Efficient syntheses of 6-prenylcoumarins and linear pyranocoumarins: Total synthesis of suberosin, toddaculin, *O*-methylapigravin (*O*-methylbrosiperin), *O*-methylbalsamiferone, dihydroxanthyletin, xanthyletin and luvangetin

Raghao S. Mali,* Priya P. Joshi, Paramjeet Kaur Sandhu and Anita Manekar-Tilve

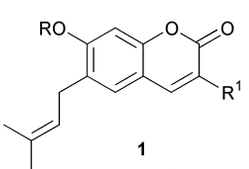
Garware Research Center, Department of Chemistry, University of Pune, Pune-411 007, India. E-mail: rsmali@chem.unipune.ernet.in; Fax: + (91) 020-5691728, 5693899

Received (in Cambridge, UK) 22nd October 2001, Accepted 3rd December 2001
First published as an Advance Article on the web 16th January 2002

Synthesis of naturally occurring 6-prenylcoumarins (**1a**, **2c** and **3a**) and their derivatives **1c**, **1d**, **1e**, **2d** and **3b–d** starting from 2-prenyloxybenzaldehydes (**8**, **12** and **14**) using tandem Claisen rearrangement and Wittig reaction is described. The coumarins **1a**, **1e** and **2c** are converted to dihydropyranocoumarins (**5a–e**). The conversion of dihydroxanthyletin **5a** and dihydroluvangetin **5d** to the naturally occurring linear pyranocoumarins xanthyletin **6a** and luvangetin **6b** is also described.

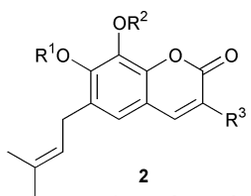
Introduction

Coumarins constitute an important class of naturally occurring[1] oxygen-ring compounds. The interest in these compounds has been mainly because of the wide range of activity exhibited[1] by them. Every year a large number of coumarins, having varied substitution patterns, are isolated from Nature. Several 6-prenylcoumarins such as suberosin **1a**, balsamiferone **1b**, brosiperin **2a**, apigravin **2b** and toddaculin **3a** have been isolated[1] from natural sources. 6-Prenylcoumarins have been used as intermediates for the synthesis of biologically active compounds, such as 6-substituted coumarins and linear furocoumarins.[1–3]



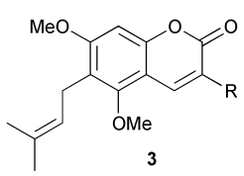
1

	R	R^1
a	Me	H
b	H	$CH_2CH=CMe_2$
c	Me	$CH_2CH=CMe_2$
d	Me	$CH_2CH=CH_2$
e	Me	Me



2

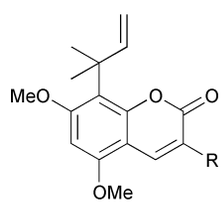
	R^1	R^2	R^3
a	Me	H	H
b	H	Me	H
c	Me	Me	H
d	Me	Me	Me



3

	R
a	H
b	Me
c	$CH_2CH=CH_2$
d	CH_2Ph

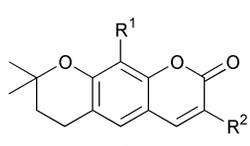
Pyranocoumarins like dihydroxanthyletin **5a**, xanthyletin **6a**, luvangetin **6b** and donatin **6c** are naturally occurring[1,4] and possess biological activities. Thus, dihydroxanthyletin **5a** isolated[5] from the whole plant of *Cassia pumila* is known for its



4

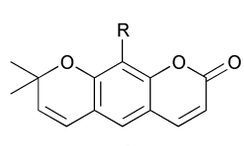
	R
a	H
b	Me
c	$CH_2CH=CH_2$
d	CH_2Ph

purgative properties.[5] Xanthyletin **6a** shows antifungal,[6] insecticidal[7] and antifeedant[8] activities. Recently it has been shown to possess anticancer[9] and anti-HIV[10] activities. Luvangetin **6b** exhibits impressive biological properties like antifeedant,[7] antiulcer,[11] antifungal[6] and antibacterial[12] activities. It is the major constituent of *Limonia acidissima*, which is also reported[13] to possess antiepileptic, purgative, and sudorific properties and is used to cure colic trouble and cardialgia.



5

	R^1	R^2
a	H	H
b	H	Me
c	OH	H
d	OMe	H
e	$OCH_2CH=CMe_2$	H



6

	R
a	H
b	OMe
c	$OCH_2CH=CMe_2$

In view of their natural occurrence and associated biological activities, various approaches have been developed for the synthesis of 6-allyl- and 6-prenylcoumarins and linear pyranocoumarins. The synthesis of 6-allyl- and 6-prenyl-7-alkoxy/hydroxycoumarins is difficult as compared with 8-allyl- and 8-prenyl-7-alkoxy/hydroxycoumarins. Claisen rearrangement

DOI: 10.1039/b109597h

of allyloxybenzene provides *o*-allylphenol; hence most of the reported methods utilize 7-allyloxycoumarins as starting materials to obtain allylcoumarins.[1] Since 7-allyloxycoumarins on Claisen rearrangement provide[1] exclusively 8-allylcoumarins, the C-8 position is blocked in order to obtain 6-allylcoumarins.[14,15] In an alternative approach,[16] 7-alkoxycoumarins have been first converted to methyl 2-allyloxy-4-alkoxycinnamates and then to 6-allylcoumarins such as suberosin **1a** and related compounds. The propynylic ether of umbeliferone has been used for the synthesis of demethylsuberosin,[17] which was subsequently converted to 3,6-diprenyl-7-hydroxycoumarin (balsamiferone) **1b**.[18] A route utilizing 3-prenyl-7-hydroxycoumarin has also been reported[19] for balsamiferone **1b**.

Literature methods[20–22] for toddaculin **3a** either involve multistep sequences and/or provide **3a** in very low yields. Most of these approaches,[21,22] utilize 5,7-dihydroxycoumarin as the starting material. As 7-(1,1-dimethylallyloxy)coumarin provides[21] 8-prenylcoumarin on Claisen rearrangement, 5-(1,1-dimethylallyloxy)-7-methoxycoumarin would be the proper starting material to obtain toddaculin **3a**. The major obstacle in this approach[21] was the selective allylation of the C-5 hydroxy group of 5,7-dihydroxycoumarin.

As indicated above, pyranocoumarins, apart from their occurrence in Nature, are reported to possess promising biological activities. In view of this, few approaches have been developed for the synthesis of linear pyranocoumarins, namely xanthyletin **6a** and luvangetin **6b**. The methods developed for **6a** involve condensation of umbeliferone (7-hydroxycoumarin) with 2-methylbut-3-yn-2-ol[23]/3-chloro-3-methylbut-l-yne[24] and provide xanthyletin **6a** in poor yield along with its angular isomer seselin. In order to avoid the formation of the angular pyranocoumarin (seselin), the C-8 position of umbeliferone is blocked by iodine.[25] The other method reported for **6a** utilizes 7-hydroxy-2,2-dimethyldihydropyran[26] or 6-formyl-7-hydroxy-2,2-dimethylpyran[27] as starting material. These compounds are then converted to xanthyletin **6a** using further reactions. Recently, Nicolaou *et al.*[28] have achieved the synthesis of xanthyletin **6a** from 2,4-dihydroxy-5-prenylbenzaldehyde using a selenium-based solid-phase reaction.

