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THE SYNTHESIS AND REACTIONS OF *ortho* BROMOPHENYLLITHIUM *

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Summary

Experimental conditions have now been developed whereby *o*-bromophenyllithium(II) may be prepared in excellent yields and used as an organometallic intermediate for the synthesis of a variety of *ortho* bromo substituted phenyl compounds (o-BrC_6H_4X). The thermal stability, decomposition products and reactions of II were studied. Reactions between II and a variety of substrates, e.g., CO_2, dimethylformamide, fluorinated esters, hexafluorobenzene, and organosilicon chlorides were examined.

Introduction

The synthesis of *ortho* halophenyllithium(I) compounds, through the metal—halogen exchange reaction in diethyl ether solvent, has been previously reported by Gilman and Gorich [1]. Reduced reaction temperatures had to be used since above their thermal stability, lithium halide elimination led to the formation of benzyne [2] as the initial decomposition product. Carbonation of I yielded *o*-halobenzoic acid and excellent yields of *o*-fluorobenzoic acid (83%) and *o*-chlorobenzoic acid (93%) were produced at —60° C and —90° C respectively. The *o*-bromophenyllithium however had to be prepared at —100° C and carbonation at this temperature produced the *o*-bromobenzoic acid in only 23% yield. The thermal stability of I was indicated as F > Cl >> Br. Nefedov and Dyachenko [3] subsequently studied the stability of I in various solvents and concluded that the *o*-bromophenyllithium prepared in hexane/tetrahydrofuran (THF) mixture had a substantial increase of 20—30° C in thermal stabil-

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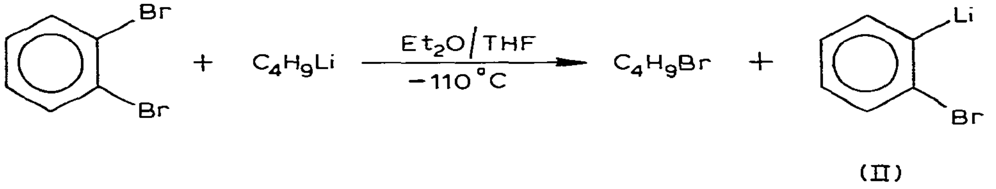
ity (as determined by differential thermal analysis) as compared to diethyl ether as a solvent.

Use of *o*-bromophenyllithium as a synthesis intermediate has not been reported due perhaps to the low temperatures required and poor yields of derivatized products [1]. We have found experimental conditions which provide moderate to excellent yields of derivatized products and are now reporting our results.

