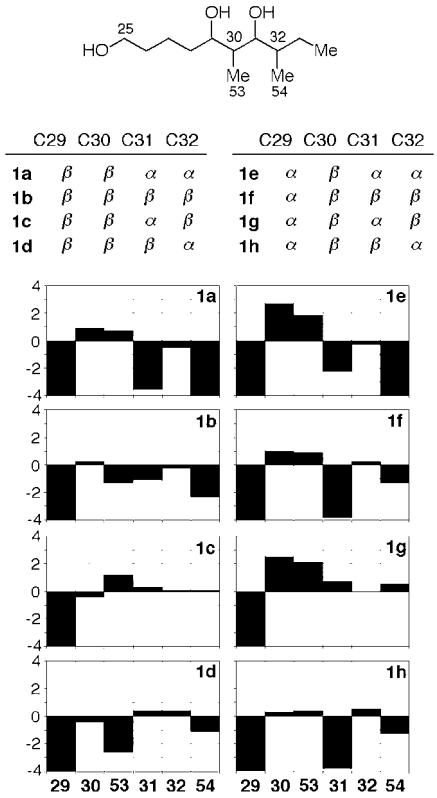

Figure 1. First mode of structural correlation. Difference between the chemical shifts of the carbon atoms of oasomycin B and those of each of **1a**–**h** (100 MHz, [D$_6$]DMSO). The *x*- and *y*-axes represent the carbon number and $\Delta\delta$ (δ**1a**–**h** – δoasomycin B), respectively, for all the charts in this paper.

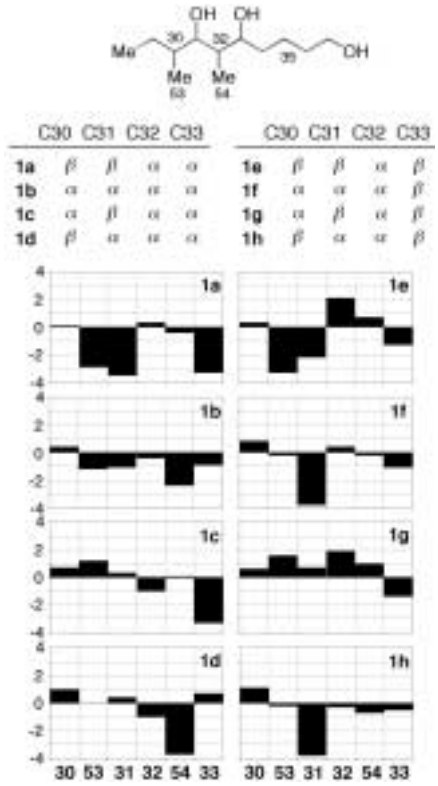

Figure 2. Second mode of structural correlation. Difference between the chemical shifts of the carbon atoms of oasomycin B and those of each of **1a**–**h** (100 MHz, [D$_6$]DMSO).

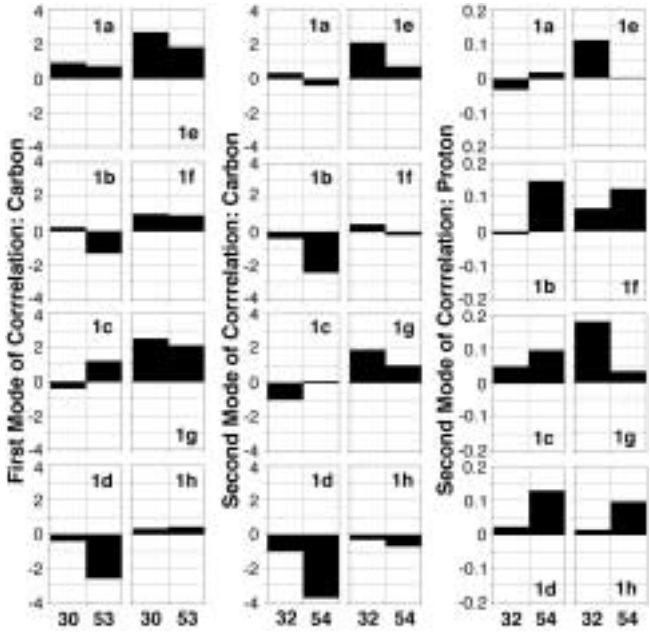

Figure 3. Structural correlation only at C30 and C53, and at C32 and C54. Difference between the chemical shifts of the carbon atoms (100 MHz, [D$_6$]DMSO) and protons (500 MHz, [D$_6$]DMSO) of oasomycin B and those of each of **1a**–**h**.

