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Introduction and Extension of Ethynyl Group Using 1,1-Dichloro-2,2-difluoroethylene. A Convenient Route to Lithium Acetylides and Derived Acetylenic Compounds[1a]

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Applicability of the following two-step reaction sequence was examined for conversion of organolithium and -magnesium compounds into lithium acetylides having two more carbon atoms: RLi or RMgBr + $CF_2{=}CCl_2 \rightarrow RCF{=}CCl_2$, $RCF{=}CCl_2 + n\text{-}C_4H_9Li \rightarrow RC{\equiv}CLi$. The reaction of RLi with $CF_2{=}CCl_2$ was accompanied by formation of RCl as a result of the Cl–Li exchange to a widely varying extent depending on the nature of R. Between butyllithium and $CF_2{=}CCl_2$, only the Cl–Li exchange was observed, and the formation of 2,2-dichloro-1-fluorovinyllithium confirmed. The conversion of $RCF{=}CCl_2$ into lithium acetylides proceeded with great ease in yields presumed to be nearly quantitative in typical cases. The resulting acetylides were treated with $CF_2{=}CCl_2$, and compounds of the type $RC{\equiv}CCF{=}CCl_2$ were isolated in overall (from RH or RBr) yields up to 69% where R is phenyl, substituted phenyl ($o\text{-}CH_3O$, $p\text{-}CH_3O$, $p\text{-}CH_3$, p-Cl, p-Br, $m\text{-}CF_3$), 1-naphthyl, 2-furyl, 2-thienyl, and ferrocenyl. In some cases $RC{\equiv}CH$ and $RC{\equiv}CCO_2H$ were also isolated. For example, 2-ethynylthiophene was prepared from thiophene in an overall yield of 63%. Previously unreported 2-ethynylbenzothiazole was also obtained. Stepwise extension of the terminal acetylenic bond is possible in a similar method as illustrated in the synthesis of $C_6H_5(C{\equiv}C)_nCF{=}CCl_2$ (n = 2, 3, 4) from $C_6H_5(C{\equiv}C)_{n-1}CF{=}CCl_2$ and $n\text{-}C_4H_9(C{\equiv}C)_2CF{=}CCl_2$ from $n\text{-}C_4H_9C{\equiv}CCF{=}CCl_2$. An efficient preparative method of 1,1,1,2-tetracholoro-2,2-difluoroethane, from which $CF_2{=}CCl_2$ is obtained by dechlorination, is described.

During the course of a study of nucleophilic reactions of fluorochloro olefins, we encountered a reaction which seemed to have a potential synthetic utility for acetylenic compounds. Thus, when β,β-dichloro-α-fluorostyrene was treated with phenyllithium, the expected fluorochlorostilbene was not detected. Instead, the formation of lithium phenylacetylide was indicated. As the starting compound was obtained from phenyllithium[2] or from phenylmagnesium bromide[3] on treatment with 1,1-dichloro-2,2-difluoroethylene (1), the whole transformation is represented by the following sequence:

$$C_6H_5Li\ (C_6H_5MgBr) \rightarrow C_6H_5CF{=}CCl_2 \rightarrow C_6H_5C{\equiv}CLi$$

This suggested a general two-step conversion of organolithiums 4 or Grignard reagents 5 into lithium acetylides 7 having two more carbon atoms. By a combination of existing methods an equivalent transformation generally requires many steps, though somewhat similar conversion of RMgBr into $RC{\equiv}CCl$ using dichloroacetylene is reported.[4] Therefore, it was decided to examine the applicability of the proposed sequence to various R groups. This sequence may be compared with a recently reported two-step conversion of aldehydes into the corresponding acetylides having one more carbon atom.[5]

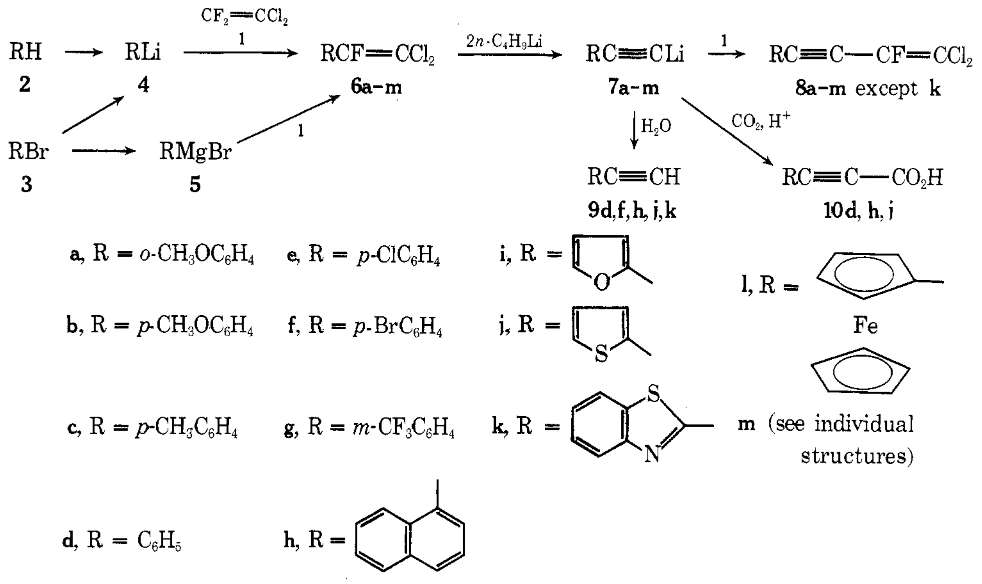
$$RCHO \rightarrow RCH{=}CBr_2 \rightarrow RC{\equiv}CLi$$

The results described herein indicate that the proposed sequence is a convenient synthetic route to some types of acetylenic compounds as well as a useful method for the stated conversion. It was also found that a similar method can be used for conversion of a lithium acetylide into the corresponding lithium acetylide having an extra conjugated acetylenic bond.

Results and Discussion

Reaction of Organolithium Compounds with $CF_2{=}CCl_2$. Lithium compounds 4 were prepared from RH (2) and RBr (3) and added to ether solutions containing excess 1 (Scheme I). The reactions occurred typically at −30 °C. For completion of the reaction the mixtures were allowed to warm to 0 °C or refluxed for up to 4 h. The inverse addition method was used, except for **4l** and **4m**, in order to minimize the possibility of reaction of the initially formed 6 with 4. The yields of 6 obtained by distillation (in some cases by crystallization) are given in Table I. When 4 was prepared by Li–Br exchange from the corresponding bromo compounds (3) using butyllithium, it was necessary to keep the preparations cold in order to avoid the formation of $RC_4H_9\text{-}n$.[6] The preparation of p-methoxyphenyllithium (**4b**) from p-bromoanisole (**3b**) is complicated by the formation of 2-methoxy-5-bromophenyllithium.[7] From these complications and from the formation of side products

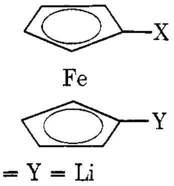
Scheme I



(RCl), the route via **4** is considered inferior to the route via Grignard reagents **5** where bromo compounds **3** are used to prepare **6b–h.** On the other hand, the preparation of **4** by lithiation[8] and subsequent treatment with **1** is considered satisfactory as a route to **6a, 6i, 6j,** and **6k.**

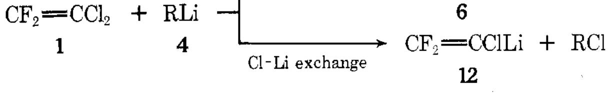
2-Benzothiazolyllithium (**4k**) is reported to be unstable above −35 °C.[9] Hence **1** was added to a solution of **4k** at −70 °C, and the resulting mixture allowed to warm slowly. The yield of **6k** was very low. However, it was found that the yield is greatly increased if the temperature is rapidly raised. This finding and subsequent experiments led to the procedure described in the Experimental Section.

