# A Facile Synthesis of Isopongaflavone, Atalantoflavone Dimethylether, Racemoflavone Dimethyleter, and Methylenedioxy Isopongaflavone

K. J. Rajendra Prasad, P. A. Periasamy, and C. S. Vijayalakshmi

*J. Nat. Prod.*, **1993**, 56 (2), 208-214• DOI:
10.1021/np50092a004 • Publication Date (Web): 01 July 2004

*Journal of Natural Products*
*Vol. 56, No. 2, pp. 208-214, February 1993*

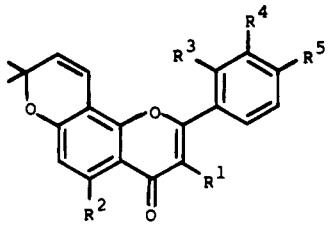
# A FACILE SYNTHESIS OF ISOPONGAFLAVONE, ATALANTOFLAVONE DIMETHYLETHER, RACEMOFLAVONE DIMETHYLETHER, AND METHYLENEDIOXY ISOPONGAFLAVONE

K.J. RAJENDRA PRASAD,* P.A. PERIASAMY, and C.S. VIJAYALAKSHMI

*Department of Chemistry, Bharathiar University, Coimbatore 641 046, Tamil Nadu, India*

ABSTRACT.—A convenient route to pyranoflavones (natural and synthetic) from acetyl hydroxychromans via the corresponding dihydro analogues by employing the Baker-Venkataraman rearrangement is reported.

Flavones possessing prenyl substituents and those with a 2,2-dimethylpyran ring system occur frequently (1,2). Since the naturally occurring pyranoflavanoids possess interesting pharmacological properties (3–5), several methods for their synthesis have been developed (6–14). There has been continued interest in our laboratory (15,16) in the synthesis of pyranoflavones from *O*-hydroxyacetyl-2,2-dimethylchroman. Some health tonics prescribed for curing diseases are extracts of *Morbus bombycis,* or related plants that contain morusin [**1**] and/or its hydrate (5). Isopongaflavone [**2**], otherwise known as candidin (17), was very active as an antifeedant against *Maruca testualis* and *Eldana saccharina* (3). Atalantoflavone dimethylether [**3**] also displayed significant insecticidal activity (4).

