23/24, 23/25, 24/22, 24/23, 24/25, 25/23, and 25/24.

Metachromin G (4): a purple oil; $[\alpha]^{20}_D$ -18° (c 0.2, C_6H_6); IR (neat) ν_{max} 3300, 1590, 1510, 1380, and 1210 cm^{-1}; UV (MeOH) λ_{max} 211 (ϵ 29700), 324 (14700), and 508 nm (800); ^1H NMR ($CDCl_3$) δ 0.83 (1 H, m, H-2'), 0.99 (1 H, m, H-3'), 1.01 (3 H, s, H_3-14), 1.02 (3 H, d, J = 6.6 Hz, H_3-12), 1.19 (1 H, m, H-1'), 1.46 (1 H, m, H-1), 1.50 (1 H, m, H-7'), 1.57 (1 H, m, H-7) 1.58 (1 H, m, H-2), 1.73 (1 H, m, H-3), 1.75 (3 H, s, H_3-15), 1.97 (2 H, m, H_2-8), 2.33 (1 H, m, H-4), 2.95 (2 H, t, J = 7.0 Hz, H_2-23), 3.09 (2 H, d, J = 7.0 Hz, H-11), 3.42 (2 H, q, J = 7.0 Hz, H_2-22), 4.68 (1 H, s, H-13'), 4.71 (1 H, s, H-13), 5.16 (1 H, t, J = 7.0 Hz, H-10), 5.39 (1 H, s, H-19), 6.45 (1 H, brt, NH), 7.20 (2 H, d, J = 8.0 Hz, H-25, 25'), 7.27 (1 H, t, J = 8.0 Hz, H-27), and 7.34 (2 H, t, J = 8.0 Hz, H-26, 26'); EIMS m/z (%) 447 (M^+, 90), 356 (60), 296 (20), 257 (60), 166 (90), 123 (30), 105 (100), and 91 (45); HREIMS m/z 447.2768 (M^+, calcd for $C_{29}H_{37}NO_3$, 447.2673); HMBC (H/C) 1/14, 1'/14, 7/6, 7/14, 8/9, 8/10, 10/8, 11/10, 11/16, 11/21, 12/3, 12/4, 13/4, 13/6, 14/1, 14/6, 14/7, 15/8, 15/9, 15/10, 19/17, 19/21, 22/20, 22/23, 22/24, 23/22, 23/24, 23/25, 25/26, 25/27, 26/24, 26/25, and 27/26.

Metachromin H (5): a purple oil; $[\alpha]^{19}_D$ -9° (c 0.2, C_6H_6); IR (neat) ν_{max} 3300, 3250, 1570, 1520, 1380, and 1200 cm^{-1}; UV (MeOH) λ_{max} 324 (ϵ 12800) and 512 nm (700); ^1H NMR ($CDCl_3$) δ 0.83 (1 H, m, H-2'), 0.94 (6 H, d, J = 6.6 Hz, H-25, 25') 0.98 (1 H, m, H-3') 1.01 (3 H, s, H_3-14), 1.02 (3 H, d, J = 6.6 Hz, H_3-12), 1.21 (1 H, m, H-1'), 1.40 (1 H, m, H-24), 1.46 (1 H, m, H-1), 1.52 (2 H, m, H_2-7), 1.56 (2 H, m, H_2-23), 1.58 (1 H, m, H-2), 1.73 (1 H, m, H-3), 1.76 (3 H, s, H_3-15), 2.31 (1 H, m, H-4), 3.10 (2 H, d, J = 7.0 Hz, H_2-11), 3.15 (2 H, m, H_2-22), 4.68 (1 H, s, H-13'), 4.71 (1 H, s, H-13), 5.17 (1 H, t, J = 7.0 Hz, H-10), 5.35 (1 H, s, H-19), 6.40 (1 H, brs, NH), and 8.20 (1 H, brs, OH); EIMS m/z (%) 413 (M^+, 65), 356 (8), 289 (15), 275 (12), 262 (30), 223 (100), 166 (30), 152 (30), and 123 (15); HREIMS m/z 413.2920 (M^+, calcd for $C_{26}H_{39}NO_3$, 413.2930).

