

tautomer II reveals that each of these substances contains the molecular fragment  $-\text{CH}-a-\text{N}-b-\text{CH}-c-\text{C}(\text{CH}_2\text{CH}_2\text{NH}_2)-$ . As  $\beta$ -(3-pyridyl)-ethylamine is devoid of any histamine-like activity, we conclude, on the basis of the preceding argument, that tautomer II is likewise devoid of any histamine-like activity. This conclusion is in accord with and supports the previous contention that tautomer I is the structure responsible for the histamine-like activity of histamine and that the principle obligatory structural requirement for histamine-like activity is the molecular fragment  $-\text{CH}-a-\text{N}-b-\text{C}(\text{CH}_2\text{CH}_2\text{NH}_2)-c-\text{CH}-$ .

### Experimental<sup>9</sup>

**$\beta$ -(3-Pyridyl)-ethylamine Dihydrochloride.**—A mixture of 1 g. of *dl*- $\beta$ -(3-pyridyl)-alanine<sup>2</sup> and 20 g. of diphenylamine was heated to 245–250° and maintained at that temperature for two hours.<sup>3</sup> The reaction mixture was digested with 40 ml. of 3 *N* hydrochloric acid and the digest allowed to cool to 25° with vigorous stirring. The diphenylamine was removed by extraction with ether, an excess of aqueous sodium hydroxide added to the aqueous phase and the latter extracted with ether. The ethereal solution was dried over sodium sulfate and then acidified with dry hydrogen chloride. The amine dihydrochloride separated as an oil, which was collected and crystallized from 20–25 ml. of hot absolute ethanol. This product (0.4 g.) was recrystallized from a mixture of absolute ethanol and ether to give  $\beta$ -(3-pyridyl)-ethylamine dihydrochloride, m. p. 195–205° with decomposition.

(9) Microanalyses by Dr. G. Oppenheimer and G. A. Swinehart.

*Anal.* Calcd. for  $\text{C}_7\text{H}_{12}\text{N}_2\text{Cl}_2$  (195.1): C, 43.1; H, 6.2; N, 14.4; Cl, 36.4. Found: C, 43.3; H, 6.3; N, 14.4; Cl, 36.4.

**Preliminary Pharmacological Report.**<sup>10</sup>—In the cat both  $\beta$ -(3-pyridyl)-ethylamine and  $\beta$ -(4-pyridyl)-ethylamine are pressor in minimally active and higher doses, being about one-fifth to one-tenth as active as  $\beta$ -phenylethylamine. In the rabbit the pressor responses are not great with minimally active doses and with higher doses an initial depressor effect may be noted that is, however, unlike that of histamine, and is shown in similar degree by both  $\beta$ -(3-pyridyl)-ethylamine and  $\beta$ -(4-pyridyl)-ethylamine. In sufficient concentration both  $\beta$ -(3-pyridyl)-ethylamine and  $\beta$ -(4-pyridyl)-ethylamine decrease movement and tone of isolated rabbit jejunum preparations. This resembles the activity of more than minimally active concentrations of  $\beta$ -phenylethylamine, and is the reverse of the effect of histamine. No stimulant effect in concentrations up to  $10^{-3}$  molar was noted upon isolated guinea-pig ileum preparations though this same concentration of  $\beta$ -phenylethylamine causes some increase in tone and concentrations of but  $10^{-6}$  molar histamine are very active upon such preparations.

### Summary

$\beta$ -(3-Pyridyl)-ethylamine has been prepared and it has been found that this amine, in common with  $\beta$ -(4-pyridyl)-ethylamine and in contrast to  $\beta$ -(2-pyridyl)-ethylamine, has pressor activity. The relation between structure and histamine-like activity is discussed.

(10) The authors are indebted to Dr. G. A. Alles for this report and to Dr. L. A. Walter for samples of  $\beta$ -(2-pyridyl)-ethylamine and  $\beta$ -(4-pyridyl)-ethylamine.

