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APPROACHES TO THE PREPARATION OF 2,2'-DIHALOGENOBIPHENYLS IN WHICH THE TWO HALOGENS ARE DIFFERENT AND THE SYNTHESIS OF SUBSTITUTED TRIPHENYLENES FROM 2-CHLORO-2'-LITHIOBIPHENYL

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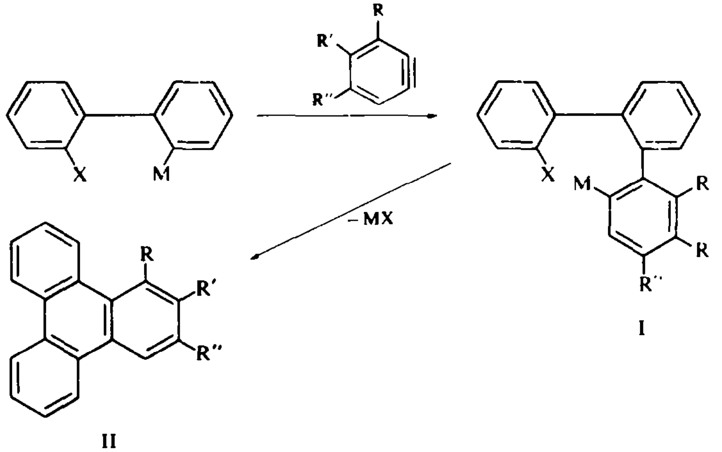
Abstract—Various possible routes to the synthesis of 2,2'-dihalogenobiphenyls have been investigated. The pyrolysis of biphenylene iodonium chloride affords 2-chloro-2'-iodobiphenyl in useful yield. 2-Chloro-2'-lithiobiphenyl has been used in the synthesis of 4-trifluoromethyl-; 3,4-dimethyl-; 3,5-dimethyl-; and 3,4-dimethoxytriphenylene.

CERTAIN substituted triphenylenes may be prepared from 4,4'-dimethyl-2-fluoro-2'-biphenylyl-Grignard, and -lithium-reagents by reaction with suitably substituted benzyne intermediates.[2]

We now report various approaches to the preparation of 2,2'-dihalogenobiphenyls and the use of one of these in the extension of our method of synthesis of substituted triphenylenes.



Two basic approaches to the synthesis of 2,2'-dihalogenobiphenyls were considered. The first method consists of the stepwise introduction of the two halogens, using a suitable 2,2'-disubstituted biphenyl.

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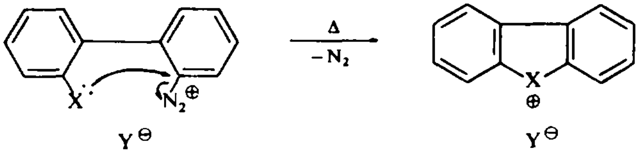
Clearly a choice is available as to which halogen is introduced in the first stage, and two starting materials, 2-amino-2'-nitrobiphenyl, and 2-acetylamino-2'-aminobiphenyl suggest themselves. However, although 2-iodo-2'-nitrobiphenyl,[3] and 2-bromo-2'-nitrobiphenyl can be obtained in reasonable yield from 2-amino-2'-nitrobiphenyl, 2-fluoro-2'nitrobiphenyl cannot. Almost quantitative yields of 2-nitro-2'-biphenyldiazonium-fluoroborate, and -hexafluorophosphate were obtained using recently described procedures,[4,5] but a variety of decomposition methods failed to raise the yield of 2-fluoro-2'-nitrobiphenyl above 5%. The reduction of 2,2'-dinitrobiphenyl to 2,2'-diaminobiphenyl was achieved in excellent yield by using iron powder (reduced by hydrogen) in ethanolic solution, and a catalytic quantity of hydrochloric acid. Controlled acetylation of the diamine yields 2-acetylamino-2'-amino-biphenyl.[6,7] Diazotization of this amine in fluoroboric acid or in the presence of ammonium hexafluorophosphate yielded diazonium salts which decomposed on attempted isolation; the decomposition in aqueous suspension only gave low yields of 2-acetylamino-2'-fluorobiphenyl.