For the following two reasons we have reached the conclusion that, of the three candidates emerging from the second mode of correlation, **1a** ($\beta\beta\alpha\alpha$) represents the relative stereochemistry at C30, C31, C32, and C33. First, the relative stereochemistry from C30 to C32 needs to be shared by both modes of correlation, but **1f** ($\alpha\alpha\alpha\beta$) and **1h** ($\beta\alpha\alpha\beta$) do not meet with this condition. Second, as recognized in many cases previously studied,[8] the ^{13}C and ^{1}H NMR characteristics are complementary for this type of comparison. Comparison of the chemical shifts of the protons attached at C32 and C54 (Figure 3)[9] clearly demonstrates that only **1a** ($\beta\beta\alpha\alpha$) matches the corresponding structural portion of the natural products at a satisfactory level.[6]

In order to extend the stereochemical information beyond the C29–C33 portion of desertomycins/oasomycins we required a new NMR database.[10] In line with the analysis presented above, we recognized a possibility that the central carbon atom in a 1,3,5-triol such as $-CH(OH)CH_2CH(OH)CH_2CH(OH)-$ may exhibit a distinctive chemical shift which is *dependent* on the relative stereochemistry at 1/3 and 3/5, but is *independent* of the functional groups present outside of this structural motif. We have demonstrated this indeed to be the case.[11, 12] The chemical shifts for the central carbon atom of **3a**–**d** are summarized in Scheme 2 as an example. In general, the chemical shifts for the central carbon atoms of 1,3,5-triols are classified into three subgroups, with those of *anti*/*anti* triols clustering around $\delta = 64$ ([D$_6$]DMSO), those of *anti*/*syn* and *syn*/*anti* triols around $\delta = 66$, and those of *syn*/*syn* triols around $\delta = 68$. Comparison of this NMR database with the chemical shifts of the carbon atoms reported for the C25 ($\delta = 63.7$ in [D$_6$]DMSO), C27 (66.7), and C35 (63.8) carbon atoms of desertomycins/oasomycins[4b] immediately predicts the rela-

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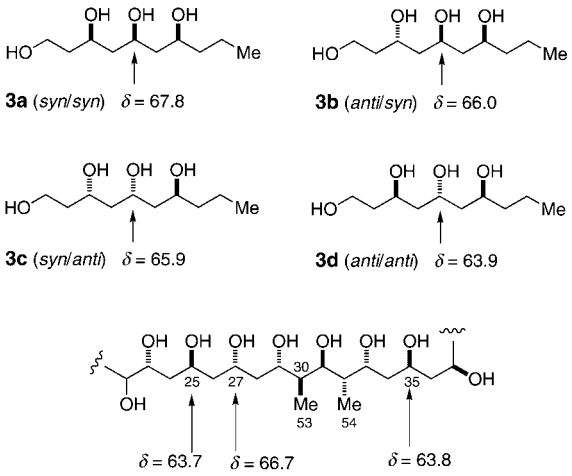
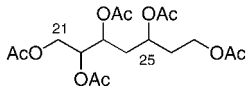


Scheme 2. Chemical shifts (100 MHz, [D$_6$]DMSO) of the central carbon atoms in 1,3,5-triols **3a**–**d** and the relevant portion of oasomycin A.

tive stereochemistry at C23, C25, C27, and C29 as well as at C33, C35, and C37 to be the one depicted in Scheme 2.

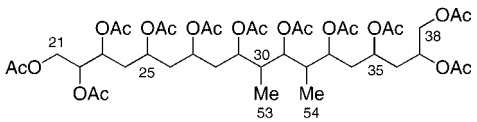
Finally, in order to address the relative stereochemistry of C22 and C23 we have created one additional NMR database for a 1,2,3,5-tetraol peracetate represented by **4a**–**d**.[5, 13] Comparison of this database with the chemical shifts for the carbon atoms found for the C21–C38 degradation product **5**[3] (Scheme 3) allows the relative stereochemistry at C22 and C23 to be assigned to that found in **4b**.



4a (C22=α, C23=α, C25=β) **4b** (C22=β, C23=α, C25=β)
4c (C22=α, C23=β, C25=β) **4d** (C22=β, C23=β, C25=β)

^{13}C NMR Chemical Shifts ($CDCl_3$)

	4a	4b	4c	4d
C21	62.4	61.9	61.6	62.2
C22	71.5	71.9	71.7	70.8
C23	67.4	67.9	68.7	68.4



5

δ ($CDCl_3$): C21=61.9; C22=71.8; C23=67.9

Scheme 3. Chemical shifts (100 MHz, $CDCl_3$) for 1,2,3,5-tetraol peracetates **4a**–**d** and the relevant portion of the C21–C38 degradation product **5**.