Conversion of Metachromin B (7) into Metachromin E (2) by Oxidative Demethylation. Aqueous ceric ammonium nitrate (24 μL, 0.5 M, 12.0 μmol) was added to a solution of metachromin B (7, 1.5 mg) in CH_3CN/H_2O (2:1, 1 mL) at 25 °C. After 30 min the mixture was diluted with water (2 mL) and extracted with EtOAc (4 mL × 2). The combined organic extracts were washed brine and dried over magnesium sulfate, and the solvent was removed to give metachromin E (2, 1.1 mg, 74%).

Ozonolysis of Metachromins A (6) and F-H (3-5). A solution of 6 (20.0 mg) in MeOH (4 mL) was saturated with ozone at -78 °C for 10 min. After excess ozone was removed by a nitrogen stream, dimethyl sulfide (0.04 mL) was added, and the mixture was stirred at 0 °C for 30 min and then at room temperature for 30 min. The solvent and excess reagent were evaporated under reduced pressure. The residue was purified by a silica gel column (1.0 × 20 cm), eluting with hexane/EtOAc (3:1) to afford compound 8 (6.7 mg, 61%): a colorless oil; $[\alpha]^{18}_D$ -39° (c 1.0, $CHCl_3$); IR (neat) ν_{max} 1700, 1450, 1350, and 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (3 H, d, J = 6.2 Hz, H_3-12), 1.17 (3 H, s, H_3-14), 1.30 (1 H, qd, J = 13.1 and 3.7 Hz, H-3'), 1.55 (1 H, m, H-1'), 1.61 (1 H, m, H-1), 1.65 (1 H, m, H-2'), 1.71 (2 H, t, J = 8.1 Hz, H_2-7), 1.88 (1 H, tt, J = 13.1 and 3.7 Hz, H-2), 2.04 (1 H, dddd, J = 12.1, 6.2, 5.5 and 2.9 Hz, H-3), 2.15 (3 H, s, H_3-15), 2.42 (1 H, dt, J = 16.8 and 8.1 Hz, H-8'), 2.55 (1 H, dt, J = 16.8 and 8.1 Hz, H-8) and 2.62 (1 H, qd, J = 6.2 and 5.5 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 14.87 (q, C-12), 21.21 (t, C-2), 23.32 (q, C-14), 29.83 (q, C-15), 32.28 (t, C-7), 36.53 (t, C-3), 39.09 (t, C-1), 39.22 (t, C-8), 41.08 (d, C-4), 47.56 (s, C-6), 209.26 (s, C-9), and 216.71 (s, C-5); EIMS m/z (%) 196 (M^+), 139 (3), 126 (10), 111 (5), 95 (15), and 43 (100); HREIMS m/z 196.1478 (M^+, calcd for $C_{12}H_{20}O_2$, 196.1463).

According to essentially the same procedure as described above, 3 (6.5 mg), 4 (3.0 mg), and 5 (7.4 mg) afforded 8 [2.7 mg (85%) from 3, $[\alpha]^{19}_D$ -32° (c 0.4, $CHCl_3$); 0.6 mg (46%) from 4, $[\alpha]^{17}_D$ -32° (c 0.05, $CHCl_3$); and 1.0 mg (29%) from 5, $[\alpha]^{20}_D$ -32° (c 0.1, $CHCl_3$)]. Spectral data (^1H NMR, IR, and EIMS) of the ozonized compounds were identical with those of compound 8 derived from 6.

