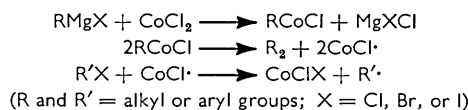**1302.** *The Production of Free Radicals in the Reaction of Grignard Reagents with Organic Halides in the Presence of Cobaltous Chloride*

By D. I. DAVIES, D. H. HEY, and MARCELLO TIECCO

The reaction between a Grignard reagent and an organic halide in the presence of cobaltous chloride results in the production of free radicals, chiefly from the halide. These radicals have been detected by reaction with an aromatic solvent used as a diluent. With monosubstituted aromatic solvents and with bromobenzene as the halide, the isomer ratio of the biphenyls produced has been measured. The percentage of *ortho* substitution is found to decrease by approximately ten, the percentage of *meta* substitution being similarly increased, compared with the isomer distribution found when benzoyl peroxide is the source of the phenyl radical.
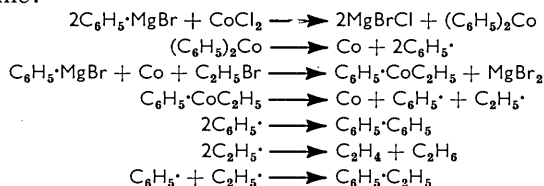
KHARASCH and FIELDS [1] discovered that the reaction of a Grignard reagent with an organic halide in the presence of a catalytic quantity of cobaltous chloride gave a coupling product derived from two molecules of the Grignard reagent. They postulated the following free-radical chain reaction in which cobalt sub-chloride is the chain carrier:

$$RMgX + CoCl_2 \longrightarrow RCoCl + MgXCl$$
$$2RCoCl \longrightarrow R_2 + 2CoCl\cdot$$
$$R'X + CoCl\cdot \longrightarrow CoClX + R'\cdot$$
(R and R' = alkyl or aryl groups; X = Cl, Br, or I)

The following alternative mechanism involving metallic cobalt as the chain carrier was subsequently suggested by Wilds and McCormack,[2] who considered that the continuously regenerated metal was in a favourable state of subdivision and activity. However,

$$2RMgX + CoCl_2 \longrightarrow R_2Co + 2MgXCl$$
$$R_2Co \longrightarrow R_2 + Co$$
$$2R'X + Co \longrightarrow 2R'\cdot + CoX_2$$
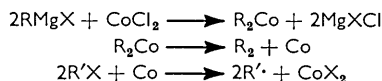
Smith [3] prepared active cobalt by reduction of cobaltous chloride with the sodium–naphthalene radical ion, and found that it did not react with ethyl bromide. This was confirmed by Frey,[4] who also observed that addition of a Grignard reagent to a suspension of metallic cobalt in an ethereal solution of ethyl bromide produced an immediate reaction. Further, when the Grignard reagent was added to cobaltous chloride in tetrahydrofuran, metallic cobalt was obtained in a dark brown, finely-divided state. Addition of ethyl bromide to this mixture produced no significant reaction but a second addition of the Grignard reagent produced an immediate reaction. Frey thus concluded that, as suggested by Wilds and McCormack, metallic cobalt is the active intermediate but that both the Grignard reagent and ethyl bromide must be present to effect reaction. Ethane, ethylene, biphenyl, and ethylbenzene were qualitatively identified as products from the cobalt-catalysed reaction of phenylmagnesium bromide and ethyl bromide, and this led Frey to suggest the following reaction scheme:

$$2C_6H_5\cdot MgBr + CoCl_2 \longrightarrow 2MgBrCl + (C_6H_5)_2Co$$
$$(C_6H_5)_2Co \longrightarrow Co + 2C_6H_5\cdot$$
$$C_6H_5\cdot MgBr + Co + C_2H_5Br \longrightarrow C_6H_5\cdot CoC_2H_5 + MgBr_2$$
$$C_6H_5\cdot CoC_2H_5 \longrightarrow Co + C_6H_5\cdot + C_2H_5\cdot$$
$$2C_6H_5\cdot \longrightarrow C_6H_5\cdot C_6H_5$$
$$2C_2H_5\cdot \longrightarrow C_2H_4 + C_2H_6$$
$$C_6H_5\cdot + C_2H_5\cdot \longrightarrow C_6H_5\cdot C_2H_5$$

Evidence for an organocobalt intermediate was also provided by Tsutsui,[5] who isolated dimesitylcobalt–tetrahydrofuran complex from the related reaction of mesitylmagnesium

[1] M. S. Kharasch and E. K. Fields, *J. Amer. Chem. Soc.*, 1941, **63**, 2316.
[2] A. L. Wilds and W. B. McCormack, *J. Org. Chem.*, 1949, **14**, 45.
[3] W. B. Smith, *J. Org. Chem.*, 1959, **24**, 703.
[4] F. W. Frey, jun., *J. Org. Chem.*, 1961, **26**, 5187.
[5] M. Tsutsui, *Ann. New York, Acad. Sci.*, 1961, **93**, 133.

bromide with cobaltous chloride in tetrahydrofuran. The diaryl cobalt was considered to rearrange through various $\pi$-complexes to yield nascent metallic cobalt and a biaryl. The nascent metallic cobalt was held to regenerate cobaltous halide by reaction with the aryl halide, an aryl radical being produced in the process. Recent work by Morizur [6] on the reaction of various aryl and aralkyl Grignard reagents (and also aryl and aralkyl lithium compounds) with cobaltous chloride and either bromobenzene or *n*-butyl bromide was interpreted as being in accord with the postulates of Wilds and McCormack. [2]

All the suggested reaction schemes involve the intermediate formation of free radicals derived from the halide, but no systematic attempt has been made to determine their fate, in spite of the fact that the properties of such radicals in solution are now well documented. It was considered that dilution of the reaction mixture with an aromatic solvent should result in substitution in the solvent by any free radical present. It is clear that addition of cobaltous chloride to a Grignard reagent produces a " reactive species," which then reacts with the halide, and it was thus expected that *slow* addition of a mixture of cobaltous chloride and Grignard reagent to the halide in an aromatic solvent, or the *slow* addition of the Grignard reagent to a solution of the halide in an aromatic solvent in which cobaltous chloride was suspended, would result in the production of radicals from the halide, at a slow rate, which would be readily trapped by reaction with the aromatic solvent.