Luvangetin **6b** has been synthesized by propargylation of daphnetin[24b] or its monomethyl ether[29] followed by cyclization. The synthesis of donatin **6c** isolated[30] from the leaves of *Pilocarpus goudotianus*, has not been reported so far in the literature.

Results and discussion

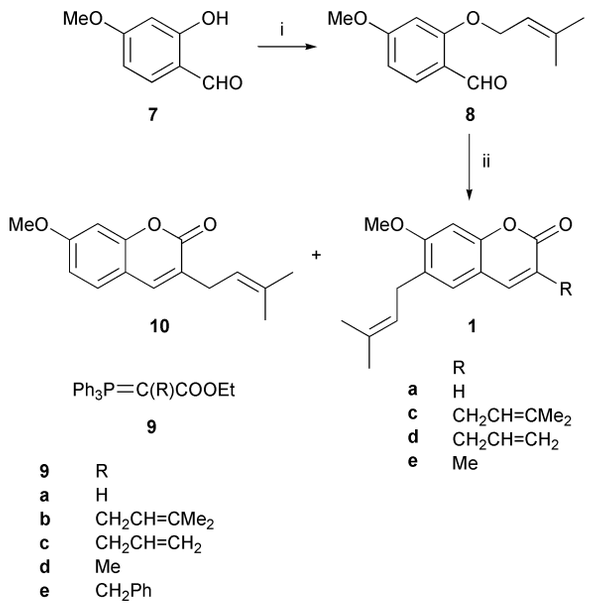
All the reported methods[16–18] for the synthesis of 6-prenyl- and 3,6-diprenylcoumarins makes use of preformed coumarins. The methods reported[23–29] for xanthyletin **6a** and luvangetin **6b** also make use of the naturally occurring coumarins or require a multi-step sequence of reactions.

Synthesis of 6-prenylcoumarins 1–3

We report[31] herein a novel and general route for naturally occurring 6-prenylcoumarins (**1a**, **2c** and **3a**) and their derivatives **1c**, **1d**, **1e**, **2d** and **3b–d** from 2-prenyloxybenzaldehydes (**8**, **12** and **14**).

2-Prenyloxybenzaldehydes **8**, **12** and **14** were prepared by prenylation of the corresponding 2-hydroxybenzaldehydes using prenyl bromide. Thus, 2-hydroxy-4-methoxybenzaldehyde **7** on reaction with prenyl bromide in the presence of K_2CO_3 in refluxing acetone provided 2-prenyloxy-4-methoxybenzaldehyde **8** in 75% yield. On similar reaction, 2-hydroxy-3,4-dimethoxybenzaldehye **11** and 2-hydroxy-4,6-dimethoxybenzaldehyde **13** provided 2-prenyloxy-3,4-dimethoxybenzaldehyde **12** and 2-prenyloxy-4,6-dimethoxybenzaldehyde **14** in 70 and 71% yield, respectively. Alternatively, these 2-prenyloxybenzaldehydes **8**, **12** and **14** were prepared in better yields by carrying out the reaction in *N,N*-dimethylformamide (DMF) solution at room temperature.

2-Prenyloxy-4-methoxybenzaldehyde **8** on reaction with the phosphorane **9a** in *N,N*-dimethylaniline at 200 °C for 6 h, under N_2 atmosphere, gave suberosin **1a**, mp 87 °C (lit.,[32] 87–88 °C) in 47% yield (Scheme 1). In this reaction along with suberosin **1a**,

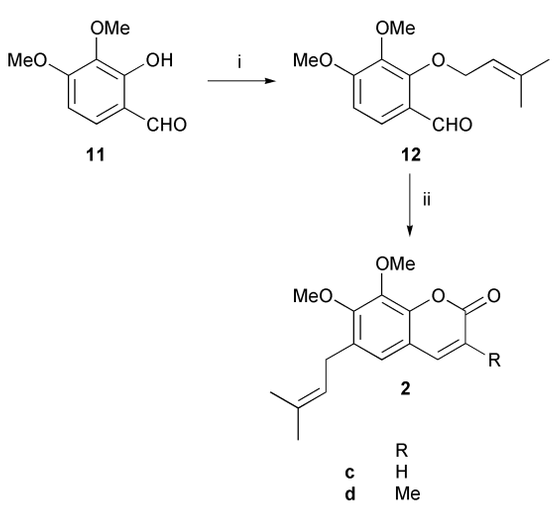


Scheme 1 *Reagents and conditions*: (i) Prenyl bromide, K_2CO_3, acetone, reflux; (ii) $Ph_3P{=}C(R)COOEt$ **9**, $PhNMe_2$, N_2, reflux.

a minor amount (7%) of 3-prenyl-7-methoxycoumarin **10**, mp 90–92 °C (lit.,[33] 91–92 °C) was obtained.

The aldehyde **8**, on similar reaction with phosphoranes **9b–d**, gave *O*-methylbalsamiferone **1c** and 6-prenyl-3-substituted coumarins **1d** and **1e** in 48–67% yield.

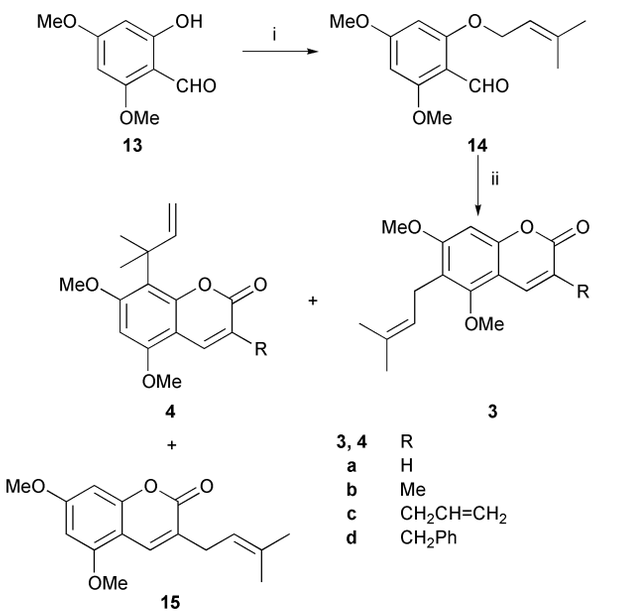
When the aldehyde **12** was treated with phosphoranes **9a** and **9d**, *O*-methylapigravin (*O*-methylbrosiperin) **2c** and its methyl derivative **2d** were obtained in 55 and 58% yield, respectively (Scheme 2).



Scheme 2 *Reagents and conditions*: (i) Prenyl bromide, K_2CO_3, acetone, reflux; (ii) $Ph_3P{=}C(R)COOEt$ **9**, $PhNMe_2$, N_2, reflux.

