The validity of this estimation depends on the following assumptions. (i) Plasma tryptophan is in rapid equilibrium with the compartment of brain tryptophan involved in the biosynthesis of HT. This assumption is supported by the relatively short average lifetime of a tryptophan molecule (calculated to be about 40 minutes from the data of Table 1) in the plasma compartment. (ii) Tryptophan hydroxylase is rate-limiting for HT biosynthesis (*7*); therefore, the rate constant for decarboxylation of 5-hydroxytryptophan must be much greater than that for tryptophan hydroxylation, and tryptophan concentration in neurons saturates the specific hydroxylase. (iii) HT stored in the brain behaves kinetically as a single compartment where newly synthesized amine rapidly mixes with already stored HT, a uniform metabolic pool being formed.

The effects of LSD and its 2-bromo derivative on the turnover rate of brain HT were measured as described. Table 2 shows that 2-bromo derivative and LSD in the doses administered neither changed the steady-state of plasma tryptophan nor altered the fractional rate constant of plasma tryptophan, as revealed indirectly by the specific activity of plasma tryptophan. In addition, Table 2 shows steady-state concentrations of brain HT, its specific activity, k_{HT}, and turnover rate of brain HT after a single injection (intraperitoneally) of LSD or the 2-bromo derivative. These data demonstrate that LSD but not its 2-bromo derivative decreased the turnover rate of brain HT. It should be mentioned that under these experimental conditions, LSD did not alter the steady-state concentration of brain HT as reported (*1*, *4*). ^{14}C-Tryptophan infusion was started 30 minutes after the injection of LSD. However, when LSD was infused intravenously together with ^{14}C-tryptophan, the brain HT concentration increased (Table 3). Hence, equations based on steady-state kinetics cannot be applied to derive k_{HT} or brain HT turnover rate under this condition. Nevertheless, the data show that LSD reduced the specific activity of HT in the brain. The conversion of ^{14}C-tryptophan to ^{14}C-HT was affected, perhaps at the rate-limiting step of tryptophan hydroxylation. The results in Table 3 also show that the 2-bromo derivative of LSD, infused in doses five-fold greater than the LSD dose, did not change the specific activity of brain HT.

Although these data support a relation between firing rate of serotonergic neurons and turnover rate of brain HT as suggested by Aghajanian *et al.* (*6*), they fail to prove this point because we have infused doses of LSD greater than those given by Aghajanian *et al.* Several problems prevent establishing a direct relation between the biochemical results and the physiological report on LSD mentioned above (*6*). It must be kept in mind that in rats the half-life of LSD is short, and our technique of measuring turnover rate of brain HT requires an infusion of ^{14}C-tryptophan lasting 40 minutes. Therefore, to measure the LSD effects on brain HT turnover rate the dose of LSD had to be increased to assure a persisting effect of this drug. In relating these data to the pharmacological profile of the two drugs tested, we note that the 2-bromo derivative of LSD, which is a much less potent hallucinogenic drug than LSD, failed to alter brain HT turnover rate.

If our results reflect an action of LSD on brain serotonergic neurons, then we propose that in the central nervous system, as well as in the periphery, LSD interacts with HT receptors (*9*). When LSD is applied to brain slices or to neurons of various brain regions in vivo through a micropipette, it facilitates or antagonizes the action of HT (*10*). The report of Aghajanian *et al.* (*6*) indicates that concentrations of LSD in tissues resulting from the doses he used may compare with the concentration of LSD in vitro that facilitates HT action (*9*, *10*). Consequently we might suggest that if LSD interacts with brain HT receptors, it may facilitate the effect of the amine on neurons as it does on the isolated uterus of rats (*9*). Regardless of the mode of action of LSD on brain HT turnover rate, the hallucinogenic effect of this drug in man may be related to the effect of LSD on HT turnover. However, no data are available suggesting that this possibility can be explored successfully. In conclusion, our results showed that LSD decreased brain HT turnover rate. The doses used were higher than those reported to decrease neuronal activity of raphe neurons (*6*).