Mixtures from lithiation of ferrocene in ether with butyllithium contained unchanged ferrocene, ferrocenyllithium (**4l**),[10,11] 1,1′-ferrocenediyldilithium (**4m**),[12,13] and a relatively large amount of unchanged butyllithium. Hence treatment with **1** afforded complex mixtures, from which **6l** was obtained as a red oil and **6m** as red crystals. Isolation of **6l** was more difficult since vaccum distillation could not be performed.[14]



4m, X = Y = Li
6m, X = Y = CF=CCl₂
7m, X = Y = C≡CLi
8m, X = Y = C≡C—CF=CCl₂
11, X = Cl; Y = CF=CCl₂

The side reaction observed is a Cl–Li exchange distinct from the substitution with elimination of lithium fluoride for the main reaction:


$$\underset{\mathbf{1}}{CF_2{=}CCl_2} + \underset{\mathbf{4}}{RLi} \begin{cases} \xrightarrow{\text{substitution}} \underset{\mathbf{6}}{RCF{=}CCl_2} + LiF \\ \xrightarrow[\text{Cl-Li exchange}]{} \underset{\mathbf{12}}{CF_2{=}CClLi} + RCl \end{cases}$$

For example, chlorobenzene and *p*-chlorotoluene were isolated in 13% yield each besides a 60% yield of **6d** and 58% yield of **6b.** When **4h** was prepared from 1-bromonaphthalene (**3h**) with lithium in ether and treated with **1**, the isolated yields (based on **3h**) were as follows: naphthalene, 15%; 1-chloronaphthalene, 24%; **6h,** 31%.[15] These chloro compounds (RCl) could arise from secondary reactions of **6** with **4**. However, chloroacetylene **13** and acetylene **9** (from **7** by hydrolysis), the coproducts of these possible reactions, were not detected though carefully sought by gas chromatography in each case.

$$\mathbf{6} + \mathbf{4} \longrightarrow \underset{\mathbf{13}}{RC{\equiv}CCl} + RCl$$

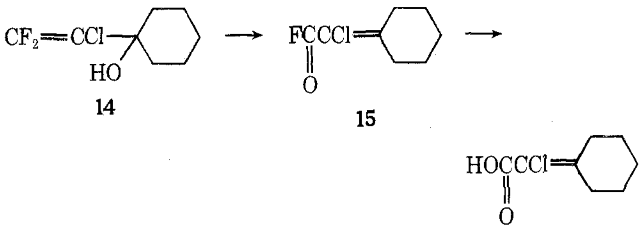
$$\mathbf{13} + \mathbf{4} \longrightarrow \mathbf{7} + RCl$$

Hence the present author sees no probable way of formation of RCl other than from the Cl–Li exchange between **1** and **4**.[16] Further, the formation of 1-chloro-2,2-difluorovinyllithium (**12**) was shown in the case of the reaction with phenyllithium (**4d**)[17] as well as in the case of the reaction with butyllithium (vide infra). Therefore, it seems reasonable to conclude that the chloro compounds (RCl) were formed from the reactions of **1** and **4**.[16] In the cases of the reactions with **4l** and **4m** there were some indications of formation of chloroferrocene and 1-chloro-1′-(2,2-dichloro-1-fluorovinyl)ferrocene (**11**). However, these products were not isolated. It is not certain either whether these were formed directly from **1**. On the other hand, no evidence of formation of the products of the Cl–Li exchange was found in the cases of the reactions of **4i** and **4j**. From isolated yields of **6** and RCl and from GC peak area ratios, the following order of increasing proportion of the Cl–Li exchange can be presented:

$$\mathbf{4i}, \mathbf{4j} < \mathbf{4g}, \mathbf{4e} < \mathbf{4d}, \mathbf{4c}, \mathbf{4a} < \mathbf{4h} < n\text{-}C_4H_9Li$$

As a rough trend it is suggested that the smaller the extent of delocalization of the negative charge in the reagent the higher the proportion of the exchange. The importance of the steric factor is also suggested from the relatively high proportion of Cl–Li exchange in the reaction of 1-naphthyllithium (**4h**). If other factors are equal, a reagent having factors of higher steric hindrance would give a higher proportion of the Cl–Li exchange.

The reaction observed between **1** and butyllithium was Cl–Li exchange, and no evidence was found of formation of the substitution product (n-$C_4H_9CF{=}CCl_2$) or a secondary product derived from this compound. The formation of 1-chloro-2,2-difluorovinyllithium (**12**) was confirmed by isolation of the cyclohexanone adduct **14** in 62% yield. The adduct was unstable and decomposed to cyclohexylidenechloroacetyl fluoride (**15**) after standing for 1 day at room temperature. The corresponding acid (16) was isolated on further standing.



14 15 16

Decompositions of this type are described in the literature.[18,19] The above results also indicate that **1** is a good source of **12**, previously obtained from 1-chloro-2,2-difluoroethylene with *N,N*-dipropyllithium amide.[20]

The exact fate of $CF_2{=}CClLi$ (**12**) in the presence of excess **1** is not known, though the final product, an undistillable, dark-colored substance, is thought to have the structure $-(CF{=}CCl)_n-$. In the presence of excess butyllithium, however, **12** was found to be converted into 1-hexynyllithium (**17**) after an exothermic reaction.

$$1 \rightarrow 12 \rightarrow \underset{17}{n\text{-}C_4H_9C{\equiv}CLi} \rightarrow \underset{18}{n\text{-}C_4H_9C{\equiv}CCF{=}CCl_2}$$

The reaction mixture yielded **18** on treatment with **1**. It should be noted that, although the reactions of **1** with excess butyllithium and with excess phenyllithium (**4d**) give similar acetylides (**17** and **7d**), the courses of formation of these are quite different from each other.

Reaction of Grignard Reagents with $CF_2{=}CCl_2$. Grignard reagents **5** were prepared in ether from the corresponding bromo compounds (**3**), **1** was added, and the resulting mixtures were refluxed for 7–20 h (not necessarily continuous). The yields of **6** isolated by distillation are included in Table I. No side product was found except small amounts of coupling compounds (e.g., biphenyl), probably formed during the preparations of **5**. The inverse addition method was not required. Higher product yields, the absence of side products (RCl), and simplicity in experimental procedure make this route (via **5**) generally preferable to the route via **4** when a bromo compound (**3**) is to be used for the synthesis of **6**.

The reactions of alkylmagnesium bromides with **1** were found to be complex and have not yet been studied well, though preliminary experiments indicated compounds of the type RCF_2CCl_2H as the main products (ca. 25% yield where R = n-C_4H_9).

Reaction of $RCF{=}CCl_2$ with *n*-Butyllithium. Although, originally, the conversion of **6d** into **7d** was discovered using phenyllithium as reagent, butyllithium was used for such purposes throughout in the present study. The reactions seemed to proceed well at −50 °C and at even lower temperatures, though in some cases higher (subzero) temperatures were used from solubility considerations. There was observed no evidence of formation of side products. The resulting mixtures containing lithium acetylides (**7**) were treated with **1**, and compounds of the type $RC{\equiv}CCF{=}CCl_2$ (**8**) were isolated (Table I). However, compound **8k** could not be obtained although 2-ethynylbenzothiazole (**9k**) was isolated in 52% yield after hydrolysis of **7k**. The reactions between lithium acetylides (**7**) and **1** were slow below 20 °C and conducted under refluxing conditions for 2–7 h. In many cases the yields of formation of **7** from **6** were suspected to be practically quantitative. Quantitative formation of ethynylbenzene (**9d**) from **6d** was confirmed by determinations by gas chromatography in duplicate experiments, in each of which butyllithium (2 equiv plus) was added to an ethereal solution of **6d** containing n-nonane as internal standard until the peak due to chloroethynylbenzene (**13d**) disappeared. Isolated yields of **9** and **10** are given in Table II.

Table I. Isolated Yield[a,b] of $RCF{=}CCl_2$ (6) and $RC{\equiv}CCF{=}CCl_2$ (8)

R	Starting compd (2 or 3)	Yield[c] of 6, % Via RLi (4)[e]	Yield[c] of 6, % Via RMgBr (5)	Yield[d] of 8, %
a	Anisole	41 (2*)		80 (2)
b	*p*-Bromoanisole	32	76 (7)	76 (6*)
c	*p*-Bromotoluene	58	74 (12*)	80 (7*)
d	Bromobenzene	60 (2)	85 (12*)	80 (6)
e	*p*-Bromochlorobenzene	56	70 (14*)	87 (6)
f	*p*-Dibromobenzene		50 (21**)	79 (2*)
g	*m*-Bromo-α,α,α-trifluorotoluene	56	67 (20*)	81 (5*)
h	1-Bromonaphthalene	31	82[f] (16*)	84 (6)
i	Furan	53 (4)		79 (5)
j	Thiophene	81 (4)		84 (5)
k	Benzothiazole	59		0
l	Ferrocene	19 (2)		61 (5)
m	Ferrocene	39 (2)		22 (6)

[a] Based on charged starting material. [b] Total refluxing times (h) with **1** in ether are indicated in parentheses; continuous (unmarked), with one overnight interruption in 2 days (*), with two overnight interruptions in 3 days (**). Where no parenthesized figure is given, the reaction mixture was hydrolyzed without refluxing. [c] Overall yield from **2** or **3**. [d] Overall yield from **6**. [e] Organolithiums **4** were obtained by reaction with ethereal butyllithium except that **4c**, **4d**, and **4h** were obtained by reaction with cut pieces of lithium. See ref 15 for **4h**. [f] Benzene used as cosolvent.

