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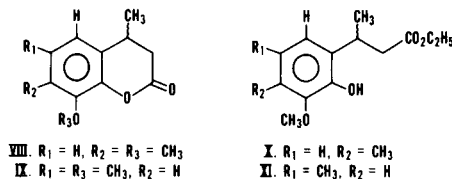
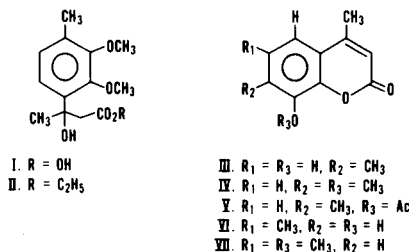
Reduction of the title coumarins at 1500 psi and 150° over 10% palladium on charcoal provides a simple route to dihydrocoumarins and/or ethyl butanoates, hydrogenolysis products of the lactone. Lower pressures and temperatures tend to yield only the dihydrocoumarin. The butanoates are readily converted to the dihydrocoumarins in polyphosphoric acid.

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Each title coumarin and their respective dihydro derivatives were needed as intermediates for an independent synthesis of an antioxidant compound that was isolated from a model, carbohydrate-amine nonenzymic browning reaction (1). Synthetic approaches to 4-alkylcoumarins are well known and are not too demanding, but the preparation of the dihydrocoumarin analogs usually require a multistep scheme of reactions. As a result, the yield of these compounds are greatly reduced.

Initially, III was prepared from I or II, but the synthesis of I and II was difficult. Direct acylation of 2,3-dihydroxytoluene is not possible because the high reactivity of the 5- and 6-positions inhibited formation of any C(4)-alkylated product (2). Consequently, 2,3-dihydroxytoluene was converted into I or II by direct carboxylation at the 4-position (3), followed by *O*-methylation of the resulting benzoic acid, formation of the acyl chloride (4), and its conversion with methyl cadmium to the acetophenone; the last step involved the Reformatsky reaction of the ketone with ethyl 2-bromoacetate to give II. Compounds I or II were converted using various acid catalysis into III or IV in poor overall yields. Because of the low overall yield from the starting phenol and the multi-step process that was needed to prepare large amounts of IV, a simpler and speedier route to coumarins IV, VII, VIII, and IX was sought. An acceptable alternative employed Pechmann reaction conditions to prepare III and VI in 93% and 20% yields, respectively; *O*-methylation of the coumarins then produced IV and VII.

The hydrogenation of the coumarin derivatives appeared to offer access to VIII and IX, because an early study had indicated that coumarin could be reduced to its dihydroderivative by low-pressure hydrogenation (5). However, subsequent work showed that, depending on the type of catalyst, the nonbenzenoid double bond could not be reduced selectively and various hydrogenation and hydrogenolysis products were formed along with the dihydrocoumarin (6). This latter finding was verified by glc examination of a reaction mixture reduced at a similar pressure and temperature (1500 psi and 150°), but the dif-



ferent reactivities of 4-un- and 4-alkyl substituted coumarins (7) suggested catalytic hydrogenation would yield the dihydrocoumarins. Low-temperature, low-pressure reduction using Raney-nickel or palladium catalysts did not reduce IV. When more rigorous conditions are used, VIII and IX formed and the product composition varied depending on the reaction parameters employed. Catalytic reduction of IV yields 13% VIII at 45 psi and 50°, 70% at 90 psi and 100°, 61% at 600 psi and 50° (in ethyl acetate), and 95% X at 1500 psi and 150°. Compound VII is reduced to 29% IX and 70% XI under the latter conditions, and the mixture obtained was easily resolved by column chromatography. The 4-methyl dihydrocoumarin syntheses are completed by cyclization of X to VIII and XI to IX, in 83% and 85% yields, respectively, using polyphosphoric acid.

Consequently, the approach to III and VI from toluene derivatives and ethyl acetoacetate is superior to the one used in the initial multistep synthesis of III, which relied on synthesis of butanoate II. Finally, one can select hydrogenation parameters (solvent, pressure, temperature) that yield either the dihydrocoumarin derivative or the corresponding butanoate or a combination of both compounds.

EXPERIMENTAL

General.