For the synthesis of toddaculin **3a** and its derivatives the 2-prenyloxy-4,6-dimethoxybenzaldehye **14** was treated with various phosphoranes. Reaction of **14** with the phosphorane **9a** in refluxing *N,N*-diethylaniline for 8 h provided toddaculin **3a**, mp 93 °C (lit.,[21] 93–94 °C) and pinnarin **4a**, mp 165 °C (lit.,[34] 166–167 °C) in 50 and 14% yield along with 3-prenyl-5,7-dimethoxycoumarin **15**, mp 108–110 °C (lit.,[33] 110–111 °C)

which is obtained in 7% yield. The aldehyde **14** when refluxed with phosphoranes **9d**, **9c** and **9e** provided toddaculin derivatives **3b–d** and pinnarin derivatives **4b–d** (Scheme 3).

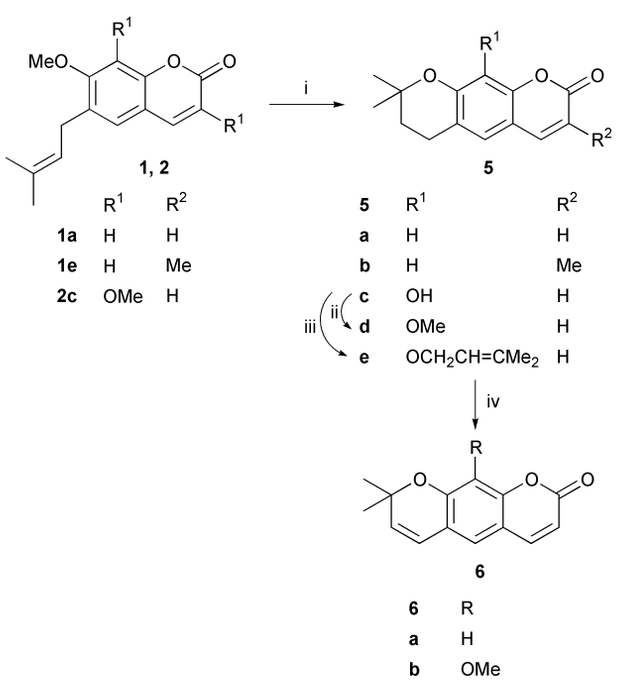


Scheme 3 *Reagents and conditions*: (i) Prenyl bromide, K_2CO_3, acetone, reflux; (ii) $Ph_3P{=}C(R)COOEt$ **9**, $PhNEt_2$, N_2, reflux.

In this approach, during the conversion of 2-prenyloxybenzaldehydes **8**, **12** and **14** into 6-prenylcoumarins **1**, **2** and **3**, Wittig reaction, isomerization of the double bond, cyclization, and Claisen rearrangement followed by Cope rearrangement occurred in one pot.

Synthesis of linear pyranocoumarins 5, 6

As discussed above, most of the methods reported[23–29] for the synthesis of linear pyranocoumarins make use of naturally occurring coumarins or require a multistep sequence of reactions. Once sizeable amounts of 6-prenylcoumarins **1**–**3** were in hand it was planned to use them for the synthesis of linear pyranocoumarins **5** and **6** (Scheme 4).



Scheme 4 *Reagents and conditions*: (i) Pyridine hydrochloride, N_2, heat; (ii) MeI, K_2CO_3, DMF, room temperature; (iii) prenyl bromide, K_2CO_3, DMF, room temperature; (iv) NBS, AIBN, benzene, K_2CO_3, N_2, reflux.

The 6-prenylcoumarin suberosin (**1a**), on heating with pyridine hydrochloride under inert atmosphere, provided dihydroxanthyletin **5a**, mp 120–122 °C (lit.,[35] 124–125 °C) in 48% yield. The 6-prenylcoumarins **1e** and **2c** on similar reaction with pyridine hydrochloride gave the dihydropyranocoumarins **5b** and **5c** in 79 and 78% yield, respectively. Dihydrodemethylluvangetin **5c**, on methylation using MeI in DMF in the presence of K_2CO_3, provided dihydroluvangetin **5d**, mp 129–131 °C (lit.,[36] 131 °C) in 86% yield. The coumarin **5c**, on prenylation using prenyl bromide in DMF in the presence of K_2CO_3, yielded dihydrodonatin **5e**, mp 65–67 °C, in 74% yield.

Dihydroxanthyletin **5a** and dihydroluvangetin **5d** on bromination followed by dehydrobromination using *N*-bromosuccinimide (NBS) in refluxing benzene containing K_2CO_3 and azoisobutyronitrile (AIBN) provided the pyranocoumarins xanthyletin **6a** and luvangetin **6b**, in 61 and 65% yield, respectively. The attempted conversion of **5e** into donatin **6c** using similar procedure, however, gave a complex mixture.

Conclusions

The present approach developed for the syntheses of 6-prenyl- and 3,6-diprenylcoumarins (**1**, **2** and **3**) does not require preformed coumarins and demonstrates the synthetic utility of tandem Claisen rearrangement and Wittig reaction. The synthesis of linear pyranocoumarins is achieved from 6-prenylcoumarins. The IR and ^1H NMR spectral data of 6-prenylcoumarins (**1a**, **2c** and **3a**) and pyranocoumarins (**5a**, **6a** and **6b**) are identical with literature data reported for natural products.

Experimental

All mps are uncorrected. IR spectra were recorded on a Perkin–Elmer FT IR-1615 spectrometer. ^1H spectra were recorded on JEOL 90 MHz, Varian Mercury 300 MHz, and Bruker AMX (500 MHz) spectrophotometers with tetramethylsilane (Me_4Si) as an internal standard in $CDCl_3$ except for the case of **5c** which was recorded in $CDCl_3$ + DMSO-d_6. Chemical shifts are expressed in δ (ppm) downfield from Me_4Si and coupling constants are in Hertz. Analyses were obtained on a Hosli's rapid carbon–hydrogen analyzer. Light petroleum (herein referred to as pet. ether) was the fraction with distillation range 60–65 °C.

General procedure for the synthesis of 2-prenyloxybenzaldehydes 8, 12 and 14

Method A. An appropriate 2-hydroxybenzaldehyde (**7**, **11** or **13**), (5 mmol) was added to a solution of prenyl bromide (1.23 ml, 10.6 mmol) in dry acetone (30 ml) containing potassium carbonate (0.86 g, 6.2 mmol) and the mixture was refluxed for 6–13 h under nitrogen atmosphere. The reaction mixture was filtered and acetone from the filtrate was removed under reduced pressure to give an oily product. It was taken up in diethyl ether (2 × 25 ml) and washed successively with aq. sodium hydroxide and water before being dried over anhydrous sodium sulfate and concentrated to afford a residue, which on purification by chromatography over silica gel gave 2-prenyloxybenzaldehydes **8**, **12** or **14**.

Method B. Prenyl bromide (1.5 ml, 13.01 mmol) was added to a solution of appropriate 2-hydroxybenzaldehyde (**7**, **11** or **13**) (5 mmol) in dry DMF (20 ml) containing potassium carbonate (1.05 g, 7.57 mmol). The reaction mixture was stirred at room temperature for 8–12 h, poured over crushed ice, and extracted with diethyl ether (3 × 10 ml). The combined extract was washed several times with 2 M aq. sodium hydroxide and then with water. The organic layer was dried over anhydrous sodium sulfate and concentrated to afford the corresponding 2-prenyloxybenzaldehyde **8**, **12** or **14**.

