

colorless crystals: mp 80–81° (lit.<sup>4</sup> 88–89); nmr (CDCl<sub>3</sub>)  $\tau$  0.84 (s, 2 H) and 1.8–2.8 (m, 10 H).

Anal. Calcd for C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>: C, 82.76; H, 5.17; N, 12.06. Found: C, 82.93; H, 5.31; N, 11.84.

The second band was recrystallized from ethanol and gave 2,6-diphenyl-3-benzylpyrazine as colorless crystals: mp 98–99° (lit.<sup>4</sup> 95°); nmr (CDCl<sub>3</sub>)  $\tau$  1.05 (s, 1 H), 1.8–2.9 (m, 15 H), and 5.75 (s, 2 H).

**Registry No.**—6, 25827-90-1; 8, 25827-91-2; 2,5-diphenyl-6-benzylpyrazine, 25827-92-3; 2,5-diphenyl-3,6-dibenzylpyrazine, 25827-93-4; 2,6-diphenylpyrazine, 25827-94-5; 2,6-diphenyl-3-benzylpyrazine, 25827-95-6.

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### Phytochemical Studies. IX. A New Flavone, Velutin<sup>1</sup>

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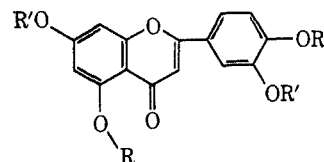
In connection with a projected phytochemical study of Washington vegetation, *Ceanothus velutinus*, a member of the Rhamnaceae or buckthorn family, was selected for initial examination. This shrub is distributed along the drier, east slopes of the Cascades and can be easily found in cleared timber areas. The leaf oil has been investigated in the past because of a pleasant odor, but only cinnamate esters were reported by earlier workers.<sup>2</sup>

A pentane extract of the leaves deposited a yellow powder, which was purified by crystallization from ethyl acetate. The resulting product or velutin analyzed for C<sub>17</sub>H<sub>14</sub>O<sub>6</sub> · 1/2 H<sub>2</sub>O; however, a true molecular weight of 314 was given by mass spectroscopy. A positive ferric chloride test indicated a phenol, and, more specifically, magnesium–hydrochloric acid suggested a flavone. The presence of two hydroxyl groups was shown by the conversion of velutin into a diacetate, C<sub>21</sub>H<sub>18</sub>O<sub>8</sub>.

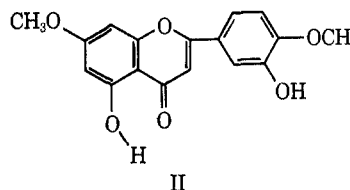
The infrared spectrum possessed a hydrogen-bonded conjugated carbonyl group and an extended aromatic ring system. In the ultraviolet, the main and secondary absorptions were similar to those reported for tetrasubstituted flavones.<sup>3</sup> Generally, the shape of the bands implied the existence of hydroxyl or methoxyl substituents at the 3' and 4' positions in the flavone ring system. The nuclear magnetic resonance spectrum contained two singlet methoxy groups, an upfield pair of doublets with typical meta-coupling constants (centered on their chemical shifts), a singlet due to an olefinic hydrogen, a broad peak of three aromatic

hydrogens, and a hydroxyl shifted downfield due to hydrogen bonding. It will be noted that 13 of the 14 protons were definitely identified here; the missing hydroxyl proton probably exchanged with the water of solvation as detected in the microanalysis. These particular assignments were facilitated by use of an extensive compilation of flavone nmr data.<sup>4</sup> A detailed solvent-shift study was not attempted because of the insolubility of velutin.<sup>5,6</sup> The mass spectral fragmentation pattern was rationalized with the aid of known models,<sup>7</sup> especially with flavones containing a 4'-hydroxyl group.<sup>8</sup>

The available chemical and spectral information was sufficient to postulate two alternative structures for the compound: 4',5'-dihydroxy-3',7'-dimethoxyflavone (Ia) or 3',5'-dihydroxy-4',7'-dimethoxyflavone (II). Ve-