Preliminary experiments (1—6) showed that addition of an ethereal solution of methyl-magnesium iodide to a benzene solution of an aryl halide in which cobaltous chloride was suspended at 80° was the most convenient method for the study of radicals produced from the halide, since the biaryls formed can only be derived from the halide. Products derived from methylmagnesium halide are gaseous. Thus the dropwise addition of methyl-magnesium iodide in ether solution to a stirred benzene solution of *p*-bromotoluene in which 10 moles % cobaltous chloride (based on halide) was suspended at 80° afforded in 16·6% yield 4-methylbiphenyl which, almost certainly, arises by substitution of a *p*-tolyl radical, derived from the halide (*p*-bromotoluene), in the solvent benzene (Expt. 5). It was note-worthy that when cobaltous chloride is added to methylmagnesium iodide in ether (Expt. 2) there is an immediate evolution of gas as the Grignard reagent reduces the cobaltous chloride to metallic cobalt. When this mixture was added to a solution of *p*-bromotoluene in benzene at 25° 4-methylbiphenyl was obtained in 7% yield compared with a 15% yield when the methylmagnesium iodide was replaced by phenylmagnesium bromide (Expt. 1). Kharasch and Fields [1] similarly observed the greater stability of a mixture of phenylmagnesium bromide and cobaltous chloride. If the reactive intermediate is an organo-cobalt compound, then this variation in yield might readily be accounted for by the increased stability of a diarylcobalt over a dialkylcobalt. Little difference would be expected between an aryl and an alkyl Grignard reagent if they are added to a suspension of cobaltous chloride in a solution of halide in the aromatic solvent, since in that case the organocobalt compound would react with the halide as soon as it was formed. This expectation is confirmed by experiment (Expts. 5 and 6).

With an aromatic Grignard reagent, substitution products derived from the Grignard reagent were formed as minor reaction products only, *e.g.*, the addition of *p*-tolylmagnesium bromide to a suspension of cobaltous chloride in a benzene solution of bromobenzene afforded only 3·3% of 4-methylbiphenyl derived from the Grignard reagent compared with 20·3% of biphenyl, a substitution and also possible dimerisation product derived from halide (Expt. 7). It is possible that the apparent substitution reaction involving the Grignard re-agent may be accounted for by exchange reactions of the type

$$CH_3 \cdot C_6H_4MgBr + C_6H_5Br \rightleftharpoons CH_3 \cdot C_6H_4Br + C_6H_5MgBr$$
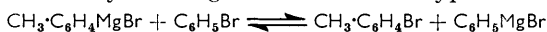
Such exchange reactions have been shown to occur. [7-9]

[6] J. P. Morizur, *Bull. Soc. chim. France*, 1964, 1331.
[7] M. S. Kharasch and C. F. Fuchs, *J. Org. Chem.*, 1945, **10**, 292.
[8] H. Gilman and H. L. Jones, *J. Amer. Chem. Soc.*, 1929, **51**, 2840.
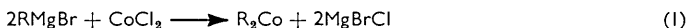[9] L. H. Slaugh, *J. Amer. Chem. Soc.*, 1961, **83**, 2734.

In reactions where the Grignard reagent and the halide were *both* aromatic, and a product separation by means of gas–liquid chromatography was possible, a search was made for reaction products other than those derived from substitution or coupling reactions. It was found that 45—50% of the halide and 25—45% of the Grignard reagent were converted into hydrocarbons by reduction (Expts. 6, 7, 12, 13). The Grignard reagent is always closely associated with several molecules of ether, which presumably provide the chief source of hydrogen in the formation of reduction products, although some of the hydro-carbon derived from the halide probably results from hydrogen abstraction from the σ-complex formed by attack by an aryl radical on the aromatic solvent.

The presence of some ether appears to be essential, since preparation of the Grignard reagent in ether solution, removal of as much ether as possible by distillation, followed by replacement with benzene, gave a product which underwent reaction only with consider-able difficulty.
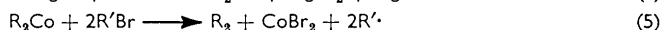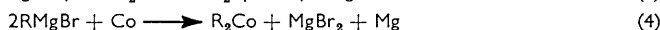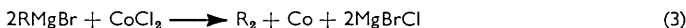
As stated above, metallic cobalt has been suggested as the active intermediate [2] and it was found that cobalt, prepared by the reduction of cobaltous chloride with methyl-magnesium halide, would not react with aryl halides (Expts. 8 and 9) but on addition of more Grignard reagent reaction readily ensued (Expt. 10), as observed by Frey,[4] there being little variation between 10 and 100 moles % cobalt catalyst (Expts. 10 and 12). Commercial metallic cobalt is also able to bring about some reaction (Expt. 11). It is thus very likely that the Grignard reagent reacts with cobaltous chloride or with metallic cobalt to give an organocobalt compound which can either react with the aryl halide to give free radicals or decompose to give a coupling product and metallic cobalt.

