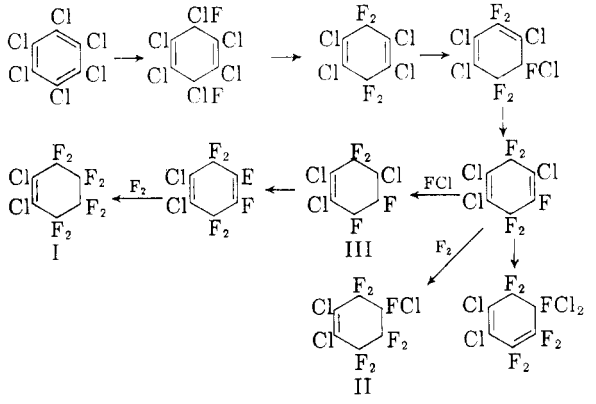
boiling CCl_4. The undissolved residue was discarded and the filtrate partially evaporated to deposit C_6Cl_6 on cooling. An infrared spectrum was run on this filtrate using a pure saturated solution of C_6Cl_6 in CCl_4 as a balance and unknown bands were found at 6.92 (m), 7.15 (s), 7.52 (m), 7.75 (w), 8.55 (m), 8.96 (w), 9.22 (w), 9.43 (w), and 14.71μ(s). An authentic sample of C_6Cl_5H in CCl_4 gave bands at 7.15 (s), 7.48 (s), 7.65 (w), 8.16 (w), 8.28 (w), 8.55 (s), 9.22 (m), and 14.68μ (s). Spectra were run of hexachlorocyclopentene and octachlorofulvene but neighter of these matched the unknown lines. Characteristic bands of octachlorocyclopentene listed in the literature[4] were also absent from this spectra. Therefore, at least one of the impurities present is C_6Cl_5H with still smaller amounts of other materials. The mechanism of the formation of IV is not known but must must come from a benzene starting material.

A mechanism for the formation of the cyclohexene compounds is shown below and is based on the usual addition-elimination mechanism found in fluorination. The conjugation of the double bond is similar to that suggested by Latif[5] in connection with the fluorination of octachlorocyclopentene.



During the initial phase of the fluorination, there will be relatively little Cl present, but as more and more SbF_3Cl_2 is produced there will be a sufficient amount present to allow chlorination of the starting material to produce $C_6F_6Cl_4$. This is the basis for the FCl addition to the intermediate $C_6F_6Cl_2$. In these reactions it is not known whether FCl or F_2 is added as a unit or by a stepwise mechanism involving SbF_4 + F and SbF_3Cl + Cl and no differentiation is made.

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(4) H. E. Ungnade and E. T. McBee, *Chem. Revs.*, **58**, 307 (1958).
(5) K. A. Latif, *J. Indian Chem. Soc.*, **30**, 525 (1953).

Synthesis of Isotopically Labeled Medicinals. II. 2-Benzylimidazoline-2-C^{14} Hydrochloride

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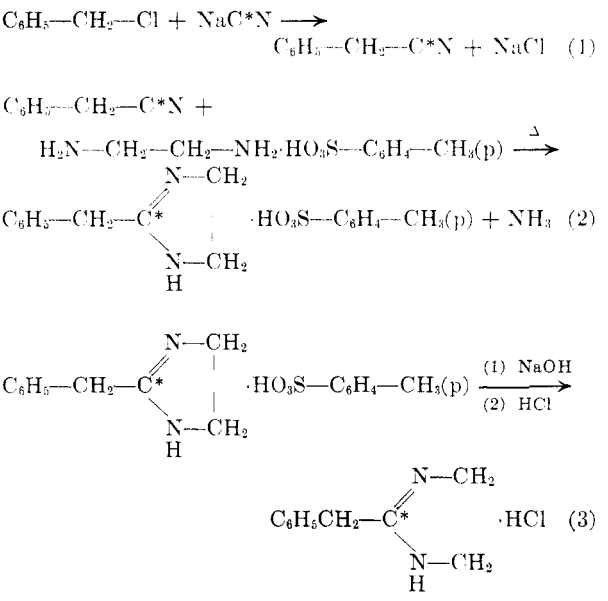
2-Benzylimidazoline hydrochloride[1] is an effective peripheral vasodilating agent and adrenergic blocking agent. A sample of this substance labeled with carbon 14 was required for fate studies in the mammalian body. Although it is manufactured commercially by the condensation of benzyl cyanide and ethylenediamine base in the presence of carbon disulfide, this reaction proved to be unsuitable in our hands on a 10-mmol. scale; only dark colored oils yielding little or none of the desired product were obtained. The modification of Oxley and Short[2] (use of ethylenediamine as the mono-*p*-toluenesulfonate) was finally employed successfully on a micro scale. The complete synthesis took the following form.



