Journal of Organometallic Chemistry
Elsevier Sequoia S.A., Lausanne
Printed in The Netherlands

SYNTHESIS AND REACTIONS OF 2,3,4,5-TETRAFLUOROPHENYLLITHIUM

CHRIST TAMBORSKI AND EDWARD J. SOLOSKI

Nonmetallic Materials Division, Air Force Materials Laboratory, Wright Patterson Air Force Base, Ohio (U.S.A.)

(Received October 30th, 1968; in revised form February 19th, 1969)

SUMMARY

The lithiation of 1,2,3,4-tetrafluorobenzene with n-butyllithium to yield 2,3,4,5-tetrafluorophenyllithium (I) and by-products is described. Reactions of this organolithium with water, carbon dioxide, trimethylchlorosilane, dimethylchlorosilane, mercuric chloride and cuprous iodide indicate the synthesis utility of this organolithium intermediate.

INTRODUCTION

In our general study on metalation of hydrofluoroaromatic compounds, we previously have reported[1] the synthesis of 2,3,4,5-tetrafluorophenyllithium (I) as a by-product from the dimetalation of 1,2,3,4-tetrafluorobenzene (II). We have examined its synthesis and utility as an intermediate in more detail.

RESULTS AND DISCUSSION

Preparation of 2,3,4,5-tetrafluorophenyllithium, (I)

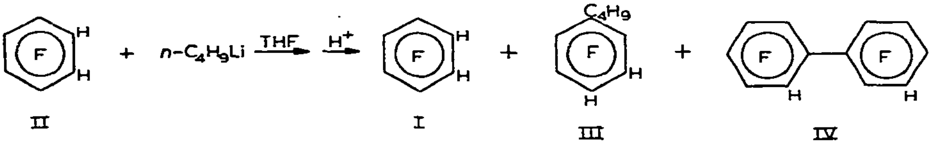
In our initial* studies on the metalation of 1,2,3,4-tetrafluorobenzene (II), the various reaction products were characterized after carbonation of the reaction mixture. A number of products indicative of both alkylation and metalation were observed. This procedure of mono and dimetalation of 1,2,3,4-tetrafluorobenzene has since been used and reported by others[2-5] in the preparation of various polyfluoroaryl compounds.

In our current studies on the monometalation of 1,2,3,4-tetrafluorobenzene, we have been able to prepare 2,3,4,5-tetrafluorophenyllithium (I) in approximately 90% yield. The by-products of this reaction are minimal and in general do not offer any difficulty in separation of derivatized products. All the reactions were carried out by the addition of an equivalent of n-butyllithium to a THF solution of 1,2,3,4-tetrafluorobenzene. The metalation is rapid (< 15 min) as indicated by the absence of

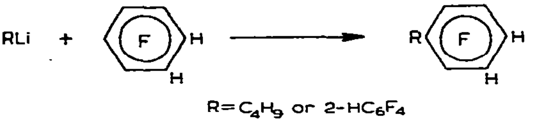
---

* Our initial studies[1] were concerned with the addition of 1,2,3,4-tetrafluorobenzene (II) to n-butyllithium (1 : 2 mole ratio) in THF or diethyl ether. In this manner, (II) was always present in an excess of n-butyllithium. Under these conditions, a mixture of organolithium compounds is obtained.

n-butyllithium determined by Color Test IIA[6]. Two minor by-products, 2,3,6-trifluoro-n-butylbenzene (III) and 2,2',3,3',4,5,6'-heptafluorobiphenyl (IV) in 1:9 ratio (VPC peak area) also were obtained when the reaction mixture was hydrolyzed at −70°. Product (III) probably was formed by a nucleophilic attack of n-butyllithium on 1,2,3,4-tetrafluorobenzene directly. Nucleophilic attack at the 2-fluorine position has been previously reported by others[5,7,8]. The formation of the biphenyl compound (IV) can be accounted for in a similar manner, *i.e.*, reaction of 2,3,4,5-tetrafluorophenyllithium (I) with 1,2,3,4-tetrafluorobenzene (II). An alternate method for the formation of the biphenyl compound (IV) through a nucleophilic reaction between 2 molecules of 2,3,4,5-tetrafluorophenyllithium (I) was considered and rejected. In this case, one would expect an increase in concentration of the biphenyl (IV) with reaction time, but when the organolithium compound (I) was allowed to stand for 4 days at −70°, no increase in biphenyl (IV) was noted. The organolithium compound was stable at this temperature, and no other new products indicative of benzyne formation from thermal decomposition of the organolithium compound were found.