Parker, Piette, Salinger, and Noller [10] recently investigated the related cuprous bromide-catalysed reaction of alkylmagnesium halides with alkyl halides, and on the basis of physical methods they concluded that the catalysts were solvated complexes of organometallic compounds with alkylmagnesium halides.
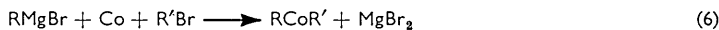
In the light of the results now reported the following reaction pathways are suggested:

$$2RMgBr + CoCl_2 \longrightarrow R_2Co + 2MgBrCl \qquad (1)$$
$$R_2Co \longrightarrow R_2 + Co \qquad (2)$$

(1) + (2) combined

$$2RMgBr + CoCl_2 \longrightarrow R_2 + Co + 2MgBrCl \qquad (3)$$
$$2RMgBr + Co \longrightarrow R_2Co + MgBr_2 + Mg \qquad (4)$$
$$R_2Co + 2R'Br \longrightarrow R_2 + CoBr_2 + 2R'\cdot \qquad (5)$$

A pathway of the form

$$RMgBr + Co + R'Br \longrightarrow RCoR' + MgBr_2 \qquad (6)$$
$$RCoR' \longrightarrow R\cdot + R'\cdot + Co \qquad (7)$$

similar to that suggested by Frey [4] must be rejected, since it implies that radicals are pro-duced equally readily from the Grignard reagent and the halide, and also suggests that crossed biaryls from the Grignard reagent and the halide should be major products of reaction. Experimentally (Expt. 13) with 4-bromobiphenyl as halide and *p*-tolylmagnesium bromide as the Grignard reagent, *p*-terphenyl, the substitution product from the halide, was formed in 16% yield and 4-methylbiphenyl, the substitution product from the Grig-nard reagent, in only 0·9% yield. The crossed coupling product, 4-(*p*-tolyl)biphenyl, was formed in 1·4% yield compared with 31% of 4,4'-dimethylbiphenyl, the coupling product from the Grignard reagent, and 1% of *pp'*-quaterphenyl, the coupling product derived from the halide. With 100 moles % cobalt as catalyst (Expt. 12) a similar product distribution was observed. These results clearly indicate that free radicals are, in general, only derived from the halide. Coupling products from the halide and crossed coupling products formed in low yield may be accounted for by the existence of an equilibrium

[10] V. D. Parker, L. H. Piette, R. M. Salinger, and C. R. Noller, *J. Amer. Chem. Soc.*, 1964, **86**, 1110.

between the Grignard reagent and the halide, and by formation of the Grignard reagent R'MgBr with the magnesium formed in reaction (4).

In the reactions under investigation free radicals are effectively produced in dilute solution as a result of the dropwise addition of the Grignard reagent to a solution of the halide in benzene in the presence of cobaltous chloride. Reactions of benzoyl peroxide in dilute solution [11-13] have been shown to give products arising from phenylcyclohexadienyl radicals, the first-formed intermediate in the reaction of phenyl radicals with benzene. These products consist of biphenyl, formed as a result of hydrogen abstraction and by disproportionation, and, particularly in dilute solution, of tetrahydroquaterphenyls formed by dimerisation. As a result of a careful examination of the reaction products from the reaction of methylmagnesium iodide with a suspension of cobaltous chloride in a solution of bromobenzene in benzene (Expt. 16) both 1',4',1'',4''-tetrahydro-*p*-quaterphenyl and *pp'*-quaterphenyl have now been isolated. Treatment of the reaction product with *o*-chloranil increased the yield of *pp'*-quaterphenyl and a trace of *op'*-quaterphenyl was also formed. The presence of 1-phenylcyclohexadiene was also detected, which arises by disproportionation of the phenylcyclohexadienyl radical. In a similar reaction (Expt. 15) between methylmagnesium iodide and a suspension of cobaltous chloride in a solution of 2-bromonaphthalene in benzene the presence of 1,4,1',4'-tetrahydro-4,4'-(di-2-naphthyl)-biphenyl among the reaction products was suspected, and 4,4'-(di-2-naphthyl)biphenyl was obtained on treatment of the crude reaction mixture with *o*-chloranil.

To obtain further evidence for the existence of free radicals as intermediates in these reactions, methylmagnesium iodide in ether solution was added dropwise to a suspension of cobaltous chloride in a solution of bromobenzene in a monosubstituted aromatic solvent (*t*-butylbenzene, cumene, or anisole) and the isomer ratio for the monosubstituted biphenyls measured by use of gas–liquid chromatography. The results are compared in Table 1 with isomer ratios obtained using other sources of phenyl radicals.

Clearly the substitution pattern is consistent with the production of phenyl radicals in the cobaltous chloride catalysed reaction of an aryl halide and a Grignard reagent, but compared with substitution by phenyl radicals derived from benzoyl peroxide the percentage of *ortho* substitution is reduced by about ten in every case. A corresponding increase in *meta* substitution of the same order is also observed, while the amount of *para* substitution is virtually unchanged.

In the experiments with t-butylbenzene as solvent and iodobenzene, bromobenzene, and chlorobenzene as halide the percentage yield and isomer ratio for the t-butylbiphenyls produced remained constant (see Table 1). These results are in agreement with the view that the reactive species which converts the halide into a free phenyl radical does so in a fast non-rate-determining step. Presumably formation of an organocobalt compound is relatively slow.

The reduction of *ortho* substitution and concomitant increase in *meta* substitution shown in Table 1 points to the attacking species' having a larger size than a phenyl radical derived from benzoyl peroxide. Thus the possibility of the attacking radical's being complexed with ether and/or either cobalt or cobaltous chloride or some other metallic or organometallic species must be regarded as possible. The presence of ether in the reaction medium may also have a bearing on the diminished degree of *ortho* substitution. These reactions give products characteristic of the formation of phenyl radicals in dilute solution and an attractive postulate is that in such dilute solutions the radicals are more selective, leading to decreased substitution at the most sterically hindered *ortho* positions. Foster and Williams [19] have, however, shown that the isomer ratios for the isopropylbiphenyls formed on phenylation of cumene with phenyl radicals from benzoyl peroxide were, within the limits of experimental error, independent of the initial peroxide concentration.