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Supplementary Material Available: All spectra of metachromins D-H (1-5) and compound 8 (47 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Regioselective Alcoholysis of Flavonoid Acetates with Lipase in an Organic Solvent

Mariapina Natoli, Giovanni Nicolosi,* and Mario Piattelli

Istituto del CNR per lo Studio delle Sostanze Naturali di Interesse Alimentare e Chimico-farmaceutico, Via del Santuario 110, 95028 Valverde CT, Italy

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Flavonoids are natural compounds widely distributed in higher plants. Many of them possess biological activities potentially exploitable in the biomedical field as antiinflammatory,[1-3] antiinfluenza virus,[4] antiulcer,[3] capillary protecting,[2] antitumor,[5-7] and in radical scavanger activity.[8-10] Inhibition of protein-tyrosine kinase[11,12] and phosphatidyl-inositol kinase[13] by flavonoids has also been reported.

Chemical elaboration of the basic flavonoid structure to obtain either rare natural compounds, for instance *O*-methyl flavonoids, or semisynthetic products often requires protection/deprotection of specific hydroxyl function(s). In a previous work we have investigated the partial hydrolysis of peracetylated di- and trihydroxyflavonoids catalyzed by a lipase from *Pseudomonas cepacea* (referred to as *Pseudomonas* sp.[14]) and we have found that this reaction takes place with a high degree of regioselectivity. In the present paper we report the results obtained by the application of this method to peracetates of additional hydroxylated compounds of the same class, namely luteolin, kaempferol, kaempferide, and quercetin. The synthesis of an *O*-methyl flavonoid, ombuin, is also described.

A flavone ester, luteolin tetraacetate (1), and three flavonol esters, kaempferol tetraacetate (2), kaempferide triacetate (3), and quercetin pentaacetate (4), were subjected to alcoholysis catalyzed by *P. cepacea* lipase in THF.

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For each substrate the amount of enzyme was chosen so as to have at the end of the reaction time (24 h) a conversion ranging from 60 to 80%. The products were then separated by chromatography and identified on the basis of UV spectra, both in the absence and presence of appropriate reagents (sodium acetate or sodium acetate–boric acid),[15,16] and ^{1}H NMR spectra.[17,18] The results are summarized in Table I. The ester group at position 3 always resists cleavage, possibly on account of inaccessibility to the enzyme, and moreover, its presence strongly affects the course of the reaction. Luteolin tetraacetate (1), which lacks the 3-acetate, gives 5,7,3′-triacetoxy-4′-hydroxyflavone (5) and a minor amount of 5,7-diacetoxy-3′,4′-dihydroxyflavone (6), while the ester groups on the A ring are not affected. In contrast, in flavonol peracetates alcoholysis of these groups can take place, and kaempferol tetraacetate (2) yields 3,5,7-triacetoxy-4′-hydroxyflavone (7) and 3,5-diacetoxy-7,4′-dihydroxyflavone (8) in comparable amounts, while kaempferide triacetate (3) gives 3,5-diacetoxy-7-hydroxy-4′-methoxyflavone (9) and 3-acetoxy-5,7-dihydroxy-4′-methoxyflavone (10). Quercetin pentaacetate (4) undergoes initial alcoholysis at position 7 to afford 3,5,3′,4′-tetraacetoxy-7-hydroxyflavone (11) followed by cleavage of the acetates at positions 4′, 5, and 3′ to yield 3,5,3′-triacetoxy-7,4′-dihydroxyflavone (12), 3,3′,4′-triacetoxy-5,7-dihydroxyflavone (13), and 3-acetoxy-5,7,3′,4′-tetrahydroxyflavone (14). The resistance to cleavage of the ester groups on the A ring of flavone acetates when a hydroxyl or methoxyl is present in position 4′ has already been observed[14] and ascribed to the fact that both these functions can conjugate with the carbonyl at C-4, thus increasing the π character of the C-2–C-1′ bond and consequently favoring a planar conformation of the molecule possibly less suitable for the catalytic site of the enzyme to accept the substrate. The effect of the presence of an OH at position 4′ on the geometry of the molecule has been now estimated by AM1 calculations in the case of flavone and 4′-hydroxyflavone. The angle between the planes of the benzopyrone system and the B ring was found to be 24° for the former and 7° for the latter.