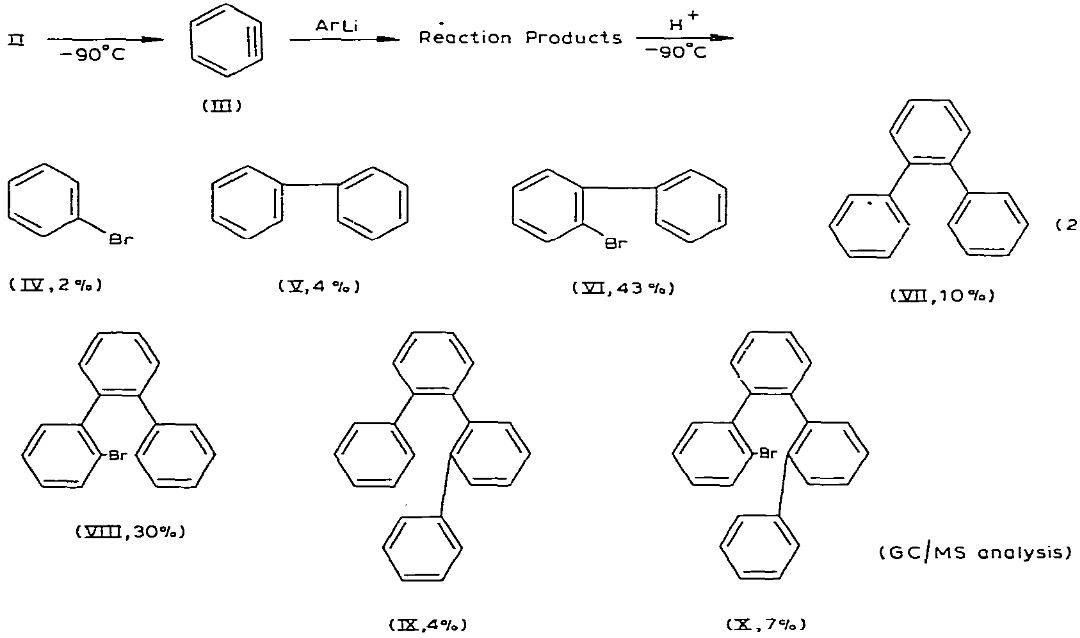
Discussion

o-Bromophenyllithium can be prepared in over 95% yield through the metal—halogen exchange reaction carried out in a mixture of diethyl ether and THF (1 : 1) at —110°C



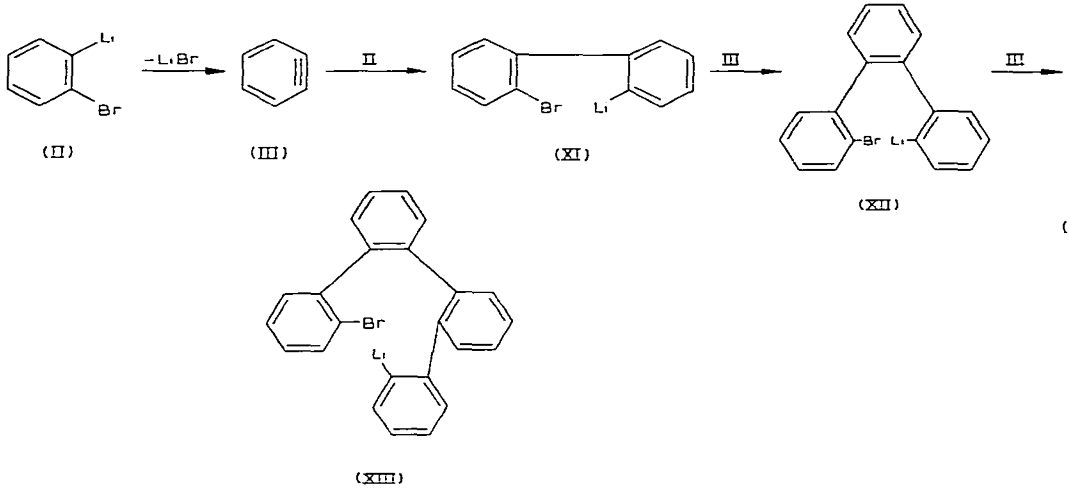
(1)

At —110°C II is stable for at least two hours. Hydrolysis of the reaction mixture at —110°C with dil. HCl produced C_6H_5Br (95%) as the major component with only trace quantities of decomposition products. If aliquot samples are withdrawn from the reaction mixture with a pipette, even though it is done rapidly, gas chromatography (GC) analysis of the removed samples indicate considerable decomposition products of II. Compound II is very temperature sensitive and when allowed to warm up to —90°C decomposes to a series of products. Within 30 min at —90°C, hydrolysis at —90°C and GC analysis of the products indicated the following:



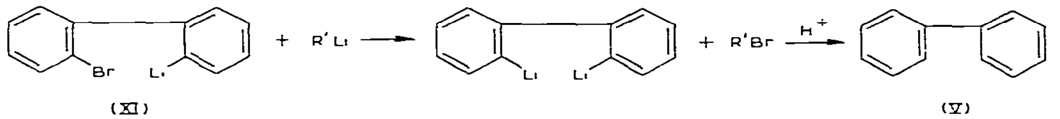
(2)

Within this short period of time most of II decomposed (~98%), as evidenced by the low percent of IV (the hydrolysis product of II) which was found. The products formed (see Experimental section) by the decomposition of II suggest the following mechanism for its decomposition and reaction with various intermediates at −90° C. This mechanism in part has been suggested by previous investigators [1,4,5].



(3)

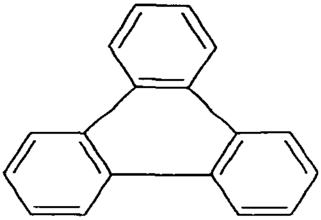
Hydrolysis of the reaction mixture (equation 2) yielded the products VI, VIII and X. It is not clear at this time how V, VII and IX are formed. Since numerous organolithium intermediates are present in the reaction mixture, some metal—halogen interchange may take place, e.g.



