Journal of Fluorine Chemistry, 35 (1987) 571–580
Received: April 29, 1986; accepted: February 12, 1987

REGIOSPECIFIC SYNTHESIS OF AROMATIC COMPOUNDS VIA ORGANOMETALLIC INTERMEDIATES. PART 5. SUBSTITUTED PERFLUOROALKYLETHER BENZENES

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SUMMARY

A new organometallic species, 3,5-$Li_2C_6H_3X$ where X = C_2F_5-(OCF_2CF_2)$_4$$OCF_2CF_2$-(IIIa) has been prepared from the corresponding dibromo compound by a metal-halogen exchange reaction. The reactions between IIIa and various substrates were examined in order to determine the usefulness of this diorganometallic reagent as a synthon.

INTRODUCTION

It has been reported recently [1] that 1,3,5-tribromobenzene could be subjected to a sequential lithium-halogen exchange followed by reaction with various substrates to yield a variety of substituted benzenes. This paper describes the preparation of a dilithio derivative (IIIa) from 3,5-$Br_2C_6H_3X$ where X = C_2F_5(OCF_2CF_2)$_4$-OCF_2CF_2-(I) by lithium-halogen exchange, and its reaction with various substrates.

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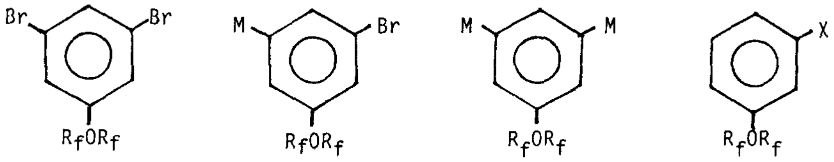
RESULTS AND DISCUSSION

The starting material I (Scheme 1) used for the preparation of the dilithio derivative IIIa was obtained by partial metal-halogen exchange of 1,3,5-tribromobenzene followed by reaction with a fluorinated ester [1] and SF_4/HF fluorination of the ketone.



