TOXIC FLUORINE COMPOUNDS

XIX. ω-FLUOROALKYNES[1]

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Received June 3, 1963

ABSTRACT

Some ω-fluoroalkynes have been prepared and shown to be valuable intermediates in the synthesis of rare long-chain ω-fluoro compounds; successful representative reactions, in all of which the C—F bond remained intact, included Grignard reactions, partial and total catalytic hydrogenation, halogenation, and miscellaneous coupling reactions.

The potential value of ω-fluoro-1-alkynes for the synthesis of unusual long-chain ω-fluoro compounds has been recognized for several years. Early work was not encouraging (2), because loss of fluorine occurred under the reaction conditions employed. More recent improvements in techniques involving acetylenic intermediates led us to re-examine the problem. In the course of the work, improved procedures for preparing ω-fluoro-1-alkynes were developed, and the importance of these compounds as intermediates was established. In illustration of their usefulness, the synthesis of two naturally occurring compounds (ω-fluoro-oleic acid and ω-fluoropalmitic acid) has already been described (1).

The preparations of the ω-fluoro-1-alkynes have been discussed (1, 2). The method of choice involves the reaction of an ω-fluoroalkyl chloride or bromide (3) with lithium acetylide stabilized as the ethylenediamine complex; the optimum reaction temperature for chlorides was 25° and for bromides 5–10°. The use of this complex obviates the need for gaseous acetylene and results in a higher yield of product. This is the only method which gives high yields of 1-alkynes directly from chlorides. Previous objections (1) to the use of alkyl chlorides, arising from the presence of unreacted chloride in the product, have been overcome by slowly warming the reaction mixture to 60° after the initial brisk reaction has ceased. This final step ensures complete reaction both of chlorides and of bromides. (Alkyl fluorides apparently do not react with the complex under the reaction conditions employed.) Yields of ω-fluoro-1-alkynes as high as 92% have thus been obtained. Physical constants are shown in Table I. The reactions which follow were undertaken to study the stability of the C—F bond under widely varying experimental conditions.

The first reactions of the ω-fluoro-1-alkynes to be studied were those involving Grignard reagents. Previous work using ethylmagnesium bromide had resulted only in fluorine-free mixtures (2). However, by using ethylmagnesium chloride under carefully controlled conditions, normal reactions occurred. The resultant Grignard reagents formed the corresponding N-α-naphthyl-ω-fluoro-2-alkynoamides with α-naphthyl isocyanate, and the corresponding ω-fluoro-2-alkynoic acids with carbon dioxide; in this work, the studies of Hollingsworth, Wotiz *et al.* (4, 5, 6) were of assistance. The first of these reactions is of value for characterizing the ω-fluoro-1-alkynes as crystalline derivatives. The second is interesting as an example of a "forced" Grignard reaction, wherein the reacting species are respectively diethylmagnesium and the di-(ω-fluoroalkynyl)magnesiums; to this end, the use of dioxane as solvent forced the Schlenk equilibrium in the desired direction.

[1]*For Part XVIII, see reference 1.*

$$F(CH_2)_nC{\equiv}CMgCl \xrightarrow{C_{10}H_7NCO} F(CH_2)_nC{\equiv}CCONHC_{10}H_7 \quad \text{(yields: 72–88\%)}$$

$$(F(CH_2)_nC{\equiv}C)_2Mg \xrightarrow{CO_2} F(CH_2)_nC{\equiv}CCOOH \quad \text{(yields: 51–95\%)}$$

Partial catalytic hydrogenation of the ω-fluoro-1-alkynes was next examined. The usual procedure, employing an alkali metal in liquid ammonia, gave fluorine-free products. However, by using hydrogen in the presence of Lindlar catalyst (7; 8, p. 200), high yields (75–86%) of the corresponding ω-fluoro-1-alkenes were obtained; uptake of hydrogen ceased abruptly after the addition of 1 mole. Oxygen-containing solvents caused total hydrogenation to the 1-fluoroalkanes; it is therefore important to use hydrocarbon solvents, such as *n*-pentane, for the reaction.