[11] D. F. DeTar and R. A. J. Long, *J. Amer. Chem. Soc.*, 1958, **80**, 4742.
[12] D. H. Hey, M. J. Perkins, and G. H. Williams, *J.*, 1963, 5604.
[13] D. H. Hey, M. J. Perkins, and G. H. Williams, *J.*, 1964, 3412.

TABLE 1

Isomer ratios of biphenyls obtained from the phenylation of mono-substituted
benzene derivatives at 80° with phenyl radicals derived from various sources

| Radical source | Mono-subd. benzene | o | m | p | Analytical method | Ref. |
|---|---|---|---|---|---|---|
| $Bz_2O_2$ | $PhC_4H_9t$ | 24 | 49 | 27 | I.R. | 14 |
| $Bz_2O_2$ | ,, | 21·2 | 49·9 | 29·0 | G.L.C. | 15 |
| $Bz_2O_2$ | ,, | 17 | 61 | 22 | I.R. | 16 |
| $Ph_3Bi$ | ,, | 10 | 63 | 27 | G.L.C. | 17 |
| $Bz_2O_2$ | ,, | 16 | 54·4 | 29·6 | G.L.C. | Expt. 24 |
| PhBr | ,, | 6·3 | 63·0 | 30·7 | G.L.C. | Expt. 17 |
| PhI | ,, | 6·0 | 64·0 | 30·0 | G.L.C. | Expt. 18 |
| PhCl | ,, | 5·2 | 65·7 | 29·1 | G.L.C. | Expt. 19 |
| $Bz_2O_2$ | $PhC_3H_7i$ | 31 | 42 | 27 | I.R. | 18 |
| $Bz_2O_2$ | ,, | 29 | 50 | 21 | I.R. | 16 |
| $Bz_2O_2$ | ,, | 30 | 42 | 28 | I.R. & G.L.C. | 19 |
| PhHgI | ,, | 24·4 | 46·0 | 29·6 | G.L.C. | 20 |
| $Ph_2Hg$ | ,, | 11·6 | 52·9 | 35·5 | G.L.C. | 20 |
| $Ph_2Hg$ * | ,, | 21·0 | 53·0 | 26·0 | I.R. | 27 |
| $Ph_2Hg$ * | ,, | 23·5 | 50·0 | 26·5 | I.R. | 27 |
| $Ph_4Pb$ * | ,, | 22·0 | 51·0 | 27·0 | I.R. | 27 |
| PhBr | ,, | 18·0 | 56·2 | 25·8 | G.L.C. | Expt. 20 |
| $Bz_2O_2$ | PhOMe | 67 | 18 | 15 | I.R. | 21 |
| $Bz_2O_2$ | ,, | 69·8 | 14·7 | 15·6 | G.L.C. | 15 |
| $Bz_2O_2$ | ,, | 70·0 | 15·5 | 14·5 | G.L.C. | Expt. 25 |
| PhBr | ,, | 54·3 | 27·9 | 17·8 | G.L.C. | Expt. 21 |
| $Bz_2O_2$ | PhCl | 50·1 | 31·6 | 18·3 | I.R. | 22 |
| $Bz_2O_2$ | ,, | 62·2 | 24·0 | 13·8 | I.R. | 23 |
| $Bz_2O_2$ | ,, | 54 | 31 | 15 | I.R. | 24 |
| $Bz_2O_2$ | ,, | 57·9 | 25·3 | 16·8 | G.L.C. | 25 |
| PhCl | ,, | 46·7 | 36·4 | 16·9 | G.L.C. | Expt. 23 |
| $Bz_2O_2$ | PhBr | 48·5 | 33·0 | 18·5 | I.R. | 24 |
| $Bz_2O_2$ | ,, | 49·3 | 33·3 | 17·4 | I.R. | 26 |
| $Bz_2O_2$ | ,, | 54·5 | 29·8 | 15·7 | G.L.C. | 25 |
| PhBr | ,, | 43·4 | 42·6 | 13·9 | G.L.C. | Expt. 22 |

* At 120°.

The consideration of the size of the attacking radical as a cause for the reduction in *ortho* substitution is supported by the results of Hey, Moulden, and Williams [28] and of Abramovitch and Saha,[29] who compared the isomer ratios of products formed by reaction of *ortho* and *para* substituted phenyl radicals in various aromatic solvents, and found a decrease in *ortho* substitution by *ortho* substituted phenyl radicals. A decision as to whether a decrease in *ortho* substitution should result largely in an increase in *meta* substitution, or whether both *meta* and *para* substitution should increase depends on the electrical and steric properties of both the solvent and the attacking radical.