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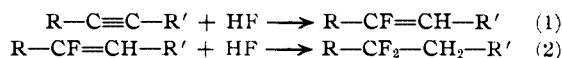
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UNIVERSAL OIL PRODUCTS COMPANY]

## The Addition of Hydrogen Fluoride to the Triple Bond<sup>1</sup>

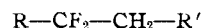
BY ARISTID V. GROSSE<sup>1a</sup> AND CARL B. LINN

We have recently demonstrated<sup>2</sup> that olefins will add hydrogen fluoride, even in the complete absence of catalysts, to give good yields of alkyl fluorides. Likewise the cyclopropane ring is opened by hydrogen fluoride to give *n*-propyl fluoride. The chemical literature contains no reference to a similar addition of hydrogen fluoride to the triple bond. In view of the ease of addition to the double bond, a similar behavior was expected of the *triple bond*. This proved to be the case and we found that unsaturates of this

type readily *add hydrogen fluoride* in the *absence of catalysts*, according to the equations



giving *difluorinated hydrocarbons* of the type



Previous to our investigation only the two simplest<sup>3</sup> members of this series were known, namely, 1,1-difluoroethane<sup>4</sup> and 2,2-difluoropropane.<sup>5</sup> Subsequently A. L. Henne, in his well known studies of aliphatic fluorine compounds, has extended the reaction of antimony or mercuric

(1) Presented before the Organic Section of the American Chemical Society at its Baltimore meeting, April, 1939 (see Abstracts, Section M., p. 27).

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(2) A. V. Grosse and C. B. Linn, *J. Org. Chem.*, **3**, 26 (1938).

(3) For  $\text{CH}_2\text{F}_2$ , see A. L. Henne, *THIS JOURNAL*, **59**, 1400 (1937).

(4) A. L. Henne and M. W. Renoll, *ibid.*, **58**, 889 (1936).

(5) A. L. Henne and M. W. Renoll, *ibid.*, **59**, 2434 (1937).

fluorides upon the corresponding dichloro compounds and recently described<sup>6</sup> 2,2-difluorobutane and -pentane. 1,1-Difluoroheptane has also been reported by him.<sup>6</sup>

We have accomplished the *addition of hydrogen fluoride to ethyne, propyne, butyne-1 and -2, pentyne-1, hexyne-1 and -3 and heptyne-1.*

The formation of an unsaturated monofluoride, according to equation 1 above, was demonstrated only in the case of acetylene where *vinyl fluoride* was isolated. Each of the other alkynes studied yielded a saturated compound analyzing for two atoms of fluorine in the molecule.

The possibility is not excluded that, under appropriate conditions, the method may be developed as a means of preparing monofluorides of the formula  $RCF=CHR'$ .

The addition of *both* hydrogen fluoride molecules takes place according to Markownikoff's rule and in line with Kharasch's theory,<sup>7</sup> leading to the attachment of *both* fluorine atoms to the *same* carbon atom.

The structure of our difluoroparaffins was definitely established in the case of the products from ethyne, propyne, butyne-1 and -2 and pentyne-1 by the identity of their physical properties with those prepared by Henne's substitution method from dichlorides of known structure (see Table I; for ethyne see p. 2291).

Further proof of the above-mentioned reaction scheme is the fact that butyne-1 and butyne-2 hydrofluorinate to give an *identical* reaction product, as can also be seen in Table I. Butyne-2 can yield no product with a fluorine attached to a terminal carbon atom and in this case it is shown that the second atom of fluorine entering goes to the already fluorinated carbon, as would be expected.

There is no reason to assume that the entering fluorine atoms take different or abnormal positions in the higher alkynes. A rigid characterization of these compounds, however, is hindered because there is no reaction, as yet, by which a fluorine atom in such a molecule may be converted into another atom or group.<sup>8</sup>

Our difluorides are completely inert and do not lose hydrogen fluoride, in contrast to aliphyl

fluorides,<sup>2</sup> a point stressed by Henne and Renoll,<sup>5</sup> relative to 2,2-difluoropropane. They have a not unpleasant odor, somewhat like straight chain paraffins. Their indices of refraction are substantially lower than those of paraffins of equal boiling points.