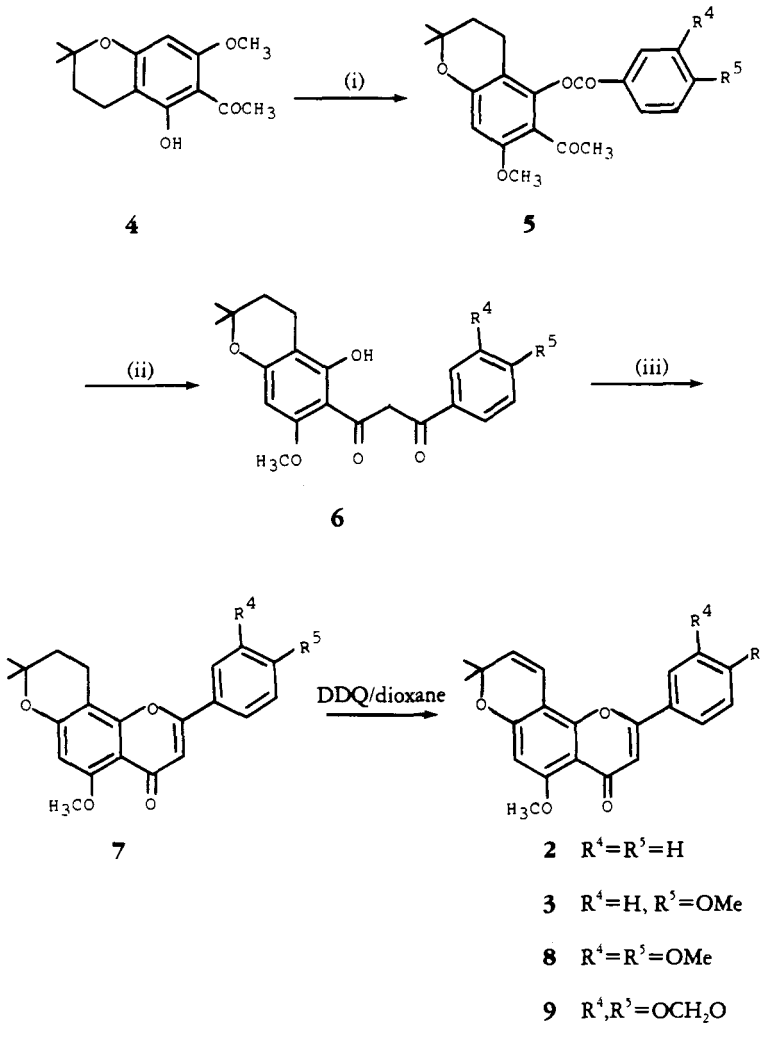


**1** $R^1$=  , $R^2=R^3=R^5=OH$, $R^4=OH$
**2** $R^1=R^3=R^4=R^5=H$, $R^2=OMe$
**3** $R^1=R^3=R^4=H$, $R^2=R^5=OMe$

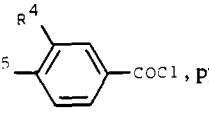
Many methods reported for the synthesis of pyranoflavones start with the simple flavone moiety. Banerji and Goomer (12) and Prasad *et al.* (15) constructed a synthetic system from chromenes and chromans, respectively. Our approach to such compounds starts with the chroman.

## RESULTS AND DISCUSSION

A convenient method for the synthesis of pyranoflavones by exploiting the Baker-Venkataraman rearrangement (18–20) is presented. In this method, *O*-aroyl derivatives of the chromans **4a–4d** were studied as a route to the dihydropyranoflavones **7a–7d**. The acetyl chromans **4a–4d** were converted to the *O*-aroyl derivatives **5a–5d** by treatment with the respective aroyl chlorides in pyridine. The esters **5a–5d** thus formed were then rearranged to the corresponding diaroylmethanes **6a–6d** which were subjected to acid-catalyzed cyclization to furnish the dihydropyranoflavones **7a–7d**, respectively. (Scheme 1).




SCHEME 1. Compounds: **a** $R^4=R^5=H$; **b** $R^4=H$, $R^5=OMe$; **c** $R^4=R^5=OMe$; **d** $R^4,R^5=OCH_2O$.

Conditions: (i)  , pyridine; (ii) KOH, pyridine; (iii) $H^+$/EtOH.

The ir spectra of **5a–5d** showed the *O*-benzoyl carbonyl absorption near 1715 $cm^{-1}$. The elemental analyses and ir spectral data of compounds **5a–5d** are listed in Table 1. Compounds **5a–5d**, when treated with KOH and pyridine, gave compounds **6a–6d**, respectively. The presence of a β-diketone group was indicated from ir absorptions at 1670 and 1620 $cm^{-1}$. The occurrence of keto and enol forms were indicated from their $^1$H-nmr spectra. Based on elemental analyses, ir, $^1$H-nmr, and ms data (Table 2), the compounds **6a–6d** were assigned as diaroylmethane derivatives. When the β-diketones **6a–6d** were subjected to acid-catalyzed cyclization, they yielded the corresponding dihydropyrano-flavones **7a–7d**. The ir, mass, $^1$H-nmr spectra, and elemental analysis data are presented in Table 3.

TABLE 1. Data for Aroyloxy Chromans **5a–5d**.

| Compound | Yield (%) | Mp[a] (EtOH) | Molecular Formula[b] | Ir(KBr) ν max ($cm^{-1}$) | Analysis % observed C,H (calcd C,H) |
|---|---|---|---|---|---|
| **5a** | 73.4 | 130–131 | $C_{21}H_{22}O_5$ (354.41) | 1715 | 70.98, 6.31 (71.17, 6.26) |
| **5b** | 70.3 | 174–175 | $C_{22}H_{24}O_6$ (384.43) | 1730 | 68.59, 6.21 (68.74, 6.29) |
| **5c** | 67.6 | 126–127 | $C_{23}H_{26}O_7$ (414.46) | 1710 | 66.56, 6.39 (66.65, 6.32) |
| **5d** | 69.3 | 168–169 | $C_{22}H_{22}O_7$ (398.42) | 1715 | 66.22, 5.48 (66.32, 5.57) |

[a]Uncorrected, measured using Mettler FP5 apparatus or a Boetius microheating table.
[b]Satisfactory microanalyses obtained: C±0.23, H±0.11.