Enzyme-catalyzed hydrolysis of flavonoid peracetates makes accessible compounds not easily obtained by chemical means, some of which can be useful intermediates in the synthesis of flavonoid derivatives. As an example, compound 12 was treated with CH_2N_2 to give 3,5,3′-triacetoxy-7,4′-dimethoxyflavone (15), which was converted by chemical hydrolysis into the rare *O*-methyl flavonoid ombuin, present in nature as a glycoside, ombuoside, originally isolated from the leaves of *Phytolacca dioica*.[19]

Experimental Section

HPLC analyses were performed on a Hypersil ODS 5-μm column, using CH_3CN/H_2O mixtures as the mobile phase. TLC was carried out with Kieselgel 60 F254 precoated silica gel on aluminum sheets. Compounds were visualized by UV light (254 nm) or by spraying with 10% solution of $Ce(SO_4)_2$ in 1 M sulfuric acid. A 1.5% solution of $FeCl_3$ in water was used as chromogenic reagent for compounds 6, 10, 13, and 14. All chemicals were of analytical grade. THF was distilled from $LiAlH_4$ and kept on 3-Å molecular sieves. Lipase from *P. cepacea* (PS) was a gift from Amano International Enzyme, Co., and was used "straight from the bottle". All flavonoids used in this work were obtained commercially. ^{1}H-NMR spectra were measured in $(CD_3)_2SO$ on a Bruker AC250 spectrometer, and chemical shifts are reported as ppm (δ) downfield from TMS. The UV spectra were recorded in absolute ethanol on an UV Perkin-Elmer 330 spectrophotometer.

Preparation of 1–4. Peracetates of luteolin, kaempferol, kaempferide, and quercetin were prepared by acetylation (Ac_2O/Py) of the corresponding flavonoids following conventional methods. The physical properties (mp, NMR) of all peracetates were in agreement with those reported in the literature.[17,20,21]

General Procedure for Lipase Catalyzed Alcoholysis. Initially, six separate experiments of enzymatic alcoholysis were carried out for each of the compounds 1–4 using different substrate/enzyme ratios. The conversion was measured after 24 h by HPLC from the decrease of the peak area of the starting material in comparison with that of an internal standard (acetophenone). The amount of enzyme used in the subsequent experiments on a larger scale (Table I) was chosen so to attain a degree of conversion from 60 to 80%. Flavone acetate (200 mg) was dissolved in anhydrous THF to 20 mM concentration (15 mM for 1). 1-Butanol (5 molar equiv) and an appropriate amount of *P. cepacea* lipase (see Table I) were added, and the suspension was shaken (300 rpm) at 42 °C. After 24 h the reaction was quenched by filtering off the enzyme and a small volume of the filtrate analyzed by HPLC to determine the percentages of the starting material and the products. The bulk of the filtrate was taken to dryness in vacuo, and the residue was subjected to chromatographic separation on a column of LiChroprep Si-gel DIOL (40–63 μm), using one of the following eluents: (1) increasing concentrations of ether in dichloromethane or (2) increasing concentrations of ethyl acetate in hexane. The isolated products were characterized by spectroscopic means (UV spectra also in the presence of fused sodium acetate or sodium acetate–boric acid; ^{1}H NMR). No product was observed in the absence of lipase.