Melting points were determined in capillaries (Thomas-Hoover Apparatus) (8) and are uncorrected. The ir spectra were obtained from chloroform solutions in a Perkin-Elmer model 621 spectrometer. Nmr spectra were recorded with a Varian HA-100 instrument and a Bruker MD 90 spectrometer from chloroform-*d* solutions, with tetramethylsilane as an internal standard. Gas-liquid chromatography was performed on a Hewlett-Packard model 5750 gas chromatograph, and glass columns were used. Mass spectra were recorded using a Nuclide model DF-90-G mass spectrometer; a direct, heated (150° to 200°) inlet was used for sample introduction.

2,3-Dihydroxy-4-methylbenzoic Acid.

Carboxylation of 2,3-dihydroxytoluene to 2,3-dihydroxy-4-methylbenzoic acid was completed in 52% yield, m.p. 203-205°, from ethanol-water (3).

2,3-Dimethoxy-4-methylbenzoic Acid.

2,3-Dihydroxy-4-methylbenzoic acid, 20 g., was treated with a half molar excess of dimethyl sulfate in aqueous sodium hydroxide at 45° for 4 hours. The reaction mixture was then refluxed for 2 hours, and after cooling, the neutralized solution was extracted with ethyl acetate. The organic phase was dried (sodium sulfate), filtered, and concentrated to an oil. Crystallization of the oil from aqueous ethanol produced the methyl ether, m.p. 125-126°, 82% yield; ms: Calcd. 196.0736, Found 196.0766, m/e (relative %) 196 (100), 181 (11), 179 (1), 167 (15), 163 (46), 151 (36), 135 (11), 123 (26), 91 (13), 79 (11), 77 (17); ¹H-nmr: δ (H) 7.39 and 7.30 (2H, aromatic, J = 8 Hz), 4.02 (3H, methoxyl, α to ring carbonyl group), 3.80 (3H, methoxyl), 2.29 (3H, ring methyl).

Anal. Calcd. for C₁₀H₁₂O₄: C, 61.20; H, 6.17. Found: C, 60.95; H, 6.09.

2-Hydroxy-3-methoxy-4-methylbenzoic Acid.

The mother liquor from the crystallization of 2,3-dimethoxy-4-methylbenzoic acid was chromatographed on a dry-packed, silica gel column (Woelm TSC, ICN Nutritional Biochemicals), using chloroform as an eluent, and two components were separated. One was the diether and the other was 2-hydroxy-3-methoxy-4-methylbenzoic acid, 12% yield, m.p. 158-159° (from ethanol-water); ms: Calcd. 182.0579, Found 182.0544, m/e (relative %) 182 (50), 165 (9), 164 (70), 149 (12), 136 (100), 135 (32), 134 (32), 123 (10), 122 (4), 121 (24), 107 (7), 106 (23), 90 (5), 77 (13), 66 (6), 65 (29); ¹H-nmr: δ (H) 6.96 and 7.20 (2H, aromatic, J_{ortho} = 8 Hz), 3.84 (3H, methoxy) 2.58 (3H, acyl methyl), 2.28 (3H, aromatic methyl).

Anal. Calcd. for C₉H₁₀O₄: C, 59.32; H, 5.54. Found: C, 59.29; H, 5.49.

2,3-Dimethoxy-4-methylbenzoyl Chloride.

2,3-Dimethoxy-4-methylbenzoic acid, 5 g., was treated with a 10 percent excess of thionyl chloride in 50 ml. of benzene, and, after removal of excess reagent by co-distillation with benzene, the product was distilled at 130° and 2 mm, yellow oil, 73% yield; ms: m/e (relative %) 214 (13), 180 (12), 179 (100), 167 (6), 164 (8), 163 (21), 151 (15), 149 (10), 136 (18), 135 (11), 123 (11), 122 (4), 121 (25), 91 (16), 77 (10); ¹H-nmr: δ (H) 7.23 and 7.16 (2H, aromatic, J_{ortho} = 8 Hz), 3.82 (3H, methoxy, α to ring carbonyl), 3.77 (3H, methoxy), 2.45 (3H, aromatic methyl).

Anal. Calcd. for C₁₀H₁₁ClO₂: C, 55.94; H, 5.17; Cl, 16.53. Found: C, 56.08; H, 5.19; Cl, 16.31.

2,3-Dimethoxy-4-methylacetophenone.