The dihydropyranoflavones **7a–7d** were dehydrogenated with DDQ in dioxane to give pyranoflavones **2**, **3**, **8**, and **9** (Scheme 1), and spectral studies supported the assigned structures (Table 4). The olefinic protons on C-9 and C-10 of **3** appeared as a clear AB system in the $^1H$ nmr, each with a coupling constant of 10 Hz, characteristic of the cis protons on olefinic carbon atoms. The 'benzylic' protons appeared substantially downfield at δ 6.32, and the other olefinic proton appeared at δ 5.62 ppm. These signals are calculated to appear at δ 6.50 ppm and 5.60 ppm, respectively, by the rule of additivity of olefinic protons (21).

## EXPERIMENTAL

Melting points were determined on a Boetius microheating table or Mettler FP 5 apparatus and are uncorrected. Chromatography was performed on columns of Si gel (Merck, 60–120 mesh). Analytical tlc was performed on Si gel-G (Merck). Ir spectra were recorded on a Perkin-Elmer 597 spectrophotometer in KBr and Nujol. $^1H$-nmr spectra were recorded on a Varian EM-360 (90 MHz), XL 100 (80 MHz), and General Electric QE-300 (300 MHz) spectrometers in $CDCl_3$. $^{13}C$-nmr spectra were obtained on General Electric QE-300 (75 MHz) and VXR-300 standard (75 MHz) spectrometers. Chemical shifts for both the $^1H$ nmr and $^{13}C$ nmr are reported downfield from TMS, and coupling constants are in Hertz. Microanalyses were performed on Carlo Erba 1106 and Perkin-Elmer Model 240 CHN analysers.

SYNTHESIS OF DIHYDROPYRANOFLAVONES BY BAKER-VENKATARAMAN REARRANGEMENT.—*Preparation of O-aroyl esters.*—A mixture of 6-acetyl-5-hydroxy-7-methoxy-2,2-dimethylchroman [**4**] (5 mmol) and aroyl chloride (5 mmol) in pyridine (5 ml) was heated on a boiling $H_2O$ bath for 2 h, cooled, and treated with cold diluted 50% aqueous HCl solution (50 ml). The separated solid was filtered, dried, and recrystallized from EtOH as colorless prisms. The physical and spectral data of *O*-aroyl esters are listed in Table 1.

*Rearrangement of the O-aroyl esters.*—To a mixture of 6-acetyl-5-*O*-aroyl-7-methoxy-2,2-dimethylchroman (3 mmol) and powdered KOH (1.13 g) was added pyridine (5 ml). The contents were stirred well for 3 h at 60°, and the resulting yellow viscous mass was acidified with diluted HCl. The solid β- diketone thus obtained was filtered, dried, and crystallized from petroleum ether/EtOAc as yellow needles. The physical and spectral data of β-diketones are listed in Table 2.

*Cyclization of the diaroylmethanes.*—A solution of diaroylmethane (1.5 mmol) in EtOH (30 ml) containing a few drops of concentrated $H_2SO_4$ was refluxed for 2 h, concentrated, and poured onto ice-$H_2O$. A colorless solid separated. The solid was filtered, dried, and purified by recrystallization from $CHCl_3$. The physical and spectral data of dihydropyranoflavones are listed in Table 3.

*Dehydrogenation of dihydropyranoflavones.*—A solution of the dihydropyranoflavone (1 mmol) in dioxane (20 ml) containing DDQ (1 mmol) was refluxed on an oil bath for 5 h, cooled, and filtered to remove the hydroquinone. The solvent was stripped from the filtrate, and the resulting residue was subjected to cc over Si gel. The pyranoflavones resulted from eluting with 15% EtOAc/petroleum ether. The physical and spectral data of pyranoflavones are presented in Table 4.

TABLE 2. Data for β-Diketones **6a–6d**.

