Structure Revision of Four Acylyphloroglucinols Isolated from the Leaves of *Syzygium polyanthum*

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**Abstract**

The structures of four 1-acyl-2,3,5-trihydroxybenzene derivatives (1–4) that inhibit the enzyme protein tyrosine phosphatase 1B, previously reported from the leaves of *Syzygium polyanthum*, have been revised based upon reinterpretation of NMR spectroscopic data. The corrected structures are all 1-acylyphloroglucinol derivatives (5–8).

**Key words**  
*Syzygium polyanthum* · Myrtaceae · phloroglucinol · NMR chemical shift analysis

**Supporting information** available online at http://www.thieme-connect.de/products

The plant family Myrtaceae is a major source of phloroglucinol natural products with potent and varied biological activities [1]. *Syzygium* is a diverse genus within the family and contains over 1000 rainforest shrub and tree species that occur mainly in South East Asia and Australasia [2]. The importance of this genus is borne out by the many species that are used as foods, medicines, and timber, with for example, the spice trade from the 17th century being based upon the exploitation of spices such as cloves, the intensely aromatic flower buds of *Syzygium aromaticum* (L.) Merr. & L.M. Perry, harvested from plants growing on a select few islands of the Indonesian archipelago, to be sold in markets in Europe [3]. Surprisingly only a relatively few papers have been reported on the non-volatile chemicals present in *Syzygium* species but acylyphloroglucinol compounds predominate, with over 20 compounds from this class being reported [1,4–6]. It was therefore surprising when Saifudin et al. reported in 2012 that the leaves of *Syzygium polyanthum* (Wight) Walp. collected in Indonesia contain four compounds with an unusual 1-acyl-2,3,5-trihydroxy-4-methylphenyl substitution pattern [7]. Three of these compounds showed micromolar inhibition of the enzyme PTP1B that has been implicated with diabetes [7]. Further investigation of the literature revealed that another study on the same species, published at about the same time by Har et al., reported compounds containing a phloroglucinol moiety rather than a 2,3,5-trihydroxybenzene moiety.

Saifudin et al. rely exclusively on the presence of a key HMBC correlation between the aromatic proton, H-6 and the acyl carbonyl carbon, C-1′ to conclude that the aromatic proton, H-1 is ortho to the acyl side chain in the four compounds isolated [7]. Using this premise the rest of their proposed structures were constructed through the logical analysis of the remaining HMBC correlations. However, no correlations from H-3 or H-5 of an aromatic moiety to the benzylic carbonyl carbon attached at C-1 have been reported for acylyphloroglucinols [8]. These correlations tend to be much weaker than the typical aromatic ortho correlations and so correlation intensity can be a useful tool to assign longer range couplings. The 2,4,6-trihydroxy substitution pattern of acylyphloroglucinols results in the aromatic carbons present in these molecules having very characteristic carbon chemical shifts, with three downfield oxygenated carbons resonating at ~160–165 ppm and three upfield aromatic carbons, each ortho to two oxygenated carbons, resonating at ~95–110 ppm [8]. In comparison the oxygenated aromatic carbons in 1,2-dihydroxyphenyl compounds typically resonate between 145–150 ppm, while protonated aromatic carbons which are ortho to only one oxygenated carbon resonate between ~110–117 ppm and quaternary aromatic carbons ortho to only one oxygenated carbon resonate between 115–120 ppm [9]. Therefore the 13C NMR data for the 2,3,5 trioxygenated phenyl structures proposed by Saifudin et al. should have two of the oxygenated aromatic carbons resonating between ~145–150 and the third between ~160–165, the protonated and one of the quaternary aromatic carbons resonating between ~110–120 ppm and the remaining aromatic carbon resonating at approximately 100 ppm. However, in all four compounds three downfield aromatic carbons were observed between δC 160.3 and 165.4 and three upfield aromatic...
carbons were observed between δC 90.9 and 105.6. This provided conclusive evidence to assign phloroglucinol structures (5–8) to the four compounds. HMBC correlations corroborated these revised structure assignments. In compound 5 for example, key HMBC correlations were observed between 3-CH3 and C-2, C-3, and C-4 and between H-5 and C-1, C-3, and C-4 however no correlation was reportedly observed to C-6 from H-5. This is unsurprising for a phloroglucinol structure since this correlation would be for a 1JCH coupling which can be quite small, but it is highly irregular in the 2,3,5-trihydroxyphenyl structure since this correlation would be between H-6 and C-2, a 3JCH coupling, which are usually between 8–10 Hz in aromatic systems [9]. Comparison of the published 13C NMR data reported for carbons associated with the 3-methyl-1-acylphloroglucinol moiety in three related compounds were in close agreement to those observed in 5–8 (see Table 3 S, Supporting Information). The corrected NMR data for compounds 5–8 are presented in Tables 1 S and 2 S in the Supporting Information.

The structures of compounds 5–8 have not been reported previously in the literature, however the methyl ester of 5, anthuminate has been reported as a constituent from the leaves of Syzygium polyanthum by Har et al. [5]. The 13C NMR data reported for anthuminate was also in close agreement with that obtained for 5. The aromatic oxygenation and methylation pattern present in the amended structures for the S. polyanthum derivatives 5–8 are typical for plants from the Myrtaceae as this family is a major source of phloroglucinol derivatives [1]. The corrected structures therefore provide useful evidence that can be used for chemotaxonomic purposes. This paper highlights a salient point, that relying solely on potentially ambiguous 2D correlations to assign compound structures without due regard for chemical shift considerations can lead to erroneous conclusions.

Supporting information
Corrected NMR assignments in two tables (Table 1 S and 2 S) and 13C NMR data for related 3-methyl-acetylphloroglucinols (Table 3 S) are available as Supporting Information.

Conflict of Interest
The author declares no conflict of interest.

References
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