2-Prenyloxy-4-methoxybenzaldehyde 8. The reaction mixture was refluxed for 6 h to give compound **8** in 75% yield (Method A) or stirred at room temperature for 10 h to provide compound **8** in 76% (Method B), mp 41–42 °C (from pet. ether) (lit.,[37] 41–42 °C); ν_{max}/cm^{-1} (Nujol) 1670; δ_H (90 MHz) 1.78 (3H, s, CH_3), 1.83 (3H, s, CH_3), 3.82 (3H, s, OCH_3), 4.55 (2H, d, *J* 6.5 Hz, OCH_2CH=), 5.3–5.58 (1H, m, OCH_2CH=), 6.3–6.6 (2H, m, C^3–H and C^5–H), 7.69 (1H, d, *J* 9 Hz, C^6–H), 10.1 (1H, s, CHO).

2-Prenyloxy-3,4-dimethoxybenzaldehyde 12. The reaction mixture was refluxed for 6 h to furnish compound **12** in 70% by using Method A or stirred at room temperature for 8 h to provide compound **12** in 87% yield (Method B), as a thick liquid; ν_{max}/cm^{-1} (neat) 1680; δ_H (90 MHz) 1.63 (3H, s, CH_3), 1.78 (3H, s, CH_3), 3.94 (3H, s, OCH_3), 4.00 (3H, s, OCH_3), 4.69 (2H, d, *J* 6 Hz, OCH_2CH=), 5.38–5.65 (1H, m, OCH_2CH=), 6.75 (1H, d, *J* 9 Hz, C^5–H), 7.6 (1H, d, *J* 9 Hz, C^6–H), 10.2 (1H, s, CHO).

2-Prenyloxy-4,6-dimethoxybenzaldehyde 14. The reaction mixture was refluxed for 13 h to provide compound **14** in 71% yield by Method A or stirred at room temperature for 12 h to obtain compound **14** in 90% yield by Method B, mp 60 °C (from pet. ether–dichloromethane); ν_{max}/cm^{-1} (Nujol) 1670; δ_H (90 MHz) 1.73 (3H, s, CH_3), 1.79 (3H, s, CH_3), 3.89 (6H, s, 2 × OCH_3), 4.56 (2H, d, *J* 6.3 Hz, OCH_2CH=), 5.48 (1H, br t, OCH_2CH=), 6.1 (2H, s, C^3–H and C^5–H), 10.43 (1H, s, CHO) (Found: C, 67.31; H, 7.17. $C_{14}H_{18}O_4$ requires C, 67.18; H, 7.25%).

General procedure for synthesis of 6-prenylcoumarins 1a, 1c–e, 2c, 2d and 3a–d and 8-isoprenylcoumarins 4a–d

A mixture of an appropriate 2-prenyloxybenzaldehyde (**8**, **12** or **14**, 1.5 mmol) and a phosphorane (**9a**, **9b**, **9c** or **9d**, 1.7 mmol) in either *N,N*-dimethylaniline or *N,N*-diethylaniline (25 ml) (see captions to Schemes 1–3) was refluxed, under nitrogen atmosphere, for 4–12 h. Excess of aniline was removed under reduced pressure. The residue obtained was extracted with ethyl acetate (3 × 10 ml). The combined extract was washed successively with dil. HCl and water, dried over anhydrous Na_2SO_4, and evaporated. The residue obtained was chromatographed over silica gel, using pet. ether–ethyl acetate (98 : 2) as eluent, to provide 6-prenylcoumarins **1a**, **1c**–**e**, **2c**, **2d** or **3a**–**d** in initial fractions. In the reaction of 2-prenyloxy-4,6-dimethoxybenzaldehyde **14** with phosphoranes **9a**–**9d** the 8-isoprenylcoumarins **4a**–**d** were obtained in initial fractions and the 6-prenylcoumarins **3a**–**d** in the later fractions.

7-Methoxy-6-prenylcoumarin (suberosin) 1a and 7-methoxy-3-prenylcoumarin 10. A mixture of 2-prenyloxy-4-methoxybenzaldehyde **8** and the phosphorane **9a** in *N,N*-dimethylaniline was refluxed for 6 h. The residue obtained was chromatographed over silica gel, using pet. ether–ethyl acetate (97 : 3) as eluent. 7-Methoxy-3-prenylcoumarin **10** (7% yield) was obtained in initial fractions, mp 90–92 °C (from pet. ether–ethyl acetate) (lit.,[33] 91–92 °C); ν_{max}/cm^{-1} (Nujol) 1708; δ_H (90 MHz) 1.69 (3H, s, CH_3), 1.81 (3H, s, CH_3), 3.24 (2H, d, *J* 7 Hz, CH_2CH=), 3.89 (3H, s, OCH_3), 5.35 (1H, m, CH_2CH=), 6.81 (1H, s, C^8–H), 6.83 (1H, d, *J* 9.2 Hz, C^6–H), 7.34 (1H, d, *J* 9.2 Hz, C^5–H), 7.4 (1H, s, C^4–H).

Further elution with the same solvent furnished suberosin **1a** (47% yield), mp 87 °C (from pet. ether–methanol) (lit.,[32] 87–88 °C); ν_{max}/cm^{-1} (Nujol) 1725; δ_H (90 MHz) 1.71 (3H, s, CH_3), 1.78 (3H, s, CH_3), 3.29 (2H, d, *J* 6 Hz, CH_2CH=), 3.89 (3H, s, OCH_3), 5.13–5.40 (1H, m, CH_2CH=), 6.22 (1H, d, *J* 10 Hz, C^3–H), 6.76 (1H, s, C^8–H), 7.16 (1H, s, C^5–H), 7.60 (1H, d, *J* 10 Hz, C^4–H) (Found: C, 73.28; H, 6.68. Calc. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60%).

***O*-Methylbalsamiferone 1c.** A mixture of 2-prenyloxy-4-methoxybenzaldehyde **8** and the phosphorane **9b** in *N,N*-dimethylaniline was refluxed for 6 h to provide *O*-methylbalsamiferone **1c** as a thick liquid in 49% yield; ν_{max}/cm^{-1} (neat) 1720; δ_H (90 MHz) 1.63 (3H, s, CH_3), 1.72 (3H, s, CH_3), 3.23 (4H, t, *J* 6 Hz, 2 × CH_2CH=), 3.82 (3H, s, OCH_3), 5.12–5.43 (2H, m, 2 × CH_2CH=), 6.76 (1H, s, C^8–H), 7.12 (1H, s, C^5–H), 7.36 (1H, s, C^4–H) (Found: C, 76.77; H, 7.70. $C_{20}H_{24}O_3$ requires C, 76.89; H, 7.74%).