Table II. Yield[a] of $RC{\equiv}CH$ (9) and $RC{\equiv}CCO_2H$ (10) Obtained from $RCF{=}CCl_2$ (6)

Compd	Yield, %		Bp, °C (mm)	$n^{20}D$ or [mp, °C]
9d	77	100[b]	50–52 (30)	1.5483
9f	58[c]	97[b]		[61–65]
9h	44[d]	97[e]	105–106 (4)	1.6500
9j	78		55–56 (30)	1.5849
9k	52			[42–43]
10d	84			[136.5–138.5]
10h	77			[137–139]
10j	72			[130–133] dec

[a] Isolated yield unless otherwise stated. Overall yield from **6**. [b] Determined yield by gas chromatography. [c] Yield obtained as crystals. [d] A red balsamlike material, believed to be mainly a polymer of **9h**, remained in the distillation pot. The weight corresponded to 96% of the weight of isolated **9h**. [e] Yield of di(1-naphthyl)butadiyne, mp 176–178 °C, obtained after treatment of crude **9h** with cupric acetate hydrate in pyridine; mp 177.5–178.5 °C (90%) after recrystallization from benzene.

The reactions of **6** except **6k**, **6l**, and **6m** with butyllithium can be monitored by gas chromatography. Each reaction mixture obtained after addition of approximately 1 equiv of butyllithium was found to contain the unchanged starting material (**6**), an intermediate, and acetylene **9** (after hydrolysis) besides butyl chloride. The intermediate is almost certainly a chloroethynyl compound (**13**)[21] though only chloroethynylbenzene (**13d**) was isolated and confirmed. In such a mixture the peak area of **13** (the total areas of the three components taken as 100%) was 70–85%

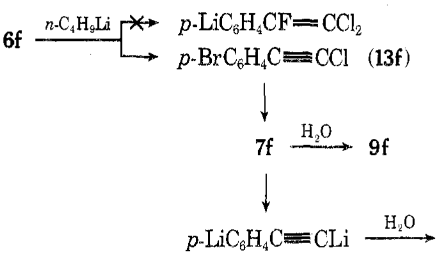
where R is phenyl or a substituted phenyl, about 55% where R is 2-furyl or 2-thienyl, and approximately 20% where R is 1-naphthyl. Some of these chloroethynyl compounds (**13**) may have only a limited stability under GC conditions. Chloroethynylferrocene (**13l**) was not detected by GC although its existence was indicated by ir. The isolated yield of **13d** was 61%. It appears that the values of k_1 and k_2 defined by the following reactions are comparable.

$$\mathbf{6} + n\text{-}C_4H_9Li \xrightarrow{k_1} \underset{\mathbf{13}}{RC\equiv CCl} + LiF + n\text{-}C_4H_9Cl$$

$$\mathbf{13} + n\text{-}C_4H_9Li \xrightarrow{k_2} \mathbf{7} + n\text{-}C_4H_9Cl$$

Specifically, for the reaction where R is phenyl the ratio k_1/k_2 was calculated to be 12 from a determined composition (**6d**, 13%; **13d**, 78%; **7d**, 9% determined as **9d**).[22]

The reaction of **6f** with butyllithium is interesting in that both the Br–Li exchange and the Cl–Li exchange[23] are possible. The Cl–Li exchange occurred exclusively unless excess butyllithium was used. The determined yield of *p*-bromoethynylbenzene (**9f**) was 97%. In the gas chromatogram the remaining 3% was accounted for by the presence of **13f** and **9d** (resulting from the dilithium compound).



When butyllithium had been added to an equimolar mixture of bromobenzene and β,β-dichloro-α-fluorostyrene (**6d**) until chloroethynylbenzene (**13d**) was almost undetectable (<1%), the conversion of bromobenzene was at most 5%. This means that the rate of the Cl–Li exchange with **6d** is at least 10^3 times the rate of the Br–Li exchange with bromobenzene (considering $k_1/k_2 = 12$ for **6d**). These facts indicate the great ease with which the Li–Cl exchange[23] occurs between **6** and butyllithium.[24]

Among the substitution in **1**, the Cl–Li exchange in **1**, and the Cl–Li exchange[23] in **6**, similarities are notable in the transition states or intermediates, in each of which a (partial) negative charge is stabilized by β-fluorine and also by α-chlorine.[25]

$$\begin{array}{lcl} & \mathbf{4} + \mathbf{1} \longrightarrow & RCF_2\bar{C}Cl_2 \\ n\text{-}C_4H_9Li \text{ or } & \mathbf{4} + \mathbf{1} \longrightarrow & CF_2{=}\bar{C}Cl \\ n\text{-}C_4H_9Li \text{ or } & \mathbf{4} + \mathbf{6} \longrightarrow & RCF{=}\bar{C}Cl \end{array}$$

The stabilizing effect of fluorine toward a negative charge at the β position has been recognized, though the mechanism of the stabilization is not unanimous.[26]

Extension of Terminal Acetylenic Bond. A formal extension of the reaction sequence shown in Scheme I gives the reaction sequence shown in Scheme II. The applicability of this sequence was demonstrated using phenyl compounds as examples. Thus treatment of **8d** with butyllithium followed by refluxing the resulting mixture with **1** afforded **19** in 84% yield. Similarly, **20** and **21** were obtained from **19** and **20**, respectively, in the yields given above. These compounds are all crystalline, and the structures are confirmed by ir, uv, ^{19}F NMR, and mass spectroscopy as well as by F and Cl elemental analysis data. The change in uv with increase in n is also consistent with the trend known for series of conjugated polynes.

Compound **22** was similarly obtained in 78% yield from **18**, which in turn was prepared from 1-hexyne by lithiation followed by treatment with **1**. The method of extension of the terminal acetylenic bond is thus shown to be applicable where R is alkyl as well as where R is aryl whereas the method of introduction of the ethynyl group is not applicable at present where R is alkyl.

Scheme II

$$R(C\equiv C)_{n-1}Li \longrightarrow R(C\equiv C)_{n-1}CF{=}CCl_2 \longrightarrow R(C\equiv C)_nLi$$

or

$$R(C\equiv C)_{n-1}CF{=}CCl_2 \longrightarrow R(C\equiv C)_nLi \longrightarrow R(C\equiv C)_nCF{=}CCl_2$$

19, R = C_6H_5; $n = 2$ (84%)
20, R = C_6H_5; $n = 3$ (76)
21, R = C_6H_5; $n = 4$ (33)
22, R = n-C_4H_9; $n = 2$ (78)

Synthetic Merits. It appears that the present method is most suited for the preparation of lithium acetylides (substituted ethynyllithiums) to be allowed to react further as such. Compounds of the type $RCF{=}CCl_2$ are as effective precursors of lithium acetylides as are the corresponding terminal acetylenes in that the conversion with butyllithium (and probably with other reagents) can be performed under very mild conditions and, unless other portions of the molecules are susceptible to attack by the reagent, in practically quantitative yield. Instead of $RC\equiv CH$, more stable $RCF{=}CCl_2$ is isolated, purified, and stored until it is converted directly into the lithium acetylide, though 2 equiv of butyllithium are required. The presence of butyl chloride (2 equiv) and lithium fluoride, which are formed as coproducts in the present route, is not expected to cause a serious detrimental effect in transformation to most derivatives. The use of a lower alkyllithium (in place of butyllithium) may be desirable in some cases.