The alternative route was no more successful. 2-Amino-2'-iodo-, 2-amino-2'-bromo- and 2-amino-2'-chloro-biphenyl were each converted in almost quantitative yield to the corresponding-diazonium-fluoroborates and -diazonium-hexafluorophosphates (III). All of these diazonium salts were found, not unexpectedly, to lose nitrogen very easily to give cyclic halonium salts IV in high yield. Biphenylenehalonium salts have been prepared on previous occasions from water soluble diazonium salts.[8,9] Our method has several advantages over the previous methods. The quantitative isolation of the diazonium salt and the fact that the cyclization may be effected by warming a suspension of the salt in a dry organic solvent, in which the ionic product also has a very low solubility is advantageous. This allows the cyclization to be achieved in a controlled manner, to yield a clean product which may be recrystallized easily or converted into other salts by simple metathetical reactions. The structures of the biphenylenehalonium salts were proved by conversion to the known iodides and which on thermal decomposition yielded the corresponding known 2-iodo-2'-halobiphenyls.



III IV

Although a large number of reactions of this general type have been reported previously no rationalization in terms of a general mechanism has been suggested. Our results suggest that these cyclization reactions of 2,2'-disubstituted biphenyls can be rationalized in terms of a S_Ni reaction. The preparation of biphenylene iodonium iodide from 2,2'-diaminobiphenyl has been reported on many occasions.[10] The step-wise decomposition of the tetrazonium salt would yield I (X = I) and hence the isolated product. Carbazole is a frequently reported by-product of the tetrazotization of 2,2'-diaminobiphenyl,[11] and its formation may involve displacement of nitrogen in the diazotized diamine III (X = NH_2). Similar results have been obtained in the diazotization of 2-amino-2'-biphenylyl ethers, oxonium salts being the isolated products III (X = OR).[12] In all of these reactions a group bearing a lone pair of electrons is present in an ideal position to attack the C atom bearing a good leaving group.

The second method of preparation of 2,2'-dihalogenobiphenyls (in which the two halogens are different) which was considered was the pyrolysis of suitable 2,2'-biphenylenehalonium halides. Although the pyrolysis of 2,2'-biphenyleneiodonium bromide is known to give 2-bromo-2'-iodobiphenyl, this dihalide was expected to be unsatisfactory for our purposes because of the possibility of the ready formation of di-organometallic reagents. The pyrolysis of 2,2'-biphenylenechloronium-bromide or -iodide yield acceptable 2,2'-dihalogenobiphenyls. The pyrolysis of 2,2'-biphenyleneiodonium chloride was at first discounted since the compound is stated not to yield 2-chloro-2'-iodobiphenyl.[13] However, the ease of preparation of large quantities of 2,2'-biphenylene-iodonium salts from 2-iodobiphenyl,[14] prompted our re-investigation of the pyrolysis of this halonium salt. The pyrolysis product was shown to be 2-chloro-2'-iodobiphenyl by comparison with a sample prepared by the pyrolysis of 2,2'-biphenylenechloronium iodide. The pyrolysis of 2,2'-biphenyleneiodonium-fluoride,-fluoroborate, and -hexafluorophosphate under a variety of conditions was shown to give 2-iodobiphenyl.

We have shown that 2-bromo-2'-iodobiphenyl reacts with magnesium (1 atomic equivalent) in ether but carboxylation yields no acids. The failure of biphenyl-Grignard reagents to give carboxylic acids in ethereal solution has been noted previously.[15] The neutral organic material in the above reaction was shown, by gas chromatography, to consist (in order of increasing retention time), of biphenyl (26·7 %), 2-bromobiphenyl (52·6 %) and 2-bromo-2'-iodobiphenyl (20·1 %). A similar reaction carried out in tetrahydrofuran solution yielded biphenyl (35·2 %), 2-bromobiphenyl (30·2%) and 2-bromo-2'-iodobiphenyl (34·5%). In view of these results we did not investigate the reaction of 2-bromo-2'-iodobiphenyl with n-butyl-lithium.

