Phytochemistry, Vol. 24, No. 6, pp. 1355–1357, 1985.
Printed in Great Britain.

0031–9422/85 $3.00 + 0.00
Pergamon Press Ltd.

SYNTHESIS OF 4-ARYLCOUMARINS FROM *COUTAREA HEXANDRA*

GIULIANO DELLE MONACHE, BRUNO BOTTA, FRANCO DELLE MONACHE and MAURIZIO BOTTA*

Centro Chimica dei Recettori del C.N.R., Università Cattolica del S. Cuore, 00168 Roma, Italy; *Dipartimento di Chimica, Università La Sapienza, Piazzale A. Moro, Roma, Italy

(*Received* 3 *October* 1984)

Key Word Index—*Coutarea hexandra*; Rubiaceae; neoflavonoids; 4-arylcoumarins; synthesis.

Abstract—The structures assigned to the 5,7-dimethoxy-4-arylcoumarins isolated from *Coutarea hexandra* have been confirmed by synthesis, via Pechmann condensation of phloroglucinol and an ethyl benzoylacetate derivative, the hydroxy groups of which were protected either by benzylation or by methylenedioxy group formation.

INTRODUCTION

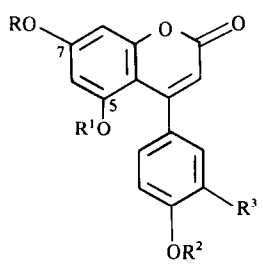
We have recently isolated the new 4-arylcoumarins **1**–**5** [1, 2] from *Coutarea hexandra*, a plant growing in north eastern Brazil and used in folk medicine [1, 3] as an antimalarial or antidiabetic agent. To confirm the assigned structures, we report now the synthesis of the five 5,7-dimethoxy-4-arylcoumarins as well as of their 5,7-dihydroxy analogues.

RESULTS AND DISCUSSION

The coumarin **1** was prepared both by Perkin cyclization of 2-hydroxy-4,6,4′-trimethoxybenzophenone and by methylation of 5,7-dihydroxy-4′-methoxy-4-phenylcoumarin, **6**, which was obtained by Pechmann condensation of ethyl *p*-methoxybenzoylacetate with phloroglucinol. The synthetic products, obtained by the two independent routes (the latter in major yield), and the natural coumarin were coincident in all respects. Coumarins having a free hydroxy group in the 4-phenyl ring like **2**–**4**, have been prepared only in poor yield by Perkin cyclization of the corresponding benzophenones [4, 5]. Conversely melanettin (6,4′-dihydroxy-7-methoxy-4-phenylcoumarin) and stevenin (6,3′-dihydroxy-7-methoxy-4-phenylcoumarin) have been synthesized [6] by condensation of *o*-methoxyhydroquinone with ethyl *p*-benzyloxybenzoylacetate and ethyl *m*-benzyloxybenzoylacetate, respectively. Similarly by condensation of ethyl *p*-benzyloxybenzoylacetate with phloroglucinol we obtained 5,7,4′-trihydroxy-4-phenylcoumarin, **7**, which by methylation with CH_2N_2 gave a mixture of **1** (43%) and **2** (50%).

We also observed that under milder conditions the Pechmann condensation product retained the benzyl group. By limiting thus the HCl gas concentration or by using a peracetylated phloroglucinol as substrate, compound **8** was obtained in good yield; it gave by methylation **9**, which by successive removal of the benzyl group afforded 4′-hydroxy-5,7-dimethoxy-4-phenylcoumarin, **2**. Both synthetic samples of **2** were coincident with the natural product. The coumarin **3** had already been obtained by partial methylation of natural **4**, together with the isomer **10** [1]; the assignment of the two structures was based on consideration of the spectral data.

Now we prepared compound **10** both by methylation of 5,7,4′-trihydroxy-3′-methoxy-4-phenylcoumarin, **11**, and by debenzylation of 5,7,3′-trimethoxy-4′-benzyloxy-4-phenylcoumarin, **12**. The synthetic **10** was identical with the unnatural monomethyl derivative of **4**, thus confirming chemically the structure of the isomer **3**. Also the coumarin **5** had been prepared by us [2], via methylenation of natural **4**. Now condensation of ethyl piperonylacetate with phloroglucinol gave **13**, which by methylation yielded 5,7-dimethoxy-3′,4′-methylenedioxy-4-phenylcoumarin, **5**. For the synthesis of **4** we considered