Where RLi and/or RMgBr are easily obtainable, the present method is suited even for the preparation of terminal acetylenes though R is restricted to be aryl at present. For example, 2-ethynylthiophene (**9j**) was prepared in the present study from thiophene in two steps in an overall yield of 63%. This method seems to be simpler than any of the previously reported ones: via 2-acetylthiophene,[27] via 2-vinylthiophene,[28b] via 2-iodothiophene,[29] via 5(2-thienyl)-2-oxazolidone.[30] Another example is the preparation of 1-ethynylnaphthalene (**9h**) via the Grignard reagent from easily available 1-bromonaphthalene. A previous synthesis of **9h** from another easily obtainable intermediate, 1-chloromethylnaphthalene, needed a considerable number of steps.[31] Though 1-acetylnaphthalene can be converted into **9h** in two steps (action of PCl_5 followed by dehydrochlorination), availability of pure 1-acetylnaphthalene, unlike that of 2-acetylnaphthalene, is not high. Acetylene **9h** may also be prepared in a good overall yield from 1-naphthaldehyde by Corey's method.[5]

Previous methods of extension of the terminal acetylenic bond by one or more acetylenic bonds are almost exclusively by Cu(I)-catalyzed unsymmetrical coupling followed by elimination of the protective group.[32–34] For example, $Et_3SiC\equiv CBr$ was used in Cadiot–Chodkiewicz coupling to prepare $Ar(C\equiv C)_nSiEt_3$, from which $Ar(C\equiv C)_nH$ ($n = 2$, 3) was generated by hydrolysis.[33] For such stepwise extension of terminal conjugated acetylenic bonds or more specifically for the preparation of monosubstituted butadiynes and hexatriynes, the present method seems to be useful. The lithium acetylides of terminal conjugated polyacetylenes are probably most easily obtainable by the present method. However, some derivatives (e.g., carboxylic acid) to be obtained from such lithium acetylides are also

Table III. Physical Properties of Compounds Having 2,2-Dichloro-1-fluorovinyl Group[a–c]

Compd	Bp, °C (mm)	n^{20}D or [mp, °C]	νC=C,[d] cm^{-1}	^{9}F NMR,[e] ppm
6a	87–91 (5)	1.5523	1660	10.9
6b	121–123 (10)	[25–26]	~1640	17.3
6c	126–126.5 (30)	1.5605	~1640	17.6
6d[f]	123–126 (60)	1.5625	1638	17.7
6e	132–133 (29)	[36–37]	~1630	18.6
6f	113–115 (10)	[40–40.5]	1637	18.7
6g	126 (60)	1.4970	~1640	19.3
6h	99–103 (1)	[45–46.5]	1648	6.9
6i	105–107 (80)	1.5418	~1640	34.4
6j	125 (48)	1.5981	1634	20.9
6k		[81–83]	1624	24.9
6l		*g*	1644	17.9
6m		[84–85]	1636	19.4
8a		[56–57]	1622	23.2
8b	123–125 (6)	[39–40]	1625	23.2
8c	103–105 (5)	1.6032	1623	23.5
8d	111 (10)	1.6043	1623	23.9
8e		[69–70]	1623	24.3
8f		[79–80]	1623	24.4
8g	112–113 (9)	1.5407	1624	25.0
8h		[37.5–38.5]	1620	23.7
8i	104–105 (20)	1.5910	1623	25.5
8j	105–106 (9)	1.6385	1618	24.2
8l		[80.5–82]	1627	21.9
8m		[122–123]	1622	23.1
18	96 (30)	1.4849	1623	22.0
22	106–108 (8)	1.5559	1612	24.9
19	~160 (4)	[65–66]	1609	25.7
20		[56–57.5]	1608	26.8
21		[67.5–68.5]	1604	27.4

[a] Satisfactory analytical results (≤±0.3% for F and ≤±0.4% for Cl) were obtained for all new compounds listed in the table. [b] A strong band assignable to νC–F appeared at 968–988 cm^{-1} for each of the compounds listed in the table. For **6h, 8g,** or **8i,** an additional peak, somewhat less strong and probably not due to νC–F, appeared at 956–966 cm^{-1}. [c] The νC≡C band for each of **8a–m** (except **k**) appeared at 2195–2205 cm^{-1}. The band for **8i** was accompanied by a somewhat stronger band at 2180 cm^{-1}. The νC≡C bands (cm^{-1}) for other compounds follow: **18,** 2225; **22,** 2230, 2150 (weak); **19,** 2200; **20,** 2165, 2100 (weak), 2200 (weak); **21,** 2125, 2170 (weak), 2200 (weak). [d] Neat for liquid and in KBr pellet for crystals. For **6** the intensity of the vinyl νC=C is generally low. [e] 20% solution in benzene (upfield relative to external CF_3CO_2H). CF_3 chemical shift −15.0 ppm for **6g** and −15.1 ppm for **8g.** [f] Bp 101 °C (12 mm) reported in ref 2; bp 89–89.9 °C (10.5 mm) and n^{26}D 1.5596 reported in ref 3. [g] Difficult to measure n^{20}D; n^{30}D 1.6416.

obtainable directly by Cadiot–Chodkiewicz coupling as well as by dehydrohalogenation reactions.

The 2,2-dichloro-1-fluorovinyl group has spectroscopic features advantageous for characterization. In mass spectra of **6** and **8** the parent peaks, confirmed easily by the characteristic relative intensities of isotope (Cl) peaks, were generally the strongest peaks, and fragments derived from the parents by loss of one and two chlorines, respectively, were also clearly observed except for ferrocene derivatives. Structural correlation of ^{19}F NMR chemical shift and of νC=C frequency, as seen in Table III, may be useful for such purposes. Anomalies for **6a** and **6h** probably originate from steric repulsion by the methoxy group and by the peri hydrogen, respectively.

During the course of this investigation the following three cases have been noted as potentially hazardous: (1) distillation in one-flask preparation of **9j,**[35] (2) distillation stated in ref 14, (3) exothermic reaction described under the heading of "Reaction of CF_2=CCl_2 with Excess Butyllithium" in the Experimental Section. The toxicity of **1** may be inferred to be comparable to those of chloroacetyl chloride, methyl acrylate, etc.,[36] or to be intermediate between those of methyl dichloroacetate and methyl chloroacetate.[37]

Experimental Section

All melting and boiling points are uncorrected. ^{19}F NMR spectra were recorded on a Hitachi R-20BK using trifluoroacetic acid as external standard. Uv spectra were recorded on a Perkin-Elmer 202. Ir spectra were recorded on a Hitachi EPI-G3. Mass spectra were obtained on a Hitachi RMU-7. GC works were performed using a 4-m column of Silicon-DC 550. GC peak area ratios were obtained by weighing papers under curves. Quantitative analysis by GC was made on the basis of the assumed proportionality in peak height using reference solutions in each of which the ratio of the internal standard to the compound to be determined was equal or almost equal to that for the solution to be analyzed. Merck alumina (activity II–III) was used for elution chromatography. All reactions of organolithium and -magnesium compounds were conducted under an atmosphere of nitrogen using a T-tube for nitrogen inlet and outlet. Sodium-dried ether was exclusively used as reaction solvent except that benzene was added as cosolvent for the reaction of **5h** with **1.** Each stock solution (ca. 600 ml, ca. 520 g) of butyllithium was prepared from 1 mol of butyl bromide at about −20 °C, stored in a brown bottle at −20 °C, and used generally within a few months. The amount of butyllithium in a solution taken from a stock solution is expressed by the nominal amount calculated by weight assuming 100% yield from butyl bromide. 1,1-Dichloro-2,2-difluoroethylene (**1**) was obtained by dehalogenation of 1,1,1,2-tetrachloro-2,2-difluoroethane,[38] which was prepared as described below, with zinc in ethanol, distilled twice from phosphorus pentoxide under nitrogen, stored in brown bottles at −20 °C, and used generally within several months after each preparation. Refluxing with **1** (bp 19 °C) was conducted using a condenser circulated with ice water. Refluxing was discontinued overnight if indicated, for example, as "refluxed for 20 h in 2 days".