The reaction between 2-chloro-2'-iodobiphenyl and magnesium was not studied since we expected that the reaction with n-butyl-lithium would afford a synthetically useful 2-halo-2'-lithio-biphenyl, whereas the reaction with magnesium might yield another complex mixture of Grignard reagents together with much unchanged starting material. 2-Chloro-2'-iodobiphenyl was found to react cleanly with n-butyl-lithium in a mixture of ether and pentane and on carboxylation gave 2-carboxy-2'-chlorobiphenyl (45%). The neutral organic material was shown, by gas chromatography, to consist of biphenyl (< 1%), 2-chlorobiphenyl (77%), 2-iodobiphenyl (18%), and 2-chloro-2'-iodobiphenyl (4%). It is interesting to note the presence of 2-iodobiphenyl in this reaction product, since very few examples of halogen-metal interconversion between an aryl chloride and n-butyl-lithium have been reported.[16]

We have used this mixture of organolithium reagents in order to synthesize 1,3-dimethyl-, 2,3-dimethyl-; 2,3-dimethoxy-; and 2-trifluoromethyltriphenylene, using an appropriately substituted aryne, generated *in situ* from substituted *o*-dihalobenzenes and n-butyl-lithium. The yields of the products obtained were, however, low. 3,5-Dimethyl- and 4,5-dimethylbenzyne, which we have used previously,[2] gave 1,3-dimethyl-, and 2,3-dimethyltriphenylene in 21% and 10% yield respectively. 4-trifluoromethylbenzyne was generated from 4-chloro-3-lithiobenzotrifluoride which was prepared by the reaction of n-butyl-lithium with 4-chloro-3-

iodobenzotrifluoride. 2-Trifluoromethyltriphenylene was obtained in this reaction in 11% yield. 3-Bromo-4-iodoveratrole has been reported not to react with magnesium under a variety of conditions.[17] However, we find that 3,4-dimethoxybenzyne is produced in the reaction of 3-bromo-4-iodoveratrole with n-butyl-lithium since, in the presence of 2-chloro-2'-lithiobiphenyl, 2,3-dimethoxytriphenylene was isolated in 10% yield.

The structures assigned to the triphenylenes prepared are based on analytical results, and UV (Table) and PMR spectroscopy (Experimental).

TABLE 1. UV ABSORPTION MAXIMA (mμ) IN ETHANOL, ($\log_{10} \varepsilon$ IN PARENTHESES)

Triphenylene derivative									
1,3-Dimethyl-	256·5 (4·83)	262·5 (4·97)	287·5 (4·12)			324 (2·56)	334 (2·56)	339 (2·48)	348·5 (2·16)
2,3-Dimethyl-	252·5 (5·05)	260·5 (5·26)	276 (4·44)	287 (4·37)	314 (2·93)	321·5 (2·75)	330 (2·76)	336·5 (2·51)	345·5 (2·44)
2,3-Dimethoxy-	258 (4·88)	264 (5·00)	293 (4·14)				335 (3·22)		351 (3·23)
2-Trifluoromethyl	250 (4·74)	258·5 (4·96)	273·5 (4·07)	285 (4·02)	300·5 (3·25)	316 (2·68)	322 (2·55)	330 (2·78)	346 (2·47)

The UV spectra of the compounds prepared show the general trend noted previously.[26, 18] Substituents in a bay position result in a greater bathochromic shift than those in a peninsular position. The presence of peninsular methoxyl groups results in bathochromic shifts of the same order as shown by bay Me groups. This may be ascribed to the participation of the non-bonding electrons in the resonance of the aromatic system.

