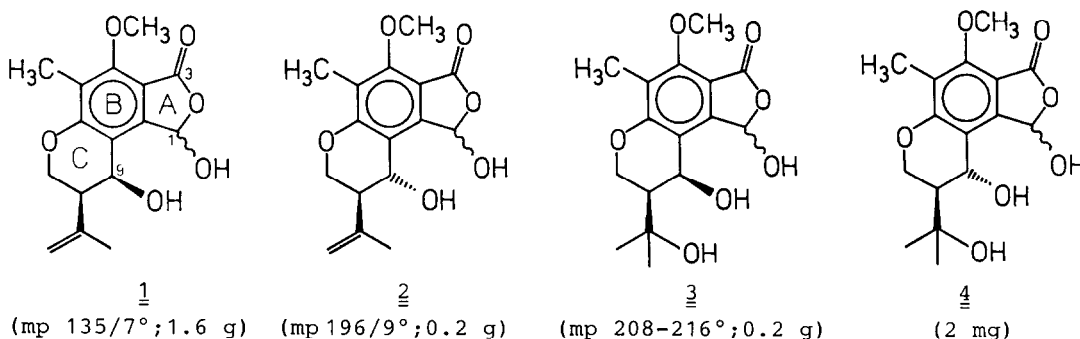


HIGHLY SUBSTITUTED CHROMANOLS FROM CULTURES OF ASPERGILLUS DURICAULIS

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Summary: The new compounds 1 - 4 and 8 have been isolated from cultures of Aspergillus duricaulis

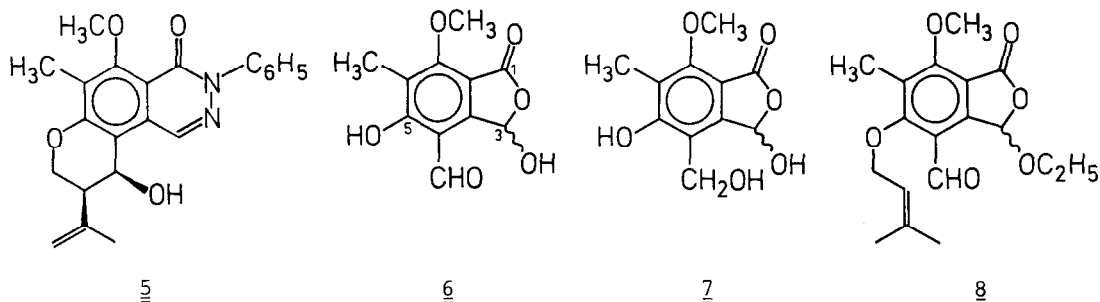
By chromatography of the ethyl acetate extract from cultures of Aspergillus duricaulis the highly substituted chromanols 1 - 4 were isolated.



The kind of substituents at ring B and the structural details of ring C were deduced from the ¹H-nmr spectra. Ring-chain tautomerism of the hydroxyphthalide ring A generates diastereomers and therefore is responsible for comparatively broad ¹H-nmr signals, which appear as two sharp signals each, when the ¹H-nmr is run in completely acid-free solvent. In aqueous solution, ring A is opened to the tautomeric phthalaldehydic acid on addition of NaHCO₃ (1). In agreement with the given formulae are the results of chemical reactions: a) on acetylation (Ac₂O/py) 1 - 3 yield two diastereomeric diacetyl derivatives [δ C-CH₂-C(=O)OCH₃: 7.12 - 7.31 in CDCl₃], which can be separated chromatographically; b) with phenylhydrazine, 1 reacts to the corresponding phthalazinone 5 [mp 161/3 °C; δ (-CH=N-): 8.51 in CDCl₃]; c) the benzylic hydroxy group at C-9 is partly removed under catalytical hydrogenation. The stereochemistry of ring C can be deduced from the coupling constants in the ¹H-nmr spectra (2).

The pattern of substitution at ring B in 1 - 3 was deduced from the ^{13}C -nmr data, which closely correlate with those of cyclopaldic acid (6) and cyclopolic acid (7) (3).

The deduced structures were proven by proton-catalyzed cyclisation of 8 to the 1-O-ethyl derivatives of 1 and 2.



Besides the main compounds 1, 2, 3 and 3-O-ethyl 7 (3), 4 and 8 were isolated as very minor components from fermentations of *Aspergillus duricaulis*. This observation corroborates, that 5-O-isopentenyl cyclopaldic acid might be the immediate precursor of the chromanols 1 to 4.

Though 1 - 4 posses two chiral centers, they did not exhibit any optical rotation nor a Cotton effect. With the shift reagent $\text{Eu}(\text{tfc})_3$, most of the ^1H -nmr signals of the diacetyl derivatives from 1 - 3 duplicated in a ratio of 1:1 (peak integrals) indicating racemic solutions.

On the other hand, whereas the isomeric compounds 1 and 2 are isolated from the cultures in an approximate 8:1 ratio, the proton-catalyzed "in vitro"-cyclisation mentioned above yields the isomers in a 1:1 ratio.

Therefore, it can not be decided with certainty wether 1 to 4 are genuine natural compounds or products from an easily occuring proton-catalyzed cyclisation reaction during fermentation or work-up.

Whereas the chromanols 1 - 4 were found to be inactive in the plate diffusion test, 8 shows pronounced antibiotic activity against various microorganisms.

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