Halogenation of the acetylenic hydrogen was accomplished using sodium hypobromite, or by treating the lithium derivative with *p*-toluenesulphonyl chloride. The bromination reaction was based on the work of Straus *et al.* (9). For the lower members, the reaction proceeded well in the aqueous medium; but the low solubility of the higher members made the use of dioxane as solvent, and a higher reaction temperature, necessary for satisfactory yields. Yields of 1-bromo-ω-fluoro-1-alkynes ranged from 67–87%. The chlorination reaction was examined only in the case of 8-fluoro-1-octyne. Extending the observations of Truchet (10), who advocated the use of the sodium or potassium derivative of a 1-alkyne, we found that the preparation of the lithium derivative, using *n*-butyllithium in a hydrocarbon solvent, was more convenient, because it avoided the use of liquid ammonia; the subsequent reaction with *p*-toluenesulphonyl chloride proceeded smoothly to give 1-chloro-8-fluoro-1-octyne in an overall yield of 42%.

$$F(CH_2)_nC{\equiv}CH + NaOBr \rightarrow F(CH_2)_nC{\equiv}CBr + NaOH$$

$$F(CH_2)_6C{\equiv}CLi + CH_3C_6H_4SO_2Cl \rightarrow F(CH_2)_6C{\equiv}CCl + CH_3C_6H_4SO_2Li$$

Attempts were then made to prepare 1-fluoro-1-alkynes by reaction of metal derivatives of 1-alkynes with perchloryl fluoride. It is known that the fluorine atom in this compound displays, under appropriate conditions, electrophilic reactivity towards many types of carbanions. However, reaction of alkynyl anions, formed from 1-alkynes and *n*-butyllithium, with perchloryl fluoride gave only a low yield (16.5%) of the symmetrical diyne, $RC{\equiv}C{\cdot}C{\equiv}CR$. The reactions of alkynyl anions with various aromatic sulphonyl fluorides were equally unsuccessful in forming 1-fluoro-1-alkynes.

Of greater importance to the overall objective of preparing long-chain compounds were various coupling reactions. ω-Fluoro-1-alkynes, in the presence of lithium amide, formed *in situ* in liquid ammonia, reacted with ω-fluoroalkyl iodides to form α,ω-difluoroalkynes. ω-Chloroalkyl iodides similarly gave the corresponding α-chloro-ω-fluoroalkynes (1), which were then utilized in the synthesis of ω-fluoro-oleic and ω-fluoropalmitic acids. Yields in these simple couplings were good (65–89%). Successful couplings between the dilithium derivative of diacetylene (11) and ω-fluoroalkyl iodides have also been carried out; the former is conveniently prepared *in situ* from 1,4-dichloro-2-butyne and four equivalents of lithium amide in liquid ammonia. Overall yields fell in the range 40–50%. The diacetylene route is of value only for forming symmetrical diynes. The method of Chodkiewicz (12) was therefore employed for preparing unsymmetrical diynes; this involves the reaction of 1-alkynes with 1-bromo-1-alkynes in the presence of a cuprous salt and a primary amine. Yields were good (55–71%).

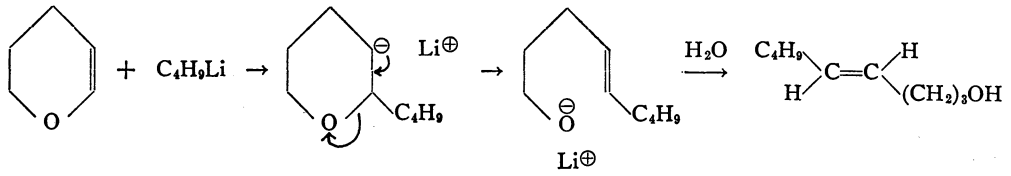
$$F(CH_2)_nC{\equiv}CLi + I(CH_2)_mF \rightarrow F(CH_2)_nC{\equiv}C(CH_2)_mF + LiI$$

$$2F(CH_2)_nI + LiC{\equiv}C{\cdot}C{\equiv}CLi \rightarrow F(CH_2)_nC{\equiv}C{\cdot}C{\equiv}C(CH_2)_nF + 2LiI$$

$$F(CH_2)_nC{\equiv}CH + BrC{\equiv}C(CH_2)_mF \rightarrow F(CH_2)_nC{\equiv}C{\cdot}C{\equiv}C(CH_2)_mF + HBr$$

Catalytic hydrogenation of the conjugated diynes using platinum gave the α,ω-difluoroalkanes in about 60% yield; ethanol was found to be a much better solvent for this than ethyl acetate. Previous preparations of α,ω-difluoroalkanes have usually involved anodic couplings, giving members containing an even number of carbon atoms. The acetylenic route is equally satisfactory for the even members, and provides a ready means of preparing the less accessible odd members.