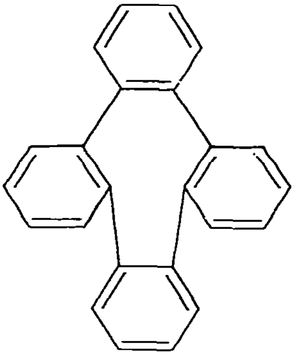
(4)

In the same manner XII and XIII could yield VII and IX. More detailed work should be done to clarify this proposal.

In previous reported [1,4,5] studies of II some other decomposition products have been noted. This is probably due to the different reaction conditions which have been used, e.g., solvent and temperature. This is shown more clearly by allowing the decomposition of II to take place in two stages. First, II was allowed to warm up to −90° C (30 min). Analysis of products (GC/MS) produced the results as described in equation 2. If however, at −90° C the reaction is not terminated through hydrolysis but allowed to warm up to room temperature and then hydrolyzed, two additional sets of reaction products were identified. The multiplicity of the reaction products (at least 17 components) made isolation of individual components impractical for complete and unequivocal characterization. A GC/MS analysis on each component and a GC/IR analysis on the major components was performed and the results of the mass spectral and IR data are consistent with the suggested structures. At some higher temperature, between −90° C and room temperature, one set of products XV and XVI (identified by GC/MS analyses) suggest an intramolecular cyclization of the bromolithium intermediates XII and XIII may have taken place to yield the following cyclized products:



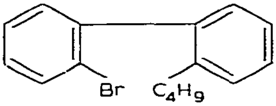
(XV)



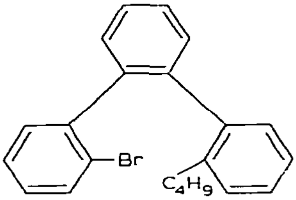
(XVI)

If sufficient quantity of XI were present in the reaction mixture, biphenylene (XIV), the first member of this cyclic series, could have been formed. Since none was detectable by GC/MS analyses of the reaction mixture, our assumption is that once XI was formed it preferred to react further with III (see equation 3) to form XII.

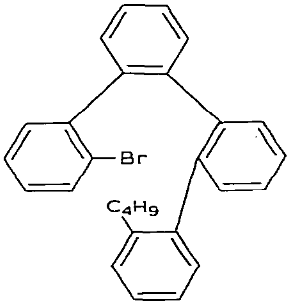
The second set of products found were those resulting through the reaction of the bromo-lithio intermediates XI, XII and XIII with the C_4H_9Br from the halogen-exchange reaction observed in equation 1 to yield the bromobutyl aromatic products:



(XVII)



(XVIII)