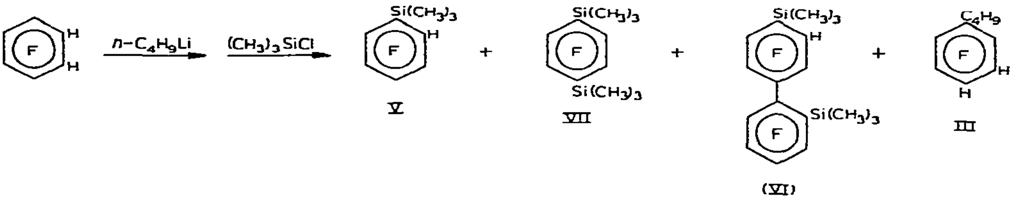
(1)



(2)

Reactions of 2,3,4,5-*tetrafluorophenyllithium*, (*I*)

In an attempt to characterize the various organolithium compounds resulting from the metalation of 1,2,3,4-tetrafluorobenzene, the reaction mixture was allowed to react with $(CH_3)_3SiCl$. Besides the principal product 2,3,4,5-tetrafluoro(trimethylsilyl)benzene (V), 2 other minor by-products were isolated (~3–4% each). VPC analysis also indicated the presence of a trace of the butylated product (III). The presence of (III), (V) and (VI) can reasonably be expected from the hydrolysis studies of the original reaction mixture prior to reaction with $(CH_3)_3SiCl$ (see eqn. 1). However, the formation of the disilylated compound (VII) is unexplainable at this time. VPC analysis of the original starting material (II) did not indicate any of the *para* dihydro isomer from which (VII) could arise by a dimetalation followed by reaction with the $(CH_3)_3SiCl$. Product (VII) was independently synthesized[9] through the reac-

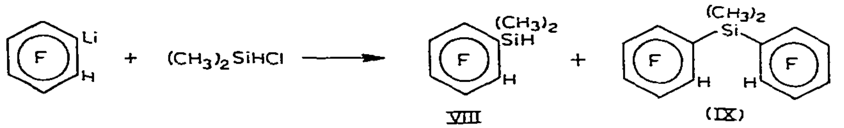


(3)

tion between 1,4-dilithiotetrafluorobenzene and $(CH_3)_3SiCl$. It was found to be identical in all respects (NMR, IR, mass spectral and VPC analysis) to the above by-product (VII).

Other reactions of (I) with various reagents, *e.g.*, $(CH_3)_2SiHCl$, $HgCl_2$, CO_2 and CuCl were carried out. Since the by-products due to the other organometallic species present were in the order of only 3–4% and did not seem to interfere with the principal reactions of (I), no attempt was made to isolate or characterize them. VPC analysis of the reaction mixture did, however, indicate small quantities of materials other than the expected product.

Reaction between the organolithium compound (I) and $(CH_3)_2SiHCl$ yielded two principal products (VIII) and (IX) (4.6 : 1 area ratio). There was no evidence of a disilylated tetrafluorobenzene. The presence of (IX) indicates that the SiH bond of (VIII) reacts competitively with the SiCl bond for the organolithium compound. Alkylation of the SiH bond with organolithium compounds is well documented in literature[10]. The bis substituted silane (IX) has recently been reported by Haiduc and Gilman[5] as a by-product from the reaction between $(CH_3)_2SiCl_2$ and a reaction mixture of mono and dilithiated tetrafluorobenzenes.