Alcoholysis of 5,7,3′,4′-Tetraacetoxyflavone (Luteolin Tetraacetate, 1). Column chromatography of the reaction mixture in solvent 1 gave 5 (90 mg) and 6 (10 mg). **5,7,3′-Triacetoxy-4′-hydroxyflavone (5):** ^{1}H NMR [$(CD_3)_2SO$] δ 7.86 (d, J = 9.0 Hz, 6′ H), 7.83 (s, 2′ H), 7.60 (d, J = 2.0 Hz, 8 H), 7.07 (d, J = 9.0 Hz, 5′ H), 7.05 (d, J = 2.0 Hz, 6 H), 6.77 (s, 3 H), 2.32 (s, Ac), 2.36 (s, 2 × Ac); UV (abs EtOH) λ_{max} 344 (ϵ 14 000), 243 nm (ϵ 13 000). Anal. Calcd for $C_{21}H_{16}O_9$: C, 61.17; H, 3.88. Found: C, 61.30; H, 3.95. **5,7-Diacetoxy-3′,4′-dihydroxyflavone (6):** ^{1}H NMR [$(CD_3)_2SO$] δ 7.57 (d, J = 2.0 Hz, 8 H), 7.41 (d, J = 9.0 Hz, 6′ H), 7.39 (s, 2′ H), 7.05 (d, J = 2.0 Hz, 6 H), 6.90 (d, J = 9.0 Hz, 5′ H), 6.62 (s, 3 H), 2.36 (s, Ac), 2.32 (s, Ac); UV (abs EtOH) λ_{max} 346 nm (ϵ 16 750), shifted to 366 on addition of fused sodium acetate–boric acid mixture, 246 nm (ϵ 15 600). Anal. Calcd for $C_{19}H_{14}O_8$: C, 61.62; H, 3.78. Found: C, 61.75; H, 3.70.

Alcoholysis of 3,5,7,4′-Tetraacetoxyflavone (Kaempferol Acetate, 2). The crude reaction mixture was subjected to column chromatography in solvent 2 to provide pure 7 (70 mg) and 8 (55 mg). **3,5,7-Triacetoxy-4′-hydroxyflavone (7):** ^{1}H NMR [$(CD_3)_2SO$] δ 7.78 (d, J = 8.8 Hz, 2′ H and 6′ H), 7.16 (d, J = 2.1 Hz, 8 H), 7.12 (d, J = 2.1 Hz, 6 H), 6.93 (d, J = 8.8 Hz, 3′ H and 5′ H), 2.32 (s, 2 × Ac), 2.31 (s, Ac); UV (abs EtOH) λ_{max} 325 (ϵ 23 000), 255 nm (ϵ 19 600), shifted to 260 on addition on fused sodium acetate. Anal. Calcd for $C_{21}H_{16}O_9$: C, 61.17; H, 3.88. Found: C, 61.35; H, 3.98. **3,5-Diacetoxy-7,4′-dihydroxyflavone (8):** ^{1}H NMR [$(CD_3)_2SO$] δ 7,72 (d, J = 8.7 Hz, 2′ H and 6′ H), 6.93 (d, J = 8.7 Hz, 3′ H and 5′ H), 6.84 (d, J = 2.2 Hz, 8 H), 6.55 (d, J = 2.2 Hz, 6 H), 2.28 (s, Ac), 2.27 (s, Ac); UV (abs EtOH) λ_{max} 318 nm (ϵ 24 100), shifted to 350 on addition of fused sodium acetate, 255 nm (ϵ 22 200), shifted to 261 on addition of fused sodium acetate. Anal. Calcd for $C_{19}H_{14}O_8$: C, 61.62; H, 3.78. Found: C, 61.45; H, 3.87.

Alcoholysis of 3,5,7-Triacetoxy-4′-methoxyflavone (Kaempferide Acetate, 3). The crude reaction mixture gave, after column chromatography with solvent 2, 85 mg of 9 and 25 mg of 10. **3,5-Diacetoxy-7-hydroxy-4′-methoxyflavone (9):** ^{1}H NMR [$(CD_3)_2SO$] δ 7.83 (d, J = 8.8 Hz, 2′ H and 6′ H), 7.13 (d, J = 8.8 Hz, 3′ H and 5′ H), 6.88 (d, J = 2.0 Hz, 8 H), 6.58 (d, J