One related reaction is of general interest. Paul and Tchelitcheff (13) have shown that dihydropyran on treatment with *n*-amylsodium forms 5-hydroxy-1-pentyne, a useful intermediate in this work. When we substituted *n*-butyllithium for *n*-amylsodium in this reaction, *trans*-1-hydroxy-4-nonene was formed in 73% yield. Thus the reaction had not followed the normal ring opening, but instead the dihydropyran had undergone addition of *n*-butyllithium followed by ether cleavage. This represents the simplest and best preparation of this unsaturated alcohol yet found.



Toxicities of some representative ω-fluoroalkynes have been given in earlier reports (1, 2). The LD_{50} results listed in Table I do not add much to the current knowledge concerning the metabolism of the alkyne grouping. The two new ω-fluoro-1-alkynes conform to the toxicity pattern previously established. The results of the three ω-fluoro-2-alkynoic acids suggest that the presence of an α,β-acetylenic bond does not affect the ultimate fate of ω-fluorocarboxylic acids; that is, the unsaturation has little effect on the toxicity. Similar observations have been made previously with ω-fluoro-2-alkenoic acids, $F(CH_2)_nCH{=}CHCOOH$ (14), and with their metabolites such as ω-fluoro-β-hydroxyacids, $F(CH_2)_nCH(OH)CH_2COOH$ (15) and ω-fluoro-β-ketoacids, $F(CH_2)_nCOCH_2COOR$ (16). The alternation of toxicity in the 1-bromo-ω-fluoro-1-alkyne series is similar to, but less pronounced than that given by the ω-fluoroalkyl halide series (3). No particular trend is apparent in the α,ω-difluoro series containing non-terminal mono- and di-yne functions.

The interpretation of the results obtained with the ω-fluoro-1-alkenes remains as obscure as ever (2). The three new α,ω-difluoroalkanes gave toxicity results in line with those described in earlier work (3).

The most important conclusion from the work described in this paper is that ω-fluoro-1-alkynes may be prepared conveniently and in good yield from ω-fluoroalkyl halides (including chlorides), and that the acetylenic function undergoes further reactions, under a wide range of experimental conditions, without loss of fluorine. The ω-fluoro-1-alkynes are thus well established as important intermediates in the synthesis of biologically active aliphatic fluorine compounds.

EXPERIMENTAL

Many of the reactions described herein were followed by gas chromatography and infrared spectroscopy. Physical constants and analytical data for all new compounds are given in Table I. The preparations described below represent typical examples of each procedure; obvious variations for obtaining different members have not been included. Melting points (uncorrected) were determined on a Kofler hot stage, and densities with a Fisher-Davidson gravitometer. Infrared spectra were obtained with Beckman IR-7 and IR-5 infrared spectrophotometers. Analyses were performed by the Schwarzkopf Microanalytical Laboratory, Woodside, 77, N.Y. The presence of the ω-fluorine atom has previously been shown by nuclear magnetic