- Ia, R = H; R' = CH<sub>3</sub>  
 b, R = Ac; R' = CH<sub>3</sub>  
 c, R = CH<sub>3</sub>; R' = CH<sub>3</sub>  
 d, R = H; R' = H



lutin on exhaustive methylation formed luteolin tetramethyl ether (Ic), while demethylation produced luteolin (Id).<sup>9</sup> These results verified both the substitution pattern and the ring system existing in the flavone. The crucial placement of the hydroxyl groups in both the A and B rings was made through ultraviolet studies. A shift of 48 m $\mu$  with sodium ethoxide in ethanol<sup>3</sup> fixed one hydroxyl at 4' rather than 3', while a shift of 35 m $\mu$  with aluminum chloride in ethanol<sup>10</sup> confirmed the placement of another hydroxyl group at 5. Compound Ia is known in the form of a dehydrogenation product from a naturally occurring flavanol,<sup>11,12</sup> and the melting points and ultraviolet spectra of both it and the corresponding diacetate are in agreement with the present data.<sup>12</sup> Since comparison samples no longer exist,<sup>13</sup> formula II cannot be completely excluded at this time. However, the weight of the evidence greatly favors Ia; so this structure is now assigned to velutin.

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Experimental Section<sup>14</sup>

Velutin (4',5-Dihydroxy-3',7-dimethoxyflavone) (Ia).—A collection of *Ceanothus velutinus* was made in late October 1969, about 5 km north along the Lake Kachess Dam Road, near Snoqualmie Pass, Wash. The leaves were air-dried for 1 week, and then ground in a Wiley mill and extracted with hot pentane for 10 days. On standing, the dark solution deposited a yellow powder, which was collected, washed, dried, and crystallized from a large volume of ethyl acetate to yield the analytical sample (0.80 g, from 1.6 kg of leaves): mp 225–227° (lit.<sup>10</sup> 223–224°);  $R_f$  0.66;  $\nu_{\max}$  3440 (OH), 2950 (CH), 1660 (C=O), 1605 (C=C), and 847  $\text{cm}^{-1}$  (1,2,3,5 tetrasubstitution);  $\lambda_{\max}$  238, 250, 268, and 348  $\text{m}\mu$  (log  $\epsilon$  4.04, 4.05, 4.01, and 4.16);  $\delta$  3.85 (OCH<sub>3</sub>), 3.92 (OCH<sub>3</sub>), 6.35 and 6.75 (6-H and 8-H), 6.90 (3-H), 7.01 (5'-H), 7.5–7.7 (6',2'-H), and 12.93 (5-OH); mass spectrum 314 (parent), 284 (M - 30), and 137 (C<sub>7</sub>H<sub>5</sub>O<sub>3</sub>). The flavone produced a brown color with ferric chloride, and a red-orange with magnesium-hydrochloric acid. The ultraviolet shifts with aluminum chloride (10%) were almost identical with those of 3',7-di-*O*-methylfluteolin.<sup>10</sup>

*Anal.* Calcd for C<sub>17</sub>H<sub>14</sub>O<sub>6</sub>· $\frac{1}{2}$ H<sub>2</sub>O (323.29): C, 63.15; H, 4.61. Found: C, 63.51; H, 4.29.

Treatment with acetic anhydride and a drop of sulfuric acid formed the diacetate (Ib), as colorless needles from benzene, mp 207° (lit.<sup>12</sup> 207°).

Methylation with dimethyl sulfate–potassium carbonate afforded luteolin tetramethyl ether (Ic), purified by sublimation at 175° (0.01 mm): mp 192–194° (lit.<sup>16</sup> 192–193°); mass spectrum 342 (parent), 313 (M - 29), 312 (M - 30), 181 (C<sub>9</sub>H<sub>9</sub>O<sub>4</sub>), 180 (C<sub>8</sub>H<sub>8</sub>O<sub>4</sub>), 162 (C<sub>10</sub>H<sub>10</sub>O<sub>2</sub>), 152 (C<sub>8</sub>H<sub>8</sub>O<sub>3</sub>), 147 (C<sub>9</sub>H<sub>9</sub>O<sub>2</sub>), and 137 (C<sub>7</sub>H<sub>5</sub>O<sub>3</sub>).

Demethylation with hydrogen iodide (49%) gave luteolin (Id), as yellow crystals from ethanol, mp 328–330° (lit.<sup>15</sup> 330–331°).

Registry No.—Ia, 25739-41-7.

**Acknowledgment.**—We thank the National Center for Urban and Industrial Health (Public Health Service Grant No. U1 00697) for the support of this work.

(14) Melting points are uncorrected. Microanalyses were provided by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Spectral measurements were made as follows: infrared (potassium bromide), ultraviolet (95% ethanol), and nuclear magnetic resonance (deuteriodimethyl sulfoxide, internal tetramethylsilane, 60 MHz). The mass spectrum was obtained on a double-focusing instrument. Thin layer chromatography employed silica gel G as the support, ethyl acetate as the developer, and iodine for detection.

