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NOTES

Paniculatin, a New Coumarin from *Murraya paniculata* (L.) Jack[1]

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The coumarin derivatives osthol and coumurrayin were isolated from foliage of *Murraya paniculata* (Rutaceae). In addition, a new coumarin, *paniculatin*, was obtained. By means of chemical degradation and u.v., n.m.r., and mass spectroscopy, the new compound was identified as 7-methoxy-8-(isovaleryloxy-2-keto-3-methylbutyl)coumarin.

L'osthol et la coumurrayine des dérivés de la coumarine, ont été isolés à partir du *Murraya paniculata* (Rutaceae). En plus, une nouvelle coumarine, la *paniculatine*, a été obtenue. En utilisant la dégradation chimique et la spectroscopie u.v., r.m.n., et de masse, le nouveau composé a été identifié comme étant le méthoxy-7 (isovaléryloxycéto-2 méthyl-3 butyl)-8 coumarine.

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The plant *Murraya paniculata* (L.) Jack (*M. exotica* L.), family Rutaceae, is known to contain coumarin derivatives. Bose and Mookerjee (1) isolated scopoletin glucoside from the petals, while from other organs Ramstad *et al.* (2) and Dreyer (3) obtained 5,7-dimethoxy-8-(3-methyl-2-butenyl)coumarin (coumurrayin), and Chakraborty *et al.* (4) 5,7-dimethyoxy-8-(2,3-dihydroxy-3-methylbutyl)coumarin (mexoticin).

Gas chromatographic examination of foliage extracts of this plant have now revealed the presence of coumurrayin and several other coumarins. Osthol (7-methoxy-8-(3-methyl-2-butenyl)coumarin) was identified by u.v. and n.m.r. spectroscopy (5) and by co-chromatography with an authentic standard, and two other 8-isopentenyl-type derivatives present only in trace amounts were partly characterized. These, isolated by gas chromatography, had the same fluorescence and u.v. absorption characteristics as osthol. In their n.m.r. spectra doublets could be discerned at δ 6.2, 7.7, 6.9, and 7.4, indicating they were 8-alkyl coumarins (5). Both showed 7-methoxyl at δ 3.9 but the aliphatic end of the spectrum was obscured by instrument noise: in one derivative signals (3H?) could be seen at δ 1.23, 1.31 and 1.70, in the other at δ 1.78 and 2.42. In addition, a new coumarin for which the name *paniculatin* is suggested, was isolated in reasonable quantities and identified as 7-methoxy-8-(1-isovaleryloxy-2-keto-3-methylbutyl)coumarin (**1**) on the basis of the following evidence. The compound had a molecular formula $C_{20}H_{24}O_6$, determined by mass spectroscopy (calcd. and found *m/e* 360.1573), and fluoresced violet under u.v. excitation in the same way as osthol. The u.v. spectrum, λ_{max} (EtOH) 247, 256, and 320 nm, unchanged by the addition of NaOH or $AlCl_3$, was typical of 7-alkoxycoumarins. This was confirmed by the [^{1}H]n.m.r. spectrum in $DCCl_3$ (Fig. 1), in which the characteristic coumarin H-3/H-4 and H-5/H-6 doublet pairs appeared. The position of the H-4 doublet at δ 7.66 showed clearly that no oxygen function was present at C-5, a possibility not excluded by the u.v. spectrum. An oxygen function at C-5 would require the H-4 doublet to be located at $\delta > 7.9$ (6). The H-6 doublet was not meta-coupled, so C-8 must bear a carbon chain. At δ 6.94 was a sharp one-proton singlet with an extremely low field which was reminiscent of the benzylic protons of the coumarins athamantin and archangelicin (7), which resonated at δ 6.97 and 7.12, respectively, under the same conditions. The septet at δ 2.88 was shown by spin decoupling to be coupled ($J = 6.7$ Hz) to the methyl doublets at 1.03 and 1.17, forming an isopropyl group which must be adjacent to a carbon lacking protons entirely. The multiplet at 2.0–2.3 and the coupled doublet at 0.95 indicated the presence of an isovalerate residue.

Mild alkaline hydrolysis of paniculatin gave

[1]NRCC No. 12275.

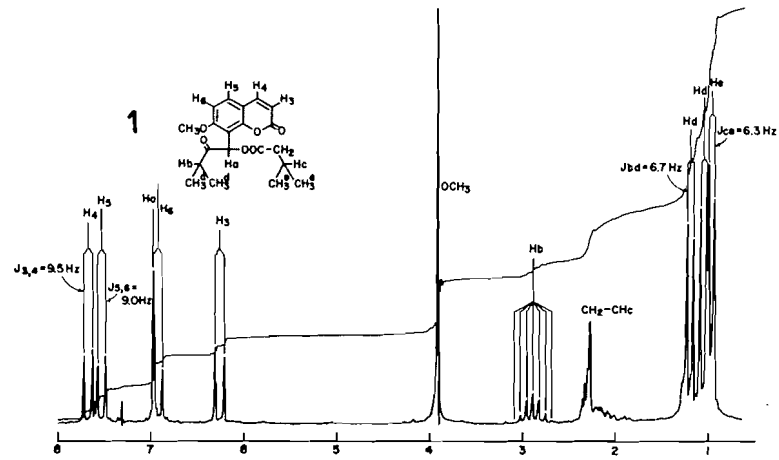

FIG. 1. The 100 MHz[^{1}H]n.m.r. spectrum of paniculatin; solvent, $DCCl_3$; TMS internal standard.

