CHEMICAL CONSTITUENTS OF *CASEARIA GRAVEOLENS*: SOME NOVEL REACTIONS AND THE PREFERRED MOLECULAR CONFORMATION OF THE MAJOR COUMARIN, MICROMELIN

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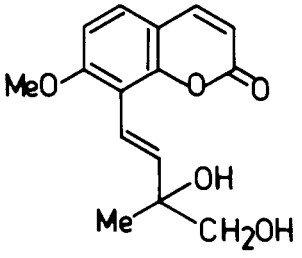
ABSTRACT.—The tree bark of *Casearia graveolens* (Samydaceae) afforded the new coumarin, casegravol (**1**) (yield 0.002%), along with three other coumarins: micromelin (**2**) (0.16%), scopoletin (0.006%). and bergapten (0.004%), as well as β-sitosterol (0.02%). This is the first report of the isolation of coumarins from Samydaceae. nOe studies of micromelin (**2**) have been used to determine its preferred molecular conformation (**3**) in terms of which the stability of the epoxy group toward 5% oxalic acid or 70% $HClO_4$ or BF_3-MeOH has been explained. Conversion of (**2**) into the dihydrobenzofuran derivatives(**4**) and (**5**), the chlorohydrins (**6**) and (**7**), the bromohydrin (**8**), the reduction product (**9**), and the epoxy ester (**10**) offered cogent chemical evidence in support of its structure and relative stereochemistry. The mass fragmentations of **2** and its reaction products have been rationalized.

Earlier we reported the isolation and structure elucidation (1) of a new monomeric coumarin casegravol (**1**) from the tree bark of *Casearia graveolens* Dalz. (Samydaceae). We now place on record the isolation and characterization of all the constituents of the plant material and report some interesting reactions of the major coumarin micromelin (**2**) in support of its structural and stereochemical features (2). The preferred molecular conformation (**3**) which presumably is responsible for the relatively stable nature of the epoxide ring has also been delineated from its nOe studies (2).



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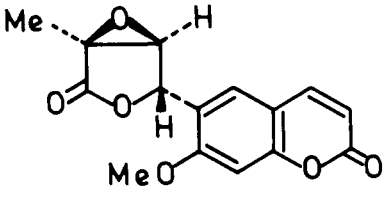

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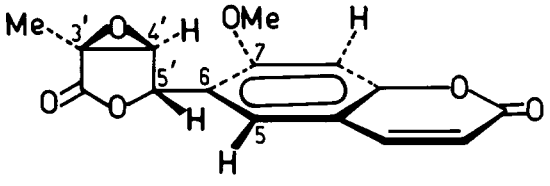

(3)

DISCUSSION

Careful chromatography of the petroleum ether and chloroform extracts of the tree bark of *C. graveolens* over silica gel afforded a new monomeric coumarin casegravol (**1**) (0.002%) in addition to three other coumarins: micromelin (3) [=micromelumin (4)]

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in an excellent yield (0.16%), scopoletin (0.006%), and bergapten (0.004%), as well as β-sitosterol (0.02%).

The structure of micromelin (**2**), isolated from the leaves of *Micromelum minutum* (Forst. f.) Seem (3) and *Micromelum pubescens* Blume (4) (Rutaceae) was settled earlier, mainly on the basis of spectral analysis and biogenetic ground (3,4) and some chemical reactions (3). The relative stereochemistry of **2** was settled as H-5′/H-4′ *trans* and H-4′/3′-CH_3 *cis* from its ^{1}H-nmr spectral analysis. Its structure was recently confirmed (5) by detailed ^{13}C-nmr studies and by conversion to the corresponding butenolide (deoxymicromelin) by refluxing with Zn-Cu in ethanol. Observance of significant nOe[2] for [3′-CH_3] (δ 1.67) ↦ H-4′ (δ 4.04) (19%) confirmed their *cis* orientation—a conclusion further reinforced by the occurrence of nOe for [H-4′] ↦ 3′CH_3 (9%). Appreciable nOe was observed for [H-4′] ↦ H-5′ (δ 5.57) (7%) and for [H-5′] ↦ H-4′ (5%) signals indicating their proximity (ϕ 90°; 2.75 Å apart as measured on Dreiding model), though *trans* disposed (6). However, absence of nOe between 3′-CH_3 and H-5′ signals ruled out the alternative formulation of micromelin with C-4′ carrying the CH_3 group.