(15) J. Gripenberg in "The Chemistry of Flavonoid Compounds," T. A. Geissman, Ed., Macmillan, New York, N. Y., 1962, p 406.

## Epoxidation of Griseofulvin. A New Reaction of the $\beta$ -Methoxyenone System

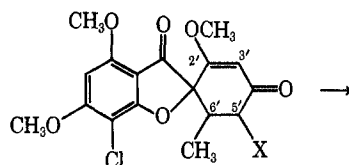
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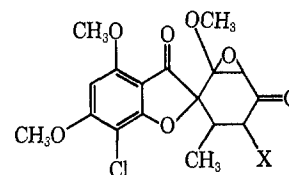
Received May 13, 1970

We would like to report that griseofulvin (1) and its 5'-bromo analog (8) are converted to their corresponding epoxy derivatives 2 and 9 in good yield by treatment with hydrogen peroxide and base. Epoxidation of 1 and its 5'-methylsulfonyl analog 5 was also achieved with benzoyl peroxide–methoxide in good yield but with poor conversion.

To the best of our knowledge this represents a new reaction of an enol ether of a  $\beta$ -diketone and would be expected to be generally applicable. We were led to this finding in the following manner.



- 1, X = H  
5, X = SO<sub>2</sub>CH<sub>3</sub>  
8, X = Br



- 2, X = H  
5a, X = SO<sub>2</sub>CH<sub>3</sub>  
9, X = Br

When we previously<sup>1</sup> attempted to introduce oxygen at C-5' in griseofulvin (1) by allowing 5'-formylgriseofulvin (3)<sup>2</sup> to react as its sodium salt with benzoyl peroxide in methanol, we obtained the overoxidized product, 5'-hydroxydehydrogriseofulvin (4), presumably owing to the ready decarbonylation of an initially formed 5'-oxygenated-5'-formyl intermediate. We hoped to circumvent this difficulty by using 5'-methylsulfonylgriseofulvin (5) in place of 3; however, we encountered another unexpected result.

Thus, on treating 5, readily obtainable from 5'-methylthiogriseofulvin<sup>3</sup> by peracid oxidation, with 1 equiv of sodium methoxide in methanol followed by 1 equiv of benzoyl peroxide, we obtained a product which was indicated by its nmr spectrum to be a 2-component mixture, in approximately a 1:1 ratio, consisting of unreacted 5 and a new substance in which the C-2'-C-3' double bond appeared to have been transformed. This was suggested by the appearance of a new OCH<sub>3</sub> signal in the spectrum at  $\delta$  3.27, 0.39 upfield from the OCH<sub>3</sub> in signal in 5, and a decrease in intensity (to  $\sim$ 0.5) of the vinyl proton of 5. Further characterization as detailed in the Experimental Section established its structure as the epoxide 5a.

Treating griseofulvin (1) in a similar manner gave a comparable result. The new product was isolated by thick layer chromatography and was formulated as epoxygriseofulvin (2) on the basis of its spectral (ir, nmr, mass spectrum) and analytical data. Its nmr spectrum additionally indicated it be a single isomer.

A significant improvement in the conversion of 1 to 2 was achieved by using hydrogen peroxide–base, the reagent commonly employed for epoxidizing  $\alpha,\beta$ -unsaturated ketones. (The epoxidation with benzoyl peroxide–methoxide is presumed to take place in a manner similar to that postulated for the hydrogen peroxide–base epoxidation,<sup>4</sup> the required benzoyl peroxy anion, PhCOO<sup>-</sup>, being generated by methoxide attack on benzoyl peroxide. The poorer conversion obtained with PhCO–OOCOPh<sup>-</sup>–OCH<sub>3</sub> could be due to the

(1) H. Newman, *J. Heterocycl. Chem.*, **7**, 957 (1970).

(2) H. Newman and T. L. Fields, *J. Org. Chem.*, **35**, 3156 (1970).

(3) (a) The facile preparation of this compound from 3 and methylthio-sylate<sup>3b</sup> will be published elsewhere shortly. (b) See R. C. Autrey and P. W. Scullard, *J. Amer. Chem. Soc.*, **90**, 4921 (1968).

(4) See the review on epoxy ketones by J. L. Pierre, *Ann. Chim. (Paris)*, **159** (1966).