(4)

Reaction between the organolithium compound (I) and mercuric chloride yielded one principal product, bis(2,3,4,5-tetrafluorophenyl)mercury (X) in a 90% yield. Carbonation of the organolithium compound (I) however, yielded two acids 2,3,4,5-tetrafluorobenzoic acid (XI) and tetrafluorophthalic acid (XII) in a ratio of 9 : 1 (VPC peak area ratio as the methyl esters). From the presence of the diacid (XII), it would appear that 1,2,3,4-tetrafluorobenzene was dilithiated to a small extent. This conclusion, however, has been discarded based on our previous observations[11] on the carbonation of 2-bromotetrafluorophenyllithium which also yielded a mixture of mono and diacids. Characterization of organolithium compound via derivatization with carbon dioxide appears to be an unpredictable method when the organolithium compound has other functional groups present capable of either metal–hydrogen or metal–halogen interconversion.

We have previously reported[12] on the oxidative-coupling reaction of perfluoroarylcopper compounds to produce good yields of biaryls. This procedure for the synthesis of such useful highly fluorinated compounds complements the other two known procedures, Ullman reaction[13,14] and thermal decomposition of perfluorotitanium compounds[2,3]. The reaction of the organolithium compound (I) with CuI followed by oxidation of the reaction mixture yielded the coupled product 2,2′,3,3′,4,4′,5,5′-octafluorobiphenyl (XIII).

EXPERIMENTAL

All organometallic reactions were carried out in an atmosphere of dry, oxygen-free nitrogen. Solvents were purified and dried by conventional methods and distilled prior to use. Melting points are uncorrected. VPC analyses were carried out on an F&M Model 500 gas chromatograph using a 6-ft. Apiezon L on Chromosorb W (60–80 mesh) column and a helium carrier gas at about 60 cc/min. The temperature was programmed at 21°/min. The ^1H and ^{19}F NMR spectra were recorded on a Varian 56–60 spectrometer. Chemical shifts are reported in ppm from internal TMS for ^1H and $CFCl_3$ for ^{19}F. Mass spectrometer analyses were performed on an AEI MS-9 spectrometer.

Reaction of 1,2,3,4-*tetrafluorobenzene with n-butyllithium*

To a precooled (−70°) stirred solution of 1,2,3,4-tetrafluorobenzene (II) (0.15 mole, 23.6 g) in 125 ml freshly distilled THF was added n-butyllithium (0.15 mole, 97.5 ml of a hexane solution) during 15 min. Fifteen min later, the reaction mixture was hydrolyzed with 100 ml of 6 *N* HCl, warmed to room temperature, phase separated, extracted with diethyl ether and the organic layer thus obtained was dried over magnesium sulfate. Concentration of the dried organic layer yielded 1.55 g of liquid. GLC analysis of this material showed the presence of 2 principal components which accounted for $>95\%$ of the mixture.

The two major products (III) and (IV) (1 : 9 area ratio) were separated by preparative gas chromatography. Product (III) was characterized as 2,3,6-trifluoro-n-butylbenzene (III). (Found: C, 63.74, 63.59; H, 6.06, 6.01. $C_{10}H_{11}F_3$ calcd.: C, 63.82; H, 5.89%.) Mass spectrometer analysis; measured, *m/e* 188.0803; calcd., 188.0813. NMR analysis*; ^1H (CCl_4 solvent, TMS standard) 7.2–6.4 ppm [m (br), 2], 2.7 ppm [m(br), 2], 1.5 ppm (m, 4), 0.93 ppm (m, 3). ^{19}F (CCl_4 solvent, $CFCl_3$ standard) 117.1 ppm (m, 1), 133.8 ppm (m, 1), 137.5 ppm (multiplet, 1). Product (IV) was characterized as 2,2′,3,3′,4,5,6′-heptafluorobiphenyl (IV). Mass spectrometer analysis; measured, *m/e* 280.0116; calcd., 280.0123, NMR analysis; ^1H (CCl_4 solvent, TMS standard) 6.6–7.5 ppm (m). ^{19}F (CCl_4 solvent, $CFCl_3$ standard) 112.6 ppm (m, 1), 129.0 ppm (m, 1), 131.5 ppm (m, 1), 131.1 ppm (m, 1), 135.3 ppm (m, 1), 147.1 ppm (m, 2).