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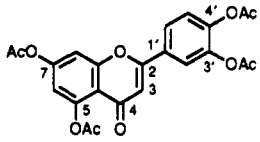
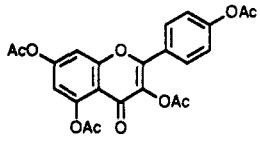
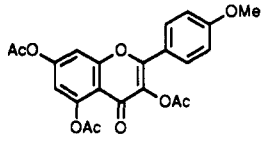
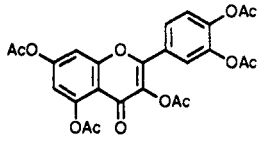
Table I. Alcoholysis of Compounds 1, 2, 3, and 4 Catalyzed by *Pseudomonas cepacea* Lipase in THF[a]

substrate	enzyme, mg/mL	conversion, %[b]	products	fraction, %[c]
 1	2	64	5,7,3′-triacetoxy-4′-hydroxyflavone (5) 5,7-diacetoxy-3′,4′-dihydroxyflavone (6)	90 10
 2	20	81	3,5,7-triacetoxy-4′-hydroxyflavone (7) 3,5-diacetoxy-7,4′-dihydroxyflavone (8)	52 48
 3	50	72	3,5-diacetoxy-7-hydroxy-4′-methoxyflavone (9) 3-acetoxy-5,7-dihydroxy-4′-methoxyflavone (10)	75 25
 4	20	80	3,5,3′,4′-tetraacetoxy-7-hydroxyflavone (11) 3,5,3′-triacetoxy-7,4′-dihydroxyflavone (12) 3,3′,4′-triacetoxy-5,7-dihydroxyflavone (13) 3-acetoxy-5,7,3′,4′-tetrahydroxyflavone (14)	49 28 13 10

[a] Substrate (200 mg) was dissolved in anhyd THF to 20 mM concentration (15 mM for 1). 1-Butanol (5 equiv) and *P. cepacea* lipase (Amano PS), "straight from the bottle" were added. The suspension was shaken (300 rpm) at 42 °C for 24 h. [b] Determined by HPLC analysis. [c] For the isolated yields, see the Experimental Section.

= 2.0 Hz, 6 H), 3.83 (s, 4′ OMe), 2.28 (s, 2 × Ac); UV (abs EtOH) λ_{max} 317 (ε 18100), 257 nm (ε 15500). Anal. Calcd for $C_{20}H_{16}O_8$: C, 62.50; H, 4.17. Found: C, 62.70; H, 4.25. **3-Acetoxy-5,7-dihydroxy-4′-methoxyflavone (10)**: ^{1}H NMR [$(CD_3)_2SO$] δ 7.82 (d, J = 8.8 Hz, 2′ H and 6′ H), 7.13 (d, J = 8.8 Hz, 3′ H and 5′ H), 6.49 (d, J = 2.0 Hz, 8 H), 6.24 (d, J = 2.0 Hz, 6 H), 3.84 (s, 4 OMe), 2.32 (s, Ac); UV (abs EtOH) λ_{max} 325 nm (ε 16000), 267 nm (ε 22000). Anal. Calcd for $C_{18}H_{14}O_7$: C, 63.16; H, 4.09. Found: C, 63.28; H, 4.17.