(I) (II) (III) (IV), X = Br
(V), X = H

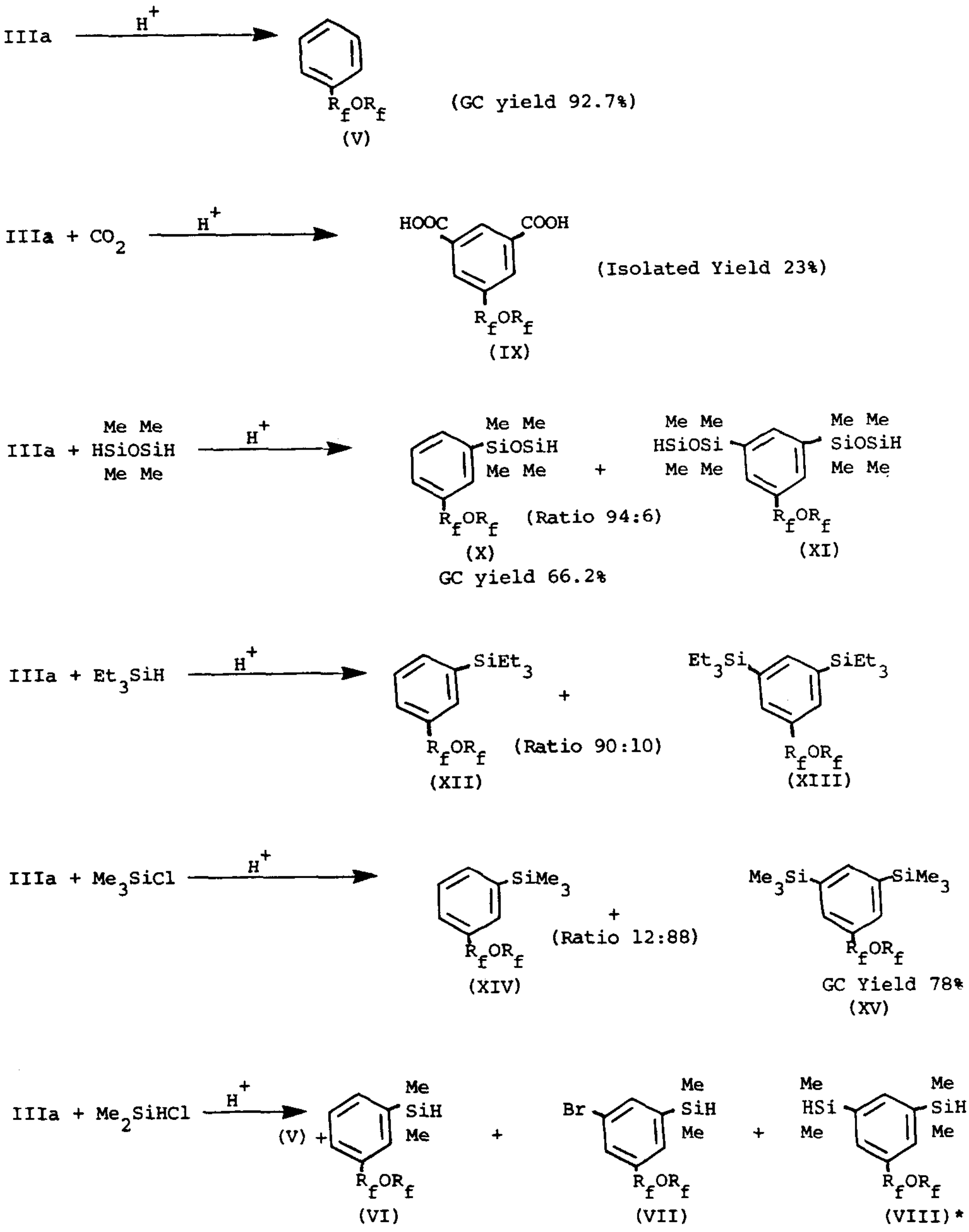
M; a = Li; b = MgBr

R_fOR_f = $-CF_2CF_2O(CF_2CF_2O)_4CF_2CF_3$

SCHEME 1

In order to determine experimental conditions suitable for the maximum conversion of the dibromide I to the dilithio derivative IIIa, several small-scale reactions were conducted with I and n-BuLi and with changes in the ratio of reactants, solvent and time at -78°C. Metal-halogen exchange at temperatures above -30°C led to extensive decomposition of the dilithio derivative IIIa. The highest yield of V (92.7 percent), in the hydrolyzed sample which represents the dilithio derivative IIIa in the reaction medium, was obtained by conducting the reaction in dry tetrahydrofuran at -78°C for about 2 h. using 3.65 molar equivalents of n-BuLi. The dilithio derivative IIIa derived from 1.0 mmole of the dibromide I, was completely soluble at -78°C in 10.0 ml of tetrahydrofuran, giving a clear, pale yellow solution. Such a freshly-prepared solution of IIIa was used for most derivatizations.

The reactivity of IIIa was studied by its interaction with various substrates. Since we were interested in obtaining silyl derivatives of IIIa, most of the substrates selected were silanes. These reactions are represented in Scheme 2. Structural assignments for compounds VII, XI, XII, XIII and XIV are based on MS data alone and are not conclusive. The experimental conditions were varied for different substrates (See experimental section). Carbonation of IIIa was done in Et_2O containing 10



$R_fOR_f = -CF_2CF_2O(CF_2CF_2O)_4CF_2CF_3$ (Isolated Yield 26.5%)

*See experimental part for relative amounts of these products.

Scheme 2. Reactions of IIIa with various substrates.

percent glyme, since Et_2O alone was not satisfactory. The Si-H bonds in Et_3SiH and $HSi(Me)_2OSi(Me)_2H$ reacted with IIIa in tetrahydrofuran, however disubstitution occurred only to a small extent. The major products XII and X were monosubstitution products. Trimethyl chlorosilane reacted readily with IIIa in tetrahydrofuran to give the disubstitution product XV as the major product.