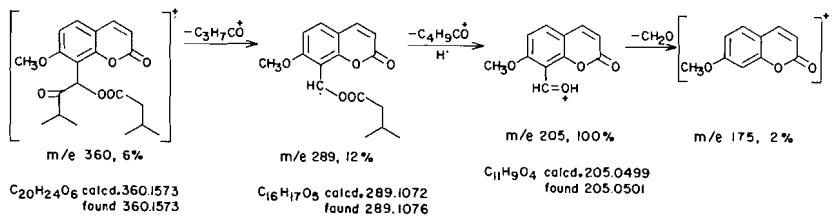

FIG. 2. Fragmentation of paniculatin, from the mass spectrum.

isovaleric acid, a coumarin identified as 7-methoxy-8-(1-hydroxy-2-keto-3-methylbutyl)-coumarin (**2**) and a trace of a compound with the same fluorescence, u.v. absorption, and chromatographic characteristics as authentic 7-methoxy-8-(2-keto-3-methylbutyl)coumarin synthesized from osthol (8). Acid hydrolysis gave a somewhat larger proportion of this last compound along with the same two major products. Isovaleric acid was identified by gas co-chromatography with authentic material on UC-W98 and FFAP columns, and on UC-W98 and 1.5% SE-52 after methylation with diazomethane. A strong odor of isovaleric acid was also apparent in the acidified hydrolyzate. Compound **2** was isolated by g.l.c. and identified by its u.v. and n.m.r. spectra; the absorption spectrum was identical with that of the parent ester. The n.m.r. spectrum was similar except for the absence of isovalerate signals, the appearance of a hydroxyl proton at δ 4.2 and the shift from δ 6.94 to 5.89 of the benzylic proton signal, thus confirming the position of the ester group.

The only structure for paniculatin in harmony with the above spectral, chromatographic, and hydrolytic data is **1**, optical configuration unknown. The mass spectrum of the coumarin supported this assignment, showing major peaks at *m/e* 360 (M) and 289 (M-71, loss of C_3H_7CO), further fragmenting with rearrangement to a very strong base peak at 205 (loss of C_4H_9CO and hydrogen transfer), then to 7-methoxycoumarin ion at *m/e* 175 (loss of CH_2O). Fragment *m/e* peaks at 43 ($C_3H_7^+$), 57 ($C_4H_9^+$), 71 ($C_3H_7CO^+$) and 85 ($C_4H_9CO^+$) corroborated this scheme; the expected metastable peaks were present at *m/e* 232.0 (360 → 289), 145.3 (289 → 205), and 149.3 (205 → 175). High resolution measurements showed the fragment formulas were $C_{16}H_{17}O_5$ at *m/e* 289 and $C_{11}H_9O_4$ at 205, consistent with the scheme shown in Fig. 2.

Paniculatin represents a novel type of coumarin in having an α-keto ester moiety, and is of some biosynthetic interest. It is doubtless derived from 7-hydroxycoumarin, probably via osthol; the subsequent stages in its formation may involve benzylic hydroxylation and esterification of meranzin (osthol epoxide) or meran-

zin hydrate (the corresponding diol). The natural occurrence of compounds very similar to these hypothetical ester intermediates (9, 10), and the common existence of benzylic esters in other classes of coumarins (7) provide some support for this idea.

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The Basicity of Aliphatic Ethers

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The pK_{BH^+} values of aliphatic ethers have been calculated from n.m.r. chemical shift data to be approximately −6.4.

Les valeurs des pK_{BH^+} d'éthers aliphatiques ont été calculées à partir des données r.m.n. des déplacements chimiques. Ces valeurs sont voisines de −6.4.

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Introduction

The basicities of aliphatic ethers is a topic of current interest and debate (1). The results of distribution studies which indicate that the pK_{BH^+}[1] values for these compounds are approximately −3 to −4 were at one time widely accepted (2, 3). However, more recent work has shown that aliphatic ethers may be less basic than the distribution studies suggested. Edward and coworkers (4, 5), on the basis of indicator measurements and n.m.r. studies, found the pK_{BH^+} of diethyl ether to be about −6, while Arnett *et al.* (6), using heats of protonation data, calculated it to be −5.1. Estimated basicity constants obtained by other methods have been tabulated elsewhere (2, 6).

We recently reported an n.m.r. method which gave reliable pK_{BH^+} values for aliphatic ketones (7) and we wish now to report results obtained when the protonation of aliphatic ethers was studied in a similar manner. Although the earlier literature (2, 4) seemed to indicate that n.m.r. chemical shifts were not suitable physical properties to use for protonation studies, later reports have shown that this procedure can be successfully employed with a wide variety of functional groups (7–13).

Edward's most recent results indicate that the chemical shifts of cations are influenced by the solvent through hydrogen bonding; hence the use of ammonium ions as internal standards introduces a potential error into the analysis (14). To overcome this we have used the difference (Δ) between the chemical shifts of α- and β-hydrogens as a measure of the extent of protonation (7). Since the α-hydrogens are closer to the site of protonation they are subject to greater shifts and consequently Δ increases with the extent of protonation. Thus when weak organic bases are dissolved in H_2SO_4 solutions

[1]In this context, pK_{BH^+} is taken to be the H_0 (15) of the solution in which the ether is one-half protonated.