In conclusion, the relative stereochemistry of the C21–C38 portion of desertomycins/oasomycins is predicted to be the one shown in the structure in Scheme 1. This prediction has been made by using only three simple universal NMR databases, and we will present the evidence to prove the predicted relative stereochemistry in the following paper.[3]

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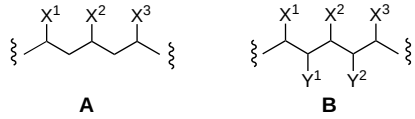
[4] For the detailed NMR data of this class of natural products, see a) desertomycins: A. Bax, A. Aszalos, Z. Dinya, K. Sudo, *J. Am. Chem. Soc.* **1986**, *108*, 8056; b) oasomycins: S. Grabley, G. Kretzschmar, M. Mayer, S. Philipps, R. Thiericke, J. Wink, A. Zeeck, *Liebigs Ann. Chem.* **1993**, 573. It is evident by comparison of the reported NMR characteristics that desertomycins and oasomycins share the same stereochemistry.
[5] The numbering used in this paper corresponds to the desertomycins/oasomycins numbering; see the structure in Scheme 1.
[6] We have found that differences in ^{13}C and ^{1}H chemical shifts are within $\Delta\delta = 0.5$ and 0.03, respectively, in the previous cases studied.
[7] Steric and/or stereoelectronic interactions between the structural motifs connected either directly or through a bridge of one methylene group are significant, whereas interactions between the structural motifs connected through a bridge of two or more methylene groups are almost negligible; see the examples given in the refs. [2a, b] and refs. [3a, b] quoted in ref. [1].
[8] W. Zheng, J. A. DeMattei, J.-P. Wu, J. J.-W. Duan, L. R. Cook, H. Oinuma, Y. Kishi, *J. Am. Chem. Soc.* **1996**, *118*, 7946.
[9] This comparison was performed without taking into account the difference in functional groups between the dipropionate model and desertomycins/oasomycins, see the structures in Scheme 1. It has been shown, at least in the case of ^{13}C NMR comparison, that no increments are necessary for a similar structural motif.[11]
[10] We created an NMR database for a 1,3-diol using the *syn* and *anti* diastereomers of $Me(CH_2)_2CH(OH)CH_2CH(OH)(CH_2)_4OH$.[11] This database was then applied in a stepwise manner to the C33/C35, C35/C37, C29/C27, C27/C25, and C25/C23 1,3-diol systems, which predicted the same relative stereochemistry as the one derived from the approach outlined in this paper. We also created an NMR database for a 1,2,4-triol peracetate using the diastereomers of $AcOCH_2CH(OAc)CH_2CH(OAc)(CH_2)_2OAc$ [^{13}C NMR (100 MHz, $CDCl_3$): *syn* diastereomer: $\delta = 60.4$ (C33), 32.9 (C34), 67.8 (C35), 35.1 (C36), 68.4 (C37), 64.6 (C38); *anti* diastereomer: $\delta = 60.6$ (C33), 33.6 (C34), 66.9 (C35), 35.3 (C36), 67.4 (C37), 65.1 (C38)]. This NMR data also suggested the same relative configuration at C35 and C37 as the one given in the text.
[11] Y. Kobayashi, C.-H. Tan, Y. Kishi, *Helv. Chim. Acta* **2000**, in press.
[12] We recognized that 1,3,5-trisubstituted acyclic compounds, represented by **A**, might exhibit this distinctive characteristic, and chose **3a**–**d** as an experimental example to demonstrate this. In our view, this phenomenon can be extended to a more generalized structure such as **B**.



A **B**

[13] **4a**–**d** were prepared in nine steps: 1) (2*S*)-[2-(phenylmethoxy)ethyl]oxirane, CH_2=CHMgBr, CuBr, THF; 2) TBSCl, imidazole, CH_2Cl_2; 3) OsO_4, NMO, acetone/H_2O, followed by $Pb(OAc)_4$, benzene; 4) CH_2=CHMgBr, THF; 5) CSA, MeOH; 6) $PhCH(OMe)_2$, CSA, benzene, followed by chromatographic separation; 7) AD-mix-α or -β, *t*BuOH/H_2O; 8) H_2, Pd/C, MeOH; 9) Ac_2O, Py, DMAP. CSA = 10-camphorsulfonic acid; DMAP = 4-dimethylaminopyridine; NMO = *N*-methylmorpholine *N*-oxide; Py = pyridine; TBS = *tert*-butyldimethylsilyl; THF = tetrahydrofuran. ^{13}C NMR (100 MHz, $CDCl_3$): **4a**: $\delta = 62.4$ (C21), 71.5 (C22), 67.4 (C23), 35.1 (C24), 66.8 (C25), 33.6 (C26), 60.5 (C27); **4b**: $\delta = 61.9$ (C21), 71.9 (C22), 67.9 (C23), 34.4 (C24), 66.7 (C25), 33.6 (C26), 60.5 (C27); **4c**: $\delta = 61.6$ (C21), 71.7 (C22), 68.7 (C23), 34.6 (C24), 68.0 (C25), 32.6 (C26), 60.4 (C27); **4d**: $\delta = 62.2$ (C21), 70.8 (C22), 68.4 (C23), 35.1 (C24), 67.8 (C25), 32.8 (C26), 60.3 (C27).

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