### Experimental

**Source of Reagents.**—The acetylene was from Prest-O-Lite welding cylinders. The propyne was prepared by us by treating methyl sulfate with sodium acetylide prepared according to the directions of G. F. Hennion.<sup>9</sup> The other alkynes<sup>10</sup> were prepared for us by Dr. Hennion at the University of Notre Dame and fractionated before use. The anhydrous hydrogen fluoride for all these preparations was supplied in cylinders by the Harshaw Chemical Company. It was over 99% pure and contained only 0.1% of water, and less than 0.04% of residue on evaporation at 100°.

**The Action of Hydrogen Fluoride on Acetylene.**—Preliminary experiments showed that there was *no reaction* when acetylene was passed into hydrogen fluoride at temperatures of -70 and 0°, respectively, although at the latter temperature there was some formation of a solid polymer. In another experiment a mixture of acetylene and hydrogen fluoride in molal ratio 1:3, was passed through a nickel reaction tube packed with nickel shavings, at a temperature of 300°. At a contact time of five seconds, the acetylene went through unreacted except for the formation of a black powder in the heated part of the reaction tube. The exit gas after being freed from hydrogen fluoride had a molecular weight of 26 (acetylene = 24) and contained no constituent of higher boiling point than acetylene. Pressure experiments, however, achieved hydrofluorination of acetylene.

**Experiment under Pressure at Room Temperature.**—Into a stainless steel autoclave of 1 liter capacity equipped with a mechanical stirrer was charged 128 g. of hydrogen fluoride. To this was connected a line supplying acetylene under pressure from a commercial cylinder. During the course of the reaction the operator was protected by a curtain of steel and remote controls were used. With the reactor at room temperature, the pressure was raised to 13 atmospheres, a temperature rise of 3° being observed. The pressure dropped slowly over a period of hours and was maintained at 8-12 atmospheres for seventy-two hours, during which time the autoclave contents was stirred continuously. The autoclave was then cooled in an ice-bath and the pressure released through a line which scrubbed out the hydrogen fluoride vapors, dried the gas; and then passed through a trap cooled to -78°. 12 g. of water-white liquid condensed in the trap. The non-condensable gas was shown to be pure acetylene. Inside the autoclave was found 30 g. of a polymer, which when washed and dried was a brittle brownish-black solid burning with difficulty.

The condensable gas was distilled on a low temperature Podbielniak column and separated into two constant boil-

(6) A. L. Henne, M. W. Renoll and H. M. Leicester, *THIS JOURNAL*, **61**, 939 (1939).

(7) M. S. Kharasch, Engelmann and Mayo, *J. Org. Chem.*, **2**, 298 (1937).

(8) Cyclohexyl fluoride readily can be converted into cyclohexyl chloride by the action of antimony trichloride (unpublished work of the authors).

(9) Paper presented before the Indiana Academy of Science at Manchester College, November 5, 1937.

(10) A comparison of some physical properties of our butyne-1 and -2 samples will be given in another paper.

ing fractions. Fraction 1, corresponding to 35 mole %, boiled at  $-72^{\circ}$  and had a molecular weight of 45 (Dumas), while fraction 2, equalling 65 mole %, boiled from  $-26$  to  $-24^{\circ}$  and had a molecular weight of 65. Approximately 15% of the acetylene reacting was converted into these two products.

These data check those described by Julius Söll of the I. G. Trust in a German patent<sup>11</sup> for physical constants of vinyl fluoride and 2,2-difluoroethane. Söll prepared them by the catalytic hydrofluorination of acetylene in the presence of mercury salts and/or activated charcoal.

Fraction 1 thus corresponds to vinyl fluoride,  $\text{CF}_2=\text{CHF}$ , mol. wt. 46; b. p.  $-72.2$  (760 mm.).<sup>11</sup>

Fraction 2 corresponds to 1,1-difluoroethane,  $\text{CH}_3-\text{CHF}_2$ , mol. wt., 66; b. p.  $-24.7$  (760 mm.).<sup>11</sup>

The refractive index ( $n_D$ ) of the 1,1-difluoroethane was 1.3011 at  $-72^{\circ}$  or extrapolated to room temperature  $\approx 1.255$ . As far as we know, this is the lowest index of refraction ever recorded for an organic or inorganic liquid compound.