1,1,1,2-Tetrachloro-2,2-difluoroethane (Precursor of 1).[39] A mixture of 1,1,2-trichloro-1,2,2-trifluoroethane (500 g, 2.67 mol; Daiflon S3, equivalent of Freon 113) and aluminum chloride (30 g, 0.22 mol; powdered reagent usable directly, granular reagent usable after brief grind) was refluxed for 3 h with vigorous mechanical stirring. Upon discontinuation of stirring and external heating, refluxing ceased temporarily but was resumed in a few minutes by the heat of isomerization ($CF_2ClCFCl_2 \rightarrow CF_3CCl_3$). After the refluxing became milder, the mixture was slowly stirred, and 1,1,2,2-tetrachloro-1,2-difluoroethane (1027 g, 5.04 mol; Daiflon S2, equivalent of Freon 112) was added at such a rate that the internal temperature was kept between 40 and 60 °C. Slow stirring was continued for an additional 50 min around 50 °C, external heating being applied toward the end of this period. Water (20 ml) was added with vigorous stirring, and the liquid portion of the resulting mixture, while warm, was transferred to a still pot by decantation. Fractional distillation afforded 1,1,1-trichloro-2,2,2-trifluoroethane, bp 45–47 °C (388 g, 2.07 mol), and 1,1,1,2-tetrachloro-2,2-difluoroethane, bp 92–93 °C (1019 g, 5.00 mol). The results were essentially reproducible in more than 20 such preparations though in some cases the yield of the tetrachlorodifluoroethane was reduced to about 900 g by disproportionation ($3CF_2ClCCl_3 \rightarrow 2CF_3CCl_3 + CCl_3CCl_3$). In no case was unisomerized 1,1,2,2-tetrachloro-1,2-difluoroethane detected (^{19}F NMR).

Work-up procedures were performed by conventional methods of hydrolysis by ice plus hydrochloric acid (procedure A) or by ice or water (procedure B) followed by extraction in ether. Reaction mixtures resulting from magnesium compounds were satisfactorily worked up by the procedure A. On the other hand, when a reaction mixture containing lithium fluoride was shaken with an aqueous solution, phase separation was generally difficult or incomplete unless lithium fluoride was removed by suction filtration. The filtration was performed only with some difficulty in many cases, particularly in the procedure B and for larger scale experiments. In some cases of the work-up procedure B, a limited amount of water was added to the active reaction mixture, and the resulting mixture refluxed for 10 min–2 h as an attempt to reduce this difficulty. After cooling, filtration was performed, or only a rough separation was achieved by decantation. The ether solutions were dried over

Na$_2$SO$_4$, after washing with aqueous sodium bicarbonate in the cases of the procedure A. Aliquots were withdrawn and reserved. The remaining solution was generally evaporated using a rotary film evaporator. The fraction (e.g., 0.90) of the solution actually subjected to the isolation procedure is necessary for yield calculation and given as "÷0.90" at the place where the yield of the main product is described. The amounts withdrawn for monitoring the reactions are neglected.

β,β-Dichloro-α-fluoro-*o*-methoxystyrene (6a). Anisole (0.75 mol) was lithiated with butyllithium under refluxing conditions for a total of 12 h, and the resulting mixture added to a solution of **1**. The yields of anisole, *o*-chloroanisole, and **6a** isolated by distillation were 15, 4, and 41%, respectively (excluding mixed fractions). The yields of these compounds determined by GC with a reserved aliquot after addition of *n*-tetradecane as internal standard were 21, 19, and 52%, respectively.

1-(2,2-Dichloro-1-fluorovinyl)naphthalene (6h). To magnesium ribbons (13.0 g, 0.53 g-atom) were added small portions of 1-bromonaphthalene (103.5 g, 0.500 mol) and ether (300 ml). After the reaction was initiated by scratching magnesium surfaces with a glass rod in twisting motions, the remaining portions were added over a period of 45 min with mechanical stirring. The resulting mixture was further refluxed for 30 min by external heating and diluted with benzene (100 ml). Upon addition of **1** (115 g, 0.87 mol) a mildly exothermic reaction occurred. Refluxing was maintained for 2 h without heating and for a total of an additional 14 h in 2 days by external heating. Work-up (A) and fractional distillation afforded 94.7 g (÷0.96, 82%) of **6h**, bp 99–103 °C (1 mm), which crystallized upon seeding. A sample recrystallized from ethanol melted at 45–46.5 °C: mass spectrum m/e (rel intensity) 240 (M$^+$ for 2 ^{35}Cl, 23), 205 (50), 170 (100), 102 (14). Without benzene cosolvent the reaction rate was less than half.

2-(2,2-Dichloro-1-fluorovinyl)thiophene (6j). To a stirred, ice-cooled solution of thiophene (79.8 g, 0.95 mol) in ether (100 ml) was added ethereal butyllithium (600 ml, 1.00 mol). The resulting solution was refluxed for 30 min and added to a solution of **1** (150 g, 1.13 mol) in ether (100 ml) over a period of 30 min at −20 to −30 °C. After 4 h of refluxing 147 g (÷0.97, 81%) of **6j**, bp 125 °C (48 mm), was obtained as the sole product: mass spectrum m/e (rel intensity) 196 (M$^+$ for 2 ^{35}Cl, 100), 161 (33), 126 (47), 117 (18), 81 (15).

2-(2,2-Dichloro-1-fluorovinyl)benzothiazole (6k). Benzothiazole (67.6 g, 0.50 mol) was added dropwise to a stirred solution (500 ml) of butyllithium (0.50 mol) in ether over a period of 74 min, during which time the internal temperature was kept between −70 and −75 °C by strong cooling with dry ice–acetone. Soon after the addition was complete, the resulting mixture was poured into an ice-cooled, stirred solution of **1** (125 g, 0.94 mol) in ether (200 ml). The temperature rose quickly to 23 °C and began to descend in a few minutes. The ice bath was removed, and the resulting mixture stirred for an additional 10 min and worked up (A). Concentration of the resulting solution followed by filtration and washing with ethanol afforded 70 g (÷0.96, 59%) of **6k**, mp 80–81.5 °C. The analytical sample, mp 81–82.5 °C, obtained after chromatography followed by recrystallization from ethanol was almost colorless: mass spectrum m/e (rel intensity) 247 (M$^+$ for 2 ^{35}Cl, 100), 212 (3), 177 (16), 168 (13), 146 (5), 108 (33), 82 (15), 69 (40).

(2,2-Dichloro-1-fluorovinyl)ferrocene (6l). An ether solution (800 ml) containing ferrocene (50.0 g, 0.269 mol) and butyllithium (0.34 mol) was left standing for 24 h at room temperature and cooled in a dry ice–acetone bath with mechanical stirring. To the resulting orange-red slurry was added **1** (88 g, 0.66 mol) in several portions keeping the internal temperature below −50 °C. From the product mixture obtained after 2 h of refluxing, work-up (A), and passage through an alumina (215 g) column as benzene solution, were removed orange crystals (19.7 g) of ferrocene. The rest of the material, which contained **6l** (83%), **11** (4%), and **6m** (13%) according to ^{19}F NMR, was steam distilled (vacuum distillation could not be performed[14]): fractions 1–2 (1 l. of H$_2$O), 10.2 g, ferrocene, **6l** (97%), **11** (3%); fractions 3–18 (9.6 l. of H$_2$O), 15.4 g, **6l** (95%), **11** (3.5%), **6m** (1.5%); residue, 9.6 g, **6l** (40%), **11** (8%), **6m** (52%).

Ferrocene (4.5 g, total 48.4%) was isolated as crystals from fractions 1–2. The total weight of the fractions 3–18 (containing practically no ferrocene) corresponds to 19% yield of **6l** based on the initially used ferrocene and to 37% yield based on the unrecovered ferrocene. The analytical sample of **6l** was obtained by a repeated steam distillation of selected fractions obtained from similar runs. Samples of **6l** obtained from chromatography had a tendency to be changed into an amorphous solid on standing whereas ones obtained in early stages of steam distillation were stable and remained as a red oil. The persistent impurity is thought to have the structure **11**. The ^{19}F NMR signal of this compound appeared between those of **6l** and **6m**. In mass spectra of samples of **6l** containing this compound, small peaks consistent as the isotopic parent peaks of **11** were observed. Mass peaks of almost pure **6l** follow: m/e (rel intensity) 298 (M$^+$ for 2 ^{35}Cl, 90), 171 (85), 153 (47), 152 (65), 123 (100).

