Notes

Meerwein Arylation of Fluorinated Olefins

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Received September 16, 1976

The Meerwein arylation—copper-catalyzed addition of Ar and X from an arenediazonium halide to an "activated" olefin $CH_2{=}CHZ$ (eq 1)—has been applied to olefins bearing diverse Z groups like aryl, vinyl, cyano, carbonyl, and chlorine.[1,2] Among the chlorine-activated olefins, chloroethene and 1,1-dichloroethene (vinyl and vinylidene chloride) give generally excellent yields of adducts. Trichloroethene and the geometrically isomeric 1,2-dichloroethenes give poorer results; tetrachloroethene fails to react.[3] Polychloroalkylalkenes like $Cl_3CCH{=}CH_2$ have not been tested. No examples have been noted where Z is one or more fluorine atoms. Where Z = CF_3, Failkov et al.[4] obtained 38–40% of adducts from *p*-nitrobenzenediazonium halides, X = Cl, Br.

$$ArN_2X + CH_2{=}CHZ \xrightarrow{CuX_2} ArCH_2CHXZ + N_2 \qquad (1)$$

The present study aimed to determine whether a fluoroalkyl chain or several fluorine atoms could promote Meerwein arylation of an otherwise not activated olefin. The olefins selected for testing, **1–8**, are depicted in Chart I. The first two are activated by electronegative fluoroalkyl groups, the third and fourth have three fluorines and one fluoroalkyl group on the double bond, the fifth has chlorine, alkyl, and two fluorines, and the sixth has chlorine and three fluorines. The last two have two or four fluorine atoms.

Chart I

$HCF_2CF_2CR{=}CH_2 + p\text{-}YC_6H_4N_2Cl$

1, R = H

2, R = CH_3

$\longrightarrow HCF_2CF_2CRClCH_2C_6H_4Y\text{-}p$

9

$\xrightarrow{KOH} HCF_2CF_2CR{=}CHC_6H_4Y\text{-}p$

Y = NO_2, Cl, CO_2H

$H(CF_2)_4CF{=}CF_2$ 3	$CF_3(CF_2)_4CF{=}CF_2$ 4	$n\text{-}C_4H_9CF{=}CFCl$ 5
$CF_2{=}CFCl$ 6	$CH_2{=}CF_2$ 7	$CF_2{=}CF_2$ 8

Olefins **1** and **2** react readily with diazonium salts bearing an electron-withdrawing substituent (Cl, NO_2, CO_2H), but not with 2,5-dimethoxybenzenediazonium chloride, under standard[1,2] Meerwein arylation conditions. Electron-releasing substituents, especially in the ortho position, often depress the yields of Meerwein adducts.[1,2] The products shown in Chart I and in Table I were obtained in 28–50% yields. In the cases studied, these were the Ar–Cl addition products **9**, not the hydrogen substitution products $ArCH{=}CHR_F$ which are often found. The latter may be prepared by dehydrochlorination of **9**.

The tetrasubstituted olefins **3–5** were not arylated under standard conditions. Most of the olefin was recovered, and the aryl group of the diazonium salt appeared as aryl halide and arene, by-products of the Sandmeyer and dediazoniation reactions which always accompany the Meerwein arylation.[1,2] Since these heavily fluorinated olefins are not very soluble in the aqueous acetone medium of the normal Meerwein arylation, a procedure was developed using acetone, a dry diazonium chloride or tetrafluoroborate, lithium trifluoroacetate as buffer, and aqueous cupric chloride to provide the copper catalyst and the small amount of water known to be essential for typical Meerwein arylations.[1,2] Using acrylonitrile as model olefin, reaction by this anhydrous procedure proceeded vigorously after a brief induction period to give 30–39% of the adduct $p\text{-}ClC_6H_4CH_2CHClCN$, which has been prepared in 37% yield under "standard" conditions.[5] However, the anhydrous procedure gave no detectable adduct with **4**. The induction period noted in all the experiments with the anhydrous procedure may reflect the time required to produce the cuprous chloride which some writers believe to be the only active catalyst in the Meerwein arylation.[1,2] However, in one attempt, use of cuprous chloride with **4** gave no better yield (zero) than did cupric chloride (also zero).

