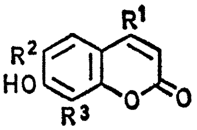
Synthesis of Some Dimethylpyrano- and 3-Methylbut-2-enyl-4-phenyl- and -4-n-propyl-coumarins

By D. E. GAMES* and N. J. HASKINS
(*Department of Chemistry, University College, P.O. Box* 78, *Cardiff* CF1 1XL)

Summary A number of dimethylbenzodipyranones and 3-methylbut-2-enyl-4-n-propyl-5,7-dihydroxycoumarins, including mammeigin and mammea's B/AA and B/AB have been synthesised, showing that MAB5 and MAB6 are mixtures, the structure of ponnalide requires revision, and that a number of these compounds are present in the seed extract of *Mammea americana* L.

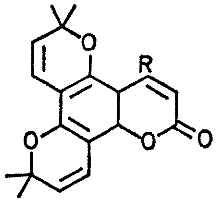
THE synthesis of a number of dimethylchromenylated naturally occurring compounds using 3-hydroxy-1,1-dimethoxy-3-methylbutane (I) has been reported by Crombie *et al.*[1] and the reaction has recently been extended to allow the introduction of two 2,2-dimethylpyran groups.[2] A number of 4-phenyl and 4-alkyl coumarins which occur in the Guttiferae family have this ring system,[3,4,6–8] and we have found that use of this reagent provides an efficient route to these compounds, enabling a number of these compounds to be detected in natural extracts, and indicating that the structure of ponnalide[4] requires revision. We have also found that reaction of 2-methylbut-3-en-2-ol and boron trifluoride etherate[9] with 4-n-propyl-5,7-dihydroxycoumarin results in the introduction of one or more 3-methylbut-2-enyl groups into the coumarin nucleus. This method has been used to synthesise the mammeas B/AA (IIa) and B/AB (IIb), coumarins isolated from *Mammea americana* L.[10] and *Mammea africana* G. Don.[8]



	R¹	R²	R³		R¹	R²	R³
(IIa)	$\mathrm{Pr^n}$	B	A	(IVc)	$\mathrm{Pr^n}$	D	H
(IIb)	$\mathrm{Pr^n}$	C	A	(IVd)	$\mathrm{Pr^n}$	E	H
(IIIa)	$\mathrm{Pr^n}$	H	C	(IVe)	$\mathrm{Pr^n}$	A	H
(IIIb)	$\mathrm{Pr^n}$	H	B	(Va)	Ph	H	C
(IIIc)	$\mathrm{Pr^n}$	H	A	(Vb)	Ph	H	B
(IVa)	$\mathrm{Pr^n}$	C	H	(VIa)	Ph	C	H
(IVb)	$\mathrm{Pr^n}$	B	H	(VIb)	Ph	B	H

Heating of 5,7-dihydroxy-4-phenylcoumarin with (I) in pyridine gave, after chromatography, the crystalline benzotripyranone (VIIa) (m.p. 177·5—178·5°) and the chromens (VIIIa) (11%) (m.p. 225·5—227°) and (XIa) (8%) (m.p. 260—263°). Orientation of (VIIIa) and (XIa) was supported by the shifts observed for 3- and 4-H of the chromen in the n.m.r. spectrum of the acetates of (VIIIa) and (XIa), which agreed with the observations of Merlini and his co-workers.[5] A similar reaction with 5,7-dihydroxy-4-n-propylcoumarin gave the benzotripyranone (VIIb) and the chromens (VIIIb) and (XIb). Structure (XIa) has been assigned to ponnalide which was isolated from *Calophyllum inophyllum*.[4] Our data for (XIa) and its acetate are not in agreement with that reported for ponnalide.†

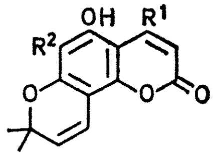
Condensation of the acetal (I) with the acyl coumarins (IIIa,b), (IVa—d), (Va,b), and (VIa,b)[6] gave the pyranocoumarins (XIIa,b) (IXa—d), (XIIIa,b), and (Xa,b) in yields varying from 30 to 80%. The coumarin (Xb) (m.p. 150—151°) was identical with mammeigin[6,7] isolated from *Mammea americana* L. and comparisons with a sample of MAB5 and a synthetic sample of MAB6, coumarins recently isolated from *Mammea africana* G. Don,[8] showed them to be mixtures consisting of (Xa) (m.p. 89·5—92°) and (Xb) for MAB5, and (IXa) (m.p. 97—98·5°) and (IXb) (m.p. 90·5—91·5°) for MAB6. The 2-methylbutyryl isomer was the major component in each case.