1,1′-Bis(2,2-dichloro-1-fluorovinyl)ferrocene (6m). An ethereal solution (500 ml) containing ferrocene (25.0 g, 0.134 mol) and butyllithium (0.34 mol) was left standing for 86 h at room temperature and cooled in a dry ice–acetone bath with stirring. After addition of **1** (61 g, 0.46 mol) the mixture was carefully allowed to warm to 18 °C in 1.5 h (exothermic around −30 °C), refluxed for 2 h, and worked up (A). The resulting solution was concentrated and steam distilled (600 ml of condensed water) to give 5.8 g of crude ferrocene. The warm hexane solution of the residue was passed through a short alumina (138 g) column. The eluate (440 ml) was concentrated to ca. 100 ml and cooled to −20 °C giving **6m** (20.1 g) as red crystals, mp 83–84.5 °C. The second crop (1.0 g, mp 78–79 °C) increased the total yield to 39% (÷0.97). The compound was recrystallized from ethanol, mp 84–85 °C, m/e 410 (M$^+$ for 4 ^{35}Cl). The material recovered from the mother liquor was steam distilled (350 ml of H$_2$O), and the residue (11.9 g) chromatographed to give **6l** (5.3 g, 14%), which was, however, unstable (see the last part of the description for **6l**).

1,1-Dichloro-2-fluoro-4-phenyl-1-buten-3-yne (8d). To a stirred, cooled solution of **6d** (38.2 g, 0.200 mol) in ether (100 ml) was added ethereal butyllithium (260 ml, 0.45 mol) over a period of 2 h at −60 °C. The temperature was allowed to rise to 0 °C in 1 h, **1** (50 g, 0.38 mol) was added, and the resulting mixture was refluxed for 6 h and worked up (B). Fractional distillation afforded 32.6 g (÷0.95, 80%) of **8d**: bp 111 °C (10 mm); m/e (rel intensity) 214 (M$^+$ for 2 ^{35}Cl, 100), 179 (14), 160 (3), 144 (62). The ir spectrum of the sample was indistinguishable from that of **8d** obtained in 76% yield from ethynylbenzene (1.00 mol) after treatment with butyllithium and refluxing with **1** for 9 h.

***p*-Bromoethynylbenzene (9f).** The ir (KBr) agreed with a published one[40] except that our spectrum was devoid of three weak bands (4.32, 9.92, 12.35 μ). Mass spectrum m/e (rel intensity) 182 (M$^+$ for ^{81}Br, 99), 180 (M$^+$ for ^{79}Br, 100), 101 (65). Lit.[41] mp 63 °C.

2-Ethynylthiophene (9j). To a stirred, cooled solution of **6j** (59.1 g, 0.300 mol) in ether (100 ml) was added ethereal butyllithium (380 ml, 0.68 mol) over a period of 2 h at −40 to −60 °C. Work-up (A) and fractional distillation afforded 23.7 g (÷0.94, 78%) of **9j**, bp 55–56 °C (30 mm), n^{20}D 1.5849 [lit.[27] bp 31–33 °C (3 mm), n^{20}D 1.5886; lit.[28b] bp 40 °C (12 mm), n^{20}D 1.5851; lit.[30] bp 54–60 °C (20 mm)].

2-Ethynylbenzothiazole (9k). To a stirred, cooled slurry of **6k** (12.4 g, 0.050 mol) in ether (150 ml) was added ethereal butyllithium (70 ml, 0.114 mol) over a period of 40 min at about −50 °C. The solution obtained after work-up (B) was dried over Na$_2$SO$_4$ and evaporated. Steam distillation of the residual oil (7.3 g) afforded 3.46 g (÷0.84, 52%) of **9k**, mp 39–41 °C. The compound, upon standing in the absence of solvent, had a tendency to be converted into fiberlike crystals: mp 42–43 °C; mass spectrum m/e (rel intensity) 159 (M$^+$, 100), 108 (19), 70 (20); ir (KBr) 3420 ($\equiv$CH), 2105 cm^{-1} (C$\equiv$C).

Anal. Calcd for C$_9$H$_5$NS: C, 67.89; H, 3.17; N, 8.80. Found: C, 67.94; H, 3.02; N, 8.89.

In a similar run where the whole mixture obtained after hydrolysis was directly subjected to steam distillation, the yield of **9k** was considerably lower, the major compound in later distilled fractions being 2-methylbenzothiazole, confirmed by comparison of the ir with that of an authentic sample. Apparently, **9k** was converted (via hydration followed by decarbonylation) into 2-methylbenzothiazole during the steam distillation probably by the catalytic action of lithium hydroxide or fluoride.

Phenylpropiolic Acid (10d). To a stirred solution of **6d** (19.1 g, 0.100 mol) in ether (100 ml) was added ethereal butyllithium (130 ml, 0.217 mol) around −50 °C. Pieces of dry ice (ca. 50 g) were added to the reaction mixture in several portions over a period of 30 min, initially the temperature being kept below −20 °C by cooling. After addition of 120 ml of water, the whole mixture was shaken vigorously and filtered in order to remove lithium fluoride. The aqueous layer was separated, washed with ether, and acidified (aqueous HCl). Filtration followed by drying afforded 12.2 g (84%) of **10d**, mp 133–136 °C. The identity of a recrystallized sample, mp 136.5–138.5 °C, from carbon tetrachloride was confirmed by its undepressed mixture melting point with an authentic sample (mp 137–138 °C).

Chloroethynylbenzene (13d) was obtained in 61% yield from 0.30 mol of **6d** and 0.31 mol of butyllithium, bp 70 °C (20 mm), $n^{20}\mathrm{D}$ 1.5794 [lit.[25a] bp 65 °C (10 mm), $n^{20}\mathrm{D}$ 1.5783]. The ir spectrum was identical with a reported one.[42]

Reaction of $CF_2{=}CCl_2$ with Butyllithium Followed by Addition to Cyclohexanone. To a stirred, well-cooled solution of **1** (20 g, 0.15 mol) in ether (100 ml) were added ethereal butyllithium (65 ml, 0.102 mol) over a period of 25 min and then a solution of cyclohexanone (9.8 g, 0.10 mol) in ether (30 ml) over a period of 20 min. A dark blue mixture resulted. The internal temperature was maintained around −70 °C during these additions and allowed to rise gradually to 17 °C in 1.7 h. The crude product obtained after work-up (B) followed by brief rotary evaporation indicated an AB pattern (4.7, 8.0 ppm, J = 22 Hz) in ^{19}F NMR. Fractional distillation was performed using a packed column washed with aqueous alkali with a small amount of potassium carbonate powder added in the still pot. 1-(1-Chloro-2,2-difluorovinyl)cyclohexanol (**14**), bp 68–72 °C (8 mm) (12.4 g, 62%), was obtained in three fractions, the first two of which were contaminated with a small amount of cyclohexanone (lit.[20] bp 72–75 °C). The fractions decomposed in succession within a few hours after standing in stoppered flasks for 1 day at room temperature. When the decomposition occurred in each flask, the stopper was expelled and the content became hot generating an irritating fume (presumed to be HF). These observations and the change in ir, disappearance of the 1728-cm^{-1} peak ($CF_2{=}CCl$–), and appearance of an 1800-cm^{-1} peak (acyl fluoride), are consistent with the transformation to **15**. The decomposed liquid samples changed to crystals of cyclohexylidenechloroacetic acid (**16**) upon further standing for several months. After recrystallization from hexane a total of 5.2 g (29%) of **16**, mp 101–102 °C, was collected: mass spectrum m/e (rel intensity) 176 (M^+ for ^{37}Cl, 9), 174 (M^+ for ^{35}Cl, 31), 68 (100); ir (KBr) 2900 (carboxylic OH, br), 1690 (C=O), 1618 cm^{-1} (C=C).

Anal. Calcd for $C_8H_{11}O_2Cl$: C, 55.02; H, 6.35; Cl, 20.3. Found: C, 54.80; H, 6.16; Cl, 20.1.

