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REVISED STRUCTURE OF PAEDEROSIDE, A NOVEL MONOTERPENE S-METHYL THIOCARBONATE

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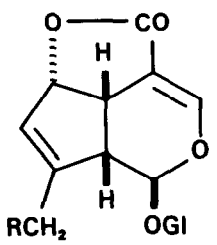
Abstract. On the basis of its mass spectrum, nmr and hydrolysis products, the iridoid glucoside, paederoside, is identified as an S-methyl thiocarbonate.

We wish to propose a revised structure (1) for paederoside, an iridoid glucoside found in two Paederia species (Rubiaceae).

Inouye and coworkers[1] first isolated paederoside in 1969 from P. scandens and assigned it the structure of a thioacetate (2) on the basis of elemental analysis, ir, uv, nmr, partial degradation and comparison with the known asperuloside (3) which occurs in the same plant. Recently we obtained these two compounds from P. foetida[2] and noted that the mass spectrum of paederoside indicated a molecular weight 16 mass units higher than that given by formula 2. We have now extended the mass spectral work, reexamined the hydrolysis products and the nmr of paederoside, and we have come to the conclusion that this iridoid is a thiocarbonate instead of a thioacetate.

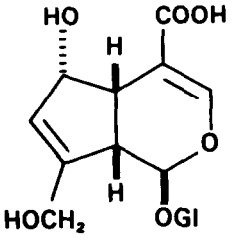


1 R = $CH_3SC(=O)-O-$

2 R = $CH_3C(=O)-S-$

3 R = $CH_3C(=O)-O-$

4



In 1967, Bentley, Johnstone and Grimshaw[3] showed that underivatized iridoid glucosides could be examined directly by electron impact mass spectrometry. In contrast with the mass spectra of most glycosides which are often dominated by the ions formed from the sugar residue, the mass spectra of iridoid glucosides are characteristic of the aglucones and usually the largest fragment observed corresponds to the aglucone moiety. As we reported in our earlier paper[2], asperuloside and paederoside exhibit closely related EI mass spectra. The largest fragment in the paederoside spectrum, however, is at m/z 284 rather than m/z 268, the aglucone molecular ion corresponding to structure 2. The base peak in the spectrum of asperuloside (3) is at m/z 43 (CH_3CO^+), and a similar intense peak would also be expected from paederoside if it possessed structure 2[4]; in fact

there is only a very minor peak at m/z 43 in the spectrum of paederoside. Intense ions at m/z 47, 48 and 75 are present in the spectrum of paederoside but not in that of asperuloside. While a thioacetate[4] could give a fragment ion at m/z 75 (CH_3COS^+) as well as a rearrangement ion at m/z 47 (CH_3S^+), they would be expected to be much lower in intensity than the CH_3S^+ and CH_3SCO^+ ions generated by a thiocarbonate such as 1.

The chemical ionization spectra of the two iridoids also supported structure 1 for paederoside The methane CI mass spectra of asperuloside and paederoside showed aglucone + H^+ ions at m/z 253 and 285 respectively, and in the ammonia CI spectrum of paederoside a weak ($M + NH_4^+$) was observed at m/z 464 as well as an intense ion at m/z 302 corresponding to the NH_4^+ adduct ion of the aglucone, the latter suggesting that the loss of the glucose moiety is a thermal process.

Inouye and coworkers[1] reported that the hydrolysis of paederoside in aqueous barium hydroxide gives deacetylasperulosic acid (4), along with thioacetic and acetic acids which were identified by gas chromatography. They ascribed the abnormal reaction products to the allylic position of the S-acetyl group in 2. We repeated the hydrolysis and obtained methyl mercaptan in accord with structure 1 but no thioacetic acid[5].

Both of these observations are compatible with the thiocarbonate rather than the thioacetate formula. The nmr of paederoside is also consistent with structure 1. The methyl resonance of paederoside (δ 2.35) would fit just as well for a S-methyl thiocarbonate as for a thioacetate[6]

As far as we know, paederoside is the first example of a naturally occurring S-methyl thiocarbonate. As we showed earlier[2], the unpleasant odor emitted by P. foetida is due to methyl mercaptan. It may be present as such in the plant, but more probably it is formed from the crushed plant through enzymic hydrolysis of paederoside.

References and notes

1. H. Inouye, S. Inouye, N. Shimokawa and M. Okiwaga, Chem. Pharm. Bull., 17, 1942 (1969)
2. Y. N. Shukla, H. A. Lloyd, J. F. Morton and G. J. Kapadia, Phytochemistry, 15, 1989 (1976)
3. T. W. Bentley, R. A. W. Johnstone and J. Grimshaw, J. Chem. Soc. (C), 2234 (1967)
4. W. H. McFadden, R. M. Seifert and J. Wasserman, Anal. Chem. 37, 560 (1965)
5. Paederoside (50 mg) was placed in a flask containing 6% $Ba(OH)_2$ (5 ml); after 18 hrs at room temperature, the flask was connected to a trap containing a 0.2% $Hg(CN)_2$ solution (10mg.). The reaction mixture was acidified with dilute H_2SO_4 and nitrogen was passed through it. The white precipitate (mp. 172° C.) which formed in the trap was identified as $(CH_3S)_2Hg$ (15mg., 69% yield) by comparison with an authentic sample (mp., mixed mp., ms.). This salt is stable and liberates CH_3SH upon addition of dilute acid. In contrast, the Hg salt of thioacetic acid darkens immediately in the air.
6. O-Benzyl-S-methyl thiocarbonate was prepared from benzyl chloroformate and methyl mercaptan. Mass spectrum: m/z (%), 182 M^+ (1.5), 138 (3), 91 (100), 77 (5), 75 (3), 65 (10), 51 (5). GC retention time on 6 ft. 3% OV 17 column, at 100°C. : 8 minutes (under the same conditions, retention times for benzyl alcohol, 0.7 min.; benzyl acetate, 1.4 min.; benzyl thioacetate, 4.3 min.). Nmr ($CDCl_3$), δ 2.35 (s. 3H), 5.26 (s. 2H), 7.36 (5H).
Benzyl thioacetate : nmr ($CDCl_3$). δ 2.34 (s. 3H), 4.12 (s. 2H), 7.28 (s. 5H).

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