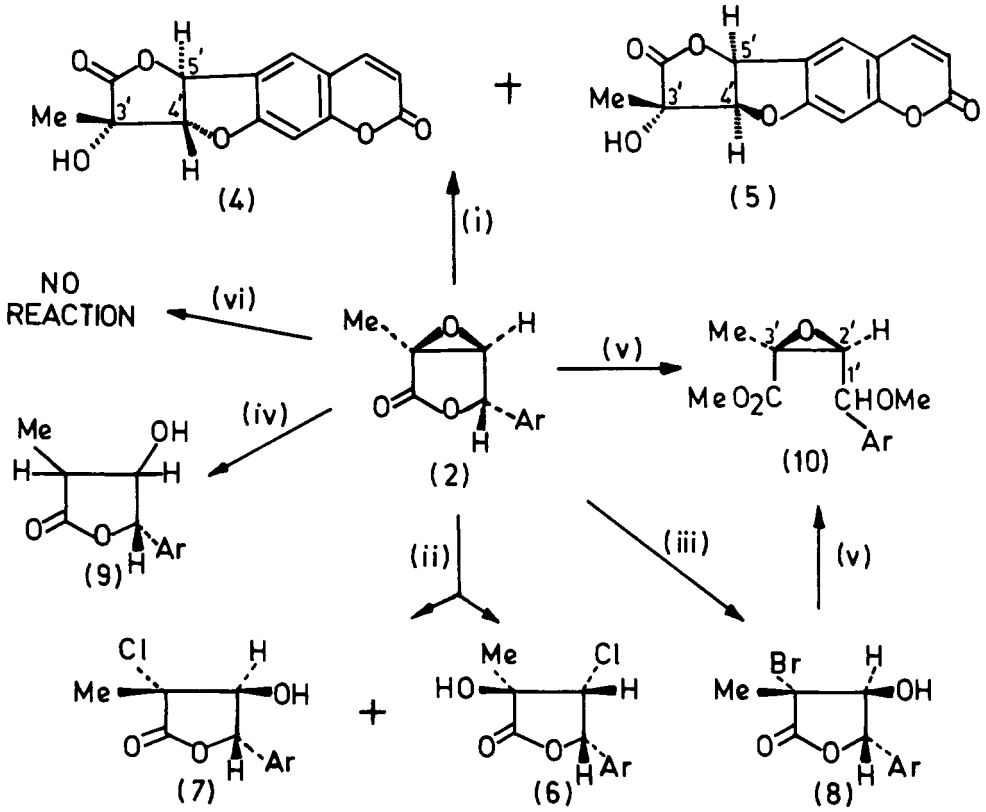
Sufficient nOe for [H-5′] ↦ H-5 (δ 7.38) (13%) showed their proximity, which was only possible if the benzene ring of the coumarin residue and the γ-lactone ring were approximately in perpendicular planes with C-5 H and C-5′ H bonds *syn* coplanar allowing H-5 and H-5′ to come quite close to each other (**3**) (2.45 Å as measured in Dreiding model). On the other hand, absence of nOe between signals at δ 7.38 (H-5) and δ 4.04 (H-4′) (~3.8 Å apart) as well as between signals at δ 4.04 and 3.96 (7-OCH_3) supported this preferred molecular conformation (**3**) for micromelin (**2**) and ruled out either of the two possible conformations in which the benzene ring and γ-lactone ring approach coplanarity. The presence of nOe for [7-OCH_3] ↦ H-8 (δ 6.88) (10%) indicating their *ortho* location and, thus, confirmed the assignment of the H-8 signal. The nOe studies unambiguously confirmed the relative stereostructure (**2**) and settled its preferred molecular conformation (**3**). The absolute configuration, however, still remains unsettled.

Attempts to open the epoxide ring present in the pendant five-membered lactonic moiety in **2** with 5% oxalic acid in dioxane or aqueous solution, or with 70% perchloric acid in dioxane solution, or with boron trifluoride in methanol met with failure. Also, **2** did not form any iodohydrin when treated with sodium iodide in presence of sodium acetate in acetic acid (7). The stability of the epoxy ring of micromelin seems to stem from a combination of at least two steric factors: (a) the preferred conformation (**3**) of micromelin has a freely rotating methoxyl group on the backside of the epoxide ring, which offers steric interference to nucleophilic attack, particularly at 4′ position, (b) the bond-eclipsing strain arising in the five-membered lactone after opening of the epoxide ring more than offsets the angle strain present in it (8). With boron tribromide, micromelin (**2**) formed a mixture of the dihydrobenzofuran derivatives **4** and **5** in the ratio of 5:3 (^{1}H-nmr evidence), which could not be separated. This reaction demonstrated the role of the conformational factor in this acid-catalyzed epoxide ring opening. Demethylation of **2** generated the phenolic hydroxyl group ideally placed to engage itself in an attack at C-4′ carbonium ion formed from the initial adduct of the boron tribromide with the epoxy oxygen (9), thus finally giving a mixture of **4** and **5** as revealed from the ^{1}H-nmr as well as from ms data of the mixture (M^+ 274). Upon refluxing with concentrated hydrochloric acid in methanol, micromelin furnished a mixture of chlorohydrins **6** and **7** in the ratio of 2:1 (^{1}H-nmr). The *cis* orientation of H-4′ and H-5′ in **6** was revealed from its ^{1}H-nmr spectra. The crude product significantly dis-