| Compound (keto:enol) | Mp (solvent) | Yield (%) | Ir (KBr) ν max ($cm^{-1}$) | Molecular Formula | Analysis % observed C,H (calcd C,H) | Mass $[M]^+$ (m/z) | $^1H$ nmr ($CDCl_3$), δ ppm J in Hz |
|---|---|---|---|---|---|---|---|
| **6a** (1:3) | 117–118 (Petroleum ether/ EtOAc) | 35 | 1650, 1610 | $C_{21}H_{22}O_5$ | 71.14, 6.19 (71.17,6.26) | 354 | 1.35, 1.37 (2s, 6H, 2-$Me_2$), 1.80, 2.62 (2t, 4H, $J$=7), 3.89 (s, 3H, 7-OMe), 4.55 (s, 2H, $COCH_2CO$), 5.91 (s, 1H, olefinic), 7.67 (m, 7H, six arom-H and 7-OH), 13.78 (s, 1H, enolic OH) |
| **6b** (2:1) | 139–140 (Petroleum ether/ EtOAc) | 32 | 1660, 1620 | $C_{22}H_{24}O_6$ | 66.76, 6.29 (66.65, 6.32) | 384 | 1.43, 1.45 (2s, 6H, 2-$Me_2$), 1.72, 2.55 (2t, 4H, $J$=7), 3.40, 3.80 (2s, 6H, 7-OMe and 4′-OMe), 4.45 (s, 2H, $COCH_2CO$), 5.70 (s, 1H, H-8), 5.85 (s, 1H, olefinic), 6.90 (d, 2H, H-3′ and H-5′, $J$=9), 7.90 (d, 2H, H-2′ and H-6′, $J$=9), 10.95 (s, 1H, 7-OH), 15.60 (s, 1H, enolic OH) |
| **6c** (1:6) | 219–220 (Petroleum ether/ EtOAc) | 35 | 1670, 1610 | $C_{23}H_{26}O_7$ | 66.79, 6.29 (66.65, 6.32) | 414 | 1.35, 1.36 (2s, 6H, 2-$Me_2$), 1.79, 2.61 (2t, 4H, $J$=7), 3.46, 3.94, 3.97 (3s, 9H,7-OMe, 3′- OMe, 4′- OMe), 4.52 (s, 2H, -$COCH_2CO$), 5.76 (s, 1H, H-8), 5.91 (s, 1H, olefinic), 6.92 (d, 1H, H-5′, $J$=10), 7.55 (s, 1H, H-2′), 7.56 (d, 1H, H-6′, $J$=10), 13.78 (s, 1H, enolic OH), 14.09 (s, 1H, 7-OH) |
| **6d** (1:6) | 148–149 (Petroleum ether/ EtOAc) | 37 | 1650, 1620 | $C_{22}H_{22}O_7$ | 66.23, 5.59 (66.32, 5.57) | 398 | 1.43, 1.45 (2s, 6H, 2-$Me_2$), 1.80, 2.70 (2t, 4H, $J$=7), 3.90 (s, 3H, 7-OMe), 4.60 (s, 2H, $COCH_2CO$), 5.90 (s, 1H, olefinic), 6.05 (s, 2H, $OCH_2O$), 7.05 (m, 3H, H-5′, H-6′, and 5-OH), 7.75 (s, 2H, H-8 and H-2′), 14.75 (s, 1H, enolic OH) |

TABLE 3. Data for Dihydropyranoflavones **7a–7d**.

| Compound | Mp[a] | Yield (%) | Ir (KBr) $\nu$ max ($cm^{-1}$) | Molecular Formula[b] | Analysis % observed C,H (calcd C,H) | Mass $[M]^+$ (*m/z*) | $^1H$ nmr ($CDCl_3$), $\delta$ ppm *J* in Hz |
|---|---|---|---|---|---|---|---|
| **7a**[c] | 205–206 | 63 | 1640 | $C_{21}H_{20}O_4$ (336.69) | 74.91, 5.90 (74.98,5.99) | 336 | 1.43 (s, 6H, 2-$Me_2$), 1.94, 2.97 (2t, 4H, *J*=7), 3.95 (s, 3H, 5-OMe), 6.33 (s, 1H, H-6), 6.73 (s, 1H, H-3), 7.53 (m, 3H, H-3′, H-4′, and H-5′), 7.90 (m, 2H, H-2′ and H-6′) |
| **7b** | 219–220 | 69 | 1635 | $C_{22}H_{22}O_5$ (366.42) | 72.20, 5.99 (72.12, 6.05) | 366 | 1.35 (s, 6H, 2-$Me_2$), 1.85, 2.90 (2t, 4H, *J*=7), 3.82, 3.88 (2s, 6H, 5-OMe and 4′-OMe), 6.23 (s, 1H, H-6), 6.54 (2s, 1H, H-3), 6.93 (d, 2H, H-3′ and H-5′, *J*=9), 7.75 (d, 2H, H-2′ and H-6′, *J*=9) |
| **7c** | 355–356 | 67 | 1630 | $C_{23}H_{24}O_6$ (396.44) | 69.49, 6.01 (69.68, 6.10) | 396 | 1.30 (s, 6H, 2-$Me_2$), 1.80, 2.82 (2t, 4H, *J*=7), 3.85 (s, 9H, 5-OMe, 3′-OMe, 4′-OMe), 6.20 (s, 1H, H-6), 6.50 (s, 1H, H-3), 6.85 (d, 1H, H-5′, *J*=10), 7.25 (s, 1H, H-2′), 7.40 (d, 1H, H-6′, *J*=10) |
| **7d** | 279–280 | 65 | 1635 | $C_{22}H_{20}O_6$ (380.40) | 69.30, 5.24 (69.46, 5.30) | 380 | 1.50 (2s, 6H, 2-$Me_2$), 1.93, 2.95 (2t, 4H, *J*=7), 3.95 (s, 3H, 5-OMe), 6.10 (s, 2H, $OCH_2O$), 6.35 (s, 1H, H-6), 6.60 (s, 1H, H-3), 6.90 (d, 1H, H-5′, *J*=10), 7.35 (s, 1H, H-2′), 7.50 (d, 1H, H-6′, *J*=10) |