3-Allylsuberosin 1d. A mixture of the 2-prenyloxybenzaldehyde **8** and the phosphorane **9c** in *N,N*-dimethylaniline was refluxed for 3.5 h to give 3-allylsuberosin **1d** in 67% yield, mp 91–93 °C (from pet. ether–ethyl acetate); ν_{max}/cm^{-1} (Nujol) 1709; δ_H (90 MHz) 1.68 (3H, s, CH_3), 1.77 (3H, s, CH_3), 3.29 (4H, d, *J* 7.5 Hz, CH_2CH=CMe_2 and CH_2CH=CH_2), 3.85 (3H, s, OCH_3), 5.15 (3H, m, CH_2CH=CMe_2 and CH_2CH=CH_2), 5.9 (1H, m, CH_2CH=CH_2), 6.75 (1H, s, C^8–H), 7.14 (1H, s, C^5–H), 7.42 (1H, s, C^4–H) (Found: C, 75.90; H, 7.04. $C_{18}H_{20}O_3$ requires C, 76.03; H, 7.09%).

3-Methylsuberosin 1e. A mixture of 2-prenyloxy-4-methoxybenzaldehyde **8** and the phosphorane **9d** in *N,N*-dimethylaniline was refluxed for 6 h to furnish 3-methylsuberosin **1e** in 48% yield, mp 108–110 °C (from pet. ether–ethyl acetate); ν_{max}/cm^{-1} (Nujol) 1730; δ_H (90 MHz) 1.62 (3H, s, CH_3), 1.68 (3H, s, CH_3), 2.1 (3H, s, CH_3), 3.25 (2H, d, *J* 6 Hz, CH_2CH=), 3.82 (3H, s, OCH_3), 5.06–5.36 (1H, m, CH_2CH=), 6.7 (1H, s, C^8–H), 7.08 (1H, s, C^5–H), 7.4 (1H, s, C^4–H) (Found: C, 74.20; H, 6.98. $C_{16}H_{18}O_3$ requires C, 74.39; H, 7.02%).

***O*-Methylbrosiperin (*O*-methylapigravin) 2c.** A mixture of 2-prenyloxy-3,4-dimethoxybenzaldehyde **12** and the phosphorane **9a** in *N,N*-dimethylaniline was refluxed for 12 h to provide compound **2c** in 55% yield, mp 93 °C (from hexane) (lit.,[38] 93–95 °C); ν_{max}/cm^{-1} (Nujol) 1710; δ_H (90 MHz) 1.68 (6H, s, 2 × CH_3), 3.27 (2H, d, *J* 6 Hz, CH_2CH=), 3.92 (3H, s, OCH_3), 3.96 (3H, s, OCH_3), 5.08–5.33 (1H, m, CH_2CH=), 6.22 (1H, d, *J* 10 Hz, C^3–H), 6.93 (1H, s, C^5–H), 7.57 (1H, d, *J* 10 Hz, C^4–H) (Found: C, 70.41; H, 6.74. Calc. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61%).

3,*O*-Dimethylapigravin (3,*O*-dimethylbrosiperin) 2d. A mixture of the 2-prenyloxybenzaldehyde **12** and the phosphorane **9d** in *N,N*-dimethylaniline was refluxed for 6 h to give compound **2d** as a thick liquid in 58% yield; ν_{max}/cm^{-1} (neat) 1725; δ_H (90 MHz) 1.69 (6H, s, 2 × CH_3), 2.14 (3H, s, CH_3), 3.32 (2H, d, *J* 6 Hz, CH_2CH=), 3.94 (3H, s, OCH_3), 4.00 (3H, s, OCH_3), 5.1–5.36 (1H, m, CH_2CH=), 6.87 (1H, s, C^5–H), 7.4 (1H, s, C_4–H) (Found: C, 71.07; H, 7.17. $C_{17}H_{20}O_4$ requires C, 70.81; H, 6.99%).

Toddaculin 3a, pinnarin 4a and 5,7-dimethoxy-3-prenylcoumarin 15. A mixture of 2-prenyloxy-4,6-dimethoxybenzaldehyde **14** and the phosphorane **9a** in *N,N*-diethylaniline was refluxed for 8 h to provide 5,7-dimethoxy-3-prenylcoumarin **15** in initial fractions in 7% yield, mp 108–110 °C (from pet. ether–ethyl acetate) (lit.,[33] 110–111 °C); ν_{max}/cm^{-1} (Nujol) 1720; δ_H (90 MHz) 1.69 (3H, s, CH_3), 1.8 (3H, s, CH_3), 3.20 (2H, d, *J* 7.5 Hz, CH_2CH=), 3.84 (3H, s, OCH_3), 3.9 (3H, s, OCH_3), 5.28–5.36 (1H, m, CH_2CH=), 6.28 (1H, d, *J* 2.4 Hz, C^6–H), 6.41 (1H, d, *J* 2.4 Hz, C^8–H), 7.22 (1H, s, C^4–H).

Elution with same solvent then furnished the second compound, pinnarin **4a** in 14% yield, mp 165 °C (from pet. ether–dichloromethane) (lit.,[34] 166–167 °C); ν_{max}/cm^{-1} (Nujol) 1713; δ_H (90 MHz) 1.63 (6H, s, 2 × CH_3), 3.83 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.69–4.97 (2H, m, CMe_2CH=CH_2), 6.11 (1H, d, *J* 9.5 Hz, C^3–H), 6.22 (1H, dd, J = 10 and 17.5 Hz, CMe_2CH=CH_2), 6.31 (1H, s, C^6–H), 7.97 (1H, d, *J* 9.5 Hz,

C^4–H) (Found: C, 69.88; H, 6.76. Calc. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61%).

Further elution with the same solvent yielded toddaculin **3a** in 50% yield, mp 93 °C (from pet. ether–dichloromethane) (lit.,[21] 93–94 °C); ν_{max}/cm^{-1} (Nujol) 1720; δ_H (90 MHz) 1.66 (3H, s, CH_3), 1.77 (3H, s, CH_3), 3.33 (2H, d, *J* 6.3 Hz, C*H*$_2$CH=), 3.8 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 5.14 (1H, m, CH_2C*H*=), 6.22 (1H, d, *J* 9.5 Hz, C^3–H), 6.61 (1H, s, C^8–H), 7.83 (1H, d, *J* 9.5 Hz, C^4–H) (Found: C, 70.30; H, 6.71. Calc. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61%).

3-Methyltoddaculin 3b and 3-methylpinnarin 4b. A mixture of the 2-prenyloxybenzaldehyde **14** and the phosphorane **9d** in *N,N*-diethylaniline was refluxed for 10 h to provide 3-methylpinnarin **4b** in 26% yield in initial fractions, mp 195 °C (from pet. ether–dichloromethane); ν_{max}/cm^{-1} (Nujol) 1705; δ_H (90 MHz) 1.64 (6H, s, 2 × CH_3), 2.14 (3H, br s, CH_3), 3.83 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.72–5.0 (2H, m, CMe_2CH=C*H*$_2$), 6.27 (1H, dd, *J* 10 and 17.5 Hz, CMe_2C*H*=CH_2), 6.33 (1H, s, C^6–H), 7.8 (1H, br s, C^4–H) (Found: C, 71.01; H, 6.95. $C_{17}H_{20}O_4$ requires C, 70.81; H, 6.99%).