[2]Proton signals saturated are shown in square brackets and enhancement of the intensity in parentheses.

played, in addition to H-4′ and H-5′ of **6**, two signals at δ 4.67 and 6.13 (each d, $J=2$ Hz) attributable to two approximately *trans* disposed H-4′ and H-5′, respectively, of the isomeric chlorohydrin (**7**). It is worthwhile to mention here that no vicinal glycol monomethyl ether was obtained by methanolysis of epoxide. Besides the fact that methyl alcohol in acid medium is less likely to attack due to its poor nucleophilicity, it will also face stronger steric hindrance towards approach at 4′ position by the eclipsed 3′-CH_3 because of its greater steric bulk compared with chloride ion. The exclusive formation of bromohydrin (**8**) by reaction of **2** with hydrobromic acid also corroborates this argument. The structure of bromohydrin followed from its spectral properties, and facile formation of an acetate (M^+ 410, 412). The larger bromide ion exclusively attacks 3′ position, although it is electronically unfavorable, inasmuch as attack at 4′ position seems to be prevented by 3′-CH_3 through an eclipsing effect.

Selective reductive cleavage of the epoxide group in presence of γ-lactone by zinc

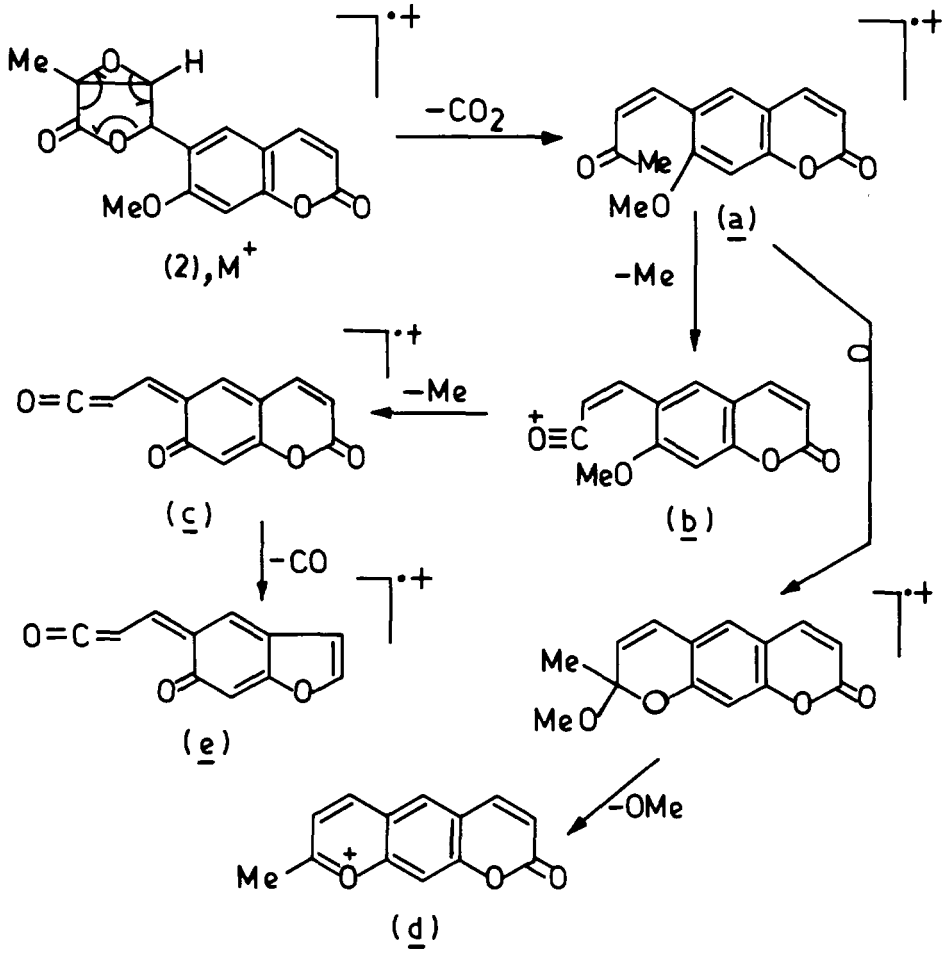


Ar=7-Methoxy-6-coumarinyl

SCHEME 1. (i) BBr_3; (ii) HCl, MeOH, reflux; (iii) HBr; (iv) Zn, MeOH, CH_3CO_2H; (v) 2% KOH-MeOH, $H_3\overset{+}{O}$; CH_2N_2 (vi) $BF_3{\cdot}Et_2O$ or 70% $HClO_4$ or 5% Oxalic acid.