	R	R¹	R²	R³
1	Me	Me	Me	H
2	Me	Me	H	H
3	Me	Me	Me	OH
4	Me	Me	H	OH
5	Me	Me	CH_2 —	O
6	H	H	Me	H
7	H	H	H	H
8	H	H	CH_2Ph	H
9	Me	Me	CH_2Ph	H
10	Me	Me	H	OMe
11	H	H	H	OMe
12	Me	Me	CH_2Ph	OMe
13	H	H	CH_2 —	O
14	Me	Me	Me	OMe
15	H	H	CH_2Ph	OMe

the preferential cleavage with BCl_3 of an aromatic methylenedioxy in the presence of methoxyls, which was applied by Teitel *et al.* in the synthesis of an isoquinoline derivative [7]. Under these conditions compound **5** was demethylenated to give in high yield (95%) compound **4**, identical with the natural specimen.

EXPERIMENTAL

General. Mps are uncorr. ^1H NMR was at 60 MHz. MS were recorded by direct inlet at 70 eV. Adsorbents used were from Merck.

2-Hydroxy-4,6,4'-trimethoxybenzophenone. To an ice cold mixture of dry $AlCl_3$ (12 g), 1,3,5-trimethoxybenzene (4.2 g) and dry Et_2O (50 ml) was added a suspension of *p*-anisoyl chloride (6 g) in dry Et_2O (50 ml). The mixture was kept at room temp for 48 hr and then treated with crushed ice and conc HCl (25 ml). The Et_2O layer was separated and the aqueous phase was extracted with CH_2Cl_2. The residue of the combined organic layers was dissolved in 10% NaOH aq and CH_2Cl_2. Acidification of the alkaline extract with dil HCl yielded crude 2-hydroxy-4,6,4'-trimethoxybenzophenone (3.6 g). The residue of the CH_2Cl_2 layer afforded on silica gel with CH_2Cl_2 further product (1.4 g, total yield 70%), mp 85–86° (MeOH); UV λ_{max}^{MeOH} nm (log ε): 225 (4.18), 286 (4.20); $\lambda_{max}^{AlCl_3}$: 221, 306, 360; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520, 1658, 1600; ^1H NMR ($CDCl_3$): δ11.78 (1H, *s*, exchang. D_2O, 2-OH), 7.48 (2H, *d*, *J* = 8.5 Hz, H-2', H-6'), 6.80 (2H, *d*, *J* = 8.5 Hz, H-3', H-5'), 6.08 (1H, *d*, *J* = 2 Hz, H-5), 5.87 (1H, *d*, *J* = 2 Hz, H-3), 3.77 + 3.75 (3H + 3H, *s* + *s*, 4-OMe + 4'-OMe), 3.44 (3H, *s*, 6-OMe); MS *m/z* (rel. int.): 288 $[M]^+$ (86), 287 (100), 273 (14), 271 (10), 270 (8), 257 (5), 255 (3), 181 $[M - ring\ B]^+$ (56), 180 (57), 166 (5), 152 (14), 137 (11), 135 $[M - ring\ A]^+$ (41), 107 (8), 77 (23); *m**: 286 (288 → 287), 257.8 (288 → 273), 241 (270 → 255), 152.1 (181 → 166), 123.5 (152 → 137), 55.4 (107 → 77). (Found: C, 66.75; H, 5.48. Calc. for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59%.)