PMR spectra of the compounds prepared (with the exception of 2-trifluoromethyltriphenylene, for which no satisfactory solvent could be found) confirm the assignment of structures, particularly when the spectra are compared with those obtained in our previous study.[19]

EXPERIMENTAL

The general methods used were as in our previous paper.[2b]

Preparation of 2,2'-diaminobiphenyl. 2,2'-dinitrobiphenyl (100 g) was dissolved in boiling EtOH (800 ml) and water (100 ml), and HCl (10 ml) added. Fe powder (reduced by hydrogen; 150 g) was added in small portions over ½ hr and the violently exothermic reaction controlled by external cooling. The mixture was stirred vigorously and heated under reflux for 4 hr. NaOH (10 g) was added and the hot mixture was filtered through a pad of "Hyflo Super Cel". The solvents were partially removed by evaporation under reduced press and gave 2,2'-diaminobiphenyl (70 g, 92%), m.p. 74–76° (lit. m.p. 79–80°) after recrystallization from aqueous EtOH.

Preparation of biphenylene-2,2'-iodonium hexafluorophosphate. 2-Amino-2'-iodobiphenyl[3] (4 g) in HCl (20 ml) and water (200 ml) was cooled to 0° and diazotized by the addition of $NaNO_2$ (1·5 g) in water (10 ml). Ammonium hexafluorophosphate (15 g) in water (50 ml) was added and after stirring for 15 min the ppt removed by filtration, washed with ether (200 ml) and dried *in vacuo* to give 2-iodobiphenyl-2'-diazonium hexafluorophosphate, (9·0 g, 100%), 91 93° (dec). The diazonium salt was suspended in dry benzene and heated under reflux for 2 hr, N_2 was evolved and filtration of the reaction mixture gave *biphenylene-2,2'-iodonium hexafluorophosphate,* (8·1 g, 97%), m.p. 185–190°. (Found: C, 34·2; H, 2·1;

$C_{12}H_8PF_6I$ requires: C, 34·0; H, 1·9%). Treatment of an aqueous soln of the above iodonium salt with a sat KI aq gave the corresponding iodide as a pale yellow solid, m.p. 220° (dec). The dry solid was heated at ~230° for ½ hr and chromatography of an ether extract gave 2,2'-di-iodobiphenyl, m.p. and mixed m.p. 104–105°, and identical IR spectra.

Preparation of biphenylene-2,2'-iodonium tetrafluoroborate. 2-Amino-2'-iodobiphenyl (5·9 g) in THF (15 ml), fluoroboric acid (40 ml, 40%) and water (10 ml), was diazotized by the dropwise addition of $NaNO_2$ 1·4 g) in water (15 ml) at 5°. After stirring the suspension for 20 min the ppt was collected, washed with aqueous fluoroboric acid (100 ml, 5%), ether: MeOH (95:5, 100 ml), and ether (200 ml), and dried *in vacuo* to give 2-iodobiphenyl-2'-diazonium tetrafluoroborate (7·5 g, 95%), 230° (dec). The diazonium salt was suspended in dry benzene and heated under reflux for 2 hr, N_2 was evolved and filtration of the reaction mixture gave *biphenylene-2,2'-iodonium tetrafluoroborate,* (7 g, 75%), m.p. 239–240° after recrystallization from water. (Found: C, 39·65; H, 2·0; $C_{12}H_8BF_4I$ requires: C, 39·4; H, 2·2%). The corresponding iodonium iodide was obtained as above.

