dissolved in 6 ml. of chloroform, and agitated overnight with 1 g. of freshly prepared manganese dioxide. The suspension was diluted with warm chloroform, filtered, washed, and concentrated to dryness. The resulting oil had a strong selective absorption around 240 mμ, but could not be crystallized even after chromatography. Acetylation in the usual manner, however, gave 127 mg. of IIIb, crystallized from hexane, m.p. 144–147°; λ_{max}^{MeOH} at 237 mμ (ϵ = 15,900); $[\alpha]_D^{25}$ +117.8; IR peaks at 5.80, 6.01, 6.18, and 8.08.

Anal. Calcd. for $C_{29}H_{32}O_5$: C, 71.10%; H, 8.30%; Found: C, 71.37%; H, 8.32%.

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Occurrence of Scopoletin in the Genus *Brunfelsia*

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Several *Brunfelsia* species (fam. *Solanaceae*) are widely used as ornamental or medicinal plants in Brazil and other South American countries and the roots of *Brunfelsia Hopeana* (Hook.) Benth. (popular name "Manacá") are listed in the Brazilian Pharmacopoeia. The older literature mentions a number of components but none seems to have been satisfactorily characterized so far. Lascelle-Scott[2] mentions the presence of an alkaloid which he named "francisceine." Lenardson[3] also reported on the alkaloid which he named "manacine." The most extensive paper is by Brandl[4] who worked on manacine and its degradation products. Later Peckolt[5] claimed to have isolated still another alkaloid which he named "brunfelsine." Although analytical data are presented by Brandl, none of the mentioned substances had been obtained in a crystalline state. The only crystalline compound mentioned thus far by Lenardson and Brandl is one which was notable because of its very strong blue fluorescence. Brandl[4] believed it to be aesculetin (6,7-dihydroxycoumarin) based on a color reaction and a combustion analysis.

In our own investigations concerning the possible occurrence of alkaloids in the mentioned plant, we could isolate the same fluorescent compound which, however, was not aesculetin but its methyl ether scopoletin, having been identified by mixture melting point and infrared and ultraviolet spectral comparison with an authentic sample.[6] Scopoletin (6-methoxy-7-hydroxycoumarin) has been found to occur in a number of plants of the *Solanaceae* and other families.[7]

Further investigation showed this compound to be present in other *Brunfelsia* species as well. It could be isolated from the following, all collected in the vicinity of Rio de Janeiro:

Brunfelsia Hopeana (Hook.) Benth. (Fraciscea uniflora Pohl.).

Brunfelsia calycina Benth. var. *macrantha* Bailey (Br. grandiflora Don.).

Brunfelsia ramosissima (Pohl.) Benth.

It was also found that the presence of the substance is not limited to the roots, but is general throughout the plants, in roots, stems, twigs, leaves, and flowers. Its remarkable fluorescence allows it to be easily detected hystologically by ultraviolet microscopy.

Isolation of scopoletin was accomplished by first extracting the ground plant material with water and then the aqueous extract continually with chloroform. The crude substance which remained after evaporation of the solvent was then purified by alternate sublimation *in vacuo* and recrystallization from ethanol. The melting point was 204°, the yield in all three species being close to 0.1%.

It is interesting to record that Lenardson, the earliest of the above mentioned investigators, thought that the crystalline compound could possibly be identical with the then recently discovered "gelseminic acid." We know today that "gelseminic acid" is, in fact, scopoletin and Lenardson's assumption was therefore quite correct.

Scopoletin has been found normally to occur only in trace amounts in plants of the family *Solanaceae* (tobacco, potato), but its concentration in the tissues increases significantly as a result of virus infection.[8,9,10] The fact that it is present in relatively high amounts in healthy plants of other genera of the same family suggests a similarity between the metabolism of healthy individuals of one genus with that of diseased individuals of another.

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Synthesis and Investigation of Organic Fluorine Compounds. XXII. The Preparation of Newer 2-Fluoroethylurethan Derivatives

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Biologically active fluorinated derivatives have been mentioned by Schrader[1] and Knunyants[2] among the derivatives of 2-fluoroethyl chloroformate. In two preceding papers[3,4] we have described a number of 2-fluoroethylurethan derivatives. Simultaneously with our investigations Sawicki, Ray, and Oliverio[5-7] have also published papers about the preparation of new fluorinated urethans.

The inhibiting action of fluoroacetic acid and 2-fluoroethanol, respectively, on the growth of experimentally produced malignant tumors has already been mentioned by us.[8,9] However, due to the rather high toxicity of both compounds, an attempt was made to find less toxic, biologically active derivatives. It appeared possible that the derivatives of 2-fluoroethylurethan would meet these requirements because their pharmacological tests[10] only show the appearance of toxic symptoms after a longer period of latency.

The compounds were too toxic in the chemotherapeutical experiments,[11] so that no significant effect could be observed. However, in some cases there was a slight but definite therapeutic activity toward cancer and we have therefore continued the preparation of further derivatives in the hope of finding less toxic members of the 2-fluoroethyl series. The new derivatives thus prepared are listed in Table I.

Some of the newly prepared derivatives have a toxicity of over 200 mg./kg./rat. The biological and probable insecticidal activity, which was observed by us in previous investigations,[12] will be reported elsewhere.

TABLE I

PREPARATION AND PROPERTIES OF 2-FLUOROETHYLURETHAN DERIVATIVES

R—NR′—$COOC_2H_4F$								
R	R′	B.P., °C.	Mm.	M.P., °C.	Method of preparation	Yield, %	Nitrogen Calcd.	Nitrogen Found
C_2H_5	H	116–117	30		A	90	13.59	13.52
iso-C_3H_7	H	110	30		A	91	9.40	9.28
C_4H_9	H	126–128	10		B	83	8.53	8.39
tert-C_4H_9	H	100	25		A	94	8.60	8.34
CH_2=$CHCH_2$	H	98–100	5		B	77	9.52	9.46
C_6H_{11}	H			63	A	88	7.43	7.27
$>CH_2$	$>CH_2$	91–93	12		B	90	9.78	9.77
o-C_2H_5-C_6H_4	H			81–82	B	79	6.66	6.36
2-CH_3-4-Cl-C_6H_3	H			88–89	B	81	6.06	6.01
2-CH_3-5-Cl-C_6H_3	H			84–85	B	77	6.06	6.00
C_6H_5	C_6H_5			83–84	C	69	5.40	5.33
p-CH_3CO-C_6H_4	H			153–154	A	81	6.25	6.14

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