2,3-Dimethoxy-4-methylbenzoyl chloride, 5 g., was converted to the acetophenone, 26% yield as a colorless oil, with methyl cadium (9). The product was purified by silica gel column chromatography (52 cm × 3 cm, dry-packed silica gel containing 10% water by weight/5 g. of ketone) (10); ms: Calcd. 194.0943, Found: 194.0893, m/e (relative %) 194 (46), 179 (100), 136 (16), 135 (3), 121 (4), 108 (3), 107 (1), 106 (4), 93 (4), 92 (2), 91 (15), 79 (2), 77 (4); ¹H-nmr: δ (H) 7.14 and 6.97 (2H, aromatic, J_{ortho} = 8 Hz), 3.82 (3H, methoxy α to ring carbonyl), 3.77 (3H, methoxy), 2.57

(3H, acyl methyl), 2.45 (3H, aromatic methyl).

Anal. Calcd. for C₁₁H₁₄O₂: C, 68.01; H, 7.27. Found: C, 67.85; H, 7.17.

2-Hydroxy-3-methoxy-4-methylacetophenone.

This acetophenone was isolated as a co-product from the preparation of 2,3-dimethoxy-4-methylacetophenone by column chromatography; the oil failed to crystallize on standing, 10% yield. Treatment of this ketone with excess diazomethane failed to convert it to the di-*O*-methyl ether; lack of reactivity is characteristic of α-hydroxy aromatic ketones; ms: Calcd. 180.0786, Found 180.0789 m/e (relative %) 180 (90), 166 (10), 165 (100), 150 (22), 147 (15), 137 (8), 123 (3), 122 (7), 119 (9), 107 (4), 78 (2), 77 (6), 53 (5); ¹H-nmr: δ (H) 7.05 and 6.96 (2H, aromatic, J_{ortho} = 8 Hz), 3.80 (3H, methoxy), 2.57 (3H, acyl methyl), 2.28 (3H, aromatic methyl).

Anal. Calcd. for C₁₀H₁₂O₃: C, 66.63; H, 6.72. Found: C, 66.51; H, 6.60.

(±)-Ethyl 3-Hydroxy-3-(2',3'-dimethoxy-4'-methyl)butanoate (II).

Treatment of 2,3-dimethoxy-4-methylacetophenone, 5 g., with a 10% molar excess of ethyl 1-bromoacetate and zinc produced II as a colorless oil (11). Following column chromatography on silica gel, II was isolated in 25% yield; ms: m/e (relative %) no parent ion, 252 (2), 207 (6), 206 (51), 191 (5), 178 (8), 165 (11), 164 (100), 163 (11), 150 (1), 149 (15), 148 (4), 145 (7), 135 (14), 134 (7), 131 (12), 122 (3), 121 (34), 115 (8), 93 (7), 92 (5), 91 (34), 79 (9), 78 (8), 77 (28); ¹H-nmr: δ (H) 7.03 and 6.98 (2H, aromatic, J_{ortho} = 8 Hz), 3.93 (3H, methoxyl), 3.73 (3H, methoxyl), 3.16 (2H, ethyl methylene, J = 16 Hz, quartet), 2.19 (3H, aromatic methyl), 1.60 (3H, chain methyl), 1.07 (3H, ethyl methyl, J = 7 Hz).

Anal. Calcd. for C₁₅H₂₂O₅: C, 63.80; H, 7.86. Found: C, 63.50; H, 7.59.

(±)-3-Hydroxy-3-(2',3'-dimethoxy-4'-methyl)butanoic Acid (I).

Acid I was prepared from 5 g. of II and 140 ml. of methanol that contained 8.42 g. of potassium hydroxide and 20 ml. of water. After 18 hours, the solution was reduced to 40 ml. and acidified with 3M hydrochloric acid. The aqueous solution was extracted with ether (three 50-ml. portions), and the combined ether extract was washed twice with water. The organic extract was dried (sodium sulfate), filtered, and concentrated. Hexane was added, and a crystalline precipitate formed, m.p. 104-107°, 97% yield; ms: m/e (relative %) 254 (15), 236 (20), 205 (17), 197 (2), 196 (18), 195 (100), 192 (37), 179 (89), 177 (91), 175 (16), 153 (19), 144 (2), 138 (15), 119 (23), 105 (16), 91 (41), 79 (12), 78 (13), 77 (22), 65 (20), 43 (79); ¹H-nmr: δ (H) 6.89 (2H, broadened quartet, aromatic), 3.98 (3H, methoxyl), 3.64 (3H, methoxyl), 2.98 (2H, methylene quartet, J = 16 Hz), 2.22 (3H, aromatic methyl), 1.62 (3H, methine methyl); ir: cm⁻¹ 3500, 3400-3000, 1745, 1705.