5,7,4'-Trimethoxy-4-phenylcoumarin, **1**; (a) via Perkin. 2-Hydroxy-4,6,4'-trimethoxybenzophenone (0.80 g), AcOK (0.28 g) and Ac_2O (1.5 ml) were heated under reflux for 24 hr. The reaction mixture was treated with ice-water and filtered to give a solid, which on silica gel with benzene–EtOAc mixtures afforded **1** (175 mg, 20%), and 2-acetoxy-4,6,4'-trimethoxybenzophenone (0.71 g, 77%), mp 116–117° (Et_2O); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765, 1658, 1600; ^1H NMR ($CDCl_3$): δ1.92 (3H, *s*, COMe); (b) via Pechmann. A cooled soln of ethyl *p*-methoxybenzoylacetate (1.25 g) and phloroglucinol (0.71 g) in abs EtOH (55 ml) was saturated with dry HCl gas. After 3 days the mixture was added with water and concentrated *in vacuo*. On filtration crude 5,7-dihydroxy-4'-methoxy-4-phenylcoumarin (1.2 g), **6**, was obtained as an orange solid (mp 258–260°). The soln was extracted with EtOAc and the organic layer mixed with 1 N NaOH aq. Acidification of the alkaline soln and extraction with EtOAc afforded further **6** (0.3 g, total yield 94%), mp 263–265° (MeOH); UV λ_{max}^{MeOH} nm (log ε): 262 (4.00), 320 (4.03); λ_{max}^{MeONa}: 276, 312, 381; IR ν_{max}^{KBr} cm^{-1}: 3320, 3190, 1688, 1678, 1630, 1595, 1548, 1510; ^1H NMR (Me_2CO-d_6): δ7.32 (2H, *d*, *J* = 8.5 Hz, H-2', H-6'), 6.93 (2H, *d*, *J* = 8.5 Hz, H-3', H-5'), 6.35 (1H, *d*, *J* = 2.5 Hz, H-8), 6.28 (1H, *d*, *J* = 2.5 Hz, H-6), 5.76 (1H, *s*; H-3), 3.82 (3H, *s*, 4'-OMe); MS *m/z* (rel. int.): 284 $[M]^+$ (100), 283 (22), 256 (95), 255 (11), 241 (39), 227 (9), 142 (13), 128 (23). (Found: C, 67.69; H, 4.22. Calc. for $C_{16}H_{12}O_5$: C, 67.60; H, 4.26%.)

Crude **6** (0.55 g), dry K_2CO_3 (1.0 g) and Me_2SO_4 (10 ml) in Me_2CO (50 ml) were heated under reflux for 1 hr. Standard work-up and purification on silica gel with $CHCl_3$–EtOH (99:1) gave pure **1** (0.51 g, 84%), mp 151–152° (EtOH), identical with the natural sample and the synthetic one obtained via Perkin (mmps 150–152°).

5,7,4'-Trihydroxy-4-phenylcoumarin (**7**). A cooled soln of ethyl *p*-benzyloxybenzoylacetate (0.6 g) and phloroglucinol (0.28 g) in EtOH (24 ml) was saturated with dry HCl gas. After 3 days the reaction mixture was added with water and concentrated *in vacuo*. Filtration gave a red solid which on CC (silica gel) with $CHCl_3$–MeOH mixtures afforded **7** (320 mg, 60%), mp 294–295° dec. ($CHCl_3$–MeOH); UV λ_{max}^{MeOH} nm (log ε): 262 (4.00), 324 (4.18); λ_{max}^{MeONa}: 275, 305, 373; IR ν_{max}^{KBr} cm^{-1}: 3510, 3235, 1662, 1590, 1550, 1510; ^1H NMR (Me_2CO-d_6): δ7.22 (2H, *d*, *J* = 8.5 Hz, H-2', H-6'), 6.83 (2H, *d*, *J* = 8.5 Hz, H-3', H-5'), 6.35 (2H, *s*, H-6, H-8), 5.74 (1H, *s*, H-3); MS *m/z* (rel. int.): 270 $[M]^+$ (100), 269 (22), 242 (88), 241 (9), 226 (8), 213 (32), 197 (11), 135 (6), 121 (5), 106.5 (4). (Found: C, 66.82; H, 3.66. Calc. for $C_{15}H_{10}O_5$: C, 66.67; H, 3.73%.) *Triacetylderivative.* Compound **7** (60 mg) treated with pyridine and Ac_2O overnight gave 5,7,4'-triacetoxy-4-phenylcoumarin (68 mg), mp 186–187° (Et_2O); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770, 1732; ^1H NMR ($CDCl_3$): δ7.38 (2H, *d*, *J* = 8.5 Hz, H-2', H-6'), 7.20 (2H, *d*, *J* = 8.5 Hz, H-3', H-5'), 7.18 (1H, *d*, *J* = 2.5 Hz, H-8), 6.81 (1H, *d*, *J* = 2.5 Hz, H-6), 2.31 (6H, 7-OAc + 4'-OAc), 1.42 (3H, *s*, 5-OAc). *Methyl derivatives.* To **7** (270 mg) in $CHCl_3$ (18 ml) and MeOH (2 ml) a satd soln of CH_2N_2 in Et_2O (20 ml) was added under stirring. After 45 min the reaction mixture was evaporated *in vacuo* and the residue passed on silica gel with benzene–EtOAc (4:1) to give **1** (135 mg, 43%) and **2** (150 mg, 50%) both identical with the natural samples.

