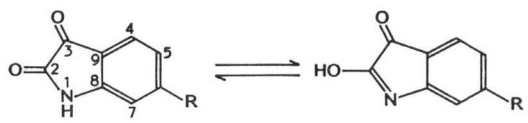
ISOLATION AND STRUCTURE ELUCIDATION OF 6-(3′-METHYL-BUTEN-2′-YL)ISATIN, AN UNUSUAL METABOLITE FROM *STREPTOMYCES ALBUS*

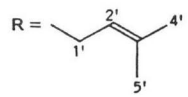
Sir:

Streptomycetes are known to generate a broad spectrum of secondary metabolites covering a wide range of chemical structures. However, up to now, the occurrence of isatin derivatives amongst the metabolites has not been reported. In this communication we describe the new metabolite **1** we have recently isolated from a strain of *Streptomyces albus*.

The strain, IMET 3453 (from the collection of the Central Institute of Microbiology and Experimental Therapy, Jena), was grown on a complex medium (glucose 2%, soybean flour 1.5%, NaCl 0.2%, $CaCO_3$ 0.1%; pH 6.2) for 4 days. Extraction of the culture liquid with 0.2 volume butyl acetate followed by repeated chromatography on silica gel columns with benzene - ether (1 : 1) and $CHCl_3$ - MeOH (9 : 1) solvent mixtures as the eluents afforded the pure **1** (yellow crystals from MeOH; mp 109~110°C; Rf 0.5 on Silufol sheets with benzene - ether 1 : 1; insoluble in water). Metabolite **1** shows weak antimicrobial activity against Gram-positive bacteria such as *Bacillus subtilis* ATCC 6633 (MIC 20 μg/ml).

The elemental composition, $C_{13}H_{13}NO_2$, of the new metabolite followed from its mass spectrum (EI-MS, direct inlet, 150°C): *m/z* 215.0935 (M^+, calcd 215.0946). From the analysis of the ^1H NMR spectrum (100 MHz, $CDCl_3$) δ_H 8.6 (1H, br, exch, NH or OH), 7.51 (1H, d, $J_{4,5}$=8.0 Hz, H4), 6.92 (1H, ddt, $J_{4,5}$=8.0 Hz, $J_{5,7}$=1.2 Hz, $J_{5,1'}$=1.3 Hz, H5), 6.76 (1H, dt, $J_{5,7}$=1.2 Hz, $J_{7,1'}$=1.3 Hz, H7), 5.28 (1H, tqq, $J_{1',2'}$=7.4 Hz, $J_{2',4'}$=$J_{2',5'}$=1.5 Hz, H2′), 3.39 (2H, ddd, $J_{1',2'}$=7.4 Hz, $J_{1',5}$=1.3 Hz, $J_{1',7}$=1.3 Hz, H1′), 1.81 (3H, d, $J_{2',5'}$=1.5 Hz, H5′), 1.74 (3H, d, $J_{2',4'}$=1.5 Hz, H4′) ppm, it became immediately evident that the carbon-bonded H atoms must be arranged as in **1** which accounts for $C_{11}H_{12}$ of the gross structure. The ^{13}C NMR spectrum (25 MHz, $CDCl_3$) δ_C 182.82 (s, C3), 160.79 (s, C2), 155.15 (s, C8), 150.17 (s, C6), 134.85 (s, C3′), 125.75 (d, C4), 124.05 (d, C5), 120.67 (d, C2′), 116.11 (s, C9), 112.76 (d, C7), 35.38 (t, C1′), 25.73 (q, C4′), 17.93 (q, C5′) ppm and the 3.6 Hz vicinal coupling between C3 and H4 indicated that the remaining atoms must be arranged either in a –COCONH– or in a –COC(OH)=N– sequence and form a five-membered hetero ring condensed with the substituted aromatic nucleus. This expectation has received full support from IR spectroscopic observations. The FT-IR spectrum of the solid sample (KBr) displayed narrow bands at 1760 and 1740 cm^{-1} attributable to the two carbonyl groups (ν_{CO}) and a sharp absorption at 3310 cm^{-1} assignable to ν_{NH}. On rerunning the spectrum in dilute $CDCl_3$ solutions, one could observe the appearance of an additional (broad) absorption at 3240 cm^{-1} (ν_{OH}) and the concomitant decrease of the ν_{NH} and one of the ν_{CO} bands, while the intensity ratios I(3310)/I(3240) and I(1760)/I(1740) changed simultaneously with the dilution. This finding clearly shows that, in solutions, the new metabolite like its parent molecule, isatin,[1] exists as a mixture of two, rapidly interconverting, tautomeric forms. Due to this property, isatin is known to behave as a chelating agent towards some trace elements[1] which might suggest that the biological function of **1** is to scavenge heavy metal ions from the medium as do many antibiotics and secondary metabolites of actinomycetes.[2]





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Acknowledgments

We thank Dr. S. HOLLY (Central Research Institute of Chemistry, Budapest) for the recording and interpretation of the IR spectra.

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(Received September 20, 1985)

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