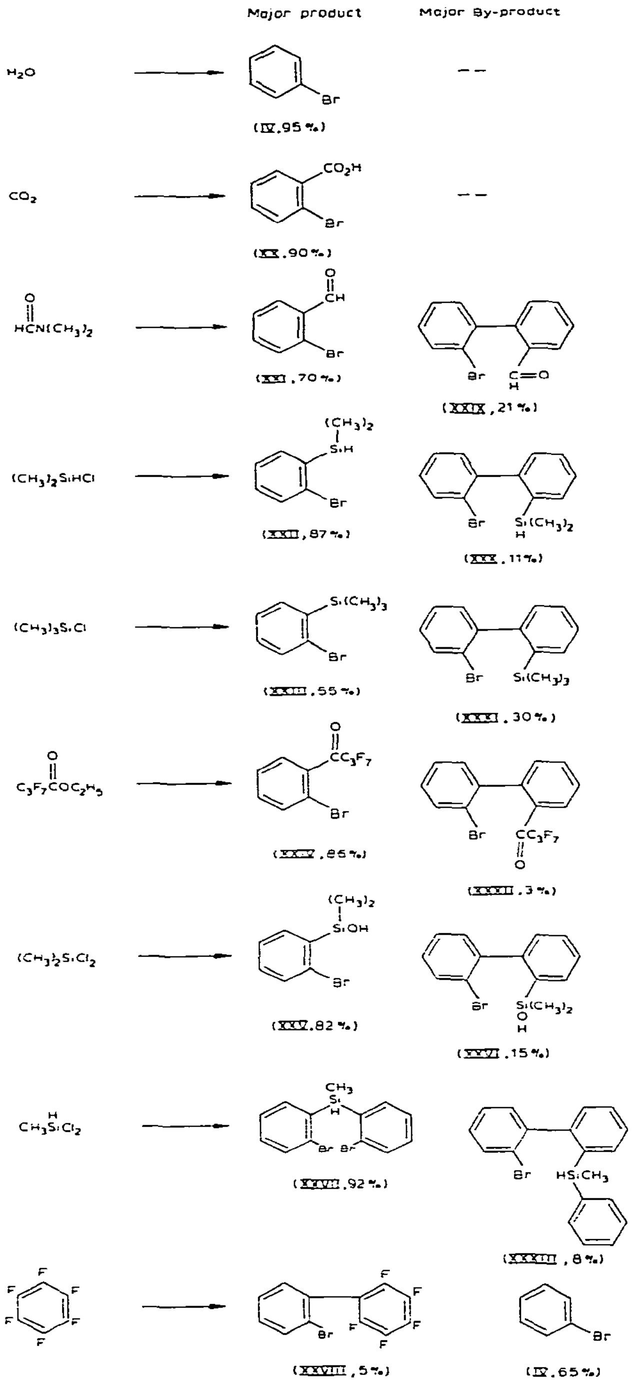
(XIX)

The third set of products found may have been formed as a result of a lithium—bromine exchange between XVII, XVIII and XIX and an organolithium species, similar to that described in equation 4 above, to yield organolithium intermediates which on protonation would yield the non-brominated compounds of XVII, XVIII and XIX.

Even though II is temperature sensitive it can be used at —110° C as an intermediate for the synthesis of *o*-substituted bromophenyl compounds. At this low temperature solubility of various substrates and their reactivity towards organolithium compounds are important considerations since they govern the rate of reaction with II. Reactions between II and various substrates which have been carried out at —110°C are summarized in Scheme 1. With reactive substrates, e.g., H_2O, CO_2, $(CH_3)_2SiHCl$ and $C_3F_7C(O)OC_2H_5$ high yields or products are obtained. By slow addition of the substrates to II, the

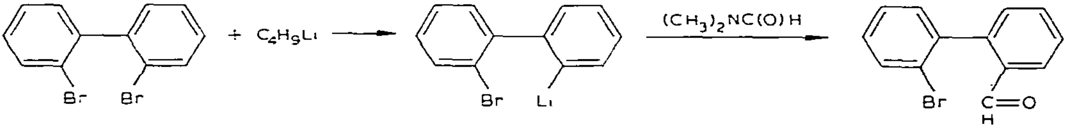
Scheme 1

Reaction of II with various substrates



temperature rise of the reaction mixture was only 3—5 degrees. This slight exotherm was sufficient however to cause some of II to decompose as evidenced by the by-product formation containing the substrate. With less reactive substrates, e.g. $(CH_3)_2NC(O)H$ or $(CH_3)_3SiCl$, requiring longer reaction time, the yields of products were decreased while the by-products were increased. With $(CH_3)_3SiCl$, substitution of a $(CH_3)_3Si$—group *ortho* to the Br (XXIII) may be sterically unfavored since the smaller $(CH_3)_2SiH$- group offered no problem and a higher yield of product (XXII) was obtained. Steric hinderance may also account for the inability to substitute both Cl's of $(CH_3)_2SiCl_2$ by the *ortho*bromophenyl group. Only one Cl was substituted and the intermediate monochloro product on hydrolysis of the reaction mixture led to the silanol XXV and the by-product XXVI. The less sterically hindered CH_3SiHCl_2 provided the disubstituted product XXVII in excellent yield. With less reactive substrates, e.g. C_6F_6, which undergo nucleophilic substitutions [7,8] readily at higher temperatures, at the low reaction temperatures used (—110° C) produced only a 5% yield of product XXVIII. The rate of reaction must be extremely slow since ~65% of C_6H_5Br (the hydrolysis product of II) was recovered along with decomposition products of II.

