Structure and Absolute Configuration of Solanapyrone D: A New Clue to the Occurrence of Biological Diels–Alder Reactions

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The structure and absolute configuration of solanapyrone D (**2**) offers further indirect evidence that solanapyrone A (**1**) and D (**2**) are biosynthesized *via* intramolecular Diels–Alder reactions.

Involvement of biological Diels–Alder reactions has been proposed in the biosynthesis of a variety of secondary metabolites.[1] Among the candidates for such a biogenetic path are the alkaloid presecamines,[2] the terpenoid heliocides,[3] and the polyketide cytochalacins.[4] However, these compounds have rarely been isolated together with their optically active regioisomer or diastereoisomer. Here we report the concurrence and isolation of an optically active diastereoisomer of solanapyrone A (**1**) which would result from *endo* cycloaddition in a biological Diels–Alder reaction.

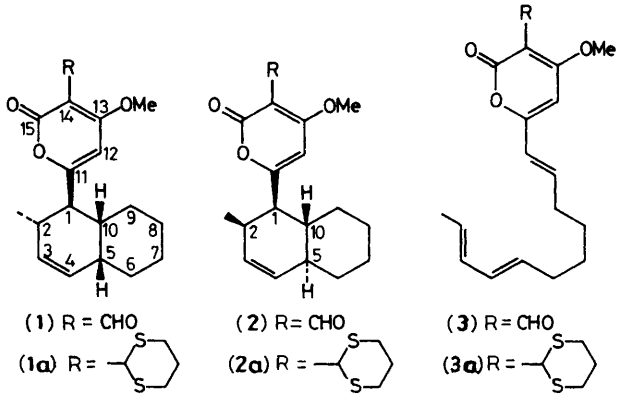


Figure 1

During the biosynthetic study of (**1**), compound (**2**), solanapyrone D, was detected and isolated as a minor component. This material was optically active {$[\alpha]_D^{24}$ −125.2° (*c* 0.8, $CHCl_3$)}, and was considered as a diastereoisomer of (**1**) from its molecular formula ($C_{18}H_{22}O_4$) and various spectral data. Eventually, the structure was identified as (**2**), depicted in Figure 1, which had been derived from a major Diels–Alder adduct in the reaction of triene (**3a**) (Figure 1).[5]

Determination of the absolute configuration of (**2**) also provides valuable information about the enzymatic reaction. This was undertaken as follows (Figure 2). A 4:1 mixture of (**1**) and (**2**) was treated with OsO_4 at −20 °C to give products (**4a**) and (**4b**), respectively. In this oxidation, the reagent attacks stereoselectively from less hindered sides, *i.e.* the convex face in (**1**) and the side opposite to the axial methyl group in (**2**). The products (**4a**) and (**4b**) are separated after

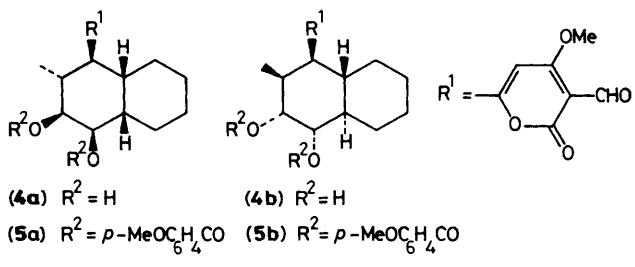
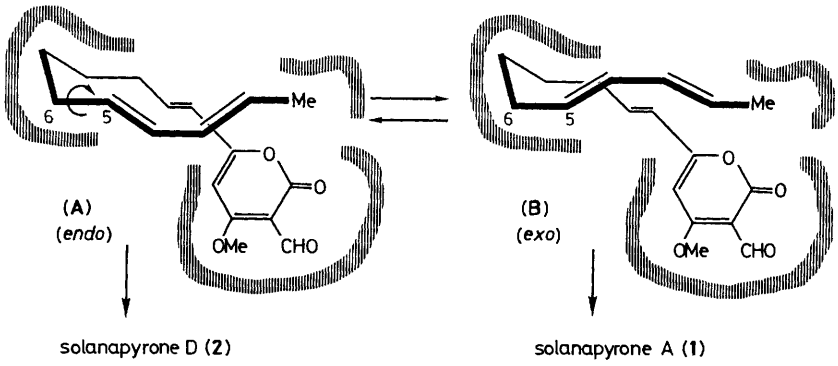


