Novel Diarylheptanoids from the Seeds of *Alpinia blepharocalyx:* Revised Structure of Calyxin A

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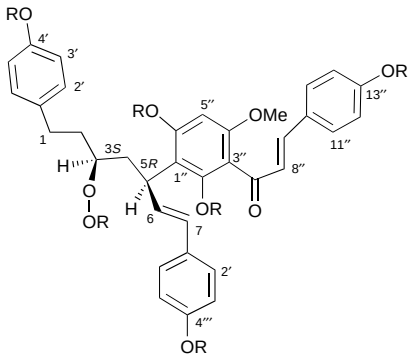
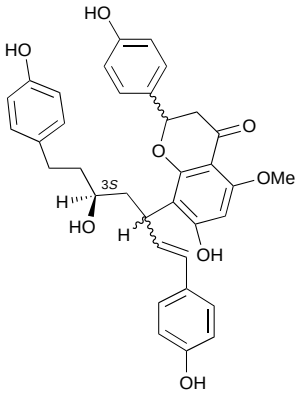
Calyxins A (**1**), E (**2**) and F (**3**), 6-hydroxycalyxin F (**4**), Calyxin G and epicalyxin G (**5** and **6**), novel diarylheptanoids having a chalcone or a flavanone moiety, were isolated from *Alpinia blepharocalyx* K. Schum. and their structures, including the corrected one of calyxin A (**1**), were elucidated by spectroscopic methods.

As part of our continuing studies on the chemistry of traditional Chinese medicine, we have examined the constituents of *Alpinia blepharocalyx* K. Schum. (Zingiberaceae). The ethanolic extract obtained from the seeds of *A. blepharocalyx* showed significant hepatoprotective activity against CCl_4-induced hepatotoxicity in rats and, therefore, it was further partitioned with hexane and diethyl ether to give hexane- and ether-soluble fractions. The ether-soluble and residual frac-



1 R = H
1a R = Ac



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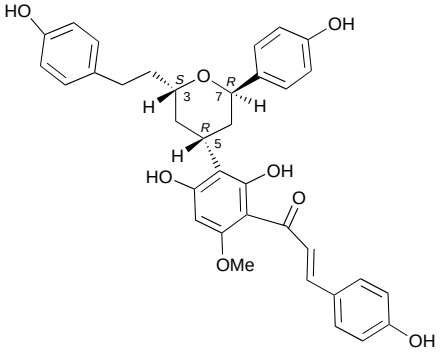

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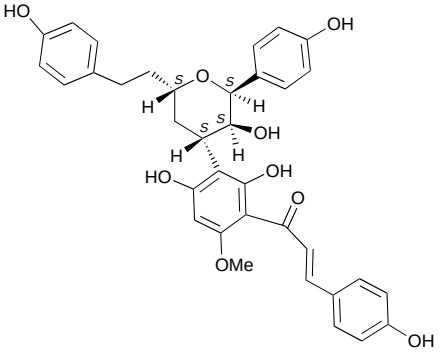

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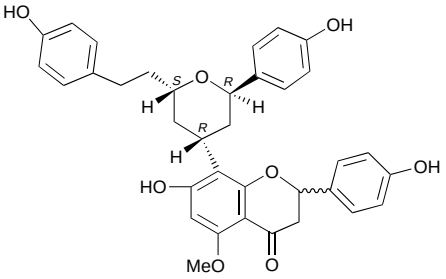

5 and **6**

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tions exhibited a more significant hepatoprotective effect than others in the same experimental liver injury model.

After repeated chromatography with silica gel and Sephadex LH-20, the ether-soluble fraction yielded a series of new diarylheptanoids having the novel feature of a diarylheptanoid part bearing a chalcone or flavanone moiety. In a previous paper,[3] we reported the isolation and structure determination of six novel diarylheptanoids named calyxin B, epicalyxin B, calyxin C, epicalyxin C, calyxin D and epicalyxin D from the seeds of *A. blepharocalyx.* Herein we report the isolation and structure determination of six additional novel diarylheptanoids, calyxins A (**1**), E (**2**) and F (**3**) and 6-hydroxycalyxin F (**4**) along with a mixture of calyxin G and epicalyxin G (**5** and **6**). Their structures have been elucidated by spectroscopic methods and the structure of calyxin A (**1**) has been corrected, as it was reported erroneously in a preliminary communication.[4]

Calyxin A (**1**) was obtained as an optically active, light yellow amorphous solid. The formula $C_{35}H_{34}O_9$, determined by high-resolution FAB–MS, and the COSY and HMQC experiments indicated **1** to be a diarylheptanoid bearing a chalcone moiety. The long-range correlations observed in the HMBC spectrum of **1** provided evidence for the attachment of the chalcone moiety to the diarylheptanoid part at the C-5 position. In our preliminary communication,[4] the location of the chalcone moiety in **1** was erroneously assigned at C-7.

The ^{13}C NMR spectral analysis of **1**, together with the inference provided by chemical reaction of an ethanolic KI solution with **1**, indicated the presence of one hydroperoxy and five hydroxy groups.[5] The absolute stereochemistry at C-3 and C-5 within **1** was determined to be *S* and *R* respectively, based on the NMR studies of the α-methoxy-α-trifluoromethylphenylacetyl (MTPA) ester of hexamethyldeoxycalyxin A.

Calyxins E (**2**) and F (**3**) had the molecular formula $C_{35}H_{34}O_8$. The ^1H and ^{13}C NMR data of both the compounds were similar to those of **1**, but **2** differed from it by having a flavanone moiety, instead of a chalcone, while **3** differed in terms of the diarylheptanoid structure. A tetrahydropyran ring like that of (−)-centrolobine[7] was found in the diarylheptanoid part of **3**. The absolute stereochemistry at C-3 of both the compounds was assumed to be *S* in view of the biogenesis. The relative stereochemistry of the protons at the three chiral centres (C-3, C-5 and C-7) within **3** was deduced to be axial on the basis of their coupling constants and an NOE experiment and the conformation of the tetrahydropyran ring was determined to be a boat-form. The absolute configuration of **3** at other chiral centres is 5*R*,7*R*, on the assumption that **3** has the same absolute configuration at C-3 (*i.e.*, *S*) as that of calyxin A (**1**).

Compound **4** appeared to be 6-hydroxycalyxin F from its spectral data. Calyxin G (**5**) and epicalyxin G (**6**) were obtained as an epimeric mixture and their NMR data indicated the presence of the same diarylheptanoid moiety as **3** and the same flavanone moiety as **2**.

Techniques used: Polarimetry, UV, IR, NMR, MS

References: 8

Tables: 2 (^1H- and ^{13}C-NMR data for **1–6**)

Scheme: 1

Figures: 3

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