As indicated in equation 2, the major decomposition product of II is 2-bromo-2'-lithiobiphenyl (XI) from which 2-bromobiphenyl (VI) results on hydrolysis of the reaction mixture. It is therefore reasonable to expect that the major by-product from the various reactions of II would be the derivative of XI (See Scheme 1). In order to clarify the 2,2'substitution of the biphenyl by-products, the 2-bromo-2'-lithiobiphenyl (XI) [1] was prepared unequivocally from the reaction between 2,2'-dibromobiphenyl and one equivalent of n-C_4H_9Li. Derivatization of XI with $(CH_3)_2NC(O)H$ produced the aldehyde derivative XXIX identical to the by-product XXIX obtained from II and $(CH_3)_2NC(O)H$. Although the remaining by-products XXX, XXXI, XXXII and XXVI were not prepared by the above method (equation 5) to confirm the 2,2'-disubstituted orientation it is reasonable to expect that the suggested structures are correct. The synthesis and reactions of XI as well as 2,2'-dilithiobiphenyl [9] will be reported at a later date.



(XI)

(XXIX)

(5)

Experimental

General comments

All reactions were carried out in flame dried glassware under an atmosphere of purified dry nitrogen. Tetrahydrofuran was dried by refluxing over metallic sodium followed by distillation from lithium aluminium hydride. Anhydrous diethyl ether (Mallinckrodt) was used without further purification. The yields reported are generally isolated yields except for those performed on small quantities where such yields were determined by gas chromatography (GC) using internal standards. GC analyses were performed on an F&M Model 700 instrument using 6 ft, 10% SE-30 on Chromosorb W column. The GC/MS analyses were performed on a Hewlett Packard 5982 GC/MS with a 5933 data system. All new principal products were characterized by elemental, mass spectral and infrared analysis. Most of the by-products of the reactions were charaterized only by GC/MS analysis, however, those produced in sufficient quantities were isolated by GC and analyzed by elemental, mass spectral and infrared analysis. In addition some of the major by-products were synthesized by an alternate method and a comparison of their infrared and mass spectral analysis were identical. Known compounds were characterized by comparing their physical properties, e.g., melting point and infrared spectra with literature data.

Preparation of o-bromophenyllithium(II). A 250 ml three-necked flask fitted with a low temperature reading thermometer, stirrer and an addition funnel was charged with anhydrous THF/Et_2O (140 ml, 1 : 1 volume ratio) and *o*-dibromobenzene (1.00 g, 4.24 mmol). The contents were cooled to —110° C (EtOH/liq. N_2 bath) and n-C_4H_9Li (2.02 ml of 2.1 *M* hexane sol., 4.24 mmol) was added over a period of 2 min. The rate of addition was controlled so as to keep the reaction temperature at —110° C. After stirring the reaction for 30 min, a cooled (—110° C) solution of conc. HCl (2 ml) and ethanol (10 ml) was added in order to hydrolyze the reaction mixture. The mixture was allowed to warm to room temperature, phase separated and the organic layer analyzed by GC. Analysis indicated C_6H_5Br in 95% yield.

Stability of II (—110 to —90° C). *o*-Bromophenyllithium prepared as described above was allowed to warm up from —110° C to —90° C over 30 min. After 30 additional min at —90° C, the reaction mixture was hydrolyzed with a cooled (—90° C) solution of conc. HCl (5 ml) and ethanol (15 ml) and then allowed to warm to room temperature. The diethyl ether layer was analyzed by GC. The analysis indicated the following compounds expressed in GC area percent: IV (2%), V (4%), VI (43%), VII (10%), VIII (30%), IX (4%) and X (7%) (see equation 2). The products were characterized by GC/MS analysis, and GC/IR analysis.

Stability of II (—110° C to room temperature). *o*-Bromophenyllithium prepared as described above was allowed to warm up to —90° C over 20 min and kept at this temperature for 30 min. The reaction mixture was then allowed to warm up to room temperature over a period of 120 min. The reaction was then hydrolyzed with 2 *M* HCl solution (200 ml) and phase separated. GC analysis indicated at least 17 components. Each component was analyzed by GC/MS.