The organolithium reagent (I), prepared as described above, was used in the following reactions.

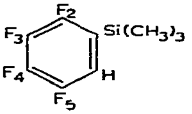
Reaction with trimethylchlorosilane

Trimethylchlorosilane (0.30 mole, 32.6 g) was added to (I) [prepared from 0.30 mole (II)] over a period of 10 min. The reaction mixture was stirred at −70° for an additional 16 h. Color Test I[15] was negative indicating the absence of the organolithium reagent. The reaction mixture was warmed to room temperature, concentrated by aspiration of the solvent and filtered from the precipitated salt. VPC analysis of the clear filtrate indicated the presence of (V), (VI) and (VII) in an area ratio of 80 : 1.2 : 2.5, respectively. Vacuum distillation yielded (V) (82%), b.p. 52°/7 mm, n_D^{22} 1.4401. The pot residue from the distillation contained primarily the two by-products (VI) and (VII) and these were separated by preparative gas chromatography and vacuum sublimation at 40°/1 mm. Product (V) was characterized as 2,3,4,5-tetrafluoro(trimethylsilyl)benzene. (Found: C, 48.54, 48.30; H, 4.49, 4.47. $C_9H_{10}F_4Si$ calcd.: C, 48.63; H, 4.54%.) Mass spectrometer analysis; measured, *m/e* 222.0490; calcd., 222.0488. NMR analysis; ^1H ($CDCl_3$ solvent, TMS standard) CH_3 0.36 ppm

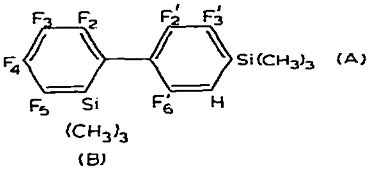
---

* s: singlet; d: doublet; t: triplet; qu: quintet; m: multiplet; br: broad.

(d, 9), Ar–H 6.94 ppm (m, 1); $J(CH_3{-}F_2)$ 1 Hz, $J(H{-}F_5)$ 9.4 Hz, $J(H{-}F_4)$ 8.4 Hz, $J(H{-}F_2)$ 4.0 Hz, $J(H{-}F_3)$ 2.7 Hz. ^{19}F ($CDCl_3$ solvent, $CFCl_3$ standard) +127 ppm (m, 1), +139.5 ppm (m, 1), +155 ppm (m, 1), +156.5 ppm (m, 1); $J(F_3{-}F_5)$ 2.5

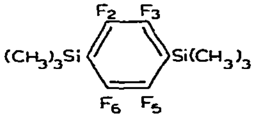


Hz, $J(F_5{-}H)$ 9.2 Hz, $J(F_2{-}F_5)$ 16 Hz, $J(F_4{-}F_5)$ 20 Hz, $J(F_2{-}F_3)$ 23 Hz, $J(F_3{-}F_4)$ 19 Hz, $J(F_4{-}H)$ 8.5 Hz, $J(F_2{-}F_4)$ 5 Hz. Product (VI) was characterized as 4′,6-bis(trimethylsilyl)-2,2′,3,3′,4,5,6′-heptafluorobiphenyl, m.p. 46–48°.