dust in methanol in the presence of a trace of acetic acid led to the isolation of the alcohol **9**. The exclusive formation of this secondary alcohol by reductive cleavage of α,β-epoxy lactone system in **2** appears to be analogous to reduction of α-halo, α-amino, α-acyloxy, and α-hydroxy ketones under similar conditions. Micromelin, in which the epoxy group is perpendicular to the plane of the lactonic carbonyl also satisfies the stereoelectronic requirement of this type of reduction (10). Similar selective reductive ring opening of epoxides has been carried out by zinc dust in ethanol in the presence of a trace of acetic acid in sesquiterpene lactones (11).

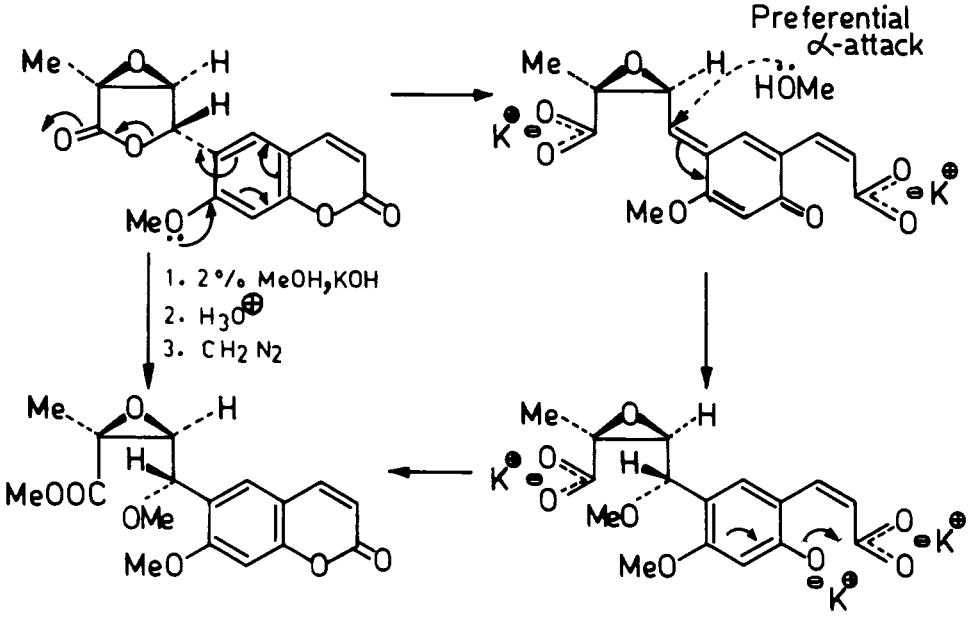
The mass fragmentation patterns of the chlorohydrin (**6**), bromohydrin (**8**), and the reduction product (**9**) are quite different from that of **2**. The high resolution mass spectrum of **2** with molecular ion at *m/e* 288.0624 ($C_{15}H_{12}O_6$) as the base peak, showed strong ion peaks at *m/e* 229.0488 (78%, $C_{13}H_9O_4$, *b*), 214.0401 (21.2%, $C_{12}H_6O_4$, *c*), 213.055 (63.1%, $C_{13}H_9O_3$, *d*) and 186.0299 (21.2%, $C_{11}H_6O_3$, *e*). These peaks were notably absent or insignificant in the mass spectra of (**6**), (**8**), and (**9**). The collapse of the lactonic epoxide moiety in the side chain of **2** with loss of carbon dioxide gave rise to the ion peak at *m/e* 244.0758 (10.1%, $C_{14}H_{12}O_4$, *a*), which readily underwent loss of a CH_3 group to generate a highly stabilized fragment ion (*b*). The genesis of other important peaks is rationalized in scheme 2. In contrast, (**6**), (**8**), and (**9**), in which the epoxide ring opened up, showed base peak at *m/e* 205.