Chlorotrifluoroethylene reacted smoothly in an autoclave under otherwise standard conditions to yield the adduct $ArCF_2CFCl_2$ in 27% yield.[6] Since it could not be dechlorinated with zinc in refluxing methanol, the isomeric structure $ArCFClCF_2Cl$ is excluded. Since this olefin reacts, but tetrachloroethene does not,[3] the intermediate complex[1,2] evidently cannot form when the double bond is too heavily substituted by large groups. Two fluorines on one carbon are not too bulky, but two chlorines are. The regioselectivity observed here further supports the statement that the aryl radical becomes attached to the less hindered terminus of the olefin.[1,2] 1,1-Dichloro-2,2-difluoroethene was not available for testing.

Vinylidene fluoride (**7**) is less reactive toward *p*-chloro- and *p*-nitrobenzenediazonium chloride than are vinylidene chloride and **6**. Apparently the radical stabilization available in the structure $Ar\text{–}C\text{–}\dot{C}\text{–}Cl$ is less important in $Ar\text{–}C\text{–}\dot{C}\text{–}F$. Most of the diazonium salt formed aryl chloride and azoarene, as well as a little ArH and phenol. About 10–15% (GC) formed the product $ArCH_2CF_2Cl$, and small amounts of telomers $Ar(C_2H_2F_2)_nCl$ were also present. Telomers are very rare in the Meerwein arylation.[1,2] Surprisingly, $ArCF_2CH_2Cl$ and $ArCH_2CF_2CF_2CH_2Cl$ were seen, showing that **7** is not nearly so regioselective in Meerwein arylations as other olefins. We have encountered such "inverse" products in radical telomerizations of R_FI with vinyl and vinylidene fluoride.[7]

Biaryls are not normally seen in Meerwein arylations. However, GC/MS detected several chlorobiphenyls in the product from *p*-chlorobenzenediazonium chloride and **7**; two were dichlorobiphenyls, one was a trichlorobiphenyl (isolated), and three were dichlorobiphenyls bearing $\text{-}CH_2CF_2Cl$ or related side chains. Except for the trichlorobiphenyl, none was formed in large amount.

This Meerwein arylation does not have preparative value under the conditions selected, partly because of the low yield, and partly because ArCl and $ArCH_2CF_2Cl$ boil very close together. However, the adduct could probably be dehydrochlorinated to $ArCH{=}CF_2$ which could be separated from ArCl.

The results with tetrafluoroethylene were less encouraging. From *p*-chlorobenzenediazonium chloride, the major products were again *p*-dichlorobenzene and 4,4′-dichloroazobenzene.

Table I. Properties of Products of Meerwein Arylation of Fluorinated Olefins p-$XC_6H_4CH_2C(R)ClCF_2CF_2H$ [a]

Registry no.	X	R	Mp or bp, °C (mm)	Recrystn solvent	Yield %[b]	Formula	Anal. Calcd, % C	Calcd, % H	Calcd, % Cl	Found, % C	Found, % H	Found, % Cl
62448-54-8	NO_2	H	33–34; 122–123 (1)[c]	MeOH	28	$C_{10}H_8ClF_4NO_2$	42.0	2.8	12.4	42.0	3.0	12.4
62448-55-9	NO_2	CH_3	95.5–97.5	EtOH	40	$C_{11}H_{10}ClF_4NO_2$	44.1	3.4		44.6	3.5	
62448-56-0	Cl	CH_3	134–135 (10)[c]		36	$C_{11}H_{10}Cl_2F_4$	45.7	3.5	24.5	45.9	3.6	24.9
62448-57-1	CO_2H	CH_3	199.8–201.6	EtOH; $PhCH_3$	50	$C_{12}H_{11}ClF_4O_2$[d]	48.4	3.4	11.9	48.5	4.0	11.6

[a] Satisfactory microanalyses were obtained for all the compounds reported in this table. [b] Yields are not corrected for recovered olefin. [c] Boiling point. [d] Neut equiv: calcd, 298; found, 298.