Details of the fate of this labeled 2-benzylimidazoline hydrochloride in the rat have been published elsewhere,[3] although it was erroneously stated in that publication that the compound bore the carbon 14 label at the methylene group between the benzene and imidazoline rings.

As is customary, the synthesis was worked out in detail using inactive sodium cyanide before making the target run using the labeled sodium cyanide. Since our sample of labeled sodium cyanide contained sodium hydroxide to minimize loss of the

(1) Tolazoline CIBA = Priscoline^R.
(2) P. Oxley and W. F. Short, *J. Chem. Soc.*, 497 (1947).
(3) B. Century, *Proc. Soc. Exptl. Biol. Med.*, **92**, 518 (1956).

label as HCN through hydrolysis, a compensatory excess of benzyl chloride was employed in the synthesis of the labeled benzyl cyanide to react with the sodium hydroxide and to conserve the active cyanide. The crude active benzyl cyanide was used directly in the next step to avoid losses attendant upon purification, and an excess of ethylene diamine mono-*p*-toluenesulfonate was used in order to conserve the labeled nitrile.

EXPERIMENTAL

Benzyl C^{14}-cyanide. The labeled sodium cyanide[4] (0.10 g.; 2 mmol., specific activity = 20 μc./mg.), containing 0.08 g. (2 mmol.) of sodium hydroxide, was placed in a 50-ml., round bottomed, ground-joint flask and diluted with 0.40 g. (8 mmol.) of inactive sodium cyanide. To this mixture was added 0.5 ml. of water, 2.0 ml. of 95% ethanol, and 1.65 g. (1.51 ml.; 13 mmol.) of benzyl chloride. The mixture was heated under reflux for 4 hr. Anhydrous ether was added and the solution was dried over anhydrous sodium sulfate and filtered. Removal of solvent *in vacuo* left a residue of crude benzyl cyanide.

2-Benzylimidazoline-2-C^{14} hydrochloride. The crude benzyl cyanide from above was treated with 3.01 g. (13 mmol.) of ethylenediamine mono-*p*-toluenesulfonate[2] and the flask was fitted with an air condenser. The mixture was heated at 200° for 1 hr., during which time ammonia gas was evolved, and then allowed to cool to room temperature. The solid was dissolved in 5 ml. of water and the solution was made strongly alkaline with 30% sodium hydroxide solution, precipitating an oil. The oil was taken up in chloroform and this solution was washed well with water. After drying over anhydrous sodium sulfate, the solvent was removed *in vacuo*. The orange gum was dissolved in 1.6 ml. of absolute ethanol and 3.2 ml. of ethyl acetate was added. After saturation with hydrogen chloride gas, 15 ml. of ether was slowly added with shaking. After standing overnight at room temperature, the supernatant liquid was decanted from the reddish brown gum, and this was washed with fresh ether by decantation. It was dissolved in the minimum amount of absolute ethanol and the solution was filtered to remove a small amount of an insoluble contaminant, m.p. 285–300° (uncorr.). The filtrate was heated to boiling and ethyl acetate was slowly added until crystallization had begun. After chilling overnight in the refrigerator, the crystalline material was collected by filtration, washed with a little fresh 6:1 ethyl acetate–absolute ethanol, ethyl acetate, ether, and finally air-dried. The pinkish crystals weighed 0.87 g., m.p. 170–174°. A second crop was obtained by combining mother liquors, adding ether, and crystallizing the resulting gum from absolute ethanol–ethyl acetate. After two additional crystallizations from the same solvent system, an additional 0.15 g. of tan crystals, m.p. 170–172° (uncorr.), was obtained. The combined crops (1.02 g.) were given a final recrystallization from absolute ethanol–ethyl acetate, affording 0.89 g. (45% of theory based on sodium cyanide), m.p. 170–172° (uncorr.) (lit. gives 175°,[2] 168–170°,[5a] 174°[5b]).