Reaction of II with CO_2. To 29.7 mmol of II, CO_2 was bubbled through for a period of 30 min. The reaction mixture was then hydrolyzed with 2 *M* HCl (400 ml) and analyzed by GC. *o*-Bromobenzoic acid (XX) was the major product, (90 GC area %) with three other additional non acidic components (ca. 10 GC area %) Extraction with dil. NaOH solution, separation of the aqueous layer and acidification of the aqueous layer, yielded 5.0 g, m.p. 148—149° C (lit. 150°C) in 84% isolated yield. The IR spectrum was identical to that of *o*-bromobenzoic acid.

Reaction of II with $(CH_3)_2NC(O)H$. To 42.4 mmol of II at —110° C was added freshly distilled $(CH_3)_2NC(O)H$ (4.64 g, 63.6 mmol) over 20 min. After an additional 120 min the reaction mixture was hydrolyzed with a cooled solution (—110° C) of conc. HCl (5.0 ml) dissolved in ethanol (15 ml). The reaction mixture was then poured into 2 *M* HCl (400 ml), phase separated and dried over $MgSO_4$. GC analysis indicated two principal products, 2-bromobenzaldehyde (XXI) (70 area %) and 2-bromo-2′-formylbiphenyl (XXIX) (21 area %). Distillation of the reaction mixture yielded XXI (isolated yield 38%), b.p. 43—44°C/0.1 mm; the infrared spectrum was identical with literature data (C=O at 1698 cm^{-1}), Mass Spec. (*m/e*) calc'd, 184, 186, found 184 (^{79}Br), 186 (^{81}Br), and XXIX (isolated yield 18%), b.p. 132—134° C/0.06 mm; infrared data C=O at 1698 cm^{-1} and 1690 cm^{-1}; Mass Spec. (*m/e*) calc. 260, 262, found 260 (^{79}Br), 262 (^{81}Br); combustion analysis, calc'd for $C_{13}H_9BrO$: C, 59.8; H, 3.47; Br, 30.6 found: C, 59.6; H, 3.74; Br, 30.6%.

Reaction of II with $(CH_3)_2SiHCl$. To 84.7 mmol of II was added a precooled (—110° C) diethyl ether (60 ml) solution of $(CH_3)_2SiHCl$ (10.0 g, 105 mmol) keeping the reaction temperature at —110° C. After 90 min the reaction mixture was hydrolyzed with a precooled (—110° C) solution of conc. HCl (5 ml) in ethanol (15 ml). The reaction was then poured into 2 *M* HCl (400 ml), phase separated and dried over $MgSO_4$. GC analysis indicated two principal products, 2-bromodimethylsilylbenzene (XXII) (87 area %) and 2-bromo-2′-dimethylsilylbiphenyl (XXX) (11 area %). Distillation of the mixture yielded XXII, b.p. 89° C/8 mm, yield 73% (isolated); Mass Spec. (*m/e*) calc'd 214, 216; found 214 (^{79}Br), 216 (^{81}Br); infrared data Si—H at 2132 cm^{-1}; combustion analysis, calc'd for $C_8H_{11}SiBr$: C, 44.65; H, 5.12; Br, 37.21; Si, 13.02; found C, 44.41; H, 5.46; Br, 37.29; Si, 12.77%, and the by-product XXX (isolated yield 11%) b.p. 89—91° C/0.005 mm; Mass Spec. (*m/e*) calc'd 290, 292; found 290 (^{79}Br), 292 (^{81}Br); infrared data Si—H at 2122 cm^{-1}; combustion analysis, calc'd for $C_{14}H_{15}SiBr$: C, 57.73; H, 5.16; Br, 27.49; Si, 9.62; found C, 57.94; H, 5.46; Br, 27.57; Si, 9.53%.