Further elution with the same solvent furnished 3-methyltoddaculin **3b** in 45% yield, mp 81 °C (from pet. ether–dichloromethane); ν_{max}/cm^{-1} (Nujol) 1720; δ_H (90 MHz) 1.66 (3H, s, CH_3), 1.77 (3H, s, CH_3), 2.17 (3H, s, CH_3), 3.36 (2H, d, *J* 6.25 Hz, C*H*$_2$CH=), 3.8 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 5.14 (1H, m, CH_2C*H*=), 6.61 (1H, s, C^8–H), 7.66 (1H, br s, C^4–H) (Found: C, 70.65; H, 6.84. $C_{17}H_{20}O_4$ requires C, 70.81; H, 6.99%).

3-Allyltoddaculin 3c and 3-allylpinnarin 4c. A mixture of 2-prenyloxy-4,6-dimethoxybenzaldehyde **14** and the phosphorane **9c** in *N,N*-diethylaniline was refluxed for 10 h to give 3-allylpinnarin **4c** in 20% yield in initial fractions, mp 110 °C (from pet. ether–dichloromethane); ν_{max}/cm^{-1} (Nujol) 1700; δ_H (90 MHz) 1.6 (6H, s, 2 × CH_3), 3.24 (2H, d, *J* 6.25 Hz, C*H*$_2$CH=CH_2), 3.79 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 4.7–4.98 (2H, m, CH_2CH=C*H*$_2$), 5.03–5.3 (2H, m, CMe_2CH=C*H*$_2$), 5.73–6.47 (2H, m, CMe_2C*H*=CH_2 and CH_2C*H*=CH_2), 6.3 (1H, s, C^6-*H*), 7.75 (1H, s, C^4–H) (Found: C, 72.57; H, 6.78. $C_{19}H_{22}O_4$ requires C, 72.59; H, 7.05%).

Further elution with the same solvent provided 3-allyltoddaculin **3c** in 40% yield, mp 65 °C (from pet. ether–dichloromethane); ν_{max}/cm^{-1} (Nujol) 1720; δ_H (90 MHz) 1.66 (3H, s, CH_3), 1.74 (3H, s, CH_3), 3.09–3.5 (4H, m, C*H*$_2$CH=CMe_2 and C*H*$_2$CH=CH_2), 3.79 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 4.95–5.39 (3H, m, CH=C*H*$_2$ and CH_2C*H*=CMe_2), 5.64–6.28 (1H, m, CH_2C*H*=CH_2), 6.61 (1H, s, C^8-*H*), 7.64 (1H, s, C^4–H) (Found: C, 72.84; H, 7.23. $C_{19}H_{22}O_4$ requires C, 72.59; H, 7.05%).

3-Benzyltoddaculin 3d and 3-benzylpinnarin 4d. A mixture of the 2-prenyloxybenzaldehyde **14** and the phosphorane **9e** in *N,N*-diethylaniline was refluxed for 14 h to give 3-benzylpinnarin **4d** in initial fractions in 17% yield, mp 95 °C (from pet. ether–dichloromethane) ν_{max}/cm^{-1} (Nujol) 1705; δ_H (90 MHz) 1.6 (6H, s, 2 × CH_3), 3.79 (3H, s, OCH_3), 3.85 (5H, s, OCH_3 and C*H*$_2$Ph), 4.67–5.0 (2H, m, CMe_2CH=C*H*$_2$), 6.22 (1H, dd, *J* 10 and 17.5 Hz, CMe_2C*H*=CH_2), 6.28 (1H, s, C^6–H), 7.28 (5H, br s, Ph), 7.66 (1H, s, C^4–H) (Found: C, 75.96; H, 6.46. $C_{23}H_{24}O_4$ requires C, 75.80; H, 6.64%).

Further elution with the same solvent afforded 3-benzyltoddaculin **3d** in 45% yield, mp 92 °C (from pet. ether–dichloromethane); ν_{max}/cm^{-1} (Nujol) 1705; δ_H (90 MHz) 1.65 (3H, s CH_3), 1.76 (3H, s, CH_3), 3.3 (2H, d, *J* 6.25 Hz, C*H*$_2$CH=), 3.68 (2H, s, C*H*$_2$Ph), 3.85 (6H, s, 2 × OCH_3), 5.08 (1H, m, CH_2C*H*=), 6.56 (1H, s, C^8–H), 7.25 (5H, br s, Ph), 7.44 (1H, s, C^4–H) (Found: C, 75.92; H, 6.48. $C_{23}H_{24}O_4$ requires C, 75.80; H, 6.64%).

General procedure for conversion of 6-prenylcoumarins 1a, 1e and 2c to dihydropyranocoumarins 5a–c

A mixture of a 6-prenylcoumarin (**1a**, **1e** or **2c**, 0.1 mmol) and pyridine hydrochloride (1 mmol) was heated at 190–200 °C under nitrogen atmosphere for 2.5–5 h (monitored by TLC). The reaction mixture was cooled to room temperature, poured over crushed ice, and made acidic with dil. hydrochloric acid before being extracted with ethyl acetate (3 × 5 ml). The combined extract was dried over anhydrous sodium sulfate and concentrated under reduced pressure to provide a residue, purification of which by column chromatography over silica gel, using pet. ether–ethyl acetate (96 : 4) as eluent, gave the corresponding dihyropyranocoumarin **5a–c**.

Dihydroxanthyletin 5a. A mixture of suberosin **1a** and pyridine hydrochloride was heated for 5 h to afford dihydroxanthyletin **5a** in 48% yield, mp 120–122 °C (from pet. ether–ethyl acetate) (lit.,[35] 124–125 °C); ν_{max}/cm^{-1} (Nujol) 1727; δ_H (300 MHz) 1.36 (6H, s, 2 × CH_3), 1.84 (2H, t, *J* 6.8 Hz, $ArCH_2$C*H*$_2$), 2.84 (2H, t, *J* 6.8 Hz, ArC*H*$_2$$CH_2$), 6.2 (1H, d, *J* 9.3 Hz, C^3–H), 6.72 (1H, s, C^{10}–H), 7.15 (1H, s, C^5–H), 7.57 (1H, d, *J* 9.3 Hz, C^4–H) (Found: C, 72.88; H, 6.11. Calc. for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13%).

3-Methyldihydroxanthyletin 5b. A mixture of 3-methylsuberosin **1e** and pyridine hydrochloride was heated for 4 h to furnish compound **5b** in 79% yield, mp 152–153 °C (from pet. ether–ethyl acetate); ν_{max}/cm^{-1} (Nujol) 1703; δ_H (500 MHz) 1.35 (6H, s, 2 × CH_3), 1.83 (2H, t, *J* 6.75 Hz, $ArCH_2$C*H*$_2$), 2.14 (3H, s, CH_3), 2.81 (2H, t, *J* 6.75 Hz, ArC*H*$_2$$CH_2$), 6.7 (1H, s, C^{10}–H), 7.07 (1H, s, C^5–H), 7.37 (1H, s, C^4–H) (Found: C, 74.10; H, 6.83. $C_{15}H_{16}O_3$ requires C, 73.75; H, 6.60%).