Reaction of $CF_2{=}CCl_2$ with Excess Butyllithium. To a stirred, cooled solution (600 ml) of butyllithium (1.00 mol) in ether was added a solution of **1** (42 g, 0.32 mol) in ether (50 ml) over a period of 30 min at −40 °C. A 1-ml portion of the reaction mixture boiled as soon as it was withdrawn to a vial. The remaining mixture was intended to be warmed slowly by adjusting the efficiency of cooling (dry ice–acetone bath). However, the temperature rise was uncontrollably rapid above −20 °C, the mixture boiled, and a partial content (estimated 100 ml) was lost from the top of the Dimroth condenser, circulated with ice-cooled water. GC indicated the formation of 1-hexyne and butyl chloride. After addition of **1** (103 g, 0.77 mol) the resulting mixture was refluxed for a total of 10 h in 2 days and worked up (B). Fractional distillation afforded **18**, bp 96–97.5 °C (30 mm), which was identical in ir and GC with the compound obtained as described below. The yield (30.3 g) corresponds to 49% based on the initially added **1**.

1,1-Dichloro-2-fluoro-1-octen-3-yne (18) was obtained in 78% yield from 0.62 mol of 1-hexyne after treatment with butyllithium followed by refluxing with **1** for 23 h in 3 days: mass spectrum m/e 194 (M^+ for 2 ^{35}Cl).

1,1-Dichloro-2-fluoro-6-phenyl-1-hexene-3,5-diyne (19). To a stirred solution of **8d** (43.0 g, 0.200 mol) in ether (80 ml) was added ethereal butyllithium (250 ml, 0.45 mol) over a period of 1.4 h at −50 °C. After 1 h the olefin **1** (50 g, 0.38 mol) was added, and the resulting mixture refluxed for 2 h and worked up (B). Recrystallization from ethanol afforded 40.2 g (84%) of **19**, mp 64–65 °C. Purified samples were colorless: mp 65–66 °C; bp ca. 160 °C (4 mm); mass spectrum m/e (rel intensity) 238 (M^+ for 2 ^{35}Cl, 43), 203 (24), 184 (5), 168 (100).

1,1-Dichloro-2-fluoro-10-phenyl-1-decene-3,5,7,9-tetrayne (21). A solution of **20** (26.3 g, 0.100 mol) was added to ethereal butyllithium below −60 °C, and the resulting mixture refluxed with **1** for 1 h. A considerable amount of carbon powderlike materials was formed. Work-up (B), chromatography, and recrystallization from ethanol afforded 9.6 g (33%) of **21**, mp 67–68 °C. Although this sample turned black in several months, recrystallization from ethanol, after removal of carbonaceous materials by filtration, regenerated beautiful, deep yellow needles, mp 67.5–68.5 °C, which showed only a slight change in appearance during storage at ambient temperature for 20 months (in the dark): mass spectrum m/e (rel intensity) 286 (M^+ for 2 ^{35}Cl, 85), 253 (51), 251 (41), 216 (100).

Uv absorption maxima are given in terms of λ, nm (log ϵ). **6d:** 207 (4.10), 256 (4.13). **8d:** 207 (4.20), 217 (4.16), 223 (4.14), 236 (4.00), 273 (4.28), 284 (4.36), 290 (shoulder), 301 (4.28). **19:** 208 (4.40), 218 (4.42), 231 (4.44), 253 (4.53), 265 (4.49), 274 (shoulder), 291 (4.29), 309 (4.44), 330 (4.39). **20:** 205 (4.45), 224 (4.41), 251 (4.65), 264 (4.86), 274 (4.78), 291 (4.77), 300 (shoulder), 320 (4.36), 343 (4.49), 369 (4.35). **21:** 209 (4.52), 277 (4.89), 292 (5.06), 301 (shoulder), 315 (4.88), 325 (shoulder), 349 (4.32), 376 (4.37), 407 (4.16). **18:** 236 (4.17), 241 (shoulder), 247 (4.13). **22:** 215 (4.49), 222 (4.53), 248 (3.84), 262 (4.15), 278 (4.35), 294 (4.29).

Registry No.—1, 79-35-6; **2a,** 100-66-3; **2i,** 110-00-9; **2j,** 110-02-1; **2k,** 95-16-9; **2l,** 102-54-5; **3b,** 104-92-7; **3c,** 106-38-7; **3d,** 108-86-1; **3e,** 106-39-8; **3f,** 106-37-6; **3g,** 402-43-7; **3h,** 90-11-9; **4** (R = C_4H_9), 109-72-8; **4a,** 31600-86-9; **4b,** 14774-77-7; **4c,** 2417-95-0; **4d,** 591-51-5; **4e,** 14774-78-8; **4f,** 22480-64-4; **4g,** 368-49-0; **4h,** 14474-59-0; **4i,** 2786-02-9; **4j,** 2786-07-4; **4k,** 39582-59-7; **4l,** 1271-15-4; **4m,** 33272-09-2; **6a,** 342-57-4; **6b,** 395-34-6; **6c,** 58228-99-2; **6d,** 394-99-0; **6e,** 58229-00-8; **6f,** 58229-01-9; **6g,** 401-06-9; **6h,** 58229-02-0; **6i,** 58229-03-1; **6j,** 58229-04-2; **6k,** 58229-05-3; **6l,** 58281-24-6; **6m,** 58281-25-7; **8a,** 58229-06-4; **8b,** 58229-07-5; **8c,** 58229-08-6; **8d,** 58229-09-7; **8e,** 58229-10-0; **8f,** 58229-11-1; **8g,** 58229-12-2; **8h,** 58229-13-3; **8i,** 58229-14-4; **8j,** 58229-15-5; **8l,** 58281-26-8; **8m,** 58281-27-9; **9d,** 536-74-3; **9f,** 766-96-1; **9h,** 15727-65-8; **9j,** 4298-52-6; **9k,** 40176-80-5; **10d,** 637-44-5; **10h,** 4843-42-9; **10j,** 4843-44-1; **13d,** 1483-82-5; **14,** 27258-83-9; **15,** 58229-16-6; **16,** 58229-17-7; **18,** 58229-18-8; **19,** 58229-19-9; **20,** 58229-20-2; **21,** 58229-21-3; **22,** 58229-22-4; 1,1,1,2-tetrachloro-2,2-difluoroethane, 76-11-9; 1,1,2-trichloro-1,2,2-trifluoroethane, 76-13-1.

References and Notes

(1) (a) Presented, in part, at the 28th Semiannual Meeting (April 1973, in Tokyo) and at the 30th Semiannual Meeting (April 1974, in Osaka) of the Japan Chemical Society. (b) Hirate Machi, Kita-ku, Nagoya, Japan.

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(14) In the first two experiments attempted separations of **6l** by vaccum distillation resulted in sudden exothermic decompositions of the whole contents of the still pots when most of unchanged ferrocene had distilled and **6l** began to distill.

(15) Naphthalene was found to be formed during the preparation of **4h**; higher temperatures favored the formation of naphthalene. In the run stated above, **4h** was prepared at about 20 °C. No substantial difference in the GC peak area ratio (0.71) of 1-chloronaphthalene/**6h** was observed with various preparations of **4h** obtained from **3h** with lithium or with butyllithium.

(16) With the reservation that a small portion of the RCl could arise from reaction of RLi with **12** and/or with its chlorine-containing derivatives, such as FC≡CCl.

(17) A product mixture obtained from reaction of **1** with **4d** at −60 °C followed by treatment with cyclohexanone contained **6d** and **14** (the cyclohexanone adduct of **12**) in an approximate ratio of 10:1 (5:1 integrated intensity ratio in ^{19}F NMR).

(18) R. N. Sterlin, R. D. Yatsenko, and L. L. Knunyants, *Khim. Nauka Prom.*, **3**, 540 (1958); *Chem. Abstr.*, **53**, 4195 (1959).

(19) (a) P. Tarrant, P. Johncock, and J. Savory, *J. Org. Chem.*, **28**, 839 (1963); (b) F. G. Drakesmith, R. D. Richardson, O. J. Stewart, and P. Tarrant, *J. Org. Chem.*, **33**, 286 (1968).

(20) H. G. Viehe and S. Y. Delavarenne, U.S. Patent 3 506 728 (1970).

(21) The reaction between chloroethynylbenzene and butyllithium is reported: H. Gilman and A. H. Haubein, *J. Am. Chem. Soc.*, **67**, 1420 (1945). See also ref 34.