SCHEME 2. *Mass fragmentation of (2).*

Treatment of **2** with 2% methanolic potassium hydroxide, followed by esterification of the resultant acid with diazomethane, afforded a yellowish white crystalline product, 6-(3′-carbomethoxy-2′,3′-epoxy-1′-methoxybutyl)-7-methoxycoumarin (**10**). This was presumably formed by the alkyl oxygen cleavage of the γ-lactone assisted by benzylic nature of 5′ position and the electron releasing 7-OCH_3, followed by methanolysis of the resonance stabilized incipient benzylic carbonium ion having an *ortho* methoxy group. The release of strain in the epoxy-lactone ring might also act as a driving force for the unexpected lactonic alkyl-oxygen cleavage. Compound **10** was also

obtained by treating **8** with methanolic potassium hydroxide solution, followed by reaction with diazomethane. The bromohydrin (**8**) underwent facile ring closure to micromelin (**2**), which then formed **10**, as explained above. The formation of the chlorohydrins **6** and **7**, the bromohydrin (**8**), the reduction product (**9**), and the epoxy ester (**10**) from micromelin gave firm chemical support in favor of its formulation (**2**) and rules out any other possibility.



SCHEME 3.

The structures of all the above reaction products are consistent with their ir, ^{1}H-nmr, and ms data, as shown in the section below.

Micromelin was found to be resistant to hydrogenation in the presence of Pd-C catalyst. Prolonged action led to the isolation of a glassy mass of uncharacterized hydroxy acid presumably resulting from hydrogenolysis of the γ-lactone and the epoxide in **2**, as evident from the disappearance of the γ-lactone band in the reduction product and presence of a broad hydroxy band (3300-3380 cm^{-1}) and also from the consumption of diazomethane. However, a detailed study of the reduction product was precluded because of its extremely low solubility in common organic solvents.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All mps were determined in open capillaries and are uncorrected. The ir spectra were taken in potassium bromide discs. The ^{1}H-nmr spectra were recorded at 100 and 80 MHz with Varian HA-100 and CFT-20 instruments, respectively, using $CDCl_3$ as solvent and TMS as internal standard, unless otherwise specified; chemical shifts are reported in ppm. The ms were run at 70 eV in an AEI MS-50 instrument using direct insertion probe, unless otherwise stated. The optical rotations were measured with a Perkin-Elmer 241 polarimeter. The organic solutions were washed with saturated sodium sulfate and evaporated on water bath. Silica gel G (Merck) was used for analytical and preparative tlc. The identity of known compounds was verified by comparison with authentic samples (mixed mp, superimposable ir, and co-tlc).

PLANT MATERIAL.—The tree bark of *Casearia graveolens* was collected from Darjeeling, West Bengal, India.

EXTRACTION.—Dried and powdered tree bark (1 kg) of *C. graveolens* was extracted in a Soxhlet apparatus successively with petroleum ether (60-80°) and chloroform for 40 h in each case. The concentrates of the different extracts were chromatographed separately over silica gel.

Bergapten. Chromatography of the concentrate of the petroleum ether extract afforded a brown, gummy, solid residue from the petroleum ether-benzene (1:1) eluate fractions. Rechromatography of this solid over silica gel (100-200 mesh) using petroleum ether-benzene (1:1) as eluent furnished bergapten, crystallizing from methanol-ethyl acetate in fine needles (40 mg), mp 185°.

β-*sitosterol.* Chromatography of the concentrate of the petroleum ether extract gave from benzene eluate fractions β-sitosterol, crystallizing from chloroform-methanol as white flakes (85 mg), mp 135-7°, $[\alpha]_D$ −33° (*c* 0.42, $CHCl_3$).

Micromelin (**2**). The concentrate of the petroleum ether extract was chromatographed over silica gel (60-120 mesh). The green solid, obtained from the chloroform eluate fractions after rechromatography over silica gel (100-200 mesh) followed by crystallization from ethyl acetate-petroleum ether, afforded white crystals of **2** (600 mg), mp 214-5°, $[\alpha]_D$ −71.6° (*c* 0.49, $CHCl_3$), Rf 0.75 [chloroform-methanol (95:5)].

Scopoletin. The later chloroform eluate fractions of the main chromatogram of the concentrate of petroleum ether extract gave a solid showing an intense violet iodine staining spot [Rf 0.50, chloroform-methanol (95:5)] in addition to that of micromelin. Repeated chromatography of this solid over silica gel (100-200 mesh) followed by crystallization from chloroform-*n*-hexane furnished light yellow needles of scopoletin (40 mg), mp 202°.

Casegravol (**1**). The solid obtained from the chloroform-methanol (96:4) eluate fractions of the chromatogram of the petroleum ether extract was subjected to rechromatography over silica gel (100-200 mesh). The chloroform-methanol (98:2) eluate fractions furnished a solid that was crystallized from chloroform-*n*-hexane in fine yellowish-white needles of **1** (20 mg), mp 158°, $[\alpha]_D \pm 0°$ ($CHCl_3$).

