Stereochemical reassignment of Mehta and Kundu's spiculoic acid A analogue

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¹H Assignment of *dia*-6

The following numbering is adopted for the spiculic acid A analogue *dia* 6.

The ¹H NMR spectrum was assigned from an analysis of the COSY spectrum using the H-7 (δ 3.86, t) signal as an entry point. Correlations were observed between H-7 and signals at δ 2.20–2.32 and δ 1.85–1.95, each corresponding to 1H. The signal at δ 1.85–1.95 correlated with a doublet at δ 1.0 (H-10). Therefore δ 1.85–1.95 was assigned as H-6 and δ 2.20–2.32 as H-8 (Figure 1).

Figure 1.

H-8 showed a correlation with H-9 (δ 2.11, 1H, t). H-9 correlated with a signal at H-5 (δ 1.95–2.05, m). H-5 also showed a correlation with H-6 (Figure 2).

Figure 2.

H-8 also showed correlations with signals at δ 1.60–1.80 (3H, m) and δ 1.30–1.40 (1H, m). Therefore δ 1.30–1.40 (1H, m) was assigned as one of the diastereotopic protons of C-11. The signal of the remaining diastereotopic proton of C-11 is mixed with that of H-13 at δ 1.60–

1.80 (3H, m) (Figure 3). In Mehta and Kundu's publication, these two signals were reported as each corresponding to two protons.

Figure 3.

Another entry point for analysis is the H-2 signal (δ 3.18, d), which correlated to both H-3 (δ 5.41, ddd) and H-4 (δ 5.60, dd), of which the former was stronger. H-4 also correlated with H-5 (Figure 4).

Figure 4.

These interpretations can be summarized in the following assignment. The H-10 coupling constant is not presented below due to a lack of information from the literature spectrum.

δ_H (400MHz, CDCl₃) 0.80–0.95 (6H, m, $-\text{CH}_3$ of C-11,13), 1.00 (3H, d, H-10), 1.10 (9H, s, $-\text{SiPh}_2^t\text{Bu}$), 1.30–1.40 (1H, m, H-11), 1.60–1.80 (3H, m, 1 x H-11 and H-13), 1.85–1.95 (1H, m, H-6), 1.95–2.05 (1H, m, H-5), 2.11 (1H, t, $J = 8.8$ Hz, H-9), 2.20–2.32 (1H, m, H-8), 3.18 (1H, d, $J = 4.8$ Hz, H-2), 3.39 (1H, $d_{1/2\text{ABq}}$, $J = 10.0$ Hz, H-12), 3.44 (1H, $d_{1/2\text{ABq}}$, $J = 10.0$ Hz, H-12), 3.65 (3H, s, $-\text{OCH}_3$), 3.86 (1H, t, $J = 5.2$ Hz, H-7), 4.47 (1H, $d_{1/2\text{ABq}}$, $J = 12.0$ Hz, $-\text{OCH}_2\text{Bn}$), 4.59 (1H, $d_{1/2\text{ABq}}$, $J = 12.0$ Hz, $-\text{OCH}_2\text{Bn}$), 5.41 (1H, ddd, $J = 1.6$ Hz, 8.0 Hz, 2.4 Hz, H-3), 5.60 (1H, dd, $J = 2.0$ Hz, 10.0 Hz, H-4), 7.20–7.45 (11H, m, $-\text{ArH}$), 7.55–7.70 (4H, m, $-\text{ArH}$).

Rationale for the Formation of Diastereoisomer *dia-6*

An illustration of the four anti and syn Diels–Alder transition states available to *dia-5* is given in Figure 5. An analysis of the strain and steric interactions present in these transition states may give an understanding of why, of the four possible diastereoisomers that could have been made, *dia-6* was formed exclusively.¹

Figure 5.

Figure 5 reveals that there is allylic strain present in both of the anti transition states (both A and B) of *dia-5*. In particular, transition state B contains significant strain between the –Et of C-7 and the vinylic –Et group.

A consideration of syn transition state C reveals that it contains significant non-bonding steric interactions between the –Et of C-7 and the diene portion of the molecule. The diene and

dienophile are therefore prevented from adopting the required alignment when in this orientation.

Comparatively, syn transition state D contains only modest strain and non-bonded steric interactions. It is therefore reasonable that this is the lowest energy transition state of the four available to **dia-5**. This theoretical rationale is in agreement with the exclusive formation of **dia-6** observed.

An interesting related example is provided by Bognár *et al.*² (Figure 6). On heating **9** in toluene, exclusive formation of cis-fused product **10** was observed.

Figure 6.

Although it was known that bulky substituents at the allylic position of the diene moiety could induce moderate stereoselectivity, such high selectivity was unprecedented. An analysis of the four possible transition states, similar to that above, again rationalizes the exclusive formation of diastereoisomer **10**.

References

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- (2) Herczegh, P.; Zsély, M.; Szilágyi, L.; Bognár, R. *Tetrahedron Lett.* **1988**, 29, 481.