### The Action of Hydrogen Fluoride on Propyne and Higher Alkyl Acetylenes

**Description of Apparatus and Procedure.**—As shown in the attached drawing (Fig. 1) the reaction chamber was a nickel cylinder 5 cm. in diameter, 35 cm. high, and open at the top. Into this was fitted a rubber stopper carrying an oil-sealed nickel stirrer, a dropping funnel, a thermocouple, and a "cold-finger" reflux cooled by dry-ice and acetone. The cylinder was surrounded by a cooling bath of acetone and dry-ice. In the case of propyne the dropping funnel was replaced by a copper tube through which the gaseous alkyne was introduced directly into the liquid hydrogen fluoride.

A distinct temperature effect was noted during the addition of alkyne, the operation requiring around forty minutes. The reaction appeared to be instantaneous. Stirring was continued for an additional thirty minutes and the product worked up immediately. When alkynes above propyne were used, cracked ice was added to the reaction mixture, it was warmed to  $0^{\circ}$  and poured into a separatory funnel where the water insoluble reaction product was quickly removed from the hydrofluoric acid, washed several times with water, dried with potassium carbonate, and then carefully distilled. With propyne, the above procedure had to be modified so that no product was lost during the dilution of the hydrogen fluoride with water. Water was added slowly from a dropping funnel in a closed system and escaping gas was washed through dilute alkali, dried with soda lime and calcium chloride and condensed in a trap cooled to  $-78^{\circ}$ .

**Anal.** The liquid difluorides were analyzed for carbon and hydrogen by the technique described by Schiemann and Pillarsky,<sup>12</sup> using, in addition to copper oxide, both lead chromate and silver gauze. The fluorine determination was carried out as previously described.<sup>13</sup>

### Results

In our experiments about one-half gram mole of the lower alkynes and one-quarter gram mole of

(11) German Patent 641,878.

(12) Schiemann and Pillarsky, *Ber.*, **62**, 3043 (1929).

(13) A. V. Grosse, R. C. Wackher and C. B. Linn, *J. Phys. Chem.*, **44**, 277 (1940).

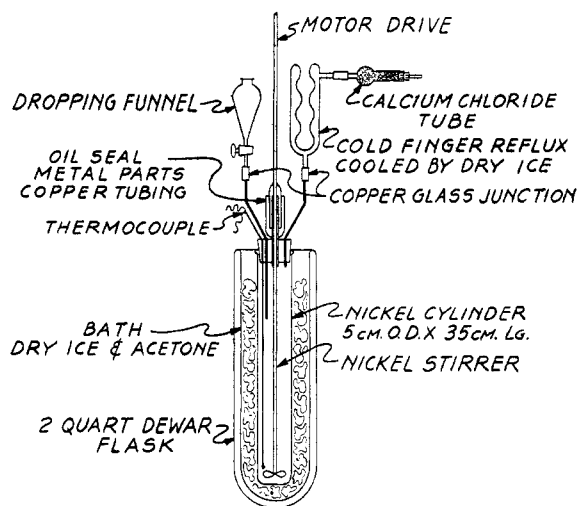


Fig. 1.

the hexynes and heptynes were charged into the reaction vessel and ten molecular equivalents of anhydrous hydrogen fluoride added. The temperature, initially  $-70^{\circ}$ , was controlled by stirring, etc., so that it did not rise more than  $5-15^{\circ}$ . The time of addition varied from one to one and one-half hours.

A crude liquid product, insoluble in water, was recovered which in every instance weighed  $1.24 \pm 0.03$  times the weight of the alkyne originally charged.

The yield of difluoride based on the alkyne charged averaged 65%, but varied between the extreme limits of 46% in the butyne-1 case and 76% in the case of hexyne-3.<sup>14</sup>

The extreme ease of hydrofluorination of the higher alkynes, which react instantly and completely at temperatures as low as  $-70^{\circ}$ , stands in contrast to the reaction of hydrogen fluoride with acetylene, where hydrofluorination was only achieved by the use of relatively high pressures and a long contact time at room temperature. This enhanced reactivity of higher alkynes contrasted to acetylene is, however, experienced in its other reactions, as recorded in the literature.

Table I gives the properties of our products as determined upon a well-fractionated and sharply boiling cut.

As can be seen from Table I the properties of difluorides formed from ethyne, propyne, butyne-1, butyne-2 and pentyne-1 are in general agreement with the predicted difluorides prepared by the method of Henne and others.