The chloroform extract of the plant yielded additional amounts of micromelin (**2**) (1 g), scopoletin (20 mg), and β-sitosterol (115 mg).

DEMETHYLATION OF 2 TO A MIXTURE OF DIHYDROFURANOCOUMARINS (4) AND (5) WITH BORON TRIBROMIDE.—A solution of micromelin (**2**) (50 mg) in dichloromethane (20 ml) was allowed to react with boron tribromide (0.4 ml) at room temperature for 4 h with continuous stirring. The complex was then decomposed by pouring it into ice. The mixture was warmed on water bath for 0.5 h and then extracted with chloroform (3 x 10 ml). The residue left on evaporation of solvent was found to be a mixture of **4** and **5**, which could not be separated by repeated column or thin layer chromatographies and crystallizations (30 mg) ir, ν max (KBr) 3300 (OH), 1775 (γ-lactone), 1715, 1620, 1570 (coumarin); ^{1}H-nmr: (d_6-DMSO, 80 MHz) δ 1.86 (6H, bs, 2 x 3′-CH_3), 4.58 (d, *J*=2 Hz, H-4′ of **4**), 4.84 (d, *J*=6 Hz, H-4′ of **5**), 5.4 (d, *J*=6 Hz, H-5′ of **5**), 6.06 (d, *J*=2 Hz, H-5′ of **4**), 6.25 and 6.27 (each d, *J*=10 Hz, 2 x H-3), 6.81 (2H, s, s x H-8), 7.53 and 7.62 (each s, 2 x H-5), 7.99 and 8.04 (each d, *J*=10 Hz, 2 x H-4); 70 eV ms: *m/e* (%) 274 (9, M^+), 256 (13, M^+-H_2O), 230 (8, M^+-CO_2), 228 (33, *m/e* 256-CO), 212 (41, *m/e* 230-H_2O), 186 (100, *m/e* 212-C_2H_2), 158 (71); CI ms (run with ammonia): *m/e* 292 (100), 275 (32), 250 (18), 248 (12), 213 (30), 204 (64), 187 (15); CI ms (run with isobutane): *m/e* 275 (28), 233 (11), 231 (13), 213 (12), 105 (12), 191 (13), 187 (100).

Chlorohydrins (**6**) *and* (**7**). Concentrated hydrochloric acid (5 ml) was added to a solution of **2** (80 mg) in dry methanol (20 ml), and the mixture was refluxed for 3 h. The reaction mixture was cooled, and the solvent was removed *in vacuo*, to give a yellow gummy solid, which was dissolved in chloroform (10 ml), washed free from acid, and dried. Removal of the solvent afforded a white, amorphous material showing two close tlc spots [Rf 0.45 (major) and 0.40 (minor), chloroform-methanol (95:5)]. This crude material was chromatographed on thin layer with chloroform-ethylacetate (90:10) as the developing solvent. The less polar band gave a white, crystalline solid (**5**) (15 mg), mp 202-4°; ir, ν max (KBr) 3400 (OH), 1780 (γ-lactone), 1708, 1620 and 1560 (coumarin); ^{1}H-nmr: δ 1.82 (s, 3′-CH_3), 2.96) bs, 3′-OH, exchangeable with D_2O), 3.96 (s, 7-OCH_3), 4.77 (d, *J*=4 Hz, H-4′), 6.10 (d, *J*=4 Hz, H-5′), 6.27 (d, *J*=10 Hz, H-3), 6.84 (s, H-8), 7.54 (s, H-5) and 7.66 (d, *J*=10 Hz, H-4); ms: *m/e* (%) 326, 324 (12.55, 38.79; M^+), 288 (3.60, M^+-HCl), 244 (5.16, *m/e* 288-CO_2 from γ-lactone side chain), 229 (1.81, *m/e* 244-3′-CH_3), 206 (12.44), 205 (100, ArCH=OH, formed by simultaneous benzylic 4′-5′ and O=C(2′)-O bond cleavages and loss of 3′-OH, initiated by electron release of 4′-Cl atom and subsequent H capture); 204 (18.67, $ArCHO^+$), 203 (100.11, ArC≡O), 189 (1.81), 1.87 (5.31), 176 (1.37), 175 (5.47, M^+-side chain), 159 (2.20), 131 (1.27)) (analysis: found: C, 55.32; H, 3.96; Cl, 10.3, $C_{15}H_{13}O_6Cl$ requires C, 55.47; H, 4.01; Cl, 10.9%).