When Me_2SiHCl was used for derivatization, both Si-Cl and Si-H bonds reacted in tetrahydrofuran, as expected, the former being more reactive than the latter leading to a mixture of products. Therefore it was necessary to prepare IIIa in tetrahydrofuran so as to obtain a high yield of the dilithio compound followed by derivatization with Me_2SiHCl in diethyl ether so as to suppress reactivity of the Si-H bond and obtain the desired derivative VIII. The best condition for derivatization of IIIa was to add the dilithiocompound in tetrahydrofuran at -78°C to Me_2SiHCl in diethyl ether at -78°C so that the final reaction mixture had tetrahydrofuran and diethyl ether in the ratio 1:2. This ratio and mode of addition suppressed reactivity of Si-H bond with the lithium reagent.

The crude reaction product contained, in addition to VIII, small amounts of V and VI which could be separated by distillation on a spinning band column. The sample of VIII thus obtained was initially believed to be pure since GC analysis, using a 6' X 1/4" O.D. SE-30 and OV-1 column at different conditions, showed only one peak. Mass spectrometry however showed that the product contained significant amounts of the brominated compound VII. These two compounds, VII and VIII however, could be seen as separate peaks on GC analysis using 12' X 1/4" O.D. Dexsil 300 (three percent) column, but their retention times were very close to each other. The amounts of VII in the product was nearly 25 percent (GC area percent).

The formation of VII in such large amounts was not anticipated nor could be readily explained in view of the high yield of the dilithio derivative, IIIa (93 percent) in the first lithiation step. Apparently VII is formed during the derivatization step. It may be remarked that we have made a similar observation during our studies on dilithiation of o-dibromobenzene in Et_2O/THF at -110°C [2]. Though o-dibromobenzene could be completely converted to the dilithio derivative by n-BuLi, derivatization has yielded significant amounts of o-bromophenyl derivatives. A possible explanation for this observation is that it may involve an equilibrium process between the lithium intermediates and n-BuBr in mixed solvent systems of Et_2O and tetrahydrofuran. Further work is necessary to understand this phenomenon.

All attempts to separate VIII from the bromo compound VII by fractionation using an efficient spinning band column failed to yield a pure sample of VIII. The mixture of VII and VIII could be reduced however with $LiAlH_4$ in dry diethyl ether whereby VII underwent debromination to VI. From this mixture of VI and VIII, pure samples could be obtained by fractional distillation under reduced pressure on an efficient spinning band column.

Attempts were also made to prepare the bis-Grignard reagent, IIIb from I and Mg in tetrahydrofuran. The reactions were very slow and incomplete. A typical reaction carried out in tetrahydrofuran at 55°C for 20 h gave about 23% of the bis-Grignard, IIIb, 10% of IIb in addition to other minor products as determined by GC analysis of the hydrolyzed reaction mixture. About 57% of the starting dibromide remained unreacted.

EXPERIMENTAL

All organometallic reactions were carried out in oven-dried glassware under an atmosphere of dry nitrogen. Commercial anhydrous Et_2O was freshly distilled from $LiAlH_4$ before use. THF was distilled from sodium-benzophenone ketyl. All melting and boiling points are uncorrected. Gas chromatographic analyses were performed on a Perkin-Elmer Sigma 1 or Sigma 2B instrument using 6' or 12' stainless steel columns (1/4" o.d.) packed with 10 percent SE-30 on Chromosorb W or three percent OV-1, three percent OV-17 or three percent Dexsil 300 on Supelcoport. Infrared spectra were taken on a Perkin-Elmer model 521 instrument. Mass spectral data were obtained on a Du Pont 21-491B instrument interfaced with a Finnigan INCOS data system.

Preparation of IIIa (nc)

Into a 100 ml four-necked flask equipped with a stirrer, low temperature thermometer, a dropping funnel and a nitrogen gas inlet and maintained under a nitrogen atmosphere, were placed anhydrous THF (20 ml) and I (1.87 g: 2.0 mmole). The contents were cooled to -78°C (2-propanol/Dry Ice bath) and n-C_4H_9 Li (5.5 ml of 1.32M solution in hexane: 7.3 mmole) was added with stirring during 10 min. while maintaining the temperature below -75°C.

Aliquot samples were taken and hydrolyzed with 2N HCl, extracted with Et_2O and analyzed by GC to monitor the extent of metal-halogen exchange. In about 2 h. the reaction mixture showed 92.7 percent of the dilithio derivative, IIIa and 2.2 percent of monolithio derivative, IIa. This solution was used to prepare the various derivatives.