(14) For additional details, see U. S. Patent 2,287,934.

TABLE I  
 PROPERTIES OF DIFLUORO-ALKANES FROM REACTION OF ALKYNES WITH HYDROGEN FLUORIDE

Difluoro-alkanes	B. p., °C.	Press., mm.	$d_{20}^{20}$	$n_D^{20}$	$n_D^{25}$	Mol. wt.	
						Calcd.	Found
2,2-Difluoropropane <sup>a</sup> (Henne's) <sup>b,h</sup>	-0.1 -0.6-0.2	760 760	0.9205 <sup>g</sup> 92	1.2904 <sup>g</sup> ..	1.3036 1.3043	80.1 80.1	79 ...
2,2-Difluoro-butane from butyne-1 <sup>c</sup> from butyne-2 <sup>d</sup> (Henne's)	30.4-30.6 30.4-30.6 30.8	747 747 760	.9016 .9016 .9012	1.3133 1.3140 1.3140	.. .. ..	94.1 94.1 94.1	93 93 ...
2,2-Difluoro-pentane (Henne's)	58.2-58 59.8	749 760	.8904 .8958	1.3352 1.3357	.. ..	108.1 108.1	109 ...
2,2-Difluoro-hexane <sup>e</sup>	86.0-2	750	.8923	1.3535	1.3744	122.1	122
3,3-Difluoro-hexane <sup>f</sup>	86.0	742	.9024	1.3546	1.3757	122.1	120
2,2-Difluoro-heptane <sup>g</sup>	111.7-9	749	.8889	1.3659	1.3866	136.1	134

<sup>a</sup> M. p., -104.8°. <sup>b</sup> M. p., -105 to -108°. <sup>c</sup> M. p., -116.9°. <sup>d</sup> M. p., -117.1°. <sup>e</sup> Calcd.: C, 58.97; H, 9.91; F, 31.12. Found: C, 56.4; H, 9.46; F, ≈34.1. <sup>f</sup> Calcd.: C, 58.97; H, 9.91; F, 31.12. Found: C, 58.76; H, 9.81; F, 31.43. <sup>g</sup> Calcd.: C, 61.70; H, 10.37; 29.93. Found: C, 61.51; H, 10.32; F, 28.17. We prepared about 20.8 g. of Henne's difluoride by treatment of antimony trifluoride with acetone dichloride; its mixed melting point with ours -108°.

It is important to note that the difluorides from butyne-1 and -2 were identical among themselves (see Table I; furthermore, the mixed melting point -116.9°, *i. e.*, showed no depression) and also with Henne's compound.

**By-Products of the Reaction.**—The hydrofluorination of propyne gave a 61% yield of the difluoride, based on the charge. The rest was accounted for in an amorphous, light brown solid (7 g. from 19 g. of propyne), similar to the solid encountered in the acetylene reaction. Elementary analysis of this solid showed it to have the composition: C, 79%; H, 9%; F, 12% (by difference) corresponding approximately to the formula  $C_6H_{13}F$  or  $3C_3H_4, HF$ . In the case of alkynes above propyne the crude products on distillation yielded liquids of higher boiling point, higher refractive index and lower density than the main product, indicating alkyne *polymers* rather than fluorides.

**Acknowledgment.**—The authors wish to thank

Mr. Willard Mann for assistance with the laboratory work pertaining to this investigation.

### Summary

1. A new reaction, the direct non-catalytic, addition of hydrogen fluoride to alkynes giving a series of difluoroparaffins, of the formula  $R-CF_2-CH_2-R'$ , has been described.

2. With the exception of acetylene the alkynes studied, namely, propyne, butyne-1, butyne-2, pentyne-1, hexyne-1, hexyne-3, and heptyne-1, all reacted at temperatures around -70° to give good yields of a difluorinated paraffin.

3. The properties of 2,2-difluoro-propane, -butane, -pentane, -hexane, -heptane and 3,3-difluoro-hexane are described.

4. The hydrofluorination of acetylene was accomplished by contacting it with liquid hydrogen fluoride in an autoclave under pressure. 1,1-Difluoro-ethane and vinyl fluoride were the reaction products isolated.

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