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Allergenic Component of a Liverwort: A Sesquiterpene Lactone

Abstract. Frullania *spp.* (*Hepaticae, Jungermanniales*) *are agents of allergies. Extraction and fractionation of* Frullania tamarisci *has given, as the only allergenic component isolated, a levorotatory crystalline substance, the structure of which is demonstrated. It is a sesquiterpene lactone. The racemic* (±) *form is isolated from a mixed sample of* Frullania tamarisci *and* Frullania dilatata; *the dextrorotatory form, from* Frullania dilatata. *The observed allergenic properties are shared by some other sesquiterpene lactones.*

Some occupational allergies (contact dermatitis) associated with the handling of European woods are caused by epiphytic Bryophytes, namely Hepaticae such as *Radula* and the ubiquitous *Frullania.* An active extract had been obtained with ether (*1*). We have now shown that it contains, besides inactive components, an active eudesmanolide (structure **1**).

Frullania tamarisci (L.) Dum., growing on oak, was collected in the Vosges in October 1968 (*2*), and it was dried at room temperature. It was extracted with ether in a soxhlet, after it was milled. Fractionation of the extract (about 3 percent of the dry weight) was monitored by patch tests applied to a cooperating patient. Chromatography (silica gel) gave a major

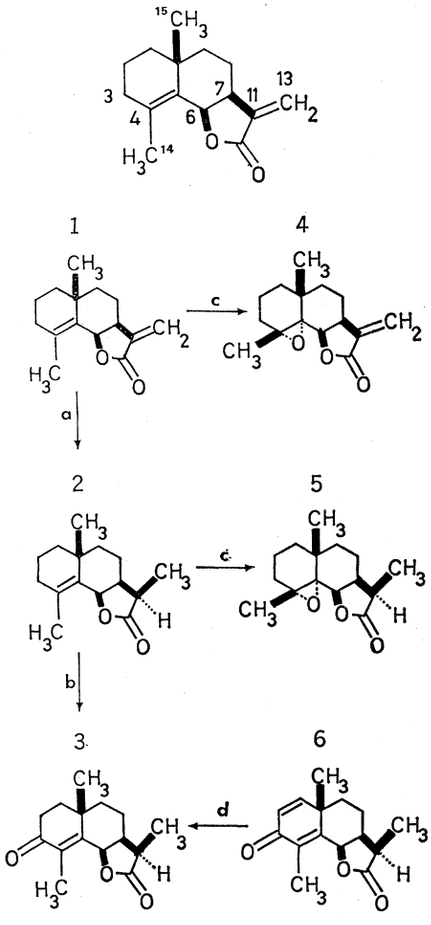

Fig. 1. The reagents used in the transformations shown were as follows. (*a*) Sodium borohydride and ethyl acetate; (*b*) sodium chromate and sodium acetate in acetic acid and acetic anhydride; (*c*) *p*-nitroperbenzoic acid and ethyl acetate; (*d*) hydrogen, tris-triphenylphosphinorhodium chloride, benzene, and ethanol. All reactions occurred at room temperature. Substances obtained were characterized as follows. Structure **2**, m.p. 69°C; infrared 1758, 1645 cm^{-1}. Structure **3**, m.p. 150°C; $[\alpha]_D$ −150°; maximum absorption (ultraviolet) at 245 nm (in ethanol) (molar extinction, 15,100). Structure **4**, m.p. 143°C, $[\alpha]_D$ −69°. Structure **5**, m.p. 183°C. Structure **6**, m.p. 193°C. All the substances mentioned gave analytical values within, at most, 0.4 percent of the theoretical values, and other spectral data are in agreement with the structures proposed.