A number of similar reactions were conducted at different conditions to arrive at the optimum conditions described above. Reactions in diethyl ether in general gave lower yields of the dilithio derivative IIIa than those conducted in THF at -78°C. In each case, the whole reaction mixture was hydrolyzed by the addition of excess 2N HCl, and extracted with Et_2O for GC estimation of yields using n-nonane as internal standard. Removal of Et_2O gave a pale yellow liquid.

Isolation of IV and V (nc)

The liquid residue obtained from a few experiments described above and containing varying amount of IV and V was combined and subjected to fractional distillation at reduced pressure. Compound V distilled at 55°C/0.3 mm as a colorless liquid. IR (neat) 3100-3000 (ArC-H), 1600 (ArC=C), 1350-1050 (C-F), 760 cm^{-1}, (monosubstitution); MS (EI) m/e 776 $[M]^+$, 177 $[M-C_{10}F_{21}O_5]^+$, 127 $[M-C_{11}F_{23}O_5]^+$, 119 $[C_2F_5]^+$. Anal. Calcd. for $C_{18}H_5F_{25}O_5$: C, 27.84; H, 0.64; F, 61.21; O, 10.31. Found: C, 27.68; H, 0.67; F, 59.04; O, 10.01.

Compound IV distilled as a colorless liquid boiling at 78-9°C/0.3 mm. IR (neat) 3070 (ArC-H), 1580 (Ar-C=C), 1450, 1420 (Ar), 1350-1050 (C-F), 780 cm^{-1} (1,3-disubstitution); MS (EI) m/e 856, 854 $[M]^+$, 257, 255 $[M-C_{10}F_{21}O_5]^+$, 207, 205 $[M-C_{11}F_{23}O_5]^+$, 119 $[C_2F_5]^+$. Anal. Calcd. for $C_{18}H_4F_{25}O_5Br$: C, 25.27; H, 0.47; Br, 9.36; O, 9.35. Found: C, 25.35; H, 0.51; Br, 9.08; O, 9.05.

Preparation of IX (nc)

To a stirred solution of IIIa in dry Et_2O/glyme (20 ml/2 ml) prepared from 1.0 mmole (0.934 g) of I, CO_2 was admitted at such a rate as to keep the solution temperature below -65°C. After the initial exotherm, CO_2 was freely admitted into the flask and the contents left overnight with stirring in a

CO_2 atmosphere, allowing it to warm up to room temperature overnight. It was then hydrolyzed with 2N HCl, extracted with Et_2O and the solvent removed to obtain a pale yellow liquid with strong smell of butyric acid. Trituration with petroleum ether gave a white solid which was recrystallized from Et_2O/petroleum ether and was identified as compound IX. Yield = 23 percent, m.p. 197-9°C. IR (KBr) 3300-2750 (broad, COOH), 1700 (C=O), 1350-1050 cm^{-1} (C-F); MS (EI) m/e 864 $[M]^+$, 847 $[M-OH]^+$, 729 $[M-OC_2F_5]^+$, 497 $[M-(OC_2F_4)_2OC_2F_5]^+$, 381 $[M-(OC_2F_4)_3OC_2F_5]^+$, 265 $[M-(OC_2F_4)_4OC_2F_5]^+$, 215 $[M-CF_2(OC_2F_4)_4OC_2F_5]^+$, 119 $[C_2F_5]^+$, 100 $[C_2F_4]^+$. Anal. Calcd. for $C_{20}H_5F_{25}O_9$: C, 27.78; H, 0.58. Found: C, 27.39; H, 0.61.

Preparation of X (nc)

A solution of IIIa prepared from I (0.934 g, 1.0 mmole) in dry THF (10 ml) at -78°C was transferred through an insulated needle to a flask containing a stirred solution of $H(Me)_2SiOSi(Me)_2H$ (0.80 g, 6.0 mmole) and n-nonane (as internal standard) in THF (2 ml) cooled to -78°C. The transfer was made as fast as possible by pressure difference in the two reaction vessels and was completed in about 2 min. The reaction mixture was stirred overnight while allowing it to warm up slowly to room temperature. It was then hydrolyzed by the addition of 2N HCl and extracted twice with Et_2O. This diethyl ether solution was subjected to GC analysis to calculate the yield and ratio of products. The ratio of the monosubstitution product, X, to the disubstitution product, XI was 94:6 based on relative peak areas.