Preparation of cyclic bromonium salts. 2-Amino-2'-bromobiphenyl (3 g) gave 2-bromobiphenyl-2'-diazonium hexafluorophosphate (4 g, 82%), 104–105° (dec), which gave *biphenylene-2,2'-bromonium hexafluorophosphate,* (2·65 g, 70%), 240° (dec). (Found: C, 38·8; H, 2·3. $C_{12}H_8BrF_6P$ requires: C, 39·1; H, 2·15%). The above amine (4·96 g) gave the corresponding diazonium tetrafluoroborate (5 g, 72%), 90° (dec) which afforded biphenylene-2,2'-bromonium tetrafluoroborate (3·35 g, 73%) m.p. 204–205° (lit[20] m.p. 199·5–200°). (Found: C, 45·5; H, 2·4. Calc. for $C_{12}H_8BrBF_4$: C, 45·2; H, 2·5%).

Preparation of cyclic chloronium salts. 2-Amino-2'-chlorobiphenyl (1 g) gave 2-chlorobiphenyl-2'-diazonium hexafluorophosphate (1·8 g, 100%) 202° (dec), which gave *biphenylene-2,2'-chloronium hexafluorophosphate* (1·3 g, 80%) 218–222° (dec). (Found: C, 43·3; H, 2·4. $C_{12}H_8ClF_6P$ requires: C, 43·1; H, 2·65%).

The above amine (1 g) gave 2-chlorobiphenyl-2'-diazonium tetrafluoroborate (1·3 g, 83%) 83–84° (dec) which afforded biphenylene-2,2'-chloronium tetrafluoroborate, (1·0 g, 84%) 182–183° (dec) (lit.[20] m.p. 169–170°). (Found: C, 52·55; H, 2·95; Calc. for $C_{12}H_8BClF_4$: C, 52·35; H, 2·9%).

2-*Chloro-2'-iodobiphenyl*

(a) 2-Amino-2'-chlorobiphenyl (4 g) in HCl (6 ml) and water (50 ml) was diazotized at 0° with $NaNO_2$ aq (1·5 g), and added to KI aq (100 ml, 10%) at 0° with vigorous stirring. After 30 min the mixture was warmed on a steam bath for 20 min and $NaHSO_3$ added until the aqueous layer became clear.

The organic layer was taken into ether and washed with $Na_2S_2O_3$aq, water and dried (Na_2SO_4). The ethereal soln was passed through a short column of alumina (Spence, Grade H) and after evaporation of the solvent gave 2-chloro-2'-iodobiphenyl, (3·1 g, 50%), m.p. 62–63° (lit.[20] m.p. 63–64°) after recrystallization from EtOH, mixed m.p. and IR spectra identical with a sample prepared by pyrolysis of biphenylene-2,2'-chloronium iodide.

(b) An aqueous soln of NaCl was added to biphenylene-2,2'-iodonium bisulphate (prepared from 2-iodobiphenyl[14]) (28 g) in hot formic acid and gave biphenylene-2,2'-iodonium chloride (26 g, 82·5%). The dry salt (26 g) was heated at 250° for 3 hr, extracted with ether, the extract washed with $Na_2S_2O_3$aq, water, dried, (Na_2SO_4) and the solvent evaporated. The residue after recrystallization from EtOH gave 2-chloro-2'-iodobiphenyl, m.p. 61–62°, identical by mixed m.p., IR and GC comparison with material prepared by method (a).

Interaction of 2-*bromo-2'-iodobiphenyl with magnesium*

(a) 2-Bromo-2'-iodobiphenyl (3·56 g) in ether (50 ml) was added dropwise to Mg (0·27 g, 1·1 At. Equiv.) and ether (10 ml). After the initial reaction subsided benzene (25 ml) was added and the mixture was refluxed for ½ hr, cooled and added to solid CO_2. No acidic material was obtained. The neutral oil was analysed by GC and was shown to contain biphenyl (26·7%), 2-bromobiphenyl (52·6%), and 2-bromo-2'-2-bromobiphenyl (52·6%), and 2-bromo-2'-iodobiphenyl (20·1%).

(b) A similar reaction in THF again resulted in the production of only neutral products. Analysis by GC showed the presence of biphenyl (40·2%), 2-bromobiphenyl (32·0%), and 2-bromo-2'-iodobiphenyl (27·7%).