The possibility that the variation in isomer ratio is due to a change in radical source must also be considered. The evidence of previous workers is conflicting. Hey, Stirling, and Williams [30] found very little variation in isomer ratio of the phenylpyridines prepared

[14] J. I. G. Cadogan, D. H. Hey, and G. H. Williams, *J.*, 1954, 3352.
[15] R. T. Morrison, J. Cazes, N. Samkoff, and C. A. Howe, *J. Amer. Chem. Soc.*, 1962, **84**, 4152.
[16] C. S. Rondestvedt, jun., and H. S. Blanchard, *J. Amer. Chem. Soc.*, 1955, **77**, 1769.
[17] D. H. Hey, D. A. Shingleton, and G. H. Williams, *J.*, 1963, 5612.
[18] D. H. Hey, B. W. Pengilly, and G. H. Williams, *J.*, 1956, 1463.
[19] W. R. Foster and G. H. Williams, *J.*, 1962, 2862.
[20] D. A. Shingleton, Ph.D. Thesis, London, 1959.
[21] T. Suehiro, *J. Chem. Soc. Japan, Pure Chem. Sect.*, 1951, **72**, 301.
[22] Chang Shih, D. H. Hey, and G. H. Williams, *J.*, 1958, 2600.
[23] D. R. Augood, D. H. Hey, and G. H. Williams, *J.*, 1953, 44.
[24] R. L. Dannley, E. C. Gregg, jun., R. E. Phelps, and C. B. Coleman, *J. Amer. Chem. Soc.*, 1954, **76**, 445.
[25] G. B. Gill, Ph.D. Thesis, London, 1963.
[26] D. R. Augood, J. I. G. Cadogan, D. H. Hey, and G. H. Williams, *J.*, 1953, 3412.
[27] J. M. Blair, D. Bryce-Smith, and B. W. Pengilly, *J.*, 1959, 3174.
[28] D. H. Hey, H. N. Moulden, and G. H. Williams, *J.*, 1960, 3769.
[29] R. A. Abramovitch and J. G. Saha, *J.*, 1964, 2175.
[30] D. H. Hey, C. J. M. Stirling, and G. H. Williams, *J.*, 1955, 3963.

by reaction of pyridine with phenyl radicals from a variety of radical sources. Blair, Bryce-Smith, and Pengilly [27] studied the photolytic decomposition of diphenylmercury and tetraphenyl-lead in cumene at 120° and their results (incorporated in Table 1) again show a reduction in *ortho* substitution and an increase in *meta* substitution, while the *para* substitution remains constant. The work of Blair, Bryce-Smith, and Pengilly [27] and of Hey, Shingleton, and Williams [17] on the photolysis of triphenylbismuth in t-butylbenzene and of Shingleton [20] on the phenylation of cumene by photolysis of diphenylmercury, and very possibly the work now reported, all involve organometallic compounds as the radical source. In each case a reduction in *ortho* substitution is observed, and this may well be due to the presence of a metal atom or ion in the transition state of the substitition step.

## EXPERIMENTAL

*Reagents.*—Anhydrous cobaltous chloride (B.D.H.) was finely powdered and dried at 160°. Aromatic solvents were purified in the conventional manner.

*Gas–Liquid Chromatography.*—For qualitative analysis the Pye Argon Chromatograph was employed with the following columns on Celite (85—100 mesh): (*A*) 10% Apiezon L, (*B*) 5% fluorosilicone fluid, (*C*) 1% neopentyl glycol adipate. Quantitative analysis was carried out using a Griffin and George Gas Density Balance Chromatograph incorporating a Martin Gas Density Balance. The method of analysis was that described by Phillips and Timms.[31] The following columns were employed on Celite (85—100 mesh): (I) 10% Apiezon L, (II) 1·5% neopentyl glycol succinate, and (III) 10% polyethylene glycol (20M) on siliconised Silocel (85—100 mesh). Compounds were identified in every case by a comparison of retention times with those of authentic samples.

*Preparation of Grignard Reagents.*—These were prepared under nitrogen in ether, and before use were filtered through glass wool, under nitrogen, into an equalising pressure dropping funnel. Methylmagnesium iodide was prepared using a slight excess of methyl iodide to ensure the magnesium was completely consumed, and the yield was based on the quantity of magnesium used. When aromatic Grignard reagents were prepared the yields were calculated on the quantity of halide used, and a slight excess of magnesium was employed to ensure complete reaction.

*Reactions of Grignard Reagents with Organic Halides.*—In each of the following experiments the reactants are first stated and this is followed by a statement of procedure. In general the reaction mixture, which became black with evolution of gaseous products, was maintained at either 80 or 25° overnight, after which dilute hydrochloric acid was added and the mixture was separated into organic and aqueous layers. The organic layer was combined with ether (2 × 50 ml.) used to wash the apparatus and to extract the aqueous layer. The combined organic layers were washed with saturated sodium hydrogen carbonate solution, water, and/or saturated sodium chloride solution, and dried over sodium sulphate. The solution was filtered and ether (100 ml.) added which had been previously used to wash the separating funnel and filtration assembly. The solution was then concentrated to 30 ml. by removal of excess of solvent by distillation. The residue was filtered through an alumina column (18 × 2 cm.) and washed through with benzene (200 ml.) previously employed to wash the fractionating column and distillation flask. The combined eluants were reduced to about 15 ml. and this solution was analysed by gas–liquid chromatography. In some cases an exhaustive column chromatography was carried out to isolate all the products of reaction.

1. Reactants: phenylmagnesium bromide (0·05 mole from bromobenzene, 7·85 g.), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·005 mole, 0·7 g.). The cobaltous chloride was added to the phenylmagnesium bromide solution and this mixture was added to the benzene solution of *p*-bromotoluene at 25°. Qualitative gas–liquid chromatography indicated the presence of toluene. A quantitative estimation gave unchanged *p*-bromotoluene (3·1 g., 73%), 4-methylbiphenyl (0·117 g., 15% based on *p*-bromotoluene consumed), and biphenyl (1·84 g., 52% based on Grignard reagent).

2. Reactants: methylmagensium iodide (0·05 mole), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·005 mole, 0·7 g.). This reaction was carried out as described for Expt. 1. Qualitative gas–liquid chromatography indicated the presence of toluene.

[31] C. S. G. Phillips and P. L. Timms, *J. Chromatog.*, 1961, **5**, 131.

A quantitative estimation gave unchanged *p*-bromotoluene (1·44 g., 34%) and 4-methylbiphenyl (0·193 g., 7% based on *p*-bromotoluene consumed).