Alcoholysis of 3,5,7,3′,4′-Pentaacetoxyflavone (Quercetin Acetate, 4). Chromatography of the crude reaction mixture using solvent 1 gave 11 (63 mg), 12 (31 mg), 13 (14 mg), and 14 (9 mg). **3,5,3′,4′-Tetraacetoxy-7-hydroxyflavone (11)**: ^{1}H NMR [$(CD_3)_2SO$] δ 7.82 (dd, J = 2.1, 8.2 Hz, 6′ H), 7.79 (d, J = 2.1 Hz, 2′ H), 7.50 (d, J = 8.2 Hz, 5′ H), 6.91 (d, J = 2.0 Hz, 8 H), 6.62 (d, J = 2.0 Hz, 6 H), 2.32 (s, 2 × Ac), 2.27 (s, 2 × Ac); UV (abs EtOH) λ_{max} 304 nm (ε 12800), shifted to 314 on addition of fused sodium acetated, 254 nm (ε 17800), shifted to 304 on addition of fused sodium acetate. Anal. Calcd for $C_{23}H_{18}O_{11}$: C, 58.73; H, 3.83. Found: C, 58.83; H, 3.95. **3,5,3′-Triacetoxy-7,4′-dihydroxyflavone (12)**: ^{1}H NMR [$(CD_3)_2SO$] δ 7.28 (d, J = 2.2 Hz, 2′ H), 7.23 (dd, J = 2.2, 4 Hz, 6′ H), 6.89 (d, J = 8.4 Hz, 5′ H), 6.84 (d, J = 1.8 Hz, 8 H), 6.57 (d, J = 1.8 Hz, 6 H), 2.29 (s, Ac), 2.27 (s, 2 × Ac); UV (abs EtOH) λ_{max} 330 nm (ε 19550), shifted to 354 on addition of fused sodium acetate, 226 nm (ε 20800), shifted to 236 on addition of sodium acetate. Anal. Calcd for $C_{21}H_{16}O_{10}$: C, 58.88; H, 3.74. Found: C, 59.01; H, 3.84. **3,3′,4′-Triacetoxy-5,7-dihydroxyflavone (13)**: ^{1}H NMR [$(CD_3)_2SO$] δ 7.82 (d, J = 9.1 Hz, 6′ H), 7.81 (s, 2′ H), 7.51 (d, J = 9.1 Hz, 5′ H), 6.52 (s, 8 H), 6.28 (s, 6 H), 2.32 (s, 3 × Ac); UV (abs EtOH) λ_{max} 265 nm (ε 22000), shifted to 275 on addition of fused sodium acetate. Anal. Calcd for $C_{21}H_{16}O_{10}$: C, 58.88; H, 3.74. Found: C, 59.05; H, 3.82. **3-Acetoxy-5,7,3′,4′-tetrahydroxyflavone (14)**: ^{1}H NMR [$(CD_3)_2SO$] δ 7.32 (d, J = 2.1 Hz, 2′ H), 7.27 (dd, J = 2.1, 8.4 Hz, 6′ H), 6.90 (d, J = 8.4 Hz, 5′ H), 6.46 (s, 8 H), 6.23 (s, 6 H), 2.32 (s, Ac); UV (abs EtOH) λ_{max} 350 nm (ε 21300), shifted to 360 on addition of fused sodium acetate and to 378 on addition of sodium acetate/boric acid mixture, 256 nm (ε 25000), shifted to 266 on addition on fused sodium acetate. Anal. Calcd for $C_{17}H_{12}O_8$: C, 59.31; H, 3.49. Found: C, 59.12; H, 3.58.

Synthesis of Ombuin (3,5,3′-Trihydroxy-7,4′-dimethoxyflavone, 16). An ethereal solution of CH_2N_2 was added to a solution of 12 (20 mg) in CH_2Cl_2 (4 mL). After 1 h excess CH_2N_2 was destroyed by addition of acetic acid, the solvent removed, and the residue chromatographed on LiChroprep Si-gel DIOL using a gradient of ether in hexane to yield 15 mg of 3,5,3′-triacetoxy-7,4′-dimethoxyflavone (15): ^{1}H NMR [$(CD_3)_2SO$] δ 7.86 (dd, J = 2.0, 8.9 Hz, 6′ H), 7.70 (d, J = 2.0 Hz, 2′ H), 7.34 (d, J = 8.9 Hz, 5′ H), 7.29 (d, J = 2.2 Hz, 8 H), 6.85 (d, J = 2.2 Hz, 6 H), 3.87 (s, OMe), 3.79 (s, OMe), 2.30 (s, 3 × Ac). Hydrolysis of 15 according to Deulofeu and Schopflocher[22] gave ombuin 16, identified by comparison of its spectral properties with those reported in the literature.[20]

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(22) Deulofeu, V.; Schopflocher, N. *Gazz. Chim. Ital.* **1953**, *83*, 449.

Acceleration of the Ortho Ester Claisen Rearrangement by Clay-Catalyzed Microwave Thermolysis: Expeditious Route to Bicyclic Lactones

Robert S. Huber and Graham B. Jones*

Department of Chemistry, Clemson University, Clemson, South Carolina 29634-1905

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The Claisen rearrangement and its variants enjoy widespread use in synthesis,[1a-g] in part due to the sim-