Bromohydrin (**8**). A solution of **2** (30 mg) in chloroform (10 ml) was stirred with 48% hydrobromic acid (5 ml) for 4 h in nitrogen atmosphere. The reaction mixture was poured into ice-cold water (50 ml) and extracted with chloroform (2 x 10 ml). The chloroform layer was washed free from acid and dried. The residue left on evaporation of the solvent gave a white material showing a single tlc spot [Rf 0.4, chloroform-methanol (95:5)]. It was chromatographed and crystallized from chloroform-*n*-hexane to yield white crytals of bromohydrin (**8**) (25 mg, yield 65%), mp 242°; ir, ν max (KBr) 3370 (OH); 1785 (γ-lactone), 1715, 1625 and 1565 cm^{-1} (coumarin); ^{1}H-nmr: δ 2.00 (3′-CH_3), 2.4 (bs, 4′-OH, exchangeable

with D_2O), 3.99 (7-OCH_3), 4.78 (bs, w½=6 Hz, H-4'), 6.12 (bs, partially merged with H-3, H-5'), 6.17 (d, J=10 Hz, H-3), 6.84 (s, H-8), 7.58 (s, H-5), 7.59 (d, J=10 Hz, H-4); ms: *m/e* (%) 3.68, 370 (39, 39; M^+), 288 (29, M^+-Hbr), 272 (14.5 *m/e* 288-0), 243 (13), 229 (2), 206 (66), 205 (100), 204 (16), 203 (32), 189 (10), 187 (12), 175 (31), 159 (9).

REDUCTION OF **2** WITH ZINC DUST IN METHANOL IN PRESENCE OF TRACE OF ACETIC ACID TO **9**.—To a stirred solution of **2** (82 mg) in dry methanol (25 ml) was added zinc dust and glacial acetic acid (0.15 ml). The reaction mixture was refluxed for 3 h (monitored by tlc), cooled, and filtered. The filtrate was concentrated *in vacuo*, diluted with ethyl acetate (80 ml), and then successively washed with 10% hydrochloric acid, 5% sodium bicarbonate, and saturated sodium chloride solution, and was finally dried. The solvent was removed *in vacuo*, yielding a crude solid, which was chromatographed on thin layer with chloroform-ethyl acetate (94:6) as the developing solvent over silica gel to yield shining white crystals of **9** (42 mg, yield 51%), mp 194°, Rf 0.5 [chloroform-methanol (95:5)]; ir ν max (KBr): 1705, 1620, 1570 (coumarin), 1780 (γ-lactone), 3340 cm^{-1} (OH); ^{1}H-nmr: (80 MHz, $CD_3CO\,CD_3$) δ 1.19 (d, J=7.3 Hz, 3'-CH_3), 3.91 (s, 7-OCH_3), 4.00-4.35 (m, H-3' and H-4'), 5.02 (bs, 4'-OH; disappeared on D_2O shake), 5.25 (d, J=5 Hz, H-5'), 6.16 (d, J=9.5 Hz, H-3), 6.90 (s, H-8), 7.56 (s, H-5), 7.84 (d, J=9.5 Hz, H-4); ms: *m/e* (%) 290 (38.5, M^+), 272 (0.7, M^+-H_2O), 206 (12.7), 205 (100, $ArCH=\overset{+}{O}H$; formed by C(2)-C(1')O bond cleavage and capture of 3'-H by O(1') and subsequent benzylic 4'-5' bond cleavage), 204 (10.8, $ArCHO^+$), 203 (6, $ArC\equiv\overset{+}{O}$), 189 (4.9), 187 (5.7), 186 (3.8), 176 (3.1), 175 (9.3, M^+ − side chain), 159 (3.4), 158 (3.4), 131 (2.3); (analysis: found C; 62.05; H, 4.74. $C_{15}H_{15}O_6$ requires: C, 62.06; H, 4.83%).

6-(3'-CARBOMETHOXY-2'-EPOXY-1'-METHOXY BUTYL)-7-METHOXYCOUMARIN (**10**).—Micromelin (**2**) (100 mg) was kept overnight with 2% methanolic potassium hydroxide (10 ml) and the resulting deep yellow reaction mixture was neutralized with dilute hydrochloric acid in cold and was then slightly acidified. Extraction with chloroform (3 x 15 ml), drying, and removal of solvent furnished a white, gummy residue. Repeated attempts to crystallize this material, even after chromatography, failed.