(22) For the consecutive reactions A → B → with common reagent Y, the following differential equations can be assumed where k_1 and k_2 are the rate constants for A and B, respectively.

$$dA/dt = -k_1AY^n$$

$$dB/dt = k_1AY^n - k_2BY^n$$

Division of the latter equation by the former and integration give the following equation where A_0 is the initial concentration of A (B absent initially):

$$\log\,[(1 - k_2/k_1)B/A + 1] + (1 - k_2/k_1)\log\,(A/A_0) = 0$$

This equation is satisfied when k_2/k_1 is approximately 1/12.1 for the values A_0 = 1, A = 0.13, B = 0.78.

One of the referees criticized this calculation as the reversibility of the reaction of **13** and butyllithium is not considered. However, the relative importance of the reverse reaction is so small that the reaction can be treated as practically irreversible in such a calculation.

(23) The most probable or most easily comprehensible course of $RC\equiv CCl$ is a Cl-Li exchange followed by elimination of LiF. However, $RCF{=}C\text{-}ClLi$ may or may not be formed at all. Hence the term "Cl-Li exchange" for these reactions is only tentative in the strict sense of the word.

(24) The reactions of halogeno olefins of other types (e.g., $RCH{=}CHCl$) with organolithiums to form acetylenic compounds have been described: M. Schlosser and V. Ladenberger, *Chem. Ber.*, **100**, 3901 (1967); G. Köbrich, *Angew. Chem.*, **77**, 75 (1965); G. Köbrich and P. Buck, "Chemistry of Acetylenes", H. G. Viehe, Ed., Marcel Dekker, New York, N.Y., 1969, Chapter 2. See also ref 5.

(25) Such considerations lead to the suspicion that the Cl-Li exchange reactivities of the chlorines in **6** would be greater than those of the respective chlorines of the corresponding trichlorovinyl compound. In a competitive experiment α,β,β-trichlorostyrene was converted into chloroethynylbenzene at 2.2 times the rate for **6d**. However, which of the chlorines of α,β,β-trichlorostyrene is preferentially exchanged is not clear.

(26) Previously the stabilization was explained by hyperconjugation by fluorine. However, this mechanism has been criticized: A. Streitwieser, Jr., and D. Holtz, *J. Am. Chem. Soc.*, **89**, 692 (1967); A. Streitwieser, Jr., A. P. Marchand, and A. H. Pudjaatmaka, *ibid.*, **89**, 693 (1968); D. Holtz, *Chem. Rev.*, **71**, 139 (1971).

(27) A. Vaitiekunas and F. F. Nord, *J. Org. Chem.*, **19**, 902 (1954).

(28) L. Brandsma "Preparative Acetylenic Chemistry", Elsevier, Amsterdam, 1971: (a) p 97; (b) p 117.

(29) R. E. Atkinson, R. F. Curtis, D. M. Jones, and J. A. Taylor, *J. Chem. Soc. C*, 2173 (1969).

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(31) D. Bertin, *C. R. Acad. Sci.*, **229**, 660 (1949); *Chem. Abstr.*, **44**, 2969*i* (1950).

(32) P. Cadiot and W. Chodkiewicz, "Chemistry of Acetylenes", H. G. Viehe, Ed., Marcel Dekker, New York, N.Y., 1969, pp 622-625.

(33) R. Eastmond and D. R. M. Walton, *Tetrahedron*, **28**, 4591 (1972).

(34) The formation of $C_6H_5(C\equiv C)_2Cl$ from the reaction between $C_6H_5C\equiv CMgBr$ and dichloroacetylene is also reported: H. G. Viehe, *Chem. Ber.*, **92**, 3064 (1959).

(35) The applicability of a one-flask procedure for the present method was tested in the case of the preparation of 2-ethynylthiophene. To a solution of thiophene (0.3 mol) was added successively ethereal butyllithium, **1** (in four portions over 12 min keeping the internal temperature between −40 and 5 °C), and ethereal butyllithium (at −50 °C), refluxing being conducted after the first and the second additions. On distillation of the product mixture obtained after work-up, exothermic decomposition of the pot residue, though not vigorous, occurred after 2-ethynylthiophene (53% yield, bp 35-37° at 10 mm) came out.

(36) C. P. Carpenter, H. F. Smyth, Jr., and U. C. Pozzani, *J. Ind. Hyg. Toxicol.*, **31**, 343 (1949); *Chem. Abstr.*, **44**, 3140*h* (1950).

(37) T. R. Torkelson, C. D Kary, M. B. Chenoweth, and E. R. Larsen, *Toxicol. Appl. Pharmacol.*, **19**, 1 (1971); *Chem. Abstr.*, **75**, 46979c (1971).

(38) W. T. Miller, Jr., E. W. Fager, and P. H. Griswald, *J. Am. Chem. Soc.*, **72**, 705 (1950).

(39) The results of related studies together with discussion of mechanistic implication of the stirring effect will be presented elsewhere.

(40) "Sadtler Standard Infrared Spectra", Sadtler Research Laboratories, Philadelphia, Pa., Midget ed, no. 7604 (sample source: Philadelphia College of Pharmacy and Science).

(41) A. D. Allen and C. D. Cook, *Can. J. Chem.*, **41**, 1084 (1963).

(42) R. D. McLachlan, *Spectrochim. Acta, Part A*, **26**, 919 (1970).

Alkylation-Reduction of Carbonyl Systems. VII. Synthesis of α-Cyclopropyl Aromatic Hydrocarbons by Cyclopropylation-Reduction of Aromatic Aldehydes and Ketones. Parameters of Cyclopropyl α, β, and γ Carbon-13 Shieldings in Cyclopropyl Aromatic Hydrocarbons

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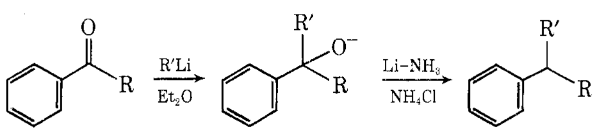
α-Cyclopropyl aromatic hydrocarbons are conveniently prepared, in excellent yields, from aromatic carbonyl compounds by tandem cyclopropylation-reduction. By this procedure cyclopropyl benzyl alkoxides, generated in situ by cyclopropylation, are reduced by lithium-ammonia-ammonium chloride to the corresponding cyclopropyl aromatic hydrocarbons. Examples include cyclopropyl(4-*tert*-butyl)phenylmethane (**8**) from 4-*tert*-butylbenzaldehyde (**1**), 1-cyclopropyl-1-phenylethane (**9**) from acetophenone (**2**), 1-cyclopropylindan (**10**) from indanone (**3**), dicyclopropylphenylmethane (**11**) from cyclopropyl phenyl ketone (**4**), cyclopropyldiphenylmethane (**12**) from benzophenone (**5**), and 1-cyclopropyl-1,3-diphenylpropane (**13**) from benzylideneacetophenone (**6**). Cyclopropylation-reduction of phenyl vinyl ketone (**7**), in contrast, yielded 3-cyclopropyl-1-phenylpropane (**14**) via 1,4 addition. Carbon magnetic resonances were assigned to the cyclopropyl aromatic hydrocarbons. A comparison of the chemical shifts with those of model compounds possessing a hydrogen in place of the cyclopropyl group allowed the estimation of the following cyclopropyl substituent parameters: 17 ± 3.7 ppm (eight values) for α, 6.1 ± 1.3 ppm (five values) for β, and −1.6 ± 0.8 ppm for the γ position (four values). These shielding parameters are smaller but in the same direction as those for a phenyl group. Those compounds possessing a chiral or prochiral center adjacent to the cyclopropyl group exhibit chemical shift nonequivalence of the cyclopropyl methylene carbons.

Synthesis. This laboratory has been exploring the potential applications of tandem alkylation-reduction of aromatic carbonyl systems as a convenient method of preparing aromatic hydrocarbons.[2] The method involves the lithium-ammonia-ammonium chloride reduction of benzyl alkoxides generated in situ by alkylation. Since the entire sequence is performed in the same reaction vessel without the isolation or purification of intermediates, the total synthesis consumes only a few hours and the isolated yield of the product is usually excellent.



The introduction of a cyclopropyl group at the α position in an aromatic hydrocarbon is a very difficult task using classical procedures. After cyclopropylation of the requisite aromatic carbonyl system, for example, the α-cyclopropyl group would not be expected to survive the dehydration[3]-hydrogenation[4] sequence.[5] On the other hand, our tandem alkylation-reduction procedure, using in this case cyclopropyllithium and an aromatic carbonyl compound, offered a potential method of preparing α-cyclopropyl aromatic hydrocarbons.