inosine, and 5′-O-acetyl-2′,3′-O-isopropylideneinosine (V) at 254, 253.5, and 253.5 mμ, respectively. These results lead to the assignment of the tetrahydro-2-pyranyl group of VII to the 5′ position of sugar moiety. Further structural proof was obtained by conversion of VII and V to their corresponding methyl derivatives (VIII, IV), respectively, by treatment with diazomethane. The ultraviolet absorption maxima of both methyl derivatives shifted to shorter wave length, 251–251.5 mμ. No band was found near the 3100-cm^{-1} region in the infrared spectrum of VIII which might be assigned to NH vibration. On the basis of the infrared and ultraviolet absorption spectra, it is concluded that the methyl group was situated on N-1 in purine ring. These facts support the structure of VII as 5′-O-(tetrahydro-2-pyranyl)-2′,3′-O-isopropylideneinosine.

Experimental Section

Paper chromatography was carried out in the following solvent systems: solvent A, *n*-butyl alcohol–acetic acid–water (32:15:8); solvent B, isopropyl alcohol–concentrated ammonium hydroxide–water (7:1:2).

9-(Tetrahydro-2-pyranyl)adenine (I).—Ten grams of adenine (0.074 mole) was dissolved in 100 ml of dimethyl sulfoxide with 12 ml of a solution of hydrogen chloride in dry dioxane (7 *N*). Twenty ml of 2,3-dihydro-4H-pyran was added to the stirred solution at 55°–60°. The mixture was kept at 55–60° for 2 hr. A white solid (15 g) precipitated and, after filtration, was dissolved in a small amount of water. The aqueous solution was adjusted to pH 7 and cooled to give 10 g (62%) of crude I. Recrystallization from ethyl acetate gave colorless crystals, mp 181–181.5°.

Anal. Calcd for $C_{10}H_{13}N_5O$: C, 54.78; H, 5.98; N, 39.95. Found: C, 54.41; H, 6.26; N, 39.86.

1,9-Di(tetrahydro-2-pyranyl)hypoxanthine (II).—Eight grams of hypoxanthine (0.058 mole) was dissolved in 100 ml of dimethyl sulfoxide with 10 ml of a solution of hydrogen chloride in dry dioxane (7 *N*) with stirring at 55–60°. 2,3-Dihydro-4H-pyran (40 ml) was added to the solution and the mixture was held at 55–60° for 15 hr. No precipitate was appeared. After 7 ml of concentrated aqueous ammonium hydroxide was added, the mixture was concentrated under reduced pressure. The resulting gum was dissolved in ethyl acetate and the solution was washed with water. The organic layer was dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure, and the residue was dissolved in ethyl acetate. A white precipitate (8 g, 45%) formed. Recrystallization from ethyl acetate gave II, colorless crystals: mp 183–184°; R_f 0.92 (A), 0.96 (B). The mother liquor was saved for the next step.

Anal. Calcd for $C_{15}H_{20}N_4O_3$: C, 59.19; H, 6.62; N, 18.41. Found: C, 59.29; H, 6.67; N, 18.66.

1,7-Di(tetrahydro-2-pyranyl)hypoxanthine (III).—Concentration of the mother liquor of II left a residual syrup which was dissolved in benzene, applied to an alumina column and eluted with benzene–ethanol (ethanol: 0, 1, 5, 10, 50%). From the fraction of 5% ethanol–benzene, II and III were obtained. Recrystallization of the latter from ethyl acetate gave colorless crystals: mp 160–162°; R_f 0.95 (A), 0.95 (B).

Anal. Calcd for $C_{15}H_{20}N_4O_3$: C, 59.19; H, 6.62; N, 18.41. Found: C, 59.36; H, 6.90; N, 18.35.

7-(Tetrahydro-2-pyranyl)xanthine (VI).—From 5 g of xanthine (0.033 mole) 4 g of crude VI was obtained in the same way. Recrystallization from acetone gave colorless crystals, which decomposed over 200°: R_f 0.74 (A), 0.54 (B).

Anal. Calcd for $C_{10}H_{12}N_4O_3$: C, 50.8; H, 5.1; N, 23.7. Found: C, 50.22; H, 5.76; N, 23.55.

5′-O-(tetrahydro-2-pyranyl)-2′,3′-O-isopropylideneinosine (VII).—The reaction of 10 g of 2′,3′-O-isopropylideneinosine (0.033 mole) with 2,3-dihydro-4H-pyran resulted 7 g of crude VII which was recrystallized from ethyl acetate to give colorless crystals: mp 191–192° (dec); R_f, 0.89 (A), 0.89 (B).

Anal. Calcd for $C_{18}H_{24}N_4O_6$: C, 55.1; H, 6.12; N, 14.28. Found: C, 55.13; H, 6.35; N, 14.14.

1-Methyl-5′-O-acetyl-2′,3′-O-isopropylideneinosine (IV).—5′-O-Acetyl-2′,3′-O-isopropylideneinosine was added to the ether solution of diazomethane prepared from N-nitrosomethylurea. The solution stood over night at room temperature and evaporated. The residue was extracted by cyclohexane. After standing the extract precipitated crude IV: mp 85–88°; R_f 0.90 (A), 0.92 (B).

