

recrystallized from MeOH to white needles, m.p. 191~191.5° (with previous softening at 187.5°), undepressed on admixture with synthetic *N*. The superimposable IR and UV spectra also established identity of the two specimens. *Anal.* Calcd. for  $C_{18}H_{16}O_6 \cdot H_2O$ : C, 62.42; H, 5.24. Found: C, 62.71; H, 5.35.

Acetylation of the product with  $Ac_2O$  and  $AcONa$  in the usual manner gave an acetate as colorless needles, m.p. 227.5~228.5° (from EtOH), undepressed on admixture with 4'-acetate of synthetic *N*.

**4'-Hydroxy-3',5,7-trimethoxyflavone (IV)**—*N* was synthesized according to Nordström and Swain<sup>1)</sup> via 4'-benzyloxy-3',5,7-trimethoxyflavone, m.p. 192~193° (reported<sup>1)</sup> m.p. 208~209° (corr.)). *Anal.* Calcd. for  $C_{25}H_{24}O_6$ : C, 71.41; H, 5.75. Found: C, 71.44; H, 5.24.

*N* crystallized from MeOH as pale yellow needles, m.p. 186° (monohydrate), and m.p. 217° (anhydrous) (reported<sup>1)</sup> m.p. 223~224° (corr.)). UV  $\lambda_{max}^{EtOH}$   $m\mu$  (log  $\epsilon$ ): 242 (4.39), 265 (4.23), 338 (4.37), unchanged on addition of  $AcONa$  and  $AlCl_3$ . UV  $\lambda_{max}^{EtOH-EtONa}$   $m\mu$  (log  $\epsilon$ ): 256 (4.28), 289 (3.93), 400 (4.49). *Anal.* Calcd. for  $C_{18}H_{16}O_6 \cdot H_2O$ : C, 62.42; H, 5.24. Found: C, 62.38; H, 5.25. *Anal.* Calcd. for  $C_{18}H_{16}O_6$ : C, 65.85; H, 4.91. Found: C, 65.75; H, 5.01.

Acetylation of *N* with  $Ac_2O$  and  $AcONa$  in the usual manner gave 4'-acetoxy-3',5,7-trimethoxyflavone as colorless needles, m.p. 228~229° (from EtOH), a compound unrecorded in the literature. *Anal.* Calcd. for  $C_{20}H_{18}O_7$ : C, 64.86; H, 4.90. Found: C, 64.85; H, 4.94.

The writer is deeply indebted to Mrs. Yukiko Tanaka and Miss Seiko Fujishima, members of the Faculty of Pharmaceutical Sciences of this University, for determining infrared spectra and carrying out the elemental analyses, and to Mr. Manabu Yamashiro of Kumamoto Daiichi High School, for taxonomical aid.

### Summary

A flavonid glycoside (I),  $C_{21}H_{20}O_{11} \cdot 3H_2O$ , m.p. 243~244° (decomp.), was isolated in pure form from the leaves of *Acer cissifolium* K. KOCH, and identified as luteolin 4'- $\beta$ -D-glucoside, first isolated by Hörhammer, *et al.*<sup>5)</sup> from *Spartium junceum* L. (Leguminosae).

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### Takashi Seki\*<sup>1</sup> and Tomio Segawa\*<sup>2</sup>: The Relation between Chemical Structures and Hypnotic Effects of Some Imidazolidinone Derivatives.

(Pharmacological Section, Research Department, Pharmaceutical  
Division, Sumitomo Chemical Co., Ltd.\*<sup>1</sup>)

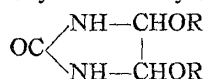
In the course of our investigation on a series of synthetic imidazolidinone derivatives we have found that some of these substances had central nervous system depressant properties in experimental animals. These compounds are 4,5-bis-alkyloxy or -alkenyloxy derivatives of 2-imidazolidinone with the following chemical structures: for the sake of convenience, they are referred to by their code numbers (Table I).

The alkenyloxy derivatives of 2-imidazolidinone are new substances which have never been disclosed in any printed articles. They are colorless, white needle, stable crystalline which are insoluble in water, soluble in methanol, chloroform and benzene.