Anal. Calcd. for C₁₃H₁₈O₅: C, 61.39; H, 4.38. Found: C, 61.21; H, 4.25.

8-Hydroxy-4,7-dimethylcoumarin (III).

Acid I, 1.16 g., was dissolved in 20 ml. of concentrated sulfuric acid, and the solution was heated for 1 hour at 80°. The cooled solution was poured into 50 ml. of ice water that was then extracted twice with 25 ml. of ether. The combined organic extract was washed twice with water (50 ml.), dried (sodium sulfate), and filtered. Solvent removal produced III, 16% yield, m.p. 204-206° from aqueous ethanol; ms: Calcd. 190.0630, Found 190.0605, m/e (relative %) 190 (100), 189 (2), 162 (54), 161 (69), 148 (3), 147 (18), 145 (5), 144 (2), 134 (8), 133 (10), 119 (13), 106 (3), 105 (11), 103 (6), 92 (3), 91 (17), 90 (1), 79 (9), 78 (6), 77 (15); ¹H-nmr: δ (H) 7.02 (2H, aromatic), 6.19 (1H, vinyl, multiplet), 6.12 (1H, hydroxy), 2.39 (3H, vinyl methyl, doublet, J = 2 Hz), 2.34 (3H, aromatic methyl).

Anal. Calcd. for C₁₁H₁₀O₂: C, 69.45; H, 5.30. Found: C, 69.51; H, 5.41.

Coumarin III was also prepared from I, in 80% yield, by heating a polyphosphoric acid solution (5 g. of acid/0.5 g. of I) at 80° for 1 hour. The product was isolated by filtration, following addition of ice water to the reaction.

4,7-Dimethyl-8-methoxycoumarin (IV).

The acid chloride of (I), 1.03 g., was dissolved in 50 ml. of methylene chloride and the solution was added in three portions to 0.485 g. of anhydrous aluminum chloride. The reaction mixture was stirred for 30

minutes; ice water was added and the organic phase was separated. The aqueous phase was extracted with methylene chloride; the combined organic phase, after drying (sodium sulfate), was concentrated, and the residue was crystallized from ethanol, IV, m.p. 134°, 74% yield; ms: Calcd. 204.9786, Found 204.9794, m/e (relative %) 204 (100), 189 (10), 176 (20), 175 (9), 161 (22), 158 (3), 145 (4), 133 (6), 115 (3), 105 (6), 79 (3), 78 (1), 77 (6); ¹H-nmr: δ (H) 7.15 and 7.07 (2H, aromatic quartet, J_{ortho} = 8 Hz), 6.17 (1H, vinyl, doublet), 3.85 (3H, methoxyl), 2.39 (3H, vinyl methyl, doublet, J = 2 Hz), 2.36 (3H, aromatic methyl); ir: (cm⁻¹) 1720 strong, 1615 strong, 1570.

Anal. Calcd. for C₁₂H₁₂O₃: C, 70.25; H, 5.90. Found: C, 70.11; H, 5.76.

Reaction of acid I, 0.5 g., with a molar equivalent of thionyl chloride and five drops of dimethylformamide in 75 ml. of methylene chloride under reflux for 2 hours, followed by the usual work-up procedure, produced IV in 50% yield.

Reaction of the acid chloride of I, 0.1 g., with zinc chloride, 0.05 g., in refluxing methylene chloride, 50 ml., yielded after the usual work-up, IV (68%).

Coumarin III by the Pechmann Reaction (12).

2,3-Diacetoxytoluene, 104 g., and 65 g. of ethyl acetoacetate were mixed into a paste, and 500 ml. of 75% (v/v) sulfuric acid was slowly added. The solution was heated at 80° for 45 minutes. Upon cooling, the reddish mixture was poured into 2 l. of stirred ice water. After stirring for 20 minutes, III was isolated by filtration; 47 g. (54% yield), m.p. 204-206° from aqueous ethanol. The spectral data for this isolate were identical to those of the previously prepared III.