5,7-Dihydroxy-4'-benzyloxy-4-phenylcoumarin (**8**). A cooled suspension of ethyl *p*-benzyloxybenzoylacetate (450 mg) and 1,3,5-triacetoxybenzene (380 mg) in EtOH (15 ml) was saturated with dry HCl gas. After 3 days the reaction mixture was added with water and reduced to small volume.

The filtered solid on silica gel with $CHCl_3$–MeOH mixtures gave **8** (245 mg, 45%) and **7** (60 mg, 15%). In another experiment a stream of dry HCl gas was passed into a cooled soln of ethyl *p*-benzyloxybenzoylacetate (300 mg) and phloroglucinol (126 mg) in EtOH for 2 min. After 3 days the reaction mixture was added with water and filtered. The soln was extracted with EtOAc. The combined solid and the residue of the extraction, on crystallization from Et_2O–MeOH, gave crude **8** (205 mg). The residue of the mother liquors on silica gel with $CHCl_3$–MeOH (97:3) gave further **8** (55 mg, total yield 72%), mp 220–221° (Et_2O–MeOH); UV λ_{max}^{MeOH} nm (log ε): 262 (4.00), 320 (4.04); λ_{max}^{MeONa}: 276, 314, 382; IR ν_{max}^{KBr} cm^{-1}: 3480, 3250, 1680, 1630, 1600, 1578, 1555, 1510; ^1H NMR (Me_2CO-d_6): δ7.60–7.20 (5H, *m*, C_6H_5), 7.30 (2H, *d*, *J* = 8.5 Hz, H-2', H-6'), 6.97 (2H, *d*, *J* = 8.5 Hz, H-3', H-5'), 6.43 + 6.38 (1H + 1H, *d* + *d*, *J* = 2.5 Hz, H-6 + H-8), 5.78 (1H, *s*, H-3), 5.05 (2H, *s*, CH_2); MS *m/z* (rel. int.): 360 $[M]^+$ (100), 332 (1), 270 (7), 269 (4), 242 (7), 241 (6), 213 (7), 185 (2), 184 (5), 115 (10). (Found: C, 73.53; H, 4.52. Calc. for $C_{22}H_{16}O_5$: C, 73.32; H, 4.48%.)

4'-Hydroxy-5,7-dimethoxy-4-phenylcoumarin (**2**). To crude **8** (160 mg) in MeOH (10 ml) a satd soln of CH_2N_2 in Et_2O (10 ml) was added. The residue on CC (silica gel) with CH_2Cl_2 gave 5,7-dimethoxy-4'-benzyloxy-4-phenylcoumarin (155 mg, 90%), **9**, mp 168–169° (MeOH); UV λ_{max}^{MeOH} nm (log ε): 255 (4.05), 318 (4.20); IR ν_{max}^{KBr} cm^{-1}: 1735, 1612, 1600, 1550, 1510; ^1H NMR ($CDCl_3$): δ7.33 (5H, *br s*, C_6H_5), 7.16 (2H, *d*, *J* = 8.5 Hz, H-2', H-6'), 6.91 (2H, *d*, *J* = 8.5 Hz, H-3', H-5'), 6.44 (1H, *d*, *J* = 2.5 Hz, H-8), 6.18 (1H, *d*, *J* = 2.5 Hz, H-6), 5.88 (1H, *s*, H-3), 5.05 (2H, *s*, CH_2), 3.79 (3H, *s*, 7-OMe), 3.40 (3H, *s*, 5-OMe). A cooled soln of **9** (78 mg) in HOAc (4 ml) and $CHCl_3$ (few drops) was saturated with dry HCl gas. After 3 days the reaction mixture was added with CCl_4 and evaporated *in vacuo*. The residue on silica gel with benzene–EtOAc gave **2** (47 mg, 78%), mp 214–215° (MeOH), identical with the natural sample (mmp 214–215°).