Demethyldihydroluvangetin 5c. A mixture of *O*-methylbrosiperin (*O*-methylapigravin), **2c** and pyridine hydrochloride was heated for 2.5 h to furnish compound **5c** in 78% yield, mp 205–206 °C (lit.,[39] 206–208 °C); ν_{max}/cm^{-1} (Nujol) 1714, 3338; δ_H (300 MHz) 1.41 (6H, s, 2 × CH_3), 1.86 (2H, t, *J* 6.7 Hz, $ArCH_2$C*H*$_2$), 2.83 (2H, t, *J* 6.7 Hz, ArC*H*$_2$$CH_2$), 6.76 (1H, s, C^5–H), 6.18 (1H, d, *J* 9.3 Hz, C^3–H), 7.6 (1H, d, *J* 9.3 Hz, C^4–H) (Found: C, 68.48; H, 5.63. Calc. for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73%).

Conversion of demethyldihydroluvangetin 5c to dihydroluvangetin 5d

lodomethane (0.05 ml, 0.8 mmol) was added to a solution of demethyldihydroluvangetin **5c** (0.1 g, 0.4 mmol) in dry DMF (3 ml) containing anhydrous potassium carbonate (0.083 g, 0.6 mmol). The reaction mixture was stirred at room temperature for 1 h, poured into ice-cold water (10 ml), and extracted with ethyl acetate (3 × 5 ml); the combined extract was washed with water, dried (Na_2SO_4), and concentrated. The residue obtained was chromatographed over silica gel, using pet. ether–ethyl acetate (95 : 5) as eluent, to furnish a solid, which on recrystallization from pet. ether–ethylacetate provided compound **5d** (0.09 g, 86%), mp 129–131 °C (lit.,[36] 131 °C); ν_{max}/cm^{-1} (Nujol) 1729; δ_H (300 MHz) 1.41 (6H, s, 2 × CH_3), 1.86 (2H, t, *J* 6.6 Hz, $ArCH_2$C*H*$_2$), 2.84 (2H, t, *J* 6.6 Hz, ArC*H*$_2$$CH_2$), 3.94 (3H, s, OCH_3), 6.21 (1H, d, *J* 9.3 Hz, C^3–H), 6.93 (1H, s, C^5–H), 7.56 (1H, d, *J* 9.3 Hz, C^4–H) (Found: C, 69.09; H, 6.13. Calc. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20%).

Conversion of demethyldihydroluvangetin 5c to dihydrodonatin 5e

Prenyl bromide (0.22 ml, 1.9 mmol) was added dropwise to a solution of demethyldihydroluvangetin **5c** (0.2 g, 0.8 mmol) in DMF (15 ml) containing potassium carbonate (0.21 g, 1.5

mmol) and the reaction mixture was stirred at room temperature for 1.5 h, diluted with water, and extracted with ethyl acetate (3 × 10 ml). The combined extract was washed with water and dried over anhydrous sodium sulfate. The residue obtained on removal of solvent was chromatographed over silica gel, using pet. ether–ethyl acetate (96 : 4) as eluent, to afford dihyrodonatin **5e** (0.19 g, 74%), mp 65–67 °C (from pet. ether–ethyl acetate); ν_{max}/cm^{-1} (Nujol) 1715; δ_H (300 MHz) 1.4 (6H, s, 2 × CH_3), 1.69 (3H, s, CH_3), 1.74 (3H, s, CH_3), 1.84 (2H, t, *J* 6.6 Hz, $ArCH_2CH_2$), 2.83 (2H, t, *J* 6.6 Hz, $ArCH_2CH_2$), 4.61 (2H, d, *J* 7.2 Hz, OCH_2CH=), 5.57–5.63 (1H, m, OCH_2CH=), 6.19 (1H, d, *J* 9.9 Hz, C^3–H), 6.91 (1H, s, C^5–H), 7.54 (1H, d, *J* 9.9 Hz, C^4–H) (Found: C, 72.48; H, 6.99. $C_{19}H_{22}O_4$ requires C, 72.59; H, 7.05%).

General procedure for conversion of dihydropyranocoumarins 5a and 5d to the pyranocoumarins xanthyletin, 6a and luvangetin 6b

A solution of dihydroxanthyletin or dihydroluvangetin (**5a** or **5d**) (0.2 mmol) and NBS (0.2 mmol) in benzene (15 ml) containing potassium carbonate (0.2 mmol) and AIBN (10 mol%) was refluxed under nitrogen for 2–2.5 h. The reaction mixture was cooled to room temperature and diluted with ice-cold water. The organic layer was separated and the aqueous layer was extracted with benzene. The combined benzene layer was dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The residue obtained was chromatographed over silica gel, using pet. ether–ethyl acetate (98 : 2) as eluent, to furnish xanthyletin **6a** or luvangetin **6b**. Both products were recrystallized from pet. ether–ethyl acetate.

Xanthyletin 6a. Yield 61%, mp 128–130 °C (lit.,[40] 128–131 °C); ν_{max}/cm^{-1} (Nujol) 1727; δ_H (300 MHz) 1.47 (6H, s, 2 × CH_3), 5.68 (1H, d, *J* 9.9 Hz, C^7–H), 6.22 (1H, d, *J* 9.6 Hz, C^3–H), 6.34 (1H, d, *J* 9.9 Hz, C^6–H), 6.72 (1H, s, C^{10}–H), 7.07 (1H, s, C^5–H), 7.58 (1H, d, *J* 9.6 Hz, C^4–H) (Found: C, 73.51; H, 5.13. Calc. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30%).

Luvangetin 6b. Yield 65%, mp 106–108 °C (lit.,[36] 108–109 °C); ν_{max}/cm^{-1} (Nujol) 1729; δ_H (300 MHz) 1.51 (6H, s, 2 × CH_3), 3.98 (3H, s, OCH_3), 5.71 (1H, d, *J* 10.2 Hz, C^7–H), 6.23 (1H, d, J 9.6 Hz, C^3–H), 6.34 (1H, d, *J* 10.2 Hz, C^6–H), 6.83 (1H, s, C^5–H), 7.57 (1H, d, *J* 9.6 Hz, C^4–H) (Found: C, 69.77; H, 5.37. Calc. for $C_{15}H_{14}O_4$: C, 69.75; H, 5.46%).

Acknowledgements

P. K. S. and A. M. T thank CSIR, New Delhi for the award of SRF, and P. P. J. thanks UGC, New Delhi for the award of JRF and SRF. Financial support from UGC, New Delhi is also gratefully acknowledged.