Interaction of 2-*chloro-2'-iodobiphenyl with n-butyl-lithium in ether*

n-BuLi (5 ml, 0·1M in hexane) was added to 2-chloro-2'-iodobiphenyl (3 g; 0·1M) in ether (60 ml). The mixture was refluxed for 2 hr, cooled, and added to solid CO_2. 4N HCl (100 ml) was added and the organic layer separated and extracted with $KHCO_3$aq. The extract, when acidified, gave 2-carboxy-2'-chlorobiphenyl (1·05 g, 45%), m.p. and mixed m.p. 136°[21] (lit.[22] m.p. 139–140°), IR spectra identical.

The neutral organic layer was analysed by GC and shown to contain biphenyl (< 1·0%), 2-chlorobiphenyl (77%), iodobiphenyl (18%), and 2-chloro-2'-iodobiphenyl (3·4%).

Synthesis of substituted triphenylenes

2-*Trifluoromethyltriphenylene*. 2-Chloro-2'-iodobiphenyl (3·15 g, 0·1M), in ether (10 ml), was added dropwise to a soln of n-BuLi (16 ml, 1·5M soln in hexane) at ambient temp. The mixture was stirred for 2 hr and 4-chloro-3-iodobenzotrifluoride (3·0 g, 0·1M) in ether (10 ml) added dropwise over ½ hr. The mixture was refluxed for 2 hr and cold 2N HCl (100 ml) added. The organic layer was dried (Na_2SO_4), evaporated, and placed on alumina in ether.

Elution with chloroform gave 2-*trifluoromethyltriphenylene*, (300 mg, 11%), m.p. 153–154° after recrystallization from trichloroethylene. (Found: C, 76·8; H, 3·75; F, 19·15; $C_{19}H_{11}F_3$ requires: C, 77·0; H, 3·70; F, 19·3%).

1,3-*Dimethyltriphenylene*. 2-Chloro-2'-iodobiphenyl (3·15 g), n-BuLi (16 ml, 1·5 M soln), and 3,5-dimethyl-2-fluorobromobenzene gave an oil from which a picrate (1·0 g, 21·5%) was obtained. The picrate on alumina gave 1,3-*dimethyltriphenylene*, m.p. 67°, after sublimation (45°/0·05 mm); τ* 1·52 (m, 4 bay protons), τ 1·8 (s, broad; proton at position 4), τ 2·52 (m, 4 peninsular protons), τ 2·78 (s, broad; proton at position 2), τ 7·0 (s, Me position 1) and τ 7·5 (s, Me position 3). (Found: C, 93·55; H, 6·4. $C_{20}H_{16}$ requires: C, 93·75; H, 6·25%).

2,3-*Dimethyltriphenylene*, as above using 4,5-dimethyl-2-fluorobromobenzene gave 2,3-dimethyltriphenylene, m.p. 148–149° (lit. m.p. 156–157°); τ 1·55 (m, 4 bay protons), τ 1·8 (s, broad, protons at positions 1 and 4), τ 2·5 (m. 4 peninsular protons), τ 7·55 (s, Me protons at positions 2 and 3). (Found: C, 93·61; H, 6·1; Calc. for $C_{20}H_{16}$: C, 93·75; H, 6·25%).

2,3-*Dimethoxytriphenylene*, as above using 4-bromo-5-iodoveratrole gave 2,3-*dimethoxytriphenylene*, m.p. 164–165°, after recrystallization from AcOH and sublimation (149° at 0·05 mm); τ 1·62 (m, 4 bay protons), τ 2·22 (s, protons at positions 1 and 4), τ 2·25 (m, 4 peninsular protons), τ 6·02 (s, OMe protons at positions 2 and 3). (Found: C, 83·2; H, 5·75; $C_{20}H_{16}O_2$ requires: C, 83·3; H, 5·55%).

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* m = multiplet; s = singlet; etc.

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