5,7,4'-Trihydroxy-3'-methoxy-4-phenylcoumarin (**11**). A cooled

suspension of ethyl (3-methoxy-4-benzyloxy)benzoylacetate (650 mg, mp 67–68°, from Et_2O) and 1,3,5-triacetoxybenzene (510 mg) in abs EtOH (33 ml) was saturated with dry HCl gas. After 3 days the reaction mixture was diluted with water, concentrated *in vacuo* and filtered. The soln was extracted with EtOAc, but the residue gave only traces of **11** and **15** (*vide infra*). The solid on CC (silica gel) with $CHCl_3$–MeOH (95:5) gave **11** (260 mg, 45%), mp 297–298° (MeOH); UV λ_{max}^{MeOH} nm (log ε): 260 (4.17), 330 (4.32); λ_{max}^{MeONa}: 250, 275, 388; IR ν_{max}^{KBr} cm^{-1}: 3410, 3290, 1688, 1595, 1560, 1508; ^1H NMR (C_5D_5N): δ10.40 (3H, *br*, exchang. D_2O, 5-OH, 7-OH, 4'-OH), 7.40–7.20 (3H, *m*, H-2', H-5', H-6'), 6.80 + 6.72 (1H + 1H, *d* + *d*, *J* = 2.5 Hz, H-6 + H-8), 6.22 (1H, *s*, H-3), 3.81 (3H, *s*, 3'-OMe); MS *m/z* (rel. int.): 300 $[M]^+$ (100), 299 (8), 285 (4), 272 (91), 257 (12), 239 (7), 229 (14), 211 (7), 150 (2), 136 (5), 128.5 (3), 114.5 (7). (Found: C, 64.12; H, 3.96. Calc. for $C_{16}H_{12}O_6$: C, 64.00; H, 4.03%.) *Methyl derivatives.* To **11** (60 mg) in MeOH (3 ml) and Et_2O (3 ml) a satd soln of CH_2N_2 in Et_2O (6 ml) was added. After 30 min the reaction mixture was evaporated *in vacuo* and the residue on prep. TLC gave 5,7,3',4'-tetramethoxy-4-phenylcoumarin (31 mg, 68%), **14**, mp 170–171° (MeOH), and 4'-hydroxy-5,7,3'-trimethoxy-4-phenylcoumarin (11 mg, **25**%), **10**, mp 174–175° (Et_2O), identical with the methyl derivatives (mmps 169–170° and 173–174°, respectively) of the natural **3** and **4** [1].

4'-Hydroxy-5,7,3'-trimethoxy-4-phenylcoumarin (**10**). A stream of dry HCl gas was passed onto a cooled soln of ethyl (3-methoxy-4-benzyloxy)benzoylacetate (650 mg) and phloroglucinol (277 mg) in EtOH for 2 min. After 3 days the reaction mixture was added with water, concentrated *in vacuo* and filtered. The soln was extracted with EtOAc and the residue gave on prep. TLC (silica gel, $CHCl_3$–MeOH, 19:1) **11** (12 mg, 2%). The solid on CC (silica gel) with $CHCl_3$–MeOH (97:3) afforded 5,7-dihydroxy-3'-methoxy-4'-benzyloxy-4-phenylcoumarin (310 mg, 40%), **15**, mp 194–195° (EtOH); UV λ_{max}^{MeOH} nm (log ε): 254 (4.19), 329 (4.28); λ_{max}^{MeONa}: 250, 277, 382; IR ν_{max}^{KBr} cm^{-1}: 3620, 3500, 1670, 1595, 1508, 1501; ^1H NMR (Me_2CO-d_6): δ9.20 + 8.75 (1H + 1H, *br s* + *br s*, exchang. D_2O, 5-OH, 7-OH), 7.60–7.20 (5H, *m*, C_6H_5), 7.15–6.80 (3H, *m*, H-2', H-5', H-6'), 6.32 (1H, *d*, *J* = 2.5 Hz, H-8), 6.23 (1H, *d*, *J* = 2.5 Hz, H-6), 5.78 (3H, *s*, H-3), 5.09 (2H, *s*, CH_2), 3.80 (3H, *s*, 3'-OMe); MS *m/z* (rel. int.): 390 $[M]^+$ (70), 300 (100), 299 (22), 272 (80), 257 (15), 239 (11), 229 (18), 211 (11), 150 (5), 136 (12), 128.5 (7), 114.5 (19). (Found: C, 70.90; H, 4.61. Calc. for $C_{23}H_{18}O_6$: C, 70.76; H, 4.65%.) To **15** (195 mg) in MeOH (10 ml) was added a satd soln of CH_2N_2 in Et_2O (10 ml). The mixture was left standing overnight and evaporated *in vacuo*. The residue on crystallization gave 5,7,3'-trimethoxy-4'-benzyloxy-4-phenylcoumarin (200 mg, 96%), **12**, mp 157–158° (Et_2O); UV λ_{max}^{MeOH} nm (log ε): 257 (4.18), 327 (4.33); IR ν_{max}^{KBr} cm^{-1}: 1726, 1610, 1553, 1512, 1490; ^1H NMR ($CDCl_3$): δ3.82 + 3.80 (3H + 3H, *s* + *s*, 7-OMe + 3'-OMe), 3.42 (3H, *s*, 5-OMe). A cooled soln of **12** (126 mg) in abs EtOH (4.5 ml) was saturated with dry HCl gas. After 4 days the reaction mixture was added with CCl_4 and evaporated *in vacuo*. The residue on prep. TLC (silica gel, benzene–EtOAc) gave starting material (51 mg) and **10** (56 mg, 57%), mp 174–175° (Et_2O), identical with the product described in the literature [1].