TABLE I

Physical constants, toxicities, and analytical results

Compound	Formula	Boiling point °C	Boiling point mm	n_D^{25} or m.p., °C	d_4^{20}	LD_{50} (mice, intraperitoneal), mg/kg (95% confidence limits)	Carbon, % Calc.	Carbon, % Found	Hydrogen, % Calc.	Hydrogen, % Found	Other, % Calc.	Other, % Found
5-Fluoro-1-pentyne	$F(CH_2)_3C{\equiv}CH$	75.5–76	742	1.3902	0.884	>100	69.74	70.00	8.20	8.26		
6-Fluoro-1-hexyne*	$F(CH_2)_4C{\equiv}CH$	106–106.5	742	1.4025		—¶						
7-Fluoro-1-heptyne†	$F(CH_2)_5C{\equiv}CH$	131.5–132	742	1.4106		—¶						
8-Fluoro-1-octyne‡	$F(CH_2)_6C{\equiv}CH$	82–82.5	60	1.4176		—¶						
9-Fluoro-1-nonyne§	$F(CH_2)_7C{\equiv}CH$	114	108	1.4221		—¶						
10-Fluoro-1-decyne	$F(CH_2)_8C{\equiv}CH$	81–82	10	1.4250	0.877	5.21 (2.74–9.46)	76.87	76.48	10.97	11.07		
N-α-Naphthyl-2-heptynoamide	$CH_3(CH_2)_3C{\equiv}CCONHC_{10}H_7$	—	—	118.5–119.5	—	—	81.24	81.30	6.82	6.83	N, 5.57	N, 5.60
N-α-Naphthyl-9-fluoro-2-nonynoamide	$F(CH_2)_6C{\equiv}CCONHC_{10}H_7$	—	—	80–80.5	—	—	76.74	76.74	6.78	6.85	N, 4.71	N, 4.90
N-α-Naphthyl-10-fluoro-2-decynoamide	$F(CH_2)_7C{\equiv}CCONHC_{10}H_7$	—	—	88–89.5	—	—	77.14	77.22	7.12	7.12	N, 4.50	N, 4.70
N-α-Naphthyl-11-fluoro-2-undecynoamide	$F(CH_2)_8C{\equiv}CCONHC_{10}H_7$	—	—	89.5–90	—	—	77.51	77.75	7.43	7.49	N, 4.31	N, 4.44
9-Fluoro-2-nonynoic acid	$F(CH_2)_6C{\equiv}CCOOH$	121	0.2	1.4593	1.075	>100	62.77	62.98	7.61	7.57		
10-Fluoro-2-decynoic acid	$F(CH_2)_7C{\equiv}CCOOH$	115	0.01	1.4599	1.064	ca. 7.5	64.49	64.67	8.12	8.22		
11-Fluoro-2-undecynoic acid	$F(CH_2)_8C{\equiv}CCOOH$	120–120.5	0.03	1.4602	1.056	42 (23.3–75.6)	65.97	66.16	8.56	8.74		
7-Fluoro-1-heptene	$F(CH_2)_5CH{=}CH_2$	117–117.5	742	1.3984	0.823	10–30	72.37	72.29	11.28	11.29		
8-Fluoro-1-octene	$F(CH_2)_6CH{=}CH_2$	140	742	1.4059	0.820	25–30	73.79	73.91	11.61	11.68		
9-Fluoro-1-nonene	$F(CH_2)_7CH{=}CH_2$	104	108	1.4128	0.812	11 (3.9–30.8)	74.94	75.20	11.88	12.06		
10-Fluoro-1-decene	$F(CH_2)_8CH{=}CH_2$	119	90	1.4179	0.815	41.5 (29.6–58.1)	75.89	76.16	12.10	12.07		
1-Bromo-6-fluoro-1-hexyne	$F(CH_2)_4C{\equiv}CBr$	62.5	12	1.4613	1.392	30 (17.1–52.5)**	40.25	40.47	4.50	4.55	Br, 44.63	Br, 44.61
1-Bromo-7-fluoro-1-heptyne	$F(CH_2)_5C{\equiv}CBr$	74	10	1.4630	1.334	>100	43.55	43.66	5.22	5.21	Br, 41.39	Br, 41.62
1-Bromo-8-fluoro-1-octyne	$F(CH_2)_6C{\equiv}CBr$	89	10	1.4634	1.272	39 (20.5–74.1)	46.40	46.54	5.84	5.95		
1-Bromo-9-fluoro-1-nonyne	$F(CH_2)_7C{\equiv}CBr$	102	10	1.4636	1.234	>100	48.89	48.80	6.38	6.33		
1-Bromo-10-fluoro-1-decyne	$F(CH_2)_8C{\equiv}CBr$	117	10	1.4639	1.194	25–40	51.08	51.20	6.86	6.71	Br, 33.98	Br, 34.17
1-Chloro-8-fluoro-1-octyne	$F(CH_2)_6C{\equiv}CCl$	112	55	1.4411		40–50**	59.08	59.12	7.44	7.54	Cl, 21.80	Cl, 21.81
1,12-Difluoro-6-dodecyne	$F(CH_2)_5C{\equiv}C(CH_2)_5F$	130.5–131	11	1.4356	0.948	55 (39.9–75.9)	71.25	71.40	9.97	10.15		
1,14-Difluoro-7-tetradecyne	$F(CH_2)_6C{\equiv}C(CH_2)_6F$	95–96	0.1	1.4394	0.925	35 (22.9–53.6)	73.00	73.23	10.50	10.39		
1,11-Difluoro-4,6-undecadiyne	$F(CH_2)_3C{\equiv}C\cdot C{\equiv}C(CH_2)_4F$	89	0.05	1.4816	1.006	>100	71.71	71.81	7.66	7.75		
1,12-Difluoro-5,7-dodecadiyne	$F(CH_2)_4C{\equiv}C\cdot C{\equiv}C(CH_2)_4F$	122	0.8	1.4819	0.994	20–25	72.70	72.95	8.14	8.18		
1,13-Difluoro-5,7-tridecadiyne	$F(CH_2)_4C{\equiv}C\cdot C{\equiv}C(CH_2)_5F$	99–100	0.03	1.4819	0.978	>100	73.55	73.47	8.55	8.40		
1,14-Difluoro-6,8-tetradecadiyne	$F(CH_2)_5C{\equiv}C\cdot C{\equiv}C(CH_2)_5F$	103–104	0.04	1.4815	0.955	97	74.30	74.49	8.91	9.21		
1,6-Difluorohexane‖	$F(CH_2)_6F$	126.5–127	742	1.3758		7.7 (6.21–9.55)	58.99	59.15	9.91	10.05		
1,11-Difluoroundecane	$F(CH_2)_{11}F$	108–108.5	11	1.4125	0.903	62.5	68.70	68.89	11.53	11.42		
1,13-Difluorotridecane	$F(CH_2)_{13}F$	135	12	1.4194	0.893	ca. 21	70.86	71.13	11.90	11.88		