8-Acetoxy-4,7-dimethylcoumarin (V).

Coumarin III was converted into its acetate derivative by treating III, 1 g., with 8 ml. of acetic anhydride, and 0.2 g. of sodium acetate for 2.5 hour at 98°. Addition of ice water and filtration yielded V, m.p. 143-146° (from aqueous ethanol); ms: Calcd. 232.0735, Found 232.0758, m/e (relative %) 232 (36), 192 (3), 191 (29), 190 (100), 162 (33), 161 (30), 160 (1), 119 (4), 105 (5), 79 (4), 78 (2), 77 (6); ¹H-nmr: δ (H) 7.31 (1H, aromatic, J_{ortho} = 8 Hz), 7.13 (1H, aromatic), 6.17 (1H, vinyl, J = 1.8 Hz), 2.39 (3H, acetyl methyl), 2.33 (3H, aromatic methyl), 2.23 (3H, vinyl methyl).

Anal. Calcd. for C₁₃H₁₂O₄: C, 67.22; H, 5.21. Found: C, 66.99; H, 5.14.

O-Methylation of III.

Coumarin III, 34.8 g., was added to 1 l. of acetone that contained 10 ml. of methyl iodide and 75 g. of anhydrous potassium carbonate. The mixture was refluxed over night and, after cooling, the reaction was filtered. The solvent was removed and the resulting residue was vigorously stirred with 300 ml. of ice water; IV was isolated by filtration (93% yield).

8-Hydroxy-4,6-dimethylcoumarin (VI).

This compound was prepared, using the Pechmann reaction described above, from 104 g. of 3,4-diacetoxytoluene, 65 g. of ethyl acetoacetate, and 500 ml. of 75% sulfuric acid. The acidic solution was poured into 2 l. of ice water that was then extracted with chloroform (five times, 500 ml. total volume). The organic phase was washed thrice with equal volumes of water and then dried (sodium sulfate). Filtration and solvent removal yielded a dark brown oil that produced crystalline VI on standing, m.p. 214-215°, aqueous ethanol (20% yield); ms: Calcd. 190.0629, Found 190.0632, m/e (relative %) 190 (100), 163 (15), 162 (49), 161 (52), 147 (11), 134 (10), 120 (3), 119 (11), 115 (4), 106 (4), 105 (6), 95 (4), 91 (14), 80 (30), 79 (5), 78 (4), 77 (9); ¹H-nmr: δ (H) 6.87 (2H, aromatic, finely split quartet), 6.20 (1H, vinyl, finely split doublet), 4.36 (1H, hydroxy, broad), 2.39 (3H, vinyl methyl, J = 2 Hz), 2.32 (3H, aromatic methyl, singlet).

Anal. Calcd. for C₁₁H₁₀O₃: C, 69.45; H, 5.30. Found: C, 69.29; H, 5.18.

4,6-Dimethyl-8-methoxycoumarin (VII).

Compound VI, using the procedure described for the preparation of IV, was converted to VII, m.p. 240.5-241.5°, aqueous ethanol (94% yield); ms: Calcd. 204.0786, Found 204.0789, m/e (relative %) 204 (100),

176 (18), 175 (15), 162 (2), 161 (13), 145 (3), 133 (11), 117 (2), 115 (3), 105 (6), 103 (4), 102 (5), 91 (2), 79 (3), 78 (2), 77 (6); ¹H-nmr: δ (H) 6.87 (2H, aromatic, finely split quartet), 6.20 (1H, vinyl, finely split doublet), 3.88 (3H, methoxyl), 2.39 (3H, vinyl methyl, J = 2 Hz), 2.32 (3H, aromatic methyl singlet).

Anal. Calcd. for C₁₂H₁₂O₃: C, 70.56; H, 5.93. Found: C, 70.45; H, 5.75.

(±)-3,4-Dihydro-8-methoxy-4,7-dimethylcoumarin (VIII) and (±)-Ethyl-3-(2'-hydroxy-3'-methoxy-4'-methylphenyl)butanoate (X).

Compound IV failed to take up hydrogen when 3.0 g. was treated with 0.5 g. of Raney-Ni (W2) in ethanol at 1500 psi and 100° for 4 hours.