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TABLE I. 4,5-Bis-alkyloxy or -alkenyloxy-2-imidazolidinones



Code numbers	R	Code numbers	R
SRC-6	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> -	SRC-14	CH <sub>3</sub> >CH-
-7	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> -	-15	CH <sub>3</sub> -CH=CH-CH <sub>2</sub> -
-8	CH <sub>3</sub> >CH-CH <sub>2</sub> -	-16	CH <sub>2</sub> =CHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> -
-9	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> -	-17	CH <sub>3</sub> CH=CHCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> -
-10	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> -	-19	CH <sub>2</sub> =CHCH <sub>2</sub> CH <sub>2</sub> -
-11	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> -	-20	CH <sub>3</sub> CH=CHCH <sub>2</sub> CH <sub>2</sub> -
-13	CH <sub>2</sub> =CH-CH <sub>3</sub> -		

In order to clarify the relation between chemical structures and their hypnotic effects we have examined the acute toxicity and hypnotic activity by administering these compounds to mice.

The suspension containing SRC-compounds and 5% gum arabic was administered in mice and the median lethal dose LD<sub>50</sub> within 24 hours was computed. The median hypnotic dose HD<sub>50</sub> was calculated as the dose which produced the loss of righting reflex in half the mice. Loss of righting reflex was said to have occurred if the mouse remains on its back for more than 20 seconds. The calculation of LD<sub>50</sub> and HD<sub>50</sub> were done by the method of Litchfield and Wilcoxon.<sup>1)</sup> The minimal hypnotic dose HD<sub>100</sub> was the dose which was necessary to produce loss of righting reflex in all mice.

### Experimental

The experimental results were summarized in Table II. Most of SRC-compounds were found to have low toxicity, produce the loss of righting reflex in mice. This effect was characterized by slow onset of and long duration of action. Lethal or near-lethal doses of SRC-compounds produced respiratory paralysis. In general it may be concluded that the hypnotic activity of these compounds is most potent when carbon number is four in alkyloxy or is five in alkenyloxy group with a few exception.

TABLE II. Acute Toxicity and Hypnotic Activity in Mice

Compd.	LD <sub>50</sub> (mg./kg.)			HD <sub>50</sub> (mg./kg.)			HD <sub>100</sub> (mg.kg.) i.p.
	s.c.	p.o.	i.p.	s.c.	p.o.	i.p.	
SRC-6	>2500	1800	840	790	520	215	300
-7	980	1430	890	440	670	350	450
-8	>2000	1780	820	1430	375	210	350
-9				>5000	>5000	>2500	
-10	>3000	>3000	620	1850	1380	245	300
-11				>5000	>5000	>5000	
-13	1650	1850	1600	820	1420	660	1000
-14				>3000	>3000	>3000	
-15	1750	1700	770	390	370	185	250
-16	621	740	450	182	239	134	175
-17				>2500	2500	1180	
-19		1480			580		
-20		>2000			1500		

1) J. T. Litchfield, Jr., F. Wilcoxon: J. Pharmacol. Exptl. Therap., 96, 99 (1949).

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### Summary

The hypnotic effects of some imidazolidinone derivatives were examined and the results suggested us that the most potent activity was obtained when carbon number is four in alkyloxy or is five in alkenyloxy group.

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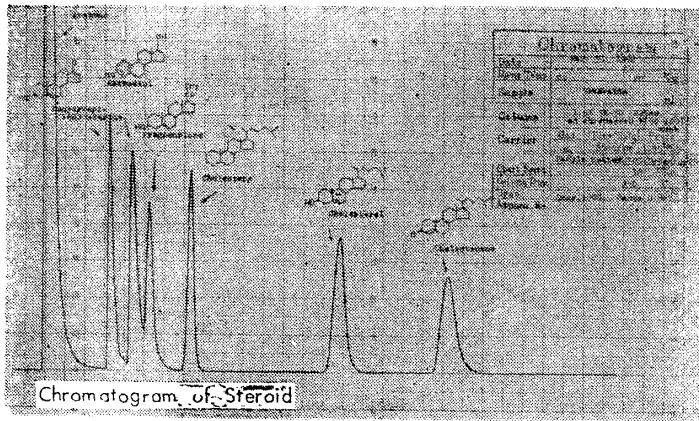
\* Top of Tops in Japan

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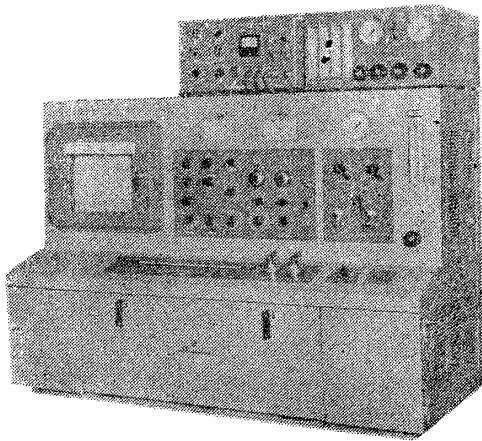
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