Perhaps 10% of the adduct $Ar(CF_2CF_2)_nCl$, $n = 1$, was formed, and decreasing amounts of the telomers $n = 2$ and 3 were also seen (GC/MS). Biaryls were not detected.

Experimental Section

Materials. The olefins 1 and 2 were prepared by vapor-phase pyrolysis (530–540 °C) of the acetates of the alcohols obtained by radical-catalyzed addition of ethanol or isopropyl alcohol to tetrafluoroethylene. They boiled at 27 and 52–53 °C, $n^{25}D$ 1.3028 and 1.3243, respectively. Olefins 3 and 4 were prepared by "dry distillation" of the sodium carboxylates $R_FCF_2CF_2COONa$, according to Hals et al.[8] They boiled respectively at 71–72 and 62–74 °C.[9] Olefin 5 was prepared from butyllithium and chlorotrifluoroethylene by the procedure of Dixon.[10] The fraction used boiled at 108.5–110 °C, $n^{25}D$ 1.3924. Chlorotrifluoroethylene was a commercial product.

General Procedure for Meerwein Arylation. The amine (0.1 mol) was diazotized conventionally with 25 mL of concentrated hydrochloric acid, 1 equiv of sodium nitrite, and ice. The filtered solution was added all at once to 0.1 mol of the olefin in 250 mL of reagent acetone, followed immediately by concentrated aqueous solutions of 0.1 mol of sodium acetate and 0.015 mol of cupric chloride. (The total volume of the aqueous solutions was 200 mL, hence the solvent was about 56% acetone.) In successful reactions, the homogeneous solution turned dark olive-green and began immediately to evolve nitrogen. In the unsuccessful reactions, the color remained clear light green. The mixture gradually reached about 33 °C, and nitrogen evolution ceased after about 0.5 h. After an additional 1 h, the mixture usually had separated into an upper dark-brown layer and a lower clear green layer.

The mixture was then distilled directly until the head temperature reached 90 °C. Unchanged olefin could be recovered from the distillate by diluting it with ice water. The residue was steam distilled, usually until 4 L had been collected. The distillate was extracted with 3 × 150 mL of methylene chloride, and the combined extracts were washed with dilute sodium hydroxide solution to remove any phenols, then with water, and then dried with potassium carbonate. In most cases, the steam-involatile material was discarded.

The extract was distilled through a small fractionating column to remove first solvent, then ArH (nitrobenzene or chlorobenzene), then ArCl (p-nitrochlorobenzene or p-dichlorobenzene) resulting from the Sandmeyer reaction, and finally the product. When the product was solid, it was crystallized from methanol or ethanol, as shown in Table I.

The procedure was modified for p-aminobenzoic acid. It was diazotized by the "inverse" method by dissolving it (0.1 mol) in sodium carbonate solution, adding sodium nitrite, and pouring the solution onto ice and hydrochloric acid. Since the extra mol of salt thus introduced impeded the solubility of the fluoro olefin 2, an extra 100 mL of water and 200 mL of acetone were added to achieve a homogeneous solution. Nitrogen evolution continued for 2.5 h, and a dark green, sticky solid precipitated. After removal of the acetone, the residue was steam distilled to remove benzoic acid (2.3 g). The residue was made strongly acidic, and the dark green solid became pale tan as the copper dissolved. The solid was collected, washed with dilute acid, then dissolved in sodium bicarbonate solution, filtered, and reprecipitated; 12.7 g was obtained. It was crystallized twice from alcohol and twice from toluene for analysis. Purification was difficult because the crude product was contaminated with p-chlorobenzoic acid.