Mass spectrometer analysis; measured, *m/e* 424.0912; calcd., 424.0914. NMR analysis; ^1H (CCl_4 solution, TMS) Ar–H, 7.0 ppm (d, 1), (A) Si–CH_3 0.4 ppm (d, 9), (B) Si–CH_3 0.1 ppm (d, 9); $J(F'_6{-}H)$ 8 Hz, $J(F'_3{-}H)$ 3 Hz, $J(F'_2{-}H)$ 2 Hz. ^{19}F (CCl_4 solution, $CFCl_3$ standard) +115 ppm (m, 1), +122 (m, 1), +129 (m, 1), +132 (m, 1), +134 (m, 1), +152 (m, 2); $J(F'_3{-}F'_6)$ 17 Hz, $J(F'_6{-}F'_3)$ 2 Hz, $J(F'_2{-}F'_3)$ 24 Hz, $J(F_4{-}F_5)$ 22 Hz, $J(F_2{-}F_5)$ 18 Hz.

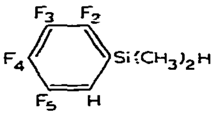
Product (VII) was characterized as 1,4-bis(trimethylsilyl)tetrafluorobenzene, m.p. 53–55°. (Found: C, 49.05, 49.06; H, 6.22, 6.26. $C_{12}H_{18}F_4Si_2$ calcd.: C, 48.95; H, 6.16%.) Mass spectrometer analysis; measured, *m/e* 294.0882; calcd., 294.0883.



NMR analysis; ^1H (CCl_4 solution, TMS standard) 0.41 ppm (qu, $J < 1$ Hz). ^{19}F (CCl_4 solution, $CFCl_3$ standard) +127 ppm [s (br)].

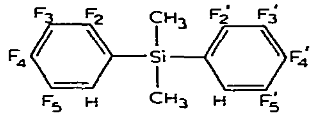
Reaction with dimethylchlorosilane

Dimethylchlorosilane (0.192 mole, 18.2 g) was added to (I) [prepared from 0.20 mole (II)] over a period of 12 min. After 1 h at −70°, Color Test I[15] was negative, indicating the absence of an organolithium compound. After one additional h, the reaction mixture was warmed to room temperature and filtered. VPC analysis of the reaction mixture (using n-decane as an internal standard) indicated two products (VIII) and (IX) (4.6 : 1 area ratio). The products were isolated by fractional distillation on a spinning band column. Compound (VIII), 26.8 g (64.3%), b.p. 155°, n_D^{25} 1.4392, was characterized as 2,3,4,5-tetrafluoro(dimethylsilyl)benzene. (Found: C, 46.13, 46,04; H, 4.00, 3.88. $C_8H_8F_4Si$ calcd.: C, 46.14; H, 3.87%.) Mass spectrometer ana-



lysis; measured, *m/e* 208.0332; calcd., 208.0332. NMR analysis; ^1H ($CDCl_3$ solvent, TMS standard) Si–CH_3 0.42 ppm (d of d, 6), Si–H 4.5 ppm (m, 1), Ar–H 7.0 ppm (m, 1); $J(CH_3–SiH)$ 4 Hz, $J(CH_3–F_2)$ 1 Hz, $J(ArH–F_5)$ 9.2 Hz, $J(ArH–F_4)$ 8.0 Hz, $J(ArH–F_2)$ 4.0 Hz, $J(ArH–F_3)$ 2.2 Hz. ^{19}F ($CDCl_3$ solution, $CFCl_3$ standard) +128 ppm (m, 1), +140 ppm (m, 1), +154 ppm (m, 1), +156 ppm (m, 1); $J(F_2–F_3)$ 23 Hz, $J(H–F_3) \sim J(F_3–F_5)$ 3 Hz, $J(F_4–F_5)$ 20 Hz, $J(F_2–F_5)$ 14 Hz, $J(F_2–F_4)$ 5 Hz, $J(F_3–F_4)$ 19 Hz, $J(H–F_5)$ 9.5 Hz, $J(H–F_4)$ 8 Hz.