*Lit. (2) b.p. 106–106.5° at 745 mm, n_D^{25} 1.4058.
†Lit. (2) b.p. 131–131.5° at 748 mm, n_D^{25} 1.4103.
‡Lit. (2) b.p. 77–78° at 50 mm, n_D^{25} 1.4165.
§Lit. (2) b.p. 66–66.5° at 12 mm, n_D^{25} 1.4192.
‖Isolated from the partial halogen exchange reaction of 1,6-dichlorohexane and potassium fluoride; lit. (18) b.p. 129.9°, n_D^{25} 1.3739.
¶The following toxicities of ω-fluoro-1-alkynes have been reported (2): $F(CH_2)_4C{\equiv}CH$, 5.7; $F(CH_2)_5C{\equiv}CH$, 53; $F(CH_2)_6C{\equiv}CH$, 7.5; $F(CH_2)_7C{\equiv}CH$, 79.
**For comparison, the toxicity of two 1-halo-1-alkynes was determined: $CH_3(CH_2)_3C{\equiv}CBr$, >100; $CH_3(CH_2)_3C{\equiv}CCl$, >100; this lack of toxicity does not bear out the statement that "the lower 1-chloroalkynes are extremely toxic" (Raphael (8, p. 57)).

resonance spectroscopy, and the significance of the spectra discussed (1). The lithium acetylide (stabilized as the ethylenediamine complex) and the *n*-butyllithium solution were purchased from Foote Mineral Co., Route 100, Exton, Pa. Ethylmagnesium chloride solution was purchased from Arapahoe Chemicals, Inc., Boulder, Colorado. The 1,4-dichloro-2-butyne was kindly presented by Antara Chemicals, General Aniline and Film Corporation, 435 Hudson Street, New York 14, N.Y.

ω-Fluoro-1-alkynes

Two methods for preparing the ω-fluoro-1-alkynes have already been described (1). By the sodium acetylide route in xylene–DMF were prepared 8-fluoro-1-octyne (from 6-fluorohexyl bromide in 50.0% yield) and 10-fluoro-1-decyne (from 8-fluoro-octyl bromide in 60.1% yield). By the lithium acetylide route were prepared the following: 5-fluoro-1-pentyne (from 3-fluoropropyl bromide in 21.4% yield[2]); 6-fluoro-1-hexyne (from 4-fluorobutyl chloride in 74.8% yield); 7-fluoro-1-heptyne (from 5-fluoropentyl chloride in 91.8% yield); 8-fluoro-1-octyne (from 6-fluorohexyl chloride in 76.4% yield); and 9-fluoro-1-nonyne (from 7-fluoroheptyl bromide in 76.4% yield). The optimum reaction temperature for the alkyl chlorides is 25° and for alkyl bromides 10°. It was previously noted (1) that incomplete reaction rendered chlorides unsuitable as starting materials, owing to the similarities in boiling points and refractive indices between the chlorides and resultant alkynes. By slowly warming the reaction mixture to 60°, after reaction at the initial low temperature has ceased, both chlorides and bromides may be caused to react completely. Unreacted starting material thus ceases to be a problem.