[a]Uncorrected, measured using Mettler FP5 apparatus or a Boetius microheating table.

[b]Satisfactory microanalyses obtained: C±0.23, H±0.11.

[c]$^{13}C$-nmr data for **7a**: 16.886 (C-10), 26.639 (8-$Me_2$), 31.873 (C-9), 56.259 (OMe), 75.993 (C-8), 96.982 (C-6), 101.380 (C-4a), 108.833 (C-3 and C-102), 125.781 (C-2′ and C-6), 128.951 (C-3′ and C-5′), 131.071 (C-4′), 131.824 (C-1′), 159.300 (C-2), 159.125 (C-6a), 159.996 (C-5, C-10b) and 177.947 ($C_4$=O) ppm.

TABLE 4. Data for Pyranoflavones **2**, **3**, **8**, and **9**.

| Compound | Mp (Lit. mp) | Yield (%) | Ir $\nu$ max ($cm^{-1}$) | Molecular Formula | Analysis % observed C,H (calcd C,H) | $^1$H nmr ($CDCl_3$), $\delta$ ppm, $J$ in Hz |
|---|---|---|---|---|---|---|
| **2** | 213–214 (215–216) (13, 22) (204–205) (23) | 66 | 1635 (Nujol) | $C_{21}H_{18}O_4$ (334.38) | 75.54, 5.38 (75.43, 5.43) | 1.56 (s, 6H, 2-$Me_2$), 4.00 (s, 3H, 5-OMe), 5.70 (d, 1H, H-9, $J$=10), 6.45 (s, 1H, H-3), 6.85 (s, 1H, H-6), 7.00 (d, 1H, H-10, $J$=10), 7.60 (m, 3H, H-3, H-4′, and H-5′), 8.30 (m, 2H, H-2′ and H-6′) |
| **3** | 208–209 (207–209) (24) | 63 | 1660 (KBr) | $C_{22}H_{20}O_5$ (364.40) | 72.43, 5.51 (72.51, 5.53) | 1.50, (s, 6H, 2-$Me_2$), 3.88 and 3.95 (2s, 6H, 4′-OMe and 5-OMe), 5.62 (d, 1H, H-9, $J$=10), 6.32 (s, 1H, H-6), 6.58 (s, 1H, H-3), 6.84 (d, 1H, H-10, $J$=10), 7.01 (d, 2H, H-3′ and H-5′, $J$=9), 7.81 (d, 2H, H-2′ and H-5′, $J$=9) |
| **8** | 194–195 (194–196) (24) | 68 | 1660 (KBr) | $C_{23}H_{22}O_6$ (394.43) | 70.15, 5.71 (70.04, 5.62) | 1.52 (s, 6H, 2-$Me_2$), 3.97, 3.98 (2s, 9H, 3′-OMe, 4′-OMe, and 5-OMe), 5.63 (d, 1H, H-9, $J$=10), 6.34 (s, 1H, H-6), 6.60 (s, 1H, H-3), 6.83 (d, 1H, H-10, $J$=10), 6.98 (d, 1H, H-5′, $J$=9), 7.32 (s, 1H, H-2′), 7.51 (d, 1H, H-6′, $J$=9) |
| **9** | 240–241 (242–244) (10, 21) | 61 | 1650 (KBr) | $C_{22}H_{18}O_6$ (378.39) | 69.93, 4.72 (69.84, 4.79) | 1.55, (s, 6H, 2-$Me_2$), 3.95 (s, 3H, 5-OMe), 5.60 (d, 1H, H-9, $J$=10), 6.05 (s, 2H, $OCH_2O$), 6.25 (s, 1H, H-6), 6.50 (s, 1H, H-3), 6.80 (d, 1H, H-10, $J$=10), 7.25 (m, 3H, arom) |