Compound (IX) 6.9 g, b.p. 115°/3 mm, n_D^{25} 1.4788, was characterized as bis(2,3,4,5-tetrafluorophenyl)dimethylsilane[5]. (Found: C, 47.56, 47.30; H, 2.38, 2.30. $C_{14}H_8F_8Si$ calcd.: C, 47.19; H, 2.26%.) Mass spectrometer analysis indicated a nominal mass *m/e* 356; calcd., *m/e* 356. NMR analysis; ^1H ($CDCl_3$ solution, TMS standard) Si–CH_3 0.80 ppm (t, $J \sim 1$ Hz), Ar–H 7.0 ppm; $J(H–F_5)$ 9.3 Hz, $J(H–F_4)$ 8.4 Hz, $J(H–F_2)$ 4.0 Hz, $J(H–F_3)$ 2.7 Hz. ^{19}F ($CDCl_3$ solution, $CFCl_3$ standard) +126 ppm (m, 1), +138 ppm (m, 1), +153 ppm (m, 1); +155 ppm (m, 1). Coupling constants similar to compound (VIII).



Reaction with mercuric chloride

Anhydrous mercuric chloride (0.10 mole, 27.15 g) was added to (I) [prepared from 0.20 mole (II)] and the resulting mixture was stirred at −70° for approximately 19 h. The reaction mixture was allowed to warm to room temperature, the solvent was aspirated and the residue extracted with benzene. Concentration of the benzene solution precipitated 54 g of crude product. A portion was recrystallized from CCl_4 to yield an analytical sample m.p. 134–136°. (Found: C, 29.09; F, 30.74; Hg, 39.99. $C_{12}H_2F_8Hg$ calcd.: C, 28.90; F, 30.48; Hg, 40.22%.)

Reaction with carbon dioxide

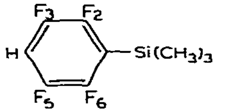
Carbon dioxide was bubbled through the organolithium reagent (I) [prepared from 0.15 mole (II)] at −70° for a period of 1 h. The reaction mixture was then allowed to warm to room temperature with continued carbonation. The reaction mixture was hydrolyzed with 80 ml of 6 *N* HCl, phase separated and the organic layer extracted with dil. NaOH. The basic aqueous layer was acidified with conc. HCl, extracted with diethyl ether, phase separated and dried ($MgSO_4$). Aspiration of the solvent yielded 29.4 g of mixed crude acids. The crude acid mixture was treated with diazomethane and the methyl esters were analyzed by VPC. Two principal products appeared in a ratio of 9 : 1 (peak area %). The first compound was characterized as methyl 2,3,4,5-tetrafluorobenzoate, b.p. 83°/15 mm, n_D^{23} 1.4477 [methyl ester of (XI)], while the second compound was characterized as dimethyl tetrafluorophthalate m.p. 76–78°, [dimethyl ester of (XII)]. These compounds were characterized by VPC retention time and comparison to known samples prepared by esterification of 2,3,4,5-tetrafluorobenzoic acid and tetrafluorophthalic acid with diazomethane.

Oxidation of (2,3,4,5-tetrafluorophenyl)copper reagent

Cuprous iodide (0.10 mole, 19.5 g) was added to the organolithium reagent (I) [prepared from 0.10 mole (II)] at −70°. The reaction mixture was stirred at −70° for 21 h and then warmed slowly to room temperature. At this point n-decane (7.5 g) was added as an internal VPC standard. Oxygen was bubbled through the reaction mixture, causing a rise in temperature. Oxidation was continued until the reaction mixture temperature returned to room temperature. The reaction mixture was hydrolyzed with 6 *N* HCl, extracted with diethyl ether, dried and analyzed by VPC. Analysis indicated one major product (69% yield), 2,2′,3,3′,4,4′,5,5′-octafluorobiphenyl (XIII)[3]. The pure product was isolated by aspirating the ether solution to dryness, dissolving the residue in petroleum ether (30–60°) and eluting from a neutral grade alumina column. The solid obtained from the alumina column chromatography was recrystallized from ethanol, m.p. 83–85°, exhibited an infrared curve identical to a known sample[3], measured, *m/e* 298, calcd., 298. (Found: C, 48.15, 47.99; H, 0.74, 0.71. $C_{12}H_2F_8$ calcd.: C, 48.34; H, 0.68%.)