N-α-Naphthyl-9-fluoro-2-nonynoamide

Ethylmagnesium chloride (5.15 ml of 3 *M* solution; 0.0156 mole) was placed in a dry 100-ml three-necked flask fitted with a nitrogen inlet, a dropping funnel, a precision-bore stirrer, and a condenser. A nitrogen atmosphere was maintained throughout. 8-Fluoro-1-octyne (2 g, 0.0156 mole) in ether (10 ml) was added slowly with stirring. The ether refluxed and the dark brown color of the original Grignard suspension lightened considerably. When gas evolution had ceased, a solution of α-naphthyl isocyanate (2.6 g, 0.0154 mole) in dry ether (10 ml) was added slowly with stirring; fast addition results in urea formation. When refluxing had ceased, the mixture was poured onto crushed ice and extracted with ether. The extract was washed with water and dried over calcium sulphate. Removal of the ether gave the amide (3.31 g, 72.2%). Recrystallization from ether – petroleum ether, followed by drying *in vacuo* at 40°, gave the pure material.

The following were prepared similarly: *N-α-naphthyl-10-fluoro-2-decynoamide* (87.6%); *N-α-naphthyl-11-fluoro-2-undecynoamide* (75.3%); and *N-α-naphthyl-2-heptynoamide* (77.0%).

Principal infrared bands of the three fluorinated amides ($CHCl_3$, cm^{-1}): 3378 and 3257 (free N—H) w; 3049 and 2985 (aromatic C—H) w; 2933 and 2857 (aliphatic C—H) m; 2232 (C≡C) m; 1664 (C=O) s; 1524 (combination N—H and C—N) s; 1488 s; 1350 m; 1256 m; 1046 and 990 (C—F) w.

9-Fluoro-2-nonynoic Acid

Precautions were observed to exclude moisture and oxygen, as in the previous procedure; the apparatus was the same. Ethylmagnesium chloride (14.5 ml of 3 *M* solution; 0.042 mole) and dry ether (29 ml) were added to the flask, thus giving a 1 *M* solution. This was stirred and heated under reflux, and dioxane (sodium dried; 3.78 g, 0.042 mole) was added. The resulting suspension was refluxed and stirred for 5 hours. 8-Fluoro-1-octyne (5 g, 0.039 mole) was added slowly, and the mixture was stirred without heating for 1 hour. It was then poured onto a mixture of powdered dry ice (150 g) suspended in dry ether (60–70 ml), and stirred for 1 hour. The mixture was hydrolyzed with saturated ammonium chloride solution and then acidified with dilute hydrochloric acid. The ether layer was extracted with sodium carbonate solution. Removal of the ether allowed recovery of unreacted alkyne. The aqueous extract was acidified and extracted with ether. Washing, drying ($CaSO_4$), and distillation gave the acid (3.39 g, 50.5%).

The following were prepared similarly: *10-fluoro-2-decynoic acid* (94.6%) and *11-fluoro-2-undecynoic acid* (75.0%).

Principal infrared bands of the three acids (CCl_4, cm^{-1}): 3521 (free O—H) w; 3077, 2660, and 2532 (bonded O—H) m; 2941 and 2865 (C—H) s; 2242 (C≡C) s; 1689 (C=O) s; 1466 (C—H) m; 1412 and 1279 (C—O and O—H) s; 1050 and 1013 (C—F) m; 919 (O—H) m.

7-Fluoro-1-heptene

Lindlar catalyst (7, 8) (200 mg) was suspended in *n*-pentane, and 5% synthetic quinoline in *n*-pentane (1 ml) was added. Upon saturation with hydrogen at room temperature and atmospheric pressure, no noticeable uptake of hydrogen occurred. 7-Fluoro-1-heptyne (4.56 g, 0.04 mole) in *n*-pentane (20 ml) was added, and hydrogenation was started. The theoretical amount of hydrogen was absorbed in just under 3 hours, after which no further uptake was observed. The catalyst was filtered off and washed with *n*-pentane. The filtrate was washed with dilute hydrochloric acid and then with water, dried ($CaSO_4$), and distilled to give the alkene (3.56 g, 80.4%).

The following were prepared similarly: *8-fluoro-1-octene* (86.0%); *9-fluoro-1-nonene* (79.8%); and *10-fluoro-1-decene* (74.9%).

[2]*The low yield is explained by the very high volatility of the product. Suitable variations in technique would undoubtedly raise the yield to that of the other members.*

Principal infrared bands of the fluoroalkenes (CCl_4, cm^{-1}): 3067 (olefinic C—H) w; 2907 and 2857 (C—H) s; 1642 (C=C) m; 1464, 1445, and 1416 (C—H) m; 1052 and 1018 (C—F) m; 952 (olefinic C—H) m; 912 (olefinic C—H) s; 722 (C—H) w.