Reaction of II with $(CH_3)_3SiCl$. To 42.4 mmol of II was added a precooled (—110° C) diethyl ether (60 ml) solution of $(CH_3)_3SiCl$ (7.4 g, 68.2 mmol) keeping the reaction temperature at —110° C. Periodic removal of aliquot samples and GC analysis indicated a slow rate of product (XXIII) formation. After 8.5 h the product was maximized. The reaction mixture was hydrolyzed with a precooled (—110° C) solution of conc. HCl (5 ml) in ethanol (15 ml). The reaction was then poured into 2 *M* HCl (400 ml), phase separated and dried over $MgSO_4$. GC analysis indicated two principal products, XXIII (55 area %), XXXI (30 area %) and four minor products (15 area %) due to thermal decomposition of II. Distillation of the mixture yielded 2-bromotrimethylsilylbenzene XXIII, b.p. 38° C/0.005 mm, yield 39% (isolated); Mass Spec. (*m/e*) calc'd 228, 230; found 228 (^{79}Br), 230 (^{80}Br); combustion analysis, calc'd for $C_9H_{13}SiBr$: C, 47.16; H, 5.68; Br, 34.93; Si, 12.23; found C, 47.02; H, 5.93; Br, 34.58; Si, 12.36%, and 2-bromo-2′-trimethylsilylbiphenyl (XXXI), b.p. 91° C/0.002 mm, yield 28% (isolated), Mass Spec. (*m/e*) calc'd 304, 306; found 304 (^{79}Br), 306 (^{81}Br); combustion analysis, calc'd for $C_{15}H_{17}SiBr$; C, 59.02; H, 5.57; Br, 26.23; Si, 9.18; found C, 59.06; H, 5.18; Br, 26.44; Si, 8.92%. The remaining four minor products were analyzed by GC/MS only and are believed to be VI, VIII, X and a trimethylsilylderivative of VIII.

Reaction of II with $C_3F_7C(O)OC_2H_5$. To 42.4 mmol of II was added precooled (—78° C) $C_3F_7C(O)OC_2H_5$ (11.3 g; 46.7 mmol) within 2 min, keeping the reaction temperature at —110° C. After 50 min the reaction mixture was hydrolyzed with a precooled (—110°C) solution of conc. HCl (5 ml) in ethanol (15 min). The reaction was then poured into 2 *M* HCl (400 ml), phase separated and dried over $MgSO_4$. GC analysis indicated one major product, 2-bromoheptafluorobutyrylbenzene (XXIV) (86 area %) and minor products as 2-bromo-2'-heptafluorobutyrylbenzene (XXXII) (3 area %) and bromobenzene (VI) (9 area %). Distillation of the mixture yielded XXIV, b.p. 107° C/20 mm; yield 76% (isolated); Mass Spec. (*m/e*) calc'd 352, 354; found 352 (^{79}Br), 354 (^{81}Br); infrared data (C=O at 1735 cm^{-1}); combustion analysis, calc'd for $C_{10}H_4F_7BrO$; C, 34.02; H, 1.14; Br, 22.64; found C, 34.02; H, 1.01; Br, 22.96%. The second minor component XXXII was isolated from the residue by preparative GC. Mass Spec. (*m/e*) calc'd 428, 430; found 428 (^{79}Br) 430 (^{81}Br); infrared data (C=O at 1724 cm^{-1}).

Reaction of II with $(CH_3)_2SiCl_2$ (2 : 1 mole ratio). To 84.8 mmol of II was added $(CH_3)_2SiCl_2$ (4.97 g, 38.6 mmol) over 20 min while keeping the temperature at —110° C. After 2 h the reaction mixture was hydrolyzed with a precooled (—110° C) solution of conc. HCl (10 ml) in ethanol (25 ml). The mixture was then poured into 2 *M* HCl (400 ml), phase separated and dried over $MgSO_4$. GC analysis indicated the major product 2-bromodimethylsilolbenzene (XXV) (82 area %) and a minor product 2-bromo-2'-dimethylsilolbiphenyl (XXVI) (15 area %). Distillation of the mixture yielded XXV, b.p. 80° C/0.25 mm; yield 70% (isolated); Mass Spec. (*m/e*) calc'd 230, 232; found 230 (^{79}Br), 232 (^{81}Br); infrared data (SiOH at 3300 cm^{-1}, broad); combustion analysis, calc'd for $C_8H_{11}SiBrO$: C, 41.56; H, 4.80; Br, 34.57; Si, 12.15; found C, 41.73; H, 4.63; Br, 34.39; Si, 11.84%. The second minor component XXVI was isolated from the residue by preparative GC. Mass Spec. (*m/e*) calc'd 306, 308; found 306 (^{79}Br), 308 (^{81}Br); infrared data (SiOH at 3312 cm^{-1}, broad).