Anal. Calcd for $C_{16}H_{20}N_4O_6$: C, 52.8; H, 5.5; N, 15.4. Found: C, 52.82; H, 6.31; N, 15.06.

1-Methyl-5′-O-(tetrahydro-2-pyranyl)-2′,3′-O-isopropylideneinosine (VIII).—From VII, crude VIII was obtained in the same way: mp 77°–80°; R_f 0.93 (A), 0.95 (B).

Anal. Calcd for $C_{19}H_{26}N_4O_6$: C, 56.3; H, 6.4; N, 13.8. Found: C, 56.17; H, 7.03; N, 13.48.

Aryliodosodifluorides

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The aryliodosodifluorides have received limited attention[1–4] as fluorinating agents, possibly because of the difficulty involved in their preparation and storage. A method is now presented which allows a simple and rapid preparation of the reagent. It involves a one-step reaction of mercuric oxide and aqueous hydrofluoric acid with the iodosodichloride in methylene chloride. The methylene chloride solution is then used directly for fluorination.

$$ArICl_2 + HgO + 2HF \longrightarrow ArIF_2 + H_2O + HgCl_2$$

1a, Ar = phenyl
b, Ar = *p*-chlorophenyl
c, Ar = *p*-tolyl
e, Ar = *p*-nitrophenyl

Previously, phenyliodosodifluoride has been prepared from iodosobenzene and hydrofluoric acid.[1] Iodosobenzene has been prepared from phenyliodosodichloride or diacetate by base hydrolysis.[5] However, iodosobenzene, upon standing, disproportionates slowly into iodobenzene and iodoxybenzene, which cannot be converted to **1a** by treatment with hydrofluoric acid.

When Bockemüller treated 1,1-diphenylethylene with **1a** he obtained a difluoro compound which he assumed to be 1,1-diphenyl-1,2-difluoroethane (**2**). The compound has now been shown by nmr studies to be 1,2-diphenyl-1,1-difluoroethane (**3**); the same difluoro derivative, **3**, is produced from 1,1-diphenylethylene and lead tetrafluoride.[6]

Ph_2CFCH_2F **2** $\qquad$ $PhCF_2CH_2Ph$ **3**

Bockmüller noted that fluorination did not proceed without some added hydrogen fluoride. The methylene chloride solution of **1** generated by our procedure has enough hydrogen fluoride dissolved in it to catalyze

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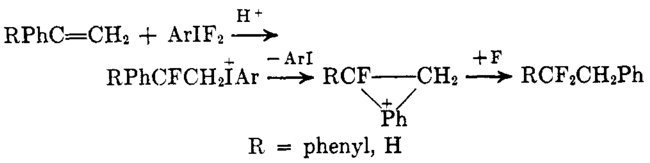
(5) (a) "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 483; (b) *ibid.*, p 482. (c) *Org. Syn.*, **43**, 60 (1963).
(6) J. Bornstein and M. R. Borden, *Chem. Ind.* (London), 441 (1958).

$$1 + PhCH{=}CH_2 \longrightarrow \underset{\mathbf{4}}{PhCH_2CF_2H}$$

the reaction with styrene. The structure of the product, 2,2-difluoroethylbenzene, was identified by its proton and ^{19}F nmr spectra. Again, as with 1,1-diphenylethylene, a rearrangement has occurred, probably *via* a phenonium ion intermediate. The role of



excess hydrofluoric acid is not clear but it appears to act solely as an acid catalyst. If the solution is filtered through magnesium oxide prior to use very little reaction occurs and **1** remains unchanged. Likewise if excess pyridine is added no reaction occurs. If the hydrofluoric acid is first removed by treatment with magnesium oxide and then replaced with trifluoroacetic acid the reaction proceeds vigorously and **4** is formed in about the same yield as if hydrofluoric acid were used. Furthermore, no evidence was obtained that the trifluoroacetate ion was incorporated in the products.

Of the various aryliodosodifluorides which have been prepared, the *p*-chlorophenyliodosodifluoride is the most convenient. Its precursor, the iodosodichloride, is easily prepared in high yield and keeps well in the refrigerator. The phenyl and tolyl iodides have a tendency to become partially chlorinated on the ring during the chlorination of the iodo group. The *p*-nitrophenyliodosodichloride is not sufficiently soluble in methylene chloride to allow convenient preparation of the difluoride.

Chloroform and benzene have also been used with success in the formation of the iodosodifluorides. Saturated hydrocarbons are not good solvents. Acetonitrile and tetrahydrofuran react with the reagents.

Experimental Section

Aryliodosodichloride.—The aryliodosodichlorides were prepared according to known procedures,[5b] or adaptations thereof.