To the dry methanolic solution (25 ml) of the combined residue obtained from the chromatography fractions was added an ether solution of diazomethane in excess, until the solution retained a permanent yellow color. Usual work-up gave a yellow residue, which was then chromatographed. The chloroform-methanol (98:2) eluate fractions were evaporated to give a residue crystallized from light petrol-chloroform mixture as yellowish-white prismatic needles of **10** (39 mg, yield 34%), mp 150°, $[\alpha]^{20}D$ −8.2° (*c* 0.73); ir, ν max (KBr) 1735, 1615, 1565 (coumarin); ^{1}H-nmr: δ 1.50 (s, 3'-CH_3), 3.18 (d, J=6 Hz, H-2'), 3.39 (s, 1'-OCH_3), 3.74 (s, 3'-$COOCH_3$), 3.86 (s, 7-OCH_3), 4.65 (d, J=6 Hz, H-1'), 6.27 (d, J=10 Hz, H-3), 6.80 (s, H-8), 7.50 (1H, s, H-5), 7.65 (d, J=10 Hz, H-4); ms: *m/e* (%) 334 (7, M^+), 303 (6, M^+-OMe from 3'-CO_2Me), 275 (10, *m/e* 303-CO), 259 (5, *m/e* 275-CO), 247 (8, *m/e* 275-CO), 232 (19, $ArCH(OMe)=CH_2^+$), 219 (100 $ArCHOMe^+$, benzylic 1'-2' bond cleavage), 203 (8, $ArC\equiv O$), 201 (20, *m/e* 232-OMe; m* 174.1), 189 (7), 176 (8), 175 (10, M^+-side chain), 159 (7), 145 (6), 131 (6), 115 (7, $MeO_2C(Me)C\overset{O}{\frown}C^+$), 102 (6, $(MeCOCO_2Me^+$); charge retention in the eliminated side chain during the genesis of *m/e* 232 gives this fragment ion) (analysis: found: C, 61.07, H, 5.28, $C_{17}H_{18}O_7$ requires: C, 61.08; H, 5.39%).

CONVERSION OF BROMOHYDRIN (**8**) TO **10**.—The bromohydrin (**8**) (8 mg) was kept overnight with 2% methanolic potassium hydroxide (3 ml). The reaction mixture was worked up as before, and the material so obtained was dissolved in methanol (5 ml) and treated with diazomethane in an ether solution. The product was worked up in the usual way to afford **10**.

HYDROGENATION OF (**2**).—A solution of (**2**) (80 mg) in ethanol (25 ml) was stirred for 3 h in presence of 10% Pd-C (20 mg) in an atmosphere of hydrogen at little over 1 atm (780 mm of Hg). Usual work-up gave a white, glassy mass, Rf 0.3 [chloroform-methanol (90:10)].

A dry methanolic solution of this glassy mass rapidly consumed diazomethane in an ether solution, although after some addition, the original compound started precipitating. The solution was kept overnight, filtered, and worked up in the usual way to give a brown, gummy mass, Rf 0.70 [chloroform-methanol (90:10)].

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LITERATURE CITED

1. S. K. Talapatra, S. P. Goswami, N. C. Ganguly, and B. Talapatra, *Chem. Ind.* (London), 154 (1980).
2. N. C. Ganguly, Ph.D. thesis, Calcutta University, 1978; S. K. Talapatra, "Symposium on Recent Developments in Organic Chemistry," Calcutta, 1979 (abstracts), p. 21; S. K. Talapatra, S. P. Goswami, N. Ganguly, and B. Talapatra, "4th Asian Symposium on Medicinal Plant and Spices," Bangkok, 1980 (abstracts), p. 232.
3. J. A. Lamberton, J. R. Price, and A. H. Redcliffe, *Aust. J. Chem.*, **20**, 973 (1967).
4. A. Chatterjee, C. P. Dutta, and S. Bhattacharyya, *Science and Culture* (India), **33**, 371 (1967).
5. J. M. Cassady, N. Ojima, C.j Chang, and J. L. McLaughlin, *J. Nat. Prod.*, **42**, 274 (1979).
6. M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).
7. J. W. Cornforth, R. H. Cornforth, and K. K. Mathew, *J. Chem. Soc.*, **112**, 2539 (1959).
8. E. L. Eliel, N. L. Allinger, S. J, Angyal, and G. A. Morrison, "Conformational Analysis," 2nd ed., Interscience Publishers, New York, 1966, p. 205.
9. R. C. Elderfield, ed. "Heterocyclic compounds," 2nd ed., John Wiley and Sons Inc., New York, 1959, Vol. 1, 37-39 (and references cited therein).
10. H. O. House, "Modern Synthetic Reactions," 2nd edn., W. A. Benjamin, Inc., Menlo Park, California, 1972, p. 158-160 (and references cited therein).
11. K. Yamakawa and K. Nishitani, *Chem. Pharm. Bull.*, **24**(11), 2810 (1976).