## LITERATURE CITED


1. K. Venkataraman, in: "The Flavanoids Part I." Ed. by J.B. Harborne, T.J. Mabry, and H. Mabry, Academic Press, New York, 1975, pp. 267–295.
2. E. Wollenweber, in: "The Flavanoids—Advances in Research" Ed. by J.B. Harborne and T.J. Mabry, Chapman and Hall, New York, 1982, pp. 189–260.
3. M.D. Bently, A. Hassanali, W. Lwande, P.G.W. Nioroge, E.N. Ole Sitayo, and M. Yatagai, *Insect. Sci. Its Appl.*, **8**, 85 (1987); *Chem. Abstr.*, **108**, 128914s (1988).
4. A. Banerji and D.L. Luthria, *Indian J. Chem., Sect. B*, **29**, 163 (1990).
5. Y. Kimura and K. Yoshiyuki, Jpn. Kokai Tokkyo Koho JP 61,291,526 [86,291,526] (1986); *Chem. Abstr.*, **106**, 155104t (1987).
6. J. Hlubucek, E. Ritchie, and W.C. Taylor, *Aust. J. Chem.*, **24**, 2347, 2355 (1971).
7. V.K. Ahluwalia, A. Jain, C. Prakash, and S. Bala, *Indian J. Chem., Sect. B*, **21**, 101 (1982).
8. A. Islam, R.K. Gupta, and M. Krishnamurthy, *Indian J. Chem., Sect. B*, **20**, 21 (1981).
9. K. Subrahmanyam, J.M. Rao, K.V.J. Rao, and T.S. Ramesh, *Indian J. Chem., Sect. B*, **14**, 339 (1976).
10. S.B. Malik, P. Sharma, and T.R. Seshadri, *Indian J. Chem., Sect. B*, **15**, 539 (1977).
11. A.C. Jain, R.G. Gupta, and A. Gupta, *Indian J. Chem., Sect. B*, **19**, 101 (1980).
12. A. Banerji and N.C. Goomer, *Synth. Commun.*, **15**, 1165 (1985).
13. D. Roy, N.N. Sharma, and R.N. Khanna, *Indian J. Chem., Sect. B*, **15**, 1138 (1977).
14. D. Roy, N.N. Sharma, and R.N. Khanna, *Indian J. Chem., Sect. B*, **16**, 463 (1978).
15. K.J. Rajendra Prasad, C.S. Rukmani Iyer and P.R. Iyer, *Indian J. Chem., Sect. B*, **22**, 278 (1983).
16. K.J. Rajendra Prasad, "Studies in Oxygen Heterocycles," Ph.D. Thesis, ITT, Bombay, India, 1982.
17. S.S. Chibber and S.K. Dutt, *Phytochemistry*, **20**, 1460 (1981).
18. L. Farkas, J. Strelisky, and B. Vermes, *Chem. Ber.*, **102**, 112 (1969).
19. K. Fukui, M. Nakayama, and T. Horie, *Bull. Chem. Soc. Jpn.*, **43**, 1524 (1970).
20. G. Devi, R.S. Kapil, and S.P. Popli, *Indian J. Chem., Sect. B*, **17**, 75 (1979).
21. U.E. Matter, E. Pascal, A.P. Pretch, A. Pross, W. Simen, and S. Sternhell, *Tetrahedron*, **25**, 691 (1969).
22. F.R. Garcez, S. Sramin, M.C. Nascimento, and W.B. Mors, *Phytochemistry*, **27**, 1079 (1988).
23. K. Subrahmanyam, J.M. Rao, and K.V.J. Rao, *Indian J. Chem., Sect. B*, **15**, 105 (1977).
24. A. Banerji, D.L. Luthria, and B.R. Prabhu, *Phytochemistry*, **27**, 3637 (1988).


*Received 11 May 1992*