After removing the solvent, the reaction mixture, a pale yellow liquid was subjected to preparative GC on a 6' X 1/4" O.D. OV-1 column (3%) to isolate a pure sample of the major product X as a colorless liquid. B.P. (Micro) 279-80°C. IR (neat) 2950 (C-H), 2115 (SiH) 1600-1570 (Ar), 1350-1050 cm^{-1} (C-F), MS (EI) m/e 880 $[M-C_2H_4]^+$, 834 $[M-Me_2SiO]^+$, 695 $[880-CF_2OC_2F_5]^+$, 463 $[880-CF_2OC_2F_4OC_2F_5]^+$, 231 $[463-(OC_2F_4)_2]^+$, 203 $[231-C_2H_4]^+$, 185 $[CF_2C_6H_4SiMe_2H]^+$, 119 $[C_2F_5]^+$, 77 $[SiMe_2F]^+$, 59 $[SiHMe_2]^+$. Anal. Calcd. for $C_{22}H_{17}F_{25}O_6Si_2$: C, 29.07; H, 1.87. Found: C, 29.62; H, 1.94.

A pure sample of X was used to derive a response factor relative to n-nonane in the calculation of yield. GC yield of X was 66.2 percent.

Preparation of XV (nc)

To a solution of IIIa (containing n-nonane as standard) prepared as described earlier from I (0.934 g, 1.0 mmole) and n-C_4H_9Li (3.0 mmole) in dry THF (10 ml), and maintained at -78°C was added with stirring Me_3SiCl (0.60 g, 5.5 mmole) in dry THF (2 ml) during 10 min. An exotherm was observed and stirring was continued while allowing the reaction mixture to warm up to room temperature overnight. The reaction mixture was hydrolyzed by the addition of 2N HCl and extracted with Et_2O. GC analysis showed that the ratio of mono- to disubstitution products, i.e., XIV to XV was 12:88 and the yield of XV calculated after isolating a pure sample by preparative GC was 78 percent. Compound XV is a colorless liquid boiling at 270°C (Micro B.P.). IR (neat) 2960 (C-H), 1630, 1575 (Ar), 1400-1050 cm^{-1} (C-F); MS (EI) m/e, 905 $[M-CH_3]^+$, 901 $[M-F]^+$, 785 $[M-OC_2F_5]^+$, 669 $[M-OC_2F_4OC_2F_5]^+$, 533 $[M-(OC_2F_4)_2OC_2F_5]^+$, 437 $[M-(OC_2F_4)_3OC_2F_5]^+$, 321 $[M-(OC_2F_4)_4OC_2F_5]^+$, 233 $[321-SiMe_4]^+$, 119 $[C_2F_5]^+$, 77 $[SiMe_2F]^+$, 73 $[SiMe_3]^+$. Anal. Calcd. for $C_{24}H_{21}F_{25}O_5Si_2$: C, 31.30; H, 2.28. Found: C, 31.27; H, 2.32.

Preparation of VI and VIII (nc)

A solution of IIIa prepared from I (18.47 g, 19.77 mmole) and C_4H_9Li (5.69 g, 89.0 mmole) in 180 ml THF at -78°C was transferred through an insulated needle, during 30 min. to a stirred solution of Me_2SiHCl (42.0 g, 0.445 mmole) in Et_2O (360 ml) maintained at -78°C. Stirring was continued while leaving the reaction flask in the cold bath and allowing it to slowly warm up to room temperature overnight. The reaction mixture was then hydrolyzed by the addition of dilute HCl, extracted twice with Et_2O and the solvent removed to obtain 18.9 g of a pale yellow liquid. GC analysis of this crude product showed 84.5 percent of a compound initially believed to be pure VIII, about 5.0 percent of VI and 2.4 percent of V (area percent) in addition to other side products. Distillation on a spinning band column gave 1.1 g of impure VI and 10.6 g of VIII which was later shown to contain VII as an impurity (see Scheme 2).