In the unsuccessful experiments, most of the olefin was recovered with the acetone. The steam distillate contained little or nothing boiling higher than the Sandmeyer product, and almost no tar remained in the steam still.

Meerwein Arylation under Anhydrous Conditions. p-Chlorobenzenediazonium chloride and tetrafluoroborate were prepared from the corresponding salts of p-chloroaniline and 1 equiv of amyl nitrite in absolute ethanol, then precipitated with dry ether. A solution of lithium trifluoroacetate was prepared by stirring 10.0 g of lithium carbonate with 250 mL of acetone while adding 34.2 g (0.3 mol) of trifluoroacetic acid slowly. To this solution was added 0.1 mol of the dry diazonium chloride, 5.3 g (0.1 mol) of acrylonitrile, and 0.015 mol of cupric chloride in 5 mL of water. The diazonium salt did not dissolve completely. Slow nitrogen evolution began immediately. After 10 min, the reaction suddenly speeded up and the temperature reached 45 °C before it could be cooled. Some material was carried out the top of the condenser by the rapid escape of nitrogen. The standard workup procedure gave 20% of p-dichlorobenzene and 7.8 g (39%) of p-$ClC_6H_4CH_2CHClCN$, bp 169–173 °C (22 mm). Alternatively, the diazonium fluoroborate with 1 equiv of lithium chloride exhibited the same behavior, giving 32% of p-dichlorobenzene and 30% of arylation product.

Chlorotrifluoroethylene.[6] An aqueous acetone solution of 0.1 mol of p-chlorobenzenediazonium chloride containing 0.1 mol of sodium acetate was placed in an autoclave, which was then chilled and evacuated. Then 25.0 g (0.214 mol) chlorotrifluoroethylene was condensed into the autoclave from a cylinder. The vessel was warmed to room temperature, and the cupric chloride solution was sucked into the autoclave. The mixture was held for 15 min at room temperature, then heated for 1.5 h at 40–50 °C. The product was isolated by the general method; 7.1 g (27%) of p-$ClC_6H_4CF_2CFCl_2$ was obtained, bp 105–107 °C (20 mm). It was identified by its mode of formation, microanalysis, and by its failure to eliminate chlorine when refluxed with zinc dust in methanol.

Dehydrochlorination. The product 9 (X = NO_2; R = H) (4.3 g) was heated for 0.5 h with a solution of 1.5 g of potassium hydroxide in 50 mL of methanol. Dilution with water gave a yellow solid, 3.6 g, which was recrystallized from methanol, mp 89.9–90.4 °C, faintly yellow needles.

Anal. Calcd for $C_{10}H_7F_4NO_2$: C, 48.2; H, 2.8. Found: C, 48.6; H, 2.6.

The other products in Table I gave precipitates of potassium chloride when treated similarly, but the olefins were not isolated or characterized.

Vinylidene Fluoride and Tetrafluoroethylene. p-Chloroaniline (0.2 mol) in 83 mL of 6 N hydrochloric acid and 80 g of ice was diazotized with 0.2 mol of sodium nitrite at 0 °C. The filtered solution was charged to the shaker tube and frozen in a −80 °C bath. Then 125 mL of acetone, 13.6 g (0.1 mol) of sodium acetate trihydrate, and 5.2 g (0.03 mol) of cupric chloride dihydrate were added without agitation. The tube was sealed, further chilled, and evacuated. Then 0.4–0.5 mol of fluoro olefin was added by vacuum transfer. The tube was then heated to 25–30 °C and maintained there with shaking for 4 h. The pressure increased about 200 psig during this time, signaling loss of nitrogen from the diazonium salt.

The tube was vented and the two-phase dark green mixture was discharged. The acetone was removed on a rotary evaporator, and the organic material was taken up in methylene chloride, washed and dried, and again evaporated. The crude product was distilled at 0.5 Torr to pot temperature 200 °C; little tar remained. The distillate was examined by GC/MS.[11] The results are given in the text.