Reduction of IV, 5 g., with 0.25 g. of 10% palladium on charcoal in 200 ml. of ethanol at 45 psi and 50° for 4 hours yielded 13% VIII and starting compound. These compounds were separated by column chromatography; 5 g. of sample was applied to a dry-packed, silica gel column (60 cm × 2.5 cm), and the column was developed with chloroform. Appropriate fractions were combined, based on the results of analytical tlc (silica gel, 10% ethyl acetate in benzene), to yield IV and VIII. Compound VIII had ms: Calcd. 206.0943, Found 206.0971, m/e (relative %) 206 (45), 191 (4), 178 (6), 165 (11), 164 (100), 149 (15), 136 (2), 135 (15), 134 (7), 131 (7), 122 (3), 121 (38), 117 (7), 116 (3), 115 (9), 105 (9), 105 (3), 103 (9), 93 (8), 92 (6), 91 (38), 79 (10), 78 (9), 77 (31); ¹H-nmr: δ (H) 6.87 and 6.80 (2H, aromatic, quartet, J = 7 Hz), 3.85 (3H, methoxyl), 3.12 (1H, center of methine, doublet of quartets), 2.66 (2H, center of methylene, octet), 2.24 (3H, aromatic methyl), 1.31 (3H, alkyl methyl, J = 7 Hz).

Anal. Calcd. for C₁₂H₁₄O₃: C, 69.87; H, 6.85. Found: C, 69.80; H, 6.80.

Hydrogenation of IV, 5.0 g., in 200 ml. ethanol with 0.25 10% palladium on charcoal at 100° and 90 psi for 4 hours yielded 70% VIII; the remainder of the isolate was IV.

Reduction of IV, 5.0 g., with 0.10 g. of 10% palladium on charcoal in 200 ml. of ethyl acetate at 50° and 600 psi for 4 hours yielded 61% VIII and starting compound.

Compound IV, 17 g., 1.0 g. of 10% palladium on charcoal and 250 ml. of ethanol were hydrogenated at 150° and 1500 psi for 6 hours. On cooling, the reaction mixture was filtered and the solvent removed. The colorless oil was distilled, b.p. (0.02 mm) 150-160°, 95% yield of X (analytical tlc on silica gel showed the product to be pure); ms: Calcd. 252.1361, Found 252.1398 m/e (relative %) 252 (12), 207 (9), 206 (48), 191 (4), 166 (3), 165 (32), 164 (100), 163 (8), 150 (7), 149 (10), 135 (9), 134 (5), 133 (5), 132 (3), 122 (3), 121 (21), 105 (12), 92 (4), 91 (26), 79 (11), 78 (7), 77 (24); ¹H-nmr: δ (H) 6.63 and 6.56 (2H, aromatic, J_{ortho} = 7.5 Hz), 4.72 (1H, hydroxy), 4.00 (2H, ethyl methylene, J = 7 Hz), 3.72 (2H, side-chain methylene, multiplet), 3.67 (3H, methoxy), 2.53 (1H, methine, multiplet), 2.17 (3H, aromatic methyl), 1.22 (3H, methine methyl, J = 7 Hz), 1.12 (3H, ethyl methyl, J = 7 Hz).

Anal. Calcd. for C₁₄H₂₀O₄: C, 66.63; H, 7.99. Found: C, 66.46; H, 7.81.

(±)-3,4-Dihydro-8-methoxy-4,6-dimethylcoumarin (IX) and (±)-Ethyl 3-(2'-hydroxy-3'-methoxy-5'-methylphenyl)butanoate (XI).

Coumarin VII was hydrogenated using the conditions for the reduction of IV. Analytical tlc indicated the isolate to be a mixture. Two components were resolved by the column chromatography previously described for the separation of IV from VIII. In this separation 10% ethyl acetate in toluene was employed as the solvent system. Compound IX was isolated as a colorless oil, 29% yield; ms: Calcd. 206.0943, Found 206.0881 m/e (relative %) 206 (45), 191 (4), 178 (6), 165 (11), 164 (100), 163 (11), 149 (16), 136 (2), 135 (16), 134 (7), 131 (13), 122 (3), 121 (39), 117 (8), 105 (9), 104 (3), 103 (9), 93 (8), 92 (6), 91 (39), 79 (10), 78 (10), 77 (33); ¹H-nmr: δ (H) 6.80 (2H, aromatic, finely split singlet), 3.82 (3H, methoxy), 3.08 (1H, center of methine, two quartets), 2.58 (2H, center of methylene multiplet), 2.30 (3H, aromatic methyl), 1.28 (3H, alkyl methyl, J = 7 Hz).