1-Bromo-6-fluoro-1-hexyne

Sodium hydroxide (10 *N*, 37 ml, 0.367 mole) was cooled in a flask surrounded by ice. Water (23 ml) was added, followed by dropwise addition of bromine (17.2 g, 0.108 mole). 6-Fluoro-1-hexyne (10 g, 0.100 mole) in ether (5 ml) was added with vigorous stirring. The mixture was then stirred overnight at room temperature. The heterogeneous mixture was poured into water and extracted with ether. The extracts were washed, dried ($CaSO_4$), and distilled to give the bromoalkyne (15.47 g, 86.4%).

The following were prepared similarly: *1-bromo-7-fluoro-1-heptyne* (86.6%), and *1-bromo-8-fluoro-1-octyne* (73.8%). The same procedure, but using dioxane (10 ml) in place of the ether and a temperature of 35°, gave: *1-bromo-9-fluoro-1-nonyne* (64.9%) and *1-bromo-10-fluoro-1-decyne* (86.4%). The 1-bromo-1-alkynes must all be distilled at reduced pressure to avoid decomposition.

Principal infrared bands (CCl_4, cm^{-1}): 2933 and 2865 (C—H) s; 2222 (C≡C) w; 1468 and 1433 (C—H) m; 1380 w; 1330 w; 1110 w; 1053 and 1012 (C—F) m; 722 (C—H) w.

1-Chloro-8-fluoro-1-octyne

The reaction was carried out in an atmosphere of dry nitrogen. 8-Fluoro-1-octyne (3.84 g, 0.03 mole) was dissolved in *n*-pentane (25 ml), and the solution was freed of any dissolved oxygen by refluxing in a stream of nitrogen for 15 minutes. *n*-Butyllithium (11.45 g of 15.2% w/w solution; 1.74 g C_4H_9Li; 0.0272 mole) in hexane was added slowly with stirring. The alkynyllithium separated. The mixture was warmed to ensure completion of the reaction. After no more butane was evolved, sodium-dried dioxane (5 ml) was added, thus dissolving most of the solid. *p*-Toluenesulphonyl chloride (freshly distilled and recrystallized, 5.7 g, 0.0298 mole) was added in dioxane, and the orange-yellow lithium sulphinate was deposited. The mixture was stirred for 15 minutes and then was poured onto crushed ice. Separation of the organic layer, ether extraction of the aqueous layer, washing, drying ($CaSO_4$), and distillation gave the chloroalkyne (2.05 g, 41.8%). Principal infrared bands (CCl_4, cm^{-1}): 2933 and 2857 (C—H) s; 2232 (C≡C) w; 1464 and 1431 (C—H) m; 1391 w; 1330 w; 1078 m; 1048 and 1012 (C—F) m.

Attempted Preparation of 1-Fluoro-1-octyne

1-Octynyllithium was prepared from 1-octyne (12.1 g) as described in the previous procedure. Dioxane was added to dissolve the solid and perchloryl fluoride was passed in at 0°. An exothermic reaction occurred and a white precipitate was deposited. Working up the mixture in the usual way gave only recovered 1-octyne (3.94 g) and 7,9-hexadecadiyne (1.35 g, 16.5%). A reaction analogous to the preparation of 1-chloro-8-fluoro-1-octyne, using *p*-toluenesulphonyl fluoride, gave no fluoroalkyne.

1,12-Difluoro-6-dodecyne and 1,14-Difluoro-7-tetradecyne

These were prepared in yields of 65.0% and 77.0% by the procedure described for 1-chloro-17-fluoro-8-heptadecyne (1). The infrared spectra of these two compounds were similar to those of the chlorofluoroalkynes (1), except that no C—Cl bands were present and the C—F bands were stronger.

1,12-Difluoro-5,7-dodecadiyne

Liquid ammonia (200 ml) was introduced into a 500-ml three-necked flask fitted with a stirrer, a dropping funnel, and a dry-ice condenser. Anhydrous ferric chloride (0.1 g) and small pieces of lithium (1.85 g, 0.264 g-atom) were added. At the end of 10 minutes, a grey suspension of lithium amide was present. 1,4-Dichloro-2-butyne (8.1 g, 0.066 mole) was added slowly. The ensuing dehydrochlorination was rapid and exothermic, being complete in about 1 minute. 4-Fluorobutyl iodide (3) (26.83 g, 0.132 mole) was added slowly, and the mixture was stirred for 4.5 hours. Ammonium chloride was added to neutralize any unreacted amide, and the ammonia was allowed to evaporate. The brown residue was extracted with ether, and the extracts were washed, dried ($CaSO_4$), and distilled, giving recovered 4-fluorobutyl iodide (3.16 g) and the required symmetrical diyne (4.83 g, 40.8%).