Reaction of II with CH_3SiHCl_2 (2 : 1 mole ratio). This reaction was carried out by a similar procedure to the one described above. GC analysis of the reaction mixture prior to distillation indicated the major product bis(2-bromophenyl)methylsilane (XXVII) (92 area %) and a minor product 2-bromo-2'-(methylphenylsilyl)biphenyl (XXXIII) (8 area %). Distillation of the mixture yielded XXVII, 158—159° C/0.005 mm; yield 79% (isolated); Mass Spec. (*m/e*) calc'd 354, 356, 358; found 354 (2 ^{79}Br), 356 (^{79}Br + ^{81}Br), 358 (2 ^{81}Br); infrared data (SiH at 2152 cm^{-1}); combustion analysis; calc'd for $C_{13}H_{12}SiBr$: C, 43.84; H, 3.40; Br, 44.88; Si, 7.89; found, C, 44.40; H, 3.44; Br, 44.76; Si, 7.84%. The second minor component XXXIII was isolated from the residue by preparative GC. Mass Spec. (*m/e*) calc'd 430, 432, 434; found 430 (2 ^{79}Br), 432 (^{79}Br + ^{81}Br), 434 (2 ^{81}Br); infrared data (SiH at 2143 cm^{-1}).

Reaction of II with C_6F_6. To 63.6 mmol of II was added a precooled (—110° C) diethyl ether (50 ml) solution of C_6F_6 (35.5 g, 191 mmol) keeping the reaction temperature at —110° C. Periodically aliquot samples were removed and analyzed by GC. Since the reaction was extremely slow (as evidence by C_6H_5Br presence) the reaction was hydrolyzed after 2 h with a precooled (—110° C) solution of conc. HCl (5 ml) in ethanol. The mixture was then poured into 2 *M* HCl (400 ml), phase separated and dried over $MgSO_4$. GC analysis indicated at least seven products. The major product (65 area %)

was C_6H_5Br (IV) from the hydrolysis of unreacted II. The remaining six products were tentatively identified by GC/MS as $C_6H_5C_6F_5$ (3.2 area %), $C_6H_4BrC_6F_5$ (XXVIII) (5.2 area %), $C_6H_4BrC_6H_5$ (19.1 area %), $C_6H_5C_6H_4C_6H_5$ (0.5 area %) $C_6H_4BrC_6H_4C_6F_5$ (0.8 area %), $C_6H_4BrC_6H_4C_6H_5$ (3.8 area %). By preparative GC product XXVIII was isolated. Mass Spec. (*m/e*) calc'd 322, 324, found 322 (^{79}Br), 324 (^{81}Br), infrared data (ArH at 3070 cm^{-1}, ArC—F, 1500—1550 cm^{-1}), combustion analysis, calc'd for $C_{12}H_4F_5Br$: C, 44.61; H, 1.25, Br, 24.74; found C, 44.97; H, 1.10; Br, 24.44%.

References

1 H. Gilman and R.D. Gorsich, J. Amer. Chem. Soc., 78 (1956) 2217.
2 G. Wittig, Naturwiss, 30 (1942) 969.
3 O.M. Nefedov and A.I. D'yachenko, Dokl. Akad. Nauk SSSR, 198 (1971) 593.
4 H. Heaney, F.G. Mann and J.T. Millar, J. Chem. Soc., (1957) 3930.
5 O.M. Nefedov and A.I. D'yachenko, Izv. Akad. Nauk SSSR, Ser. Khim., (1977) 1378.
6 R. Huisgen in H. Zeiss (Ed.), Organometallic Chemistry, Reinhold Publishing Company, New York, 1960, Chapter 2.
7 R.D. Chambers, Fluorine in Organic Chemistry, John Wiley and Sons, New York, 1973.
8 M. Hudlicky, Chemistry of Organic Fluorine Compounds, Ellis Horwood Limited, London, 1976.
9 H. Gilman and R. Gorsich, J. Amer. Chem. Soc., 77 (1955) 6380.