References

1 (*a*) R. D. H. Murray, J. Mendez and S. A. Brown, *The Natural Coumarins, Occurrence, Chemistry and Biochemistry*, Wiley Interscience, New York, 1982; (*b*) R. D. H. Murray, *Progress in the Chemistry of Organic Natural Products, Naturally Occurring Plant Coumarins*, Springer Wien, New York, 1991, vol. 58, p. 83; (*c*) R. D. H. Murray, *Progress in the Chemistry of Organic Natural Products, Naturally Occurring Plant Coumarins*, Springer Wien, New York, 1997, vol. 72, p. 1.
2 R. D. H. Murray, M. M. Ballantyne and K. P. Mathai, *Tetrahedron*, 1971, **27**, 1247.
3 T. R. Sheshadri and M. S. Sood, *Indian J. Chem.*, 1963, **1**, 291.
4 V. Kumar, N. M. Mohamed Niyaz, S. Saminathan and D. B. M. Wickramaratne, *Phytochemistry*, 1998, **49**, 215.
5 K. S. Mukherjee, C. K. Chakraborty, J. P. Chatterjee and P. Bhattacharya, *J. Indian Chem. Soc.*, 1989, **66**, 66.
6 D. P. Chakraborty, A. Das Gupta and P. K. Bose, *Ann. Biochem. Exp. Med.*, 1957, **17**, 59, (D. P. Chakraborty, A. Das Gupta and P. K. Bose, *Chem. Abstr.*, 1957, **52**, 1352g).
7 O. Kiyomi, H. Masayoshi, N. Ryochi and N. Mitsuru, *Jpn. Appl.* 7 973 12, 1977, (O. Kiyomi, H. Masayoshi, N. Ryochi and N. Mitsuru, *Chem. Abstr.*, 1977, **91**, P152771u).
8 G. S. Verma, B. R. Prabhu and A. Banerji, *J. Agric. Food. Chem.*, 1989, **37**, 1435.
9 A. A. L. Gunatilaka, D. G. I. Kingston, E. M. K. Wijeratne, B. M. R. Bandara, G. A. Hofmann and R. K. Johnson, *J. Nat. Prod.*, 1994, **57**, 518.
10 K.-H. Lee, Y. Kashiwada, L. Haung, J. J. Lee, M. Costino, J. Snider, M. Manax and L. Xie, *U.S. Appl.* 5 635 589, 1997, (K.-H. Lee, Y. Kashiwada, L. Haung, J. J. Lee, M. Costino, J. Snider, M. Manax and L. Xie, *Chem. Abstr.*, 1997, **127**, 10432b).
11 S. D. Srivastava, K. Halwe and S. K. Srivastava, *Fitoterapia*, 1997, **68**, 410, (S. D. Srivastava, K. Halwe and S. K. Srivastava, *Chem. Abstr.*, 1997, **128**, 268242j).
12 D. P. Chakraborty, M. Sen and P. K. Bose, *Trans. Bose Res. Inst.*, 1961, **24**, 31, (D. P. Chakraborty, M. Sen and P. K. Bose, *Chem. Abstr.*, 1961, **56**, 1835b).
13 A. Patra, S. K. Misra and S. K. Chaudhuri, *J. Indian Chem. Soc.*, 1988, **65**, 205.
14 M. H. Pardanani, Y. A. Shaikh and K. N. Trivedi, *J. Indian Chem. Soc.*, 1975, **52**, 45.
15 G. M. Massanet, E. Pendo, F. Rodriguez-Luis and J. Salvador, *Heterocycles*, 1987, **26**, 1541.
16 N. Cairns, L. M. Harwood and D. P. Astles, *J. Chem. Soc., Chem. Commun.*, 1986, 1264.
17 N. Cairns, L. M. Harwood and D. P. Astles, *J. Chem. Soc., Chem. Commun.*, 1986, 750.
18 N. Cairns, L. M. Harwood and D. P. Astles, *J. Chem. Soc., Chem. Commun.*, 1987, 400.
19 D. Swaroop, P. B. Sharma and R. S. Kapil, *Indian J. Chem., Sect. B, Chem. Incl. Med. Chem.*, 1983, **22B**, 408.
20 P. N. Sharma, A. Shoeb, R. S. Kapil and S. P. Popli, *Indian J. Chem., Sect. B, Chem. Incl. Med. Chem.*, 1980, **19B**, 938.
21 R. D. H. Murray, M. M. Ballantyne, T. C. Hogg and P. H. McCabe, *Tetrahedron*, 1975, **31**, 2960.
22 S. Mahey, T. R. Sheshadri and S. K. Mukerjee, *Indian J. Chem.*, 1974, **12**, 29.
23 (*a*) E. Spath and R. Hillel, *Ber. Dtsch. Chem. Ges. B*, 1939, **72**, 963; (*b*) H. D. Schroder, B. Wilheim, H. Otto and H. Schmidt, *Chem. Ber.*, 1959, **92**, 2338.
24 (*a*) J. Reisch, K. Szendrei, E. Minker and I. Novak, *Pharmazie*, 1969, **24**, 483; (*b*) J. Banerji, N. Ghoshal, S. Sarkar and M. Kumar, *Indian J. Chem., Sect. B*, 1982, **21**, 496.
25 V. K. Ahluwalia, K. Bhat and R. P. Singh, *Indian J. Chem., Sect. B, Chem. Incl. Med. Chem.*, 1982, **21B**, 403.
26 (*a*) A. K. Das Gupta and K. R. Das, *J. Chem. Soc. C*, 1969, 33; (*b*) P. Way Kole, S. Shaikh and R. N. Usgaonkar, *Indian J. Chem., Sect. B, Chem. Incl. Med. Chem.*, 1980, **19B**, 238; (*c*) M. N. Kavinde, S. A. Kulkarni and M. V. Paradkar, *Synth. Commun.*, 1990, **20**, 3259; (*d*) V. K. Ahluwalia and S. Bala, *Acta Chim. Acad. Sci. Hung.*, 1983, **113**, 143.
27 (*a*) S. Yamaguchi, R. Miyakawa, S. Yonezawa and Y. Kawase, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 3593; (*b*) Y. Kawase, S. Yamaguchi, H. Horita, J. Takeno and H. Kameyama, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 1153.
28 K. C. Nicolaou, J. A. Pfefferkorn and G.-Q. Cao, *Angew. Chem. Int., Ed.*, 2000, **39**, 734.
29 J. Hlubucek, E. Ritcher and W. C. Taylor, *Aust. J. Chem.*, 1971, **24**, 2347.
30 J. M. Amaro-Luis, G. Massanet, E. Pando, F. Rodriquez-Luis and E. Zubia, *Planta Med.*, 1990, **56**, 304.
31 For a preliminary communication of this work see R. S. Mali, P. K. Sandhu and A. Manekar-Tilve, *J. Chem. Soc., Chem. Commun.*, 1994, 251.
32 P. W. Austin and T. R. Sheshadri, *Indian J. Chem.*, 1968, **6**, 412.
33 M. D. Sindkhedkar, Ph.D. Thesis, University of Pune, Pune, India, August 1998.
34 R. D. H. Murray and M. M. Ballantyne, *Tetrahedron*, 1970, **26**, 4607.
35 W. Steck, *Can. J. Chem.*, 1971, **49**, 1197.
36 E. Spath, P. K. Bose, H. Schmidt, E. Dobrovolny and A. Mukerjee, *Ber. Dtsch. Chem. Ges. B*, 1940, **73**, 1361.
37 M. Murayama, E. Seto, T. Okuda and I. Morita, *Chem. Pharm. Bull.*, 1972, **20**, 741.
38 S. K. Garg, S. R. Gupta and N. D. Sharma, *Phytochemistry*, 1979, **18**, 1580.
39 R. B. Filho, A. F. Magalhaes and O. R. Gottlieb, *Phytochemistry*, 1972, **11**, 3307.
40 R. D. H. Murray, M. M. Ballantyne and K. P. Mathai, *Tetrahedron Lett.*, 1970, 243.