Alternate synthesis of (2,3,5,6-*tetrafluorophenyl*)*trimethylsilane and* 1,4-*bis*(*trimethylsilyl*)*tetrafluorobenzene*[9]

To a precooled (−70°) stirred solution of 1,2,4,5-tetrafluorobenzene (0.5 mole, 75.0 g) in 300 ml of anhydrous diethyl ether was added n-butyllithium (0.625 mole, 406 ml of a hexane solution) during 42 min. Thirty min after addition, Color Test IIA[6] was negative, indicating the absence of n-butyllithium. To this solution was added trimethylchlorosilane (0.70 mole, 76.0 g) over a period of 12 min. Color Test I[15] was positive after 30 min and therefore, the reaction mixture was allowed to stir at −70° for an additional 18 h. The reaction mixture then was warmed to 0°. Color Test I was negative. The precipitate was filtered and the filtrate was fractionated through a spinning band column to give two products. The major product was identified as (2,3,5,6-tetrafluorophenyl)trimethylsilane, 69.7 g (62% yield), b.p. 50°/6 mm, n_D^{27} 1.4420. NMR analysis; ^1H ($CDCl_3$ solvent, TMS standard) 0.40 ppm (t, 6), 6.98 ppm (t of t, 1); $J(CH_3\text{-}F_2)$ 1.5 Hz, $J(H\text{-}F_3)$ 9.4 Hz, $J(H\text{-}F_2)$ 7.4 Hz. ^{19}F ($CDCl_3$ solvent, $CFCl_3$ standard) +128 ppm (m, 1), +139 ppm (m, 1).



The minor product was characterized as 1,4-bis(trimethylsilyl)tetrafluorobenzene, 28.3 g (38% yield), b.p. 90°/3 mm, m.p. 58–59°.

NMR analysis data identical to that described for compound (VII) above.

ACKNOWLEDGEMENTS

The authors wish to thank R. J. De Pasquale of the Air Force Materials Laboratory for his interpretation of the NMR spectra and J. R. Boal of Mellon Institute for performing the mass spectral analysis.

REFERENCES

1 R. J. Harper, E. J. Soloski and C. Tamborski, *J. Org. Chem.*, 29 (1964) 2385.
2 S. C. Cohen and A. G. Massey, *Tetrahedron Lett.*, (1966) 4393.
3 S. C. Cohen, D. E. Fenton, A. J. Tomlinson and A. G. Massey, *J. Organometal. Chem.*, 6 (1966) 301.

4 G. H. Brooke, B. S. Furniss, W. K. R. Musgrave and Md. A. Quasem, *Tetrahedron Lett.*, (1965) 2991.
5 I. Haiduc and H. Gilman, *J. Organometal. Chem.*, 11 (1968) 55.
6 H. Gilman and J. Swiss, *J. Amer. Chem. Soc.*, 62 (1940) 1847.
7 J. Burdon and W. B. Hollyhead, *J. Chem. Soc.*, (1965) 6326.
8 R. B. King and M. B. Bisnette, *J. Organometal. Chem.*, 2 (1964) 38.
9 F. W. G. Fearon and H. Gilman, *J. Organometal. Chem.*, 10 (1967) 535.
10 V. Bažant, V. Chvalovský and J. Rathouský, *Organosilicon Compounds*, Prague, Czechoslovakia, 1965, p. 120.
11 C. Tamborski and Edward J. Soloski, *J. Organometal. Chem.*, 10 (1967) 385.
12 R. J. De Pasquale and C. Tamborski, *J. Organometal. Chem.*, 13 (1968) 273.
13 E. Nield, R. Stephens and J. C. Tatlow, *J. Chem. Soc.*, (1959) 166.
14 W. J. Pummer and L. A. Wall, *J. Res. Nat. Bur. Stand. A*, 63 (1959) 167.
15 H. Gilman and F. Schulze, *J. Amer. Chem. Soc.*, 47 (1925) 2002.