Anal. Calcd. for C₁₂H₁₄O₃: C, 69.87; H, 6.85. Found: C, 69.75; H, 6.72.

Compound XI was isolated as a colorless oil, 70% yield; ms: Calcd. 252.1361, Found 252.1378 m/e (relative %) 252 (2), 207 (6), 206 (51), 191 (5), 178 (8), 165 (11), 164 (100), 163 (11), 150 (1), 149 (15), 148 (4), 145 (7), 135 (14), 134 (7), 131 (12), 122 (3), 121 (34), 115 (8), 93 (7), 92 (5), 91 (34), 79 (9), 78 (8), 77 (28); ¹H-nmr: δ (H) 6.52 (2H, aromatic, finely split singlet), 5.59 (1H, hydroxyl), 4.06 (2H, ethyl methylene, quartet, J = 7

Hz), 3.80 (3H, methoxy), 3.70 (1H, center of two methine quartets), 2.49 (2H, side chain methylene, multiplet), 2.20 (3H, aromatic methyl), 1.27 (3H, methine methyl, $J = 7$ Hz), 1.16 (3H, ethyl methyl, $J = 7$ Hz).

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.63; H, 7.99. Found: C, 66.60; H, 8.11.

Synthesis of VIII from X and IX from XI.

The respective ethyl ester, X or XI, was treated with 5 g. of polyphosphoric acid at 90° for 6 hours. After cooling, ice water was added and the product was isolated by filtration or chloroform extraction. Dihydrocoumarin VIII was isolated in 83% yield and IX in 85% yield. The structure of each product was confirmed by glc (a 122 cm \times 2 mm glass column of 3% SE-30 on Chromosorb Q, 100° initial temperature, and programmed at 6° /minute at 220°), 1H -nmr, and ms analyses.

Hydrogenation of Coumarin.

Coumarin, 2 g., was hydrogenated using load ratios and conditions identical to those employed in the reduction of VII. Subsequent work up of the reaction mixture yielded a colorless oil, and glc analysis of the product on the SE-30 column used above showed the oil to contain eight components; one had the same retention time as the starting coumarin. No further separations or identifications were attempted.

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REFERENCES AND NOTES

- (1) F. D. Mills and J. E. Hodge, Abstracts, 178th ACS Meeting, Washington, D.C., September 1979, No. 75, Carbohydrates section.
- (2) J. D. Edwards, Jr., S. E. McGuire and C. Hignite, *J. Org. Chem.*, **39**, 3028 (1964).
- (3) M. W. Baines, D. B. Cobb, R. J. Edin, R. Fielden, J. N. Gardner, A. M. Roe, W. Tertnik and G. L. Willey, *J. Med. Chem.*, **8**, 81 (1965).
- (4) M. Braver Floyd and G. R. Allen, Jr., *J. Org. Chem.*, **35**, 2647 (1970).
- (5) E. Spath and O. Besta, *Ber.*, **66**, 754 (1933).
- (6a) P. L. De Benneville and R. Conner, *J. Am. Chem. Soc.*, **62**, 283 (1940); (b) P. L. De Benneville and R. Conner, *ibid.*, **62**, 3067 (1940).
- (7) R. C. Elderfield, Ed., "Heterocyclic Compounds," Vol. 2, Chapter 6, John Wiley and Sons, Inc., New York, N.Y., 1951.
- (8) The mention of firm names or trade products does not imply that they are endorsed or recommended by the U.S. Department of Agriculture over other firms or similar products not mentioned.
- (9) J. Cason, *J. Am. Chem. Soc.*, **68**, 2078 (1946).
- (10) B. Loev and M. M. Goodman, *Chem. Ind.*, 2026 (1967).
- (11) C. R. Hauser and D. S. Breslow, *Org. Synth.*, Coll. Vol. 3, 408 (1955).
- (12) E. B. Vilet, *ibid.*, Coll. Vol. 1, 360 (1941).