Figure 2



Scheme 1

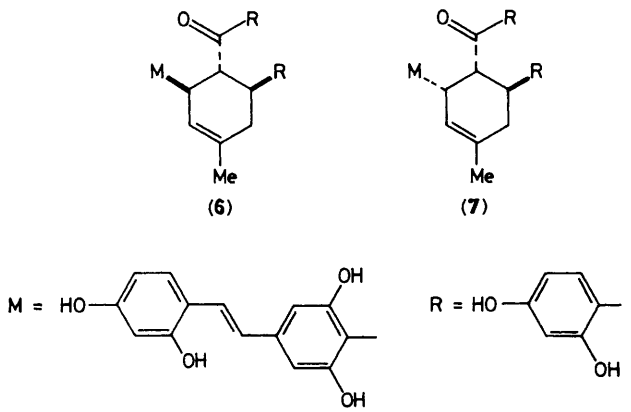


Figure 3

conversion to di-*p*-methoxybenzoates (**5a**) and (**5b**).† Based on the ^{1}H n.m.r. spectroscopy coupling constants, the relationship between 3-H and 4-H was assigned as equatorial–axial in (**5a**), and as axial–equatorial in (**5b**). The negative split in the Cotton effect [$\lambda_{max.}$ (EtOH) ($\Delta\varepsilon$): 268 (−15.5), 248 (+12.3) nm (*c* 0.032 mM)] was observed in the c.d. spectrum of (**5b**). From this result, the absolute configuration of (**2**) was assigned as depicted in Figure 1. Interaction between the *p*-methoxybenzoyl group and the pyrone moiety can be ignored because of the distance between these groups and the different location of their u.v. maxima.

The stereochemistry at C-1 and C-10 in (**2**) is the same as that of (**1**) whereas the configurations at C-2 and C-5 in (**2**) are opposite to those of (**1**).[6] These data allow speculation that the postulated enzyme which catalyses the Diels–Alder reaction recognizes the dienophile portion and terminal methyl group, and accepts two similar transition states (**A**) and (**B**) of (**3**), which can be interconverted by rotation about the C-5 to C-6 bond (Scheme 1). Thus, transition state (**A**) (*exo*) gives (**1**), and (**B**) (*endo*) gives (**2**). Consideration of Dreiding models indicates that the stability of the two transition states would be similar. In fact, this is reflected in the product ratio [(**1a**)/(**2a**) = 1/2] in the synthesis of (**1**).[5] In more than 30 decalin polyketides,[7] solanapyrones represent the only case in which the triene precursor [*e.g.*, (**3**)] does not possess any chiral centre. Possibly this accounts for the biological production of two diastereoisomers. Interestingly, kuwanones X (**6**) and Y (**7**), a pair of diastereoisomers possibly arising from *exo* and *endo* intermolecular cycloaddition, respectively, have the same stereochemical relationship as (**1**) and (**2**) (Figure 3).[8]

In conclusion, stereochemical information and isolation of a pair of possible adducts strongly suggest that (**1**) and (**2**) are biosynthesized *via* an intramolecular Diels–Alder reaction. The timing of oxidation of the C_1 unit at the pyrone ring is presently being investigated prior to incorporation experiments with trienes.

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† *Spectroscopic data.* ^{1}H n.m.r. ($CDCl_3$). (**5a**): δ 8.08 (2 H, d, *J* 8.8 Hz), 7.83 (2 H, d, *J* 8.9 Hz), 7.00 (2 H, d, *J* 8.8 Hz), 6.81 (2 H, d, *J* 8.9 Hz), 5.38 (1 H, dd, *J* 2.8, 3.0 Hz, 4-H), 5.19 (1 H, dd, *J* 2.8, 11.0 Hz, 3-H), 3.90 (3 H, s), 3.81 (3 H, s). (**5b**) δ 8.05 (2 H, d, *J* 8.8 Hz), 7.74 (2 H, d, *J* 8.9 Hz), 7.01 (2 H, d, *J* 8.8 Hz), 6.82 (2 H, d, *J* 8.9 Hz), 5.45 (1 H, dd, *J* 2.6, 2.8 Hz, 3-H), 5.22 (1 H, dd, *J* 2.6, 11.5 Hz, 4-H), 3.91 (3 H, s), 3.81 (3 H, s).

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