active fraction, which yielded the inactive triterpene ketone friedelin from a benzene solution (about 0.05 percent). The mother liquors were distilled twice at reduced pressure to give, first a more volatile, inactive fraction (probably a sesquiterpene alcohol), and then a less volatile, viscous, active distillate [about 1 percent, boiling point at 0.1 torr at 120° to 130°C (bath temperature)]. This distillate crystallized nearly completely on standing. Recrystallization from hexane gave a highly active substance (about 0.2 percent), melting at 77°C; its specific rotation $[\alpha]_D$ was − 113° in $CHCl_3$; its composition was $C_{15}H_{20}O_2$. Its infrared spectrum in KBr showed bands at 1756, 1666, and 1644 cm^{-1}; the nuclear magnetic resonance spectrum showed signals at chemical shifts (δ, ppm) from tetramethylsilane: 6.18 and 5.60 (H-13); 5.28 (H-6); 2.98 (H-7); 1.76 (H-14), 1.09 (H-15), in $CDCl_3$.

Structure **1** was deduced from the spectral properties of the substance itself and of the derivatives prepared by the reactions summarized in Fig. 1. The α,β-unsaturated ketone **3** is identical with 1,2-dihydro-6-epi-β-santonin, prepared from 6-epi-β-santonin **6** (*3*).

A mixed sample of *Frullania* spp., containing mostly *Fr. tamarisci* (L.) Dum. and *Fr. dilatata* (L.) Dum., collected from rocks in the Dordogne region (August 1968) gave, by the same procedure, a less levorotatory solid distillate (about 1 percent), which on repeated crystallization from hexane gave a pure substance, melting at 95°C, which was optically inactive. This is the racemic mixture (±) of structure **1** as shown by the identity of nuclear magnetic resonance (NMR) spectra and of infrared spectra in solution and by the slight differences of the infrared spectra in the solid state. The product of epoxidation was similarly proved to be the optically inactive (±) structure **4**.

The isolation from liverworts of eudesmanolides extends the range of distribution of this class of substances, widespread in some tribes of Compositae (*4*). Our patient gave positive allergic reactions to several sesquiterpene lactones from Compositae (damsin, parthenin), but not to others (α-santonin, desacetylconfertifolin, psilostachyin B); his sensitivity does not appear to be directly linked with any of the individual functional groups present in structure **1**.

It is quite exceptional to find sesquiterpenes belonging to enantiomeric series (*5*). It may therefore be of more than passing interest to note that another liverwort contains (−)-longifolene, the enantiomer of the common sesquiterpene, (+)-longifolene (*6*).

Note added in proof: Extraction of homogeneous *Fr. dilatata* (L.) Dum., collected in the Dordogne area on saplings of chestnuts (April 1969) led (with J.-C. Muller) to the isolation of the pure enantiomer of lactone **1**, m.p. 76°C, $[\alpha]_D + 114°$; this is also allergenically active on our patient.

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2. We thank Prof. A. Gagnieux, Mrs. N. Ourisson, and Miss A.-M. Lambert for help in locating the plants, in collecting them, and in identifying them.
3. A sample of 6-epi-β-santonin was provided by Prof. W. Cocker, University of Dublin; it was hydrogenated as indicated in Fig. 1. 1,2-Dihydro-6-epi-β-santonin thus obtained was identical with a sample donated by Prof. E. Piers, University of British Columbia, Vancouver.
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Current-Voltage Relations during Illumination: Photoreceptor Membrane of a Barnacle

Abstract. *In voltage clamped photoreceptor cells of the barnacle, light-induced membrane current varied nonlinearly with membrane potential and changed sign at about + 27 millivolts (reversal potential) independently of light intensity. Instantaneous current-voltage relations were linear and intersected the voltage axis at the reversal potential. Illumination increased membrane conductance that was dependent on membrane potential, light intensity, and time.*

Upon illumination, changes in membrane potential of photoreceptor cells occur in several marine arthropod preparations such as the *Limulus* ommatidium (*1, 2*), the *Limulus* olfactory nerve (*3–5*), and the lateral ocellus of the barnacle (*6*). The positive shift of membrane potential or depolarization due to illumination usually consists of an early transient phase followed