Isolation of Trichlorobiphenyl. The product from p-chloroaniline and vinylidene fluoride was fractionally distilled. The cut from 90–110 °C (0.3 Torr), 5.1 g, was crystallized twice from isopropyl alcohol, 1.1 g, mp 63.0–63.5 °C.

Anal. Calcd for $C_{12}H_7Cl_3$: C, 55.9; H, 2.7; Cl, 41.3. Found: C, 55.9; H, 2.5; Cl, 39.6; N, 1.6.

Since this material contained about 15% of 4,4′-dichloroazobenzene (GC), it should have the composition C, 56.1; H, 2.8; Cl, 39.4; N, 1.7. These values agree with those found.

Registry No.—**1**, 40723-71-5; **2**, 57252-78-5; **3**, 1767-94-8; **4**, 355-63-5; **5**, 367-36-2; **6**, 79-38-9; *p*-chlorobenzenediazonium chloride, 2028-74-2; *p*-nitrobenzenediazonium chloride, 100-05-0; *p*-carboxybenzenediazonium chloride, 17405-00-4; *p*-dichlorobenzene, 106-46-7; *p*-$ClC_6H_4CH_2CHClCN$, 17849-64-8; *p*-$ClC_6H_4CF_2CFCl_2$, 62448-58-2; *p*-$NO_2C_6H_4CH{=}CHCF_2CF_2H$, 62448-59-3; *p*-chloroaniline, 106-47-8; vinylidene fluoride, 116-14-3; 4,4′-dichloroazobenzene, 1602-00-2; trichlorobiphenyl, 62461-62-5.

References and Notes

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(3) A. V. Dombrovskii and V. M. Naidan, *J. Gen. Chem. USSR (Engl. Transl.)*, **32**, 1256 (1962).
(4) Ya. A. Fialkov, A. M. Aleksandrov, and L. M. Yagupol'skii, *J. Gen. Chem. USSR (Engl. Transl.)*, **38**, 1741 (1968).
(5) P. L'Ecuyer and C. A. Olivier, *Can. J. Res., Sect. B*, **27**, 689 (1949).
(6) The experiment with chlorotrifluoroethene was performed by Dr. Richard R. Merner of this laboratory.
(7) C. S. Rondestvedt, Jr., unpublished experiments in this laboratory.
(8) L. J. Hals, T. S. Reid, and G. H. Smith, *J. Am. Chem. Soc.*, **73**, 4054 (1951); T. J. Brice, J. D. La Zerte, L. H. Hals, and W. H. Pearlson, *ibid.*, **75**, 2698 (1953); R. N. Haszeldine, *J. Chem. Soc.*, 4026 (1954).
(9) Commercial perfluorooctanoic acid was used for this preparation, and it contained related compounds. The wide boiling range of **4** betokens a mixture of olefins.
(10) S. Dixon, *J. Org. Chem.*, **21**, 400 (1956).
(11) GC/MS analyses were performed by Mr. R. H. Weeks in this laboratory.

Metal-Ammonia Reduction of Fluorinated Aromatic Compounds

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Received December 23, 1976

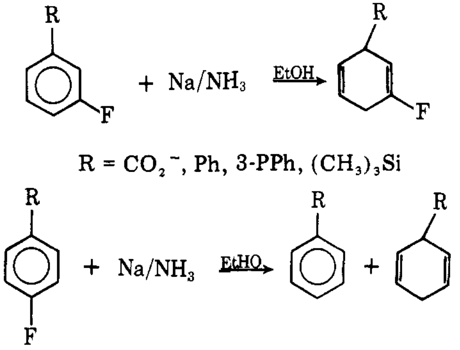
The acceptance of the hydrogenolysis of aryl carbon–halogen bonds (including fluorine) by alkali metals in liquid ammonia is evidenced by three major reviews.[1,2] Since direct metal–halogen exchange is not an attractive mechanism with fluorides,[3] and benzyne processes can be eliminated on other grounds,[4] the most likely pathway appears to be presented in eq 1.