1,14-Difluoro-6,8-tetradecadiyne was prepared similarly in 47.8% yield.

1,11-Difluoro-4,6-undecadiyne

A 250-ml flask was fitted with a gas inlet tube, a dropping funnel, a stirrer, and a condenser. The flask was purged with nitrogen, and 5-fluoro-1-pentyne (2.88 g, 0.0335 mole) in absolute methanol (25 ml) was added. To this solution was added 10 ml of a 33% v/v solution of *n*-propylamine in methanol (i.e. ca. 0.06 mole of amine), cuprous chloride (70 mg), and hydroxylamine hydrochloride (0.2 g). The mixture was cooled to 0° and a methanolic solution of 1-bromo-6-fluoro-1-hexyne (6 g, 0.0335 mole) was added dropwise and with vigorous stirring. Small crystals of hydroxylamine hydrochloride were added from time to time to maintain the copper in the reduced state. The reaction was complete after about 1 hour. The copper was complexed by the addition of sodium cyanide (1 g). The mixture was diluted with water, extracted with ether, and the extracts were washed, dried ($CaSO_4$), and distilled, yielding the unsymmetrical diyne (3.36 g, 54.6%).

1,13-Difluoro-5,7-tridecadiyne was prepared similarly in 71.4% yield.

Principal infrared bands of the four diynes (CCl_4, cm^{-1}): 2933 and 2857 (C—H) s; 2257 and 2155 (C≡C?) vw; 1477, 1458, and 1431 (C—H) m; 1391 m; 1351 w; 1326 m. The next six bands must be due to C—F, because none of them are present in the nonfluorinated analogues; all are strong: 1066, 1044, 1019, 1006, 986, and 959.

1,11-Difluoroundecane

Platinum dioxide (250 mg) was reduced in ethanol to finely divided platinum black. 1,11-Difluoro-4,6-undecadiyne (1.99 g, 0.0108 mole) in ethanol was added; hydrogenation proceeded smoothly until the theoretical quantity of hydrogen had been taken up. The catalyst was removed by filtration, and the ethanol by distillation, to give the difluoroalkane (1.98 g). Distillation gave the pure material (1.33 g, 64.0%).

1,13-Difluorotridecane was prepared similarly in 53.2% yield.

trans-1-Hydroxy-4-nonene

A 500-ml flask, fitted with a gas inlet tube, a dropping funnel, a precision-bore stirrer, and a condenser, was purged with nitrogen. *n*-Butyllithium (163 g of a 15.2% w/w solution; 24.6 g C_4H_9Li; 0.385 mole) was introduced, and dihydropyran (17.7 g, 0.19 mole based on 90% purity) was added over a period of 30 minutes. The temperature rose from 26° to 34°. The mixture was heated under reflux for 3 hours and then cooled. Excess *n*-butyllithium was destroyed by the slow addition of water, with cooling. The layers were separated and the aqueous layer was extracted with ether. Drying ($CaSO_4$) and distillation yielded the product (19.8 g, 73.0%) of b.p. 209–210° and n_D^{25} 1.4465; lit. (17) b.p. 103–104° at 14 mm, n_D^{20} 1.4494. Principal infrared bands (CCl_4, cm^{-1}): 3610 (free O—H) w; 3322 (bonded O—H) m; 2959, 2924, and 2857 (C—H) s; 1468, 1458, 1439, and 1381 (C—H) m; 1058 (C—O and O—H) s; 970 (*trans*-RCH=CHR′) s.

ACKNOWLEDGMENTS

We wish to express our indebtedness to Allied Chemical Corporation, General Chemical Division, Morristown, N.J., for financial assistance; to Dr. M. K. McPhail and Dr. C. A. deCandole, Suffield Experimental Station, Ralston, Alberta, for carrying out the toxicity determinations; to Dr. O. F. Beumel, Jr., Foote Mineral Co., Exton, Pa., for helpful advice in the use of the lithium acetylide complex; and to Antara Chemicals, General Aniline and Film Corporation, 435 Hudson Street, New York 14, N.Y., for a gift of 1,4-dichloro-2-butyne.

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