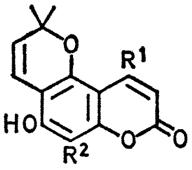


(VIIa) R = Ph, (b) R = $\mathrm{Pr^n}$

A re-examination of the seed extracts of *Mammea americana* L., using m.s., t.l.c., and n.m.r. has resulted in the identification of (Xa), (IXa), and (IXb) in these extracts together with a number of as yet unidentified homologous acylated 4-phenyl- and 4-alkyl-2,2-dimethylpyranocoumarins.

Treatment of 4-n-propyl-5,7-dihydroxycoumarin with an excess of 2-methylbut-3-en-2-ol and boron trifluoride etherate in dioxan solution at room temperature for 24 h, followed by work-up under non-acidic conditions, and chromatography, gave the coumarins (IIIc) (m.p. 180—182°)





	R¹	R²		R¹	R²
(VIIIa)	Ph	H	(XIa)	Ph	H
(VIIIb)	$\mathrm{Pr^n}$	H	(XIb)	$\mathrm{Pr^n}$	H
(IXa)	$\mathrm{Pr^n}$	C	(XIIa)	$\mathrm{Pr^n}$	C
(IXb)	$\mathrm{Pr^n}$	B	(XIIb)	$\mathrm{Pr^n}$	B
(IXc)	$\mathrm{Pr^n}$	D	(XIIIa)	Ph	C
(IXd)	$\mathrm{Pr^n}$	E	(XIIIb)	Ph	B
(Xa)	Ph	C			
(Xb)	Ph	B			

A = $\mathrm{Me_2C{:}CH{\cdot}CH_2}$, B = $\mathrm{Me_2CH{\cdot}CH_2{\cdot}CO}$, C = $\mathrm{MeCH_2{\cdot}CH(Me){\cdot}CO}$, D = $\mathrm{MeCH_2{\cdot}CH_2{\cdot}CO}$, E = $\mathrm{Me_2CH{\cdot}CO}$.

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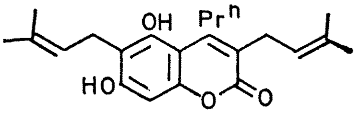
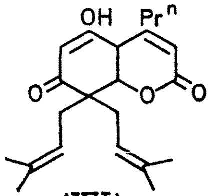
† Professor Seshadri has informed us that he has come to a similar conclusion and the structure of ponnalide is being revised.

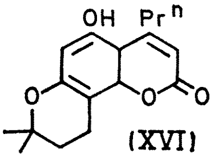
(3%) (IVe) (m.p. 166—168°) (9%) (XIV) (m.p. 131—133°) (0·3%) and the α-pyrone (XV) (m.p. 192°) (1%). The orientation of (IIIc), (IVe) and (XIV) are assigned on the basis of the Gibbs reaction and the conversion of (IIIc) and (IVe) into known 3,3-dimethylchromans.[11] With concentrated hydrochloric acid, the pyrone (XV) gave the expected 3,3-dimethylchroman (XVI)[12] and the spectral data obtained for (XV) was consistent with that reported for structurally similar compounds.[13]



(XIV)



(XV)



(XVI)

Reaction of the acyl coumarins (IVb) and (IVa)[6] with 2-methylbut-3-en-2-ol under similar conditions gave mammea B/AA (IIa) (m.p. 122·5—123°) (2%) and mammea B/AB (IIIb) (m.p. 118—120°) (2%) which were identical with the natural materials.[8,10]‡

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‡ Seshadri has recently reported[14] the synthesis of the 4-phenylcoumarin mammeisin by a similar method.

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