$$ArF \xrightarrow{e^-} [ArF]^{-\cdot} \xrightarrow{-F^-} Ar\cdot \xrightarrow{e^-} Ar^- \xrightarrow{NH_3} ArH \qquad (1)$$

Thus, addition of an electron to the aromatic ring of ArF results in a radical anion which loses fluoride ion producing an aryl radical. This radical is expected to easily accept another electron to form an aryl carbanion which is rapidly protonated by ammonia. Depending on the nature of ArF and reaction conditions (metal supply, proton source, etc.), ArH may also be reduced to cyclohexadienes and related products.

In addition to the firm establishment of the aforementioned mechanism, our results indicate that under proper conditions, the Birch reduction can, in fact, provide an important synthetic pathway for the formation of fluorinated cyclohexadienes. As illustrated in Scheme I, compounds containing fluorine meta to an activating substituent[5] can be successfully reduced with retention of fluorine, whereas fluorine in the para position is lost.[6] Thus, this observed substituent effect rules out any direct electron transfer to the Ar–F bond and establishes electron addition to the ring as the first step. Loss of fluoride from this intermediate seems more attractive than a second electron addition, since dianions are generally not formed with benzene derivatives.[1,2] Protonation of the radical anion followed by a second electron addition and then loss of fluoride may also be ruled out since this would lead to a carbene intermediate which is not consistent with product analysis.

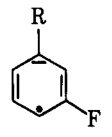
Scheme I



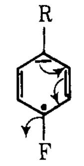
R = CO_2^-, Ph, 3-PPh, $(CH_3)_3Si$

R = CO_2^-, Ph, 4-FPh

These transformations can be rationalized in terms of the electron density distribution in the intermediate radical anions.[7] Hence, as an oversimplification, if resonance structures 1 and 2 are considered as most important in their respective cases, the process for fluorine loss in 2 can be visualized. Alternatively, we may simply consider that fluorine is expected to be lost when attached to a carbon holding increased electron density in the intermediate anion, and, conversely, when fluorine is on a carbon with decreased electron density (such as 1) it may be retained. This generates particular interest in the biphenyl case, since electron density is distributed between two rings. Nonetheless, fluorine was lost from both 4-fluorobiphenyl and 4,4′-difluorobiphenyl while it was retained with 3-fluorobiphenyl and 3,3′-difluorobiphenyl. The fact that 3-fluorobiphenyl reduces primarily in the fluorinated ring suggests that fluorine is an activating group[8] in metal/ammonia reduction, although not as activating as phenyl or trimethylsilyl in view of our present results. Since fluorine substitution is known to stabilize pyramidal or nonconjugated carbanions[8] but destabilize directly conjugated carbanions, this suggests that the effect of fluorine substitution in this position is largely inductive. However, the deactivating effect of a methyl or methoxy substituent presumably does not shift electron density away from the carbon bearing the fluorine in the intermediate, since the reduction of both *p*-fluorotoluene and *p*-fluoroanisole results in loss of fluorine.



1



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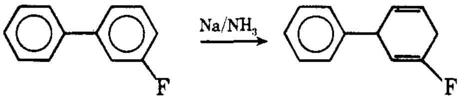

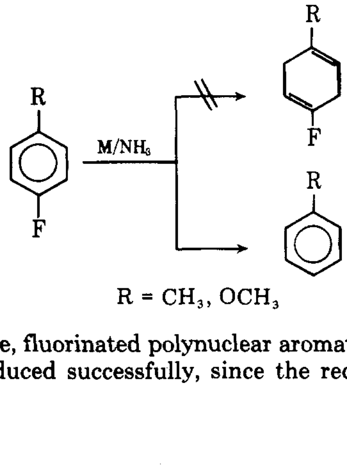

R = CH_3, OCH_3

In principle, fluorinated polynuclear aromatic compounds might be reduced successfully, since the reduction of the