Purification of VIII

An impure sample of VIII (16.1 g - from two experiments) containing VII (25 GC area percent) was dissolved in dry Et$_2$O (50 ml) and added slowly during 15 min. to a stirred suspension of LiAlH$_4$ (5.0 g) in dry Et$_2$O (200 ml) at room temperature. The reaction was followed every 15 minutes by GC analysis of aliquot samples hydrolyzed by adding to dilute HCl and was stopped when all the bromo compound VII was reduced (about 1 h.). It was found that the time required for reduction varied with the activity (purity) of LiAlH$_4$ and long reaction time led to small amounts of additional secondary products.

The reaction was stopped by very carefully adding the reaction mixture to 3N HCl and ice. The diethyl ether layer was separated and the solvent removed to yield VIII containing VI formed by reduction of VII. The crude product was subjected to fractional distillation under reduced pressure to obtain 7.11 g of pure VIII as a colorless liquid. Overall isolated yield of pure VIII was 26.5 percent, b.p. 77°/0.005 mm., IR (neat) 3060-3000 (ArC-H), 3000-2900 (Aliph C-H), 2115 (Si-H), 1580 (Ar), 1400-1050 (C-F), 890-860 cm^{-1} (SiH def). MS (EI) m/e 873 $[M-F]^+$, 872 $[M-HF]^+$, 813 $[872-SiHMe_2]^+$, 641 $[M-OC_2F_4OC_2F_5]^+$, 525 $[M-(OC_2F_4)_2OC_2F_5]^+$, 409 $[M-(OC_2F_4)_3OC_2F_5]^+$, 351 $[M-SiMe_2(OC_2F_4)_3OC_2F_5]^+$, 293 $[M-(OC_2F_4)_4OC_2F_5]^+$, 243 $[M-CF_2(OC_2F_4)_4OC_2F_5]^+$, 215 $[243-C_2H_4]^+$, 187 $[215-C_2H_4]^+$, 185 $[351-CF_2]^+$, 119 $[C_2F_5]^+$, 77 $[SiMe_2F]^+$. Anal. Calcd. for $C_{22}H_{17}F_{25}O_5Si_2$: C, 29.59; H, 1.91; F, 53.25. Found: C, 29.83; H, 1.95; F, 53.62.

During the fractionation, about 1.2 g of pure VI was also obtained as a colorless liquid b.p. 66°/0.005 mm., IR (neat) 3060-3000 (ArC-H) 3000-2800 (Aliph C-H), 2115 (Si-H), 1595 (Ar), 1400-1050 (C-F), 890-860 cm^{-1} (SiH def). MS (EI) m/e 813 $[M-F]^+$, 736 $[813-SiMe_2F]^+$, 736 $[813-SiMe_2F]^+$, 583 $[M-OC_2F_4OC_2F_5]^+$, 369 $[736-(OC_2F_4)_2OC_2F_5]^+$, 351 $[M-(OC_2F_4)_3OC_2F_5]^+$, 253 $[736-(OC_2F_4)_3OC_2F_5]^+$, 235 $[M-(OC_2F_4)_4OC_2F_5]^+$, 185 $[M-CF_2(OC_2F_4)_4OC_2F_5]^+$, 157 $[185-C_2H_4]^+$, 119 $[C_2F_5]^+$, 77 $[SiMe_2F]^+$. Anal. Calcd. for $C_{20}H_{11}F_{25}O_5Si$: C, 28.78; H, 1.32; F, 56.95. Found: C, 28.89; H, 1.35; F, 55.23.

Mass Spectrometry

The mass spectral data given for the substituted perfluoroalkylether benzenes indicate that the fragmentation pattern of these compounds proceeds mainly by fragmenting at the C-O sites of the R_fOR_f group. In general, the fragments $M^+-OC_2F_5$, $M^+-(OC_2F_4)_nOC_2F_5$ where n=1 to 4 and $M^+-CF_2(OC_2F_4)_4OC_2F_5$ can easily be identified. This pattern was effective in obtaining structural information.

REFERENCES

1 L.S. Chen, G.J. Chen and C. Tamborski, J. Organometal. Chem., 215 (1981) 281.

2 U.D.G. Prabhu, K.C. Eapen and C. Tamborski, J. Org. Chem., 49 (1984) 2792.