3. Reactants: methylmagnesium iodide (0·05 mole), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·005 mole, 0·7 g.). The methylmagnesium iodide solution was added to a suspension of the cobaltous chloride in a benzene solution of *p*-bromotoluene at 25°. Qualitative gas–liquid chromatography indicated the presence of toluene. A quantitative estimation gave unchanged *p*-bromotoluene (2·02 g., 47%) and 4-methylbiphenyl (0·24 g., 10·8% based on consumed *p*-bromotoluene).

4. Reactants: phenylmagnesium bromide (0·05 mole from bromobenzene, 7·85 g.), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·005 mole, 0·7 g.). This reaction was carried out as for Expt. 3. Qualitative gas–liquid chromatographic analysis indicated the presence of toluene. A quantitative estimation gave unchanged *p*-bromotoluene (1·83 g., 43%), 4-methylbiphenyl (0·374 g. 15·5% based on reacted *p*-bromotoluene), and biphenyl (1·44 g., 37·5% based on Grignard reagent).

5. Reactants: methylmagnesium iodide (0·05 mole), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·005 mole, 0·7 g.). This reaction was carried out as for Expt. 3 except that the temperature was 80°. Qualitative gas–liquid chromatography indicated the presence of toluene. A quantitative estimation gave unchanged *p*-bromotoluene (0·153 g., 3·5%) and 4-methylbiphenyl (0·677 g., 16·6% based on consumed *p*-bromotoluene).

6. Reactants: phenylmagnesium bromide (0·05 mole from bromobenzene, 7·85 g.), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·005 mole, 0·7 g.). As for Expt. 5. Quantitative gas–liquid chromatography gave toluene (0·98 g., 46% based on consumed *p*-bromotoluene), unchanged *p*-bromotoluene (0·27 g., 6%), 4-methylbiphenyl (0·88 g., 22% based on consumed *p*-bromotoluene), and biphenyl (1·8 g., 47% based on Grignard reagent).

7. Reactants: *p*-tolylmagnesium bromide (0·05 mole from *p*-bromotoluene, 8·5 g.), bromobenzene (0·025 mole, 3·9 g.), benzene (250 ml.), cobaltous chloride (0·005 mole, 0·7 g.). As for Expt. 5. Quantitative gas–liquid chromatography gave toluene (1·19 g., 26·2% based on Grignard reagent), unchanged bromobenzene (0·53 g., 13·5%), biphenyl (0·685 g., 20% based on bromobenzene), 4,4′-dimethylbiphenyl (2·21 g., 53% based on Grignard reagent), and 4-methylbiphenyl (0·28 g., 3·3% based on Grignard reagent).

8. Reactants: methylmagnesium iodide (0·05 mole), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·025 mole, 3·3 g.). The cobaltous chloride was added in small portions to the methylmagnesium iodide solution. When gas evolution had ceased, the benzene was added and the mixture boiled at reflux for a few hours. To this mixture a solution of the *p*-bromotoluene in benzene (20 ml.) was added dropwise during 2 hr. and the mixture was then kept at 80° overnight. Qualitative gas–liquid chromatography showed the presence of only unchanged *p*-bromotoluene.

9. Reactants: methylmagnesium iodide (0·05 mole), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·025 mole, 3·3 g.). The cobaltous chloride was suspended in benzene solution and the methylmagnesium iodide solution added dropwise during 1 hr. and the resulting mixture kept at 80° overnight. A solution of the *p*-bromotoluene in benzene (50 ml.) was then added during 2 hr. and the mixture maintained at 80° for a further 24 hr. Qualitative gas–liquid chromatography showed the presence of only unchanged *p*-bromotoluene.

10. Reactants: methylmagnesium iodide (0·015 mole), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), cobaltous chloride (0·005 mole, 0·7 g.). The cobaltous chloride was suspended in benzene at 80° and the solution of methylmagnesium iodide added dropwise. After 1 hr. the solution of *p*-bromotoluene in benzene (20 ml.) was added, followed by the dropwise addition during 2 hr. of a new solution of methylmagnesium iodide (0·05 mole). Quantitative gas–liquid chromatography gave unchanged *p*-bromotoluene (2·61 g., 61·4%) and 4-methylbiphenyl (0·114 g., 8·8% based on consumed *p*-bromotoluene).

11. Reactants: methylmagnesium iodide (0·05 mole), *p*-bromotoluene (0·025 mole, 4·25 g.), benzene (250 ml.), metallic cobalt (B.D.H.), 1 g. The cobalt was suspended in the benzene solution of *p*-bromotoluene at 80° and the methylmagnesium iodide added dropwise during 2 hr. Afterwards the mixture was boiled at reflux for 72 hr. Qualitative gas–liquid chromatography showed the presence of 4-methylbiphenyl and 4,4′-dimethylbiphenyl, the latter in the larger quantity.

12. Reactants: methylmagnesium iodide (0·05 mole), cobaltous chloride (0·022 mole,

2·9 g.), benzene (250 ml.), 4-bromobiphenyl (0·025 mole, 5·80 g.), *p*-tolylmagnesium iodide (0·05 mole from *p*-iodotoluene, 10·8 g.). The cobaltous chloride was suspended in the benzene at 80° and the solution of methylmagnesium iodide added dropwise during 2 hr. and then maintained at 80° overnight. The Grignard solution was in slight excess to ensure complete reduction of all the cobaltous chloride. The 4-bromobiphenyl dissolved in benzene (50 ml.) was then added, followed by the dropwise addition during 2 hr. of the *p*-tolylmagnesium iodide solution. The reaction was then kept at 80° for a further 24 hr. Quantitative gas–liquid chromatography gave toluene (1·65 g., 34·3% based on Grignard reagent), unchanged 4-bromobiphenyl (3·5 g., 60·4%), biphenyl (0·76 g., 50% based on consumed 4-bromobiphenyl), 4,4′-dimethylbiphenyl (1·87 g., 41% based on Grignard reagent), *p*-terphenyl (0·275 g., 12·1% based on consumed 4-bromobiphenyl), and 4-(*p*-tolyl)biphenyl (0·095 g., 0·8% based on Grignard reagent).