Anal. Calcd. for $C_{10}H_{13}N_2Cl$: N, 14.25; Cl, 18.03. Found: N, 14.44; Cl, 18.27.

The specific activity of the product was found[3] to be 1 μc./mg.

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(4) Tracerlab, Inc., 130 High Street, Boston 10, Mass.
(5a) British Patent **460,528; 514,411.**
(5b) S. R. Aspinall, *J. Am. Chem. Soc.*, 61, 3195 (1939).

Identification of Esculetin in Tobacco and in Cigarette Smoke

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In the purification of scopoletin (6-methoxy, 7-hydroxycoumarin) from cigarette smoke and from various tobacco extracts,[1,2] two or more interfering blue fluorescing compounds persisted with the scopoletin through several paper chromatographic developments. The present paper reports our identification of one of these interfering compounds as esculetin (6,7-dihydroxycoumarin).

We have identified esculetin for the first time in the leaves and flowers of oven-dried, greenhouse-grown, One-Sucker tobacco, in the tobacco of representative U. S. cigarettes, and in flue-cured and air-cured tobacco leaf samples. The mainstream smoke from representative U. S. cigarettes was found to contain esculetin in a trace amount.

The esculetin is extremely difficult to separate completely from scopoletin with such solvent systems as 15% acetic acid-water, 60% acetic acid-water; *n*-butyl alcohol–acetic acid–water (6:1:2 v./v.), and *n*-butyl alcohol–benzene-pyridine-water (5:1:3:3 v./v.), but separation on paper chromatograms may be accomplished with the solvent system nitromethane-benzene-water (2:3:5 v./v.).

In addition to its persistence with scopoletin on many paper chromatograms of various tobacco samples, esculetin may be confused on some of these chromatograms with caffeic acid. The R_f values of esculetin and caffeic acid are quite close in a number of solvent systems (Table I), and there is similarity in the bluish white fluorescence of esculetin and of caffeic acid when either is present only in low concentration on the chromatogram. Esculetin, however, behaves differently than does caffeic acid on paper chromatograms still wet with the solvent system *n*-butyl alcohol–benzene-pyridine-water. Under these conditions, esculetin fluoresces a bluish yellow when examined under long wave-length ultraviolet light (3660 Å) whereas the same concentration of caffeic acid exhibits only an extremely weak—practically imperceptible—fluorescence under the same conditions.

EXPERIMENTAL

Esculetin from tobacco flowers. Oven-dried flowers from One-Sucker tobacco plants, *Nicotiana tabacum*, grown in the greenhouse at Argonne National Laboratory, Lemont, Ill., appeared to be richer in esculetin than the leaves and other tobacco samples examined, and were, therefore, used for

(1) C. H. Yang, Y. Nakagawa, and S. H. Wender, *J. Org. Chem.*, **23**, 204 (1958).
(2) C. H. Yang, Y. Nakagawa, and S. H. Wender, *Anal. Chem.*, **30**, 2041 (1958).