Aryliodosodifluorides.—The aryliodosodifluorides were all prepared by procedures analogous to the one shown here for *p*-chlorophenyliodosodifluoride. *p*-Chlorophenyliodosodichloride (12.3 g, 0.04 mole) and 10.8 g of finely ground yellow mercuric oxide (0.05 mole) were shaken with 100 ml of methylene chloride in a polyethylene bottle.[7] Hydrofluoric acid (48%, 10 ml) was added and the bottle shaken vigorously for about 1 min. The color of the solution turned from bright yellow to nearly colorless. In some instances a small additional amount of mercuric oxide was required to completely discharge the yellow color. The methylene chloride phase was carefully decanted. The residue was shaken with 50 ml of methylene chloride, which was then decanted and combined with the original solution. The combined solution (1 ml) was analyzed by titration of the iodine liberated by reaction with aqueous potassium iodide. From the volume of the reagent solution the yield was calculated, typically in the range of 60–90%.

1,1-Difluoro-1,2-diphenylethane.—Phenyliodosodifluoride was prepared according to directions given above with 20.9 g (0.076 mole) of phenyliodosodichloride. Iodometric analysis indicated that 0.0592 moles of the iodosodifluoride was present in the 187 ml of solution. This solution was stirred at 0° while 9.43 g (0.0524 mole) of 1,1-diphenylethylene in 35 ml of methylene chloride was added over a period of 20 min. The reaction was kept at 0° for 3 hr before being washed with aqueous sodium bicarbonate solution, dried over anhydrous magnesium sulfate, and concentrated to 11.3 g of dark brown viscous oil. The oil was dissolved in 100 ml of pentane and chromatographed on 50 g of alumina. In addition to iodobenzene and recovered starting material, 5.4 g (47%) of white crystals melting at 57–63° was obtained. After recrystallization from pentane they melted at 65–67°, lit.[1] mp 66°. The nmr spectrum showed peaks at τ 2.85 and 2.97 (phenyl), and τ 6.73 (CH_2), a triplet with a splitting of 0.26 ppm.

Anal. Calcd for $C_{14}H_{12}F_2$: C, 77.04; H, 5.54; F, 17.41. Found: C, 76.76; H, 5.59; F, 17.32.

1,1-Difluoro-2-phenylethane.—*p*-Chlorophenyliodosodichloride (30.95 g, 0.1 mole) was converted to the iodosodifluoride by the method described above using 200 ml of methylene chloride, 25 g of mercuric oxide, and 30 ml of hydrofluoric acid. To the decanted methylene chloride solution was added 15 g (0.14 mole) of styrene at room temperature. After 3 hr the solution was washed with aqueous sodium bicarbonate, dried by filtration through anhydrous magnesium sulfate, and concentrated to an amber oil which was then distilled. The fraction boiling at 130–150° at atmospheric pressure (11.1 g) was analyzed by gas chromatography. A 20 ft × $^3/_8$ in. column packed with 20% FS-1265 silicone fluid (10,000 cts) on Chromosorb W was maintained at 140° with a helium flow rate of 200 cc/min. 1,1-Difluoro-2-phenylethane, retention time 9.8 min, and styrene, retention time 7.1 min, were the major constituents of the mixture. A yield of 37% based on the iodosodichloride was calculated from the gc analysis by using the corrected thermal response values of all the major components. The product was collected by preparative-scale gas chromatography on the same column. The proton nmr spectrum showed bands at τ 2.83 (phenyl), τ 4.27 (terminal proton), a triplet of triplets with J = 0.95 cps for the coupling with CF_2, τ 7.01 (CH_2), a triplet of doublets with J = 0.30 cps for the coupling with CF_2. The fluorine nmr had a pair of triplets at 115 ppm relative to trichlorofluoromethane.

Anal. Calcd for $C_8H_8F_2$: C, 67.60; H, 5.67; F, 26.73. Found: C, 67.53; H, 5.73; F, 27.01.

Acid Catalysis of the Fluorination.—The preparation of *p*-chlorophenyliodosodifluoride was repeated according to directions above. The reagent solution was divided into four parts. Styrene (5 ml) in 30 ml of methylene chloride was added to the first part, and 5.0 ml of styrene in 30 ml of pyridine was added to the second part. The third and fourth parts were each treated with 5 g of magnesium oxide and filtered. Styrene (5 ml) in 30 ml of methylene chloride was added to the third part and 1.0 ml of trifluoroacetic acid and then 5.0 ml of styrene in 30 ml of methylene chloride was added to the fourth part. After 20 hr each sample was analyzed by vpc. 1,1-Difluoro-2-phenylethane was produced in 37% yield in part 1, 0% in part 2, 3% in part 3, and 32% in part 4. Samples from parts 2 and 3 released iodine with aqueous potassium iodide solution; parts 1 and 4 did not.

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(7) Wherever possible, polyethylene ware was used to avoid the decomposition of the reagent on glass surfaces.

Synthesis of Retuline

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The isolation of a new alkaloid, retuline ($C_{21}H_{26}O_2N_2$), from an African *Strychnos* species was reported in 1951.[2] It was shown to lack O-methyl and N-methyl groups and its ultraviolet spectrum was reminiscent of that

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