5,7-Dihydroxy-3',4'-methylenedioxy-4-phenylcoumarin (**13**). A cooled soln of ethyl piperonylacetate (2.36 g, mp 37–38°, from EtOH) and phloroglucinol (1.26 g) in abs EtOH (100 ml) was saturated with dry HCl gas. After 3 days the reaction mixture was added with water and concentrated *in vacuo*. The solid on silica gel with $CHCl_3$–MeOH (19:1) gave crude **13** (2.60 g, 87%), mp 268–269° dec (Et_2O–MeOH); UV λ_{max}^{MeOH} nm (log ε): 254 (4.09), 329 (4.22); IR ν_{max}^{KBr} cm^{-1}: 3490, 3240, 1672, 1625, 1610, 1570, 1500; ^1H NMR (Me_2CO-d_6): δ6.90 (3H, *br s*, H-2', H-5', H-6'), 6.32 (1H, *d*, *J* = 2 Hz, H-8), 6.23 (1H, *d*, *J* = 2 Hz, H-6), 5.94 (2H, *s*, O–CH_2–O), 5.76 (1H, *s*, H-3); MS *m/z* (rel. int.): 298 $[M]^+$ (88), 270 (100), 241 (13), 240 (6), 212 (14), 211 (8), 184 (15), 155 (10), 149 (5), 135 (5), 134.5 (10), 134 (5), 120 (9); *m**: 244.6 (298 → 270), 215.1 (270 → 241), 213.3 (270 → 240), 187.3 (240 → 212). (Found: C, 64.64; H, 3.34. Calc. for $C_{16}H_{10}O_6$: C, 64.43; H, 3.38%.)

5,7-Dimethoxy-3',4'-methylenedioxy-4-phenylcoumarin (**5**). To crude **13** (300 mg) in MeOH (15 ml) and Et_2O (15 ml) a satd soln of CH_2N_2 in Et_2O (30 ml) was added. After 1 hr the reaction mixture was evaporated *in vacuo* and the residue on silica gel with $CHCl_3$ gave **5** (290 mg, 88%), mp 194–195° (Et_2O), identical with the natural sample (mmp 194–195°).

3',4'-Dihydroxy-5,7-dimethoxy-4-phenylcoumarin (**4**). To a cooled soln of **5** (326 mg) in CH_2Cl_2 (15 ml) was added 1 M BCl_3 in CH_2Cl_2 (2 ml). The reaction mixture was kept at room temp for 6 hr, evaporated *in vacuo*, added with MeOH and left standing overnight. The residue on silica gel with $CHCl_3$–MeOH (98:2) gave **4** (298 mg, 95%), mp 211–212° (MeOH), identical with the natural sample (mmp 210–212°).

REFERENCES

1. Delle Monache, G., Botta, B., Serafim Neto, A. and Alves de Lima, R. (1983) *Phytochemistry* **22**, 1657.
2. Delle Monache, G., Botta, B. and Alves de Lima, R. (1984) *Phytochemistry* **23**, 1813.
3. Reher, G., Kraus, Lj., Sinnwell, V. and König, W. A. (1983) *Phytochemistry* **22**, 1524.
4. Donnelly, D. M. X., O'Reilly, J. and Whalley, W. B. (1975) *Phytochemistry* **14**, 2287.
5. Donnelly, D. M. X., Thompson, J., Whalley, W. B. and Ahmad, S. (1973) *J. Chem. Soc. Perkin Trans.* 1, 1737.
6. Ahluwalia, V. K. and Dhingra, S. (1980) *Heterocycles* **14**, 1329.
7. Teitel, S., O'Brien, J. and Brossi, A. (1972) *J. Org. Chem.* **37**, 3368.