13. Reactants: *p*-tolylmagnesium iodide (0·05 mole from *p*-iodotoluene (0·8 g.), benzene (250 ml.), 4-bromobiphenyl (0·025 mole, 5·80 g.), cobaltous chloride (0·005 mole, 0·7 g.). As for Expt. 5. Quantitative gas–liquid chromatography gave toluene (2·07 g., 45·5%, based on Grignard reagent), unchanged 4-bromobiphenyl (3·65 g., 63%), biphenyl (0·645 g., 45·5%, based on consumed 4-bromobiphenyl), 4-methylbiphenyl (0·073 g., 0·9% based on Grignard reagent), 4,4′-dimethylbiphenyl (1·40 g., 31% based on Grignard reagent), *p*-terphenyl (0·358 g., 16·7% based on consumed 4-bromobiphenyl), and 4-(*p*-tolyl)biphenyl (0·163 g., 1·4% based on Grignard reagent).

Table 2 contains the gas–liquid chromatographic data for the quantitative and/or qualitative analysis of the products formed in Expts. 1—13.

14. Reactants: methylmagnesium iodide (0·15 mole), benzene (300 ml.), *p*-bromotoluene (0·05 mole, 8·5 g.), cobaltous chloride (0·0075 mole, 0·975 g.). As for Expt. 5. The concentrated reaction product on qualitative gas–liquid chromatography on column *A* at 175°, was shown to contain 4-methylbiphenyl together with a smaller quantity of 4,4′-dimethylbiphenyl and an-

TABLE 2

Method of gas–liquid chromatographic detection or estimation of products formed in reactions 1—13

| Expt. numbers | Column | Temp.° | Marker in quantitative estimations | Compounds detected or estimated |
|---|---|---|---|---|
| 1—5 | *A* | 120 | | Toluene |
| 8, 9 | *A* | 175 | | *p*-Bromotoluene |
| 11 | *A* | 175 | | 4-Methylbiphenyl, 4,4′-dimethylbiphenyl |
| 1—7, 10 | I | 174 | Naphthalene | *p*-Bromotoluene, 4-methylbiphenyl, biphenyl |
| 6, 7, 12, 13 | I | 80 or 90 | *o*-Xylene | Toluene |
| 12, 13 | I | 180 | Naphthalene | 4-Bromobiphenyl, biphenyl, 4,4′-dimethylbiphenyl, 4-methylbiphenyl (Expt. 13 only) |
| 12, 13 | II | 228 | *trans-p*-Methoxy-stilbene | *p*-Terphenyl, 4-(*p*-tolyl)biphenyl |

other compound having a rention time of 12 min. compared with 17·5 min. for 4-methylbiphenyl. The reaction product was chromatographed on an alumina column (35 × 3·5 cm. diam.) and eluted with light petroleum (b. p. 40—60°). The first fractions (400 ml.) contained an oil (0·1 g.), shown to be unsaturated by the presence of olefinic protons at 4·3 τ in the nuclear magnetic resonance spectrum. The oil solidified on standing in air to afford 4-methylbiphenyl, m. p. and mixed m. p. 40—41°. From subsequent fractions (800 ml.) 4-methylbiphenyl (2·0 g., m. p. and mixed m. p. 40—41° and identical infrared spectra), was isolated. Elution with 1 : 1 benzene–light petroleum (b. p. 60—80°) gave 600 ml. of eluant which was concentrated to 100 ml. and treated with *o*-chloranil. This afforded 0·1 g., of material, m. p. 339—341°. Elution with benzene (700 ml.) gave 0·08 g. of similar material identified as 4,4′-di(*p*-tolyl)biphenyl by comparison with a synthetic specimen.[32]

15. Reactants: methylmagnesium iodide (0·15 mole), benzene (300 ml.), 2-bromonaphthalene (0·05 mole, 10·35 g.), cobaltous chloride (0·0075 mole, 0·975 g.). The residual solution left after removal of most of the solvent contained 4,4′-di(2-naphthyl)biphenyl (0·1 g., m. p. and mixed m. p. 333—335°, identical infrared spectra). Qualitative gas–liquid chromatography on column *A* at 175° showed the presence of naphthalene, 2-bromonaphthalene, and a

[32] M. S. Kharasch, D. C. Sayles, and E. K. Fields, *J. Amer. Chem. Soc.*, 1944, **66**, 481.

compound with retention time mid-way between those of naphthalene and 2-bromonaphthalene. The residual solution was chromatographed on an alumina column (35 × 3·5 cm.). Elution with light petroleum (b. p. 40—60°) (600 ml.) afforded a semi-solid (4·65 g.) identified by quali- tative gas–liquid chromatography on column *A* at 175° as a mixture of 2-bromonaphthalene and the unidentified compound; light petroleum (b. p. 60—80°) (500 ml.) gave 2-phenyl- naphthalene (1·45 g.), m. p. and mixed m. p. 100—102°; 1 : 1 mixture (100 ml.) of light petroleum (b. p. 60—80°) and benzene gave 2,2'-binaphthyl, m. p. and mixed m. p. 187—188°; a further 600 ml. of the above solvent gave a product (1·0 g.), m. p. 110—130°, on crystallisation from light petroleum (b. p. 100—120°), which was converted, on treatment with *o*-chloranil, into 4,4'-di(2-naphthyl)biphenyl (0·3 g.), m. p. 333—335°.

16. Reactants: methylmagnesium iodide (0·114 mole), bromobenzene (0·049 mole, 7·698 g., benzene (250 ml.), cobaltous chloride (0·0114 mole, 1·485 g.). The residual solution was quanti- tatively analysed on column (I) at 175°, using bibenzyl as marker, and 1-phenylcyclohexa- 2,5-diene (0·158 g., 2% based on consumed bromobenzene), and biphenyl (1·63 g., 21% based on consumed bromobenzene) were detected. Chromatography on an alumina column (35 × 3·5 cm.) of the residual solution and elution with n-hexane (500 ml.) gave an oil shown by analysis on column *A* at 175° to be a mixture of biphenyl and 1-phenylcyclohexa-2,5-diene. Further chromatography of this oil on the same column and elution with n-hexane (50 ml. fractions) gave 1-phenylcyclohexadiene, identified by comparison of nuclear magnetic resonance spectrum with that of an authentic specimen (the spectrum contained olefinic protons at 4·28 $\tau$, and allylic protons at 6·1 and 7·3 $\tau$), and biphenyl, m. p. and mixed m. p. 70—71°. Elution of original column with a 1 : 1 mixture (250 ml.) of light petroleum (b. p. 60—80°) and benzene gave an oil (0·1 g.), which crystallised from light petroleum (b. p. 80—100°) to give 1',4',1'',4''- tetrahydro-*p*-quaterphenyl, m. p. 142—143°[11] (the nuclear magnetic resonance spectrum showed aromatic protons at 2·81 $\tau$, olefinic protons at 4·22 $\tau$, and allylic protons at 6·1 and 7·0 $\tau$), which on dehydrogenation with *o*-chloranil gave *pp*'-quaterphenyl (m. p. and mixed m. p. 315—317°, identical infrared spectra); hydrogenation over palladium on charcoal catalyst gave dodecahydroquaterphenyl (m. p. and mixed m. p. 200—202°, identical infrared spectra). Elution with a 1 : 1 mixture (600 ml.) of light petroleum (b. p. 60—80°) and benzene gave an oil (1·25 g.), which in benzene (50 ml.) with *o*-chloranil (2·0 g.) added, was boiled under reflux for 16 hr. On cooling and dilution with ethanol (25 ml.) *pp*'-quaterphenyl (0·147 g.) was precipi- tated and filtered off. The filtrate was passed through an alumina column (15 × 2 cm.) and eluted with benzene (100 ml.). Concentration of total eluant to 5 ml. followed by chromato- graphy on column *A* at 175° showed the presence of biphenyl, while column *B* at 200° and column *C* at 225° indicated biphenyl and traces of *m*-terphenyl, *p*-terphenyl, and *op*'-quaterphenyl. The amount of biphenyl (0·1 g.), subsequently isolated by column chromatography, probably

TABLE 3

Phenylation of monosubstituted aromatic compounds with phenyl radicals derived from phenyl halides

| Expt. No. | Solvent | Halide | Column for analysis of products | Temp.° | Marker | Biphenyl (g.) | Substituted biphenyl | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | *o* (g.) | *m* (g.) | *p* (g.) |
| 17 | t-Butylbenzene 125 ml. | Bromobenzene 3·85 g. | I | 200 | Phenanthrene | 0·036 | 0·025 | 0·244 | 0·119 |
| 18 | t-Butylbenzene 125 ml. | Iodobenzene 4·96 g. | I | 200 | 4-Acetoxybi- phenyl | 0·095 | 0·022 | 0·235 | 0·110 |
| 19 | t-Butylbenzene 125 ml. | Chlorobenzene 2·875 g. | I | 200 | 4-Acetoxybi- phenyl | 0·046 | 0·022 | 0·278 | 0·123 |
| 20 * | i-Propylbenzene 250 ml. | Bromobenzene 7·648 g. | I | 200 | Phenanthrene | 0·064 | 0·105 | 0·329 | 0·156 |
| 21 | Anisole 250 ml. | Bromobenzene 7·632 g. | I | 175 | 4-Acetoxybi- phenyl | 0·214 | 0·744 | 0·382 | 0·244 |
| 22 † | Bromobenzene 250 ml. | | III | 200 | Bibenzyl | 0·384 | 0·606 | 0·595 | 0·193 |
| 23 ‡ | Chlorobenzene 250 ml. | | III | 200 | Bibenzyl | 0·132 | 0·392 | 0·306 | 0·142 |

\* Also dicumyl, 2·68 g. was formed.    † Bromobenzene as solvent and radical source.    ‡ Chloro- benzene as solvent and radical source.

arises from fission of the quaterphenyls during dehydrogenation. A final elution with benzene (400 ml.) gave *pp'*-quaterphenyl, m. p. and mixed m. p. 315—317°.

*Determination of the Isomer Ratios for the Phenylation of Monosubstituted Aromatic Solvents.*— Reactions 17—23 were conducted as in Expt. 5 at 80°, and the molar ratio of reactants was methylmagnesium iodide (2 mole), cobaltous chloride (0·2 mole), radical source, *i.e.*, halide (1 mole). Table 3 summarises the results obtained by quantitative gas chromatography.

24. A mixture of t-butylbiphenyls was prepared from the reaction of benzoyl peroxide with t-butylbenzene by the method of Cadogan, Hey, and Williams [14] and analysed quantitatively on column (I) at 200° using phenanthrene as marker. The results are in Table 1.

25. A mixture of methoxyphenyls was prepared from the reaction of benzoyl peroxide with anisole and the mixture analysed quantiatively by gas–liquid chromatography on column (I) at 200° using phenanthrene as marker. The results are in Table 1.

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