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THALLIUM IN ORGANIC SYNTHESIS—XVII

PREPARATION OF BIARYLS FROM ARYLMAGNESIUM BROMIDES AND THALLIUM(I) BROMIDE[1-3]

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Abstract—Reaction of thallium(I) bromide with aromatic Grignard reagents which are unsubstituted in the *ortho* positions results in rapid reduction of the inorganic halide to metallic thallium and simultaneous formation, in high yield, of symmetrical biaryls. A sequence of redox reactions among the three thallium valence states is shown to be involved in the overall coupling process. The scope and limitations of this biaryl synthesis have been defined.

INTRODUCTION

During research in which one of the main objectives was the preparation of organothallium(I) derivatives, the reaction of phenylmagnesium bromide with thallium(I) bromide in diethyl ether was investigated. The products obtained were biphenyl (74%), diphenylthallium bromide (5–10%), elemental thallium and (apparently) unchanged thallium(I) bromide. The formation of biphenyl in high yield in this reaction immediately suggested the possibility that this procedure might be developed into a new biaryl synthesis, and accordingly a more detailed investigation was undertaken. We wish to describe in this paper the results of this study.

The reactions of Grignard reagents with thallium(III) halides, leading to organothallium(III) derivatives, are unexceptional and have been widely investigated.[4] In contrast, there are only five reports of investigations of analogous reactions involving the much more accessible thallium(I) halides. In 1904, Meyer and Bertheim[5] reported that treatment of alkylmagnesium halides with thallium(I) chloride resulted in formation of metallic thallium; the fate of the organic residue was not determined. An almost identical result was described by Goddard and Goddard,[6] whose only observation on the reaction of phenylmagnesium bromide with thallium(I) bromide was that "quantitative reduction to metallic thallium had occurred". The first successful isolation of an organothallium derivative in this type of reaction was reported in 1932 by Menzies and Cope,[7] who obtained diethylthallium bromide in 12·4% yield from the reaction of ethylmagnesium bromide with thallium(I) chloride. Gilman *et al.*[8] have since shown that the major portion of the Grignard reagent in this reaction undergoes decomposition to a mixture of ethane and ethylene. In all of these reactions diethyl ether was employed as solvent. More recently, Okhlobystin *et al.*[9] found that triethylthallium could be conveniently prepared by treatment of a mixture of ethylmagnesium bromide and ethyl bromide in tetrahydrofuran solution with thallium(I) bromide.

RESULTS

Addition of thallium(I) bromide to an ethereal solution of an equimolar amount of phenylmagnesium bromide at room temperature resulted in the instantaneous separation of a finely divided black solid, the exact constitution of which is still uncertain. When the reaction mixture was stirred and heated under reflux, the nature of the precipitate gradually changed, first to a heavy black granular deposit, then after four hours, to pellets of shiny metallic thallium. A small amount of diphenylthallium bromide crystallized from the cooled reaction mixture and, together with thallium, was removed by filtration. Standard work-up of the filtrate (Experimental) gave pure biphenyl in 74% yield.

Systematic variation of the reaction conditions then enabled approximately optimum conditions for the coupling process to be determined. Thus under otherwise identical conditions to those described above, reaction at 0° throughout proceeded sluggishly, and biphenyl was formed in only 35% yield. Admixture of the reagents at room temperature was found to be advantageous: a reduced yield of biphenyl, 51%, was obtained when thallium(I) bromide was added to a refluxing solution of the Grignard reagent. The order of addition of the reagents, on the other hand, had little significant effect on the yield of biaryl. Completion of reaction required heating under reflux for approximately four hours; standard titrimetric analysis of aliquots of the reaction mixture established that $> 95\%$ of the Grignard reagents had been consumed after this period.

Initial attempts to extend this coupling reaction to substituted aromatic Grignard reagents were disappointing. Biaryls were formed, but in low yields (15–35%), and isolation of the products was complicated by the presence of substantial amounts of diarylthallium bromide by-products. Fortunately this latter problem was easily eliminated by avoiding the use of diethyl ether as solvent. When tetrahydrofuran was employed, either alone or diluted with benzene, reaction proceeded smoothly and cleanly, and in the majority of cases studied no diarylthallium bromide was produced. Despite these various modifications of the experimental conditions, however, yields of biaryls (with the sole exception of biphenyl) were consistently in the range 45–50%, indicating under-utilization of the available Grignard reagent.

It was therefore evident that biaryl production was not properly represented by the simple stoichiometry shown in Eq 1 and 2, and the relative proportions

$$\mathrm{ArMgBr + TlBr \rightarrow ArTl + MgBr_2} \tag{1}$$

$$\mathrm{2ArTl \rightarrow Ar{-}Ar + 2Tl} \tag{2}$$

of the reagents, selected on this basis, were incorrect. Both by variation of the amount of thallium(I) bromide used, and from considerations of probable mechanisms for the coupling reaction, it was found that the optimum Grignard reagent: thallium(I) bromide ratio was in fact 1:1·5. With this ratio of reactants, and using the standard reaction conditions described in the Experimental, aromatic Grignard reagents were converted in high yield to the corresponding biaryls. Details of these conversions are listed in Table 1. Secondary aliphatic Grignard reagents (cyclohexyl, cyclopentyl, isopentyl) also underwent coupling in satisfactory yield, but the reactions of primary aliphatic Grignard reagents were anomalous, di-n-alkylthallium bromides being the sole products of reaction (Eq 3).[10]

$$\mathrm{2RCH_2MgBr + 3TlBr \rightarrow (RCH_2)_2TlBr + 2Tl + 2MgBr_2} \tag{3}$$

From the data in Table 1 it is evident that the Grignard reagent/thallium(I) bromide reaction constitutes an extremely simple, high yield synthesis of symmetrical biaryls. The reaction failed, however, when applied to *ortho* substituted aromatic Grignard reagents; the products in these cases were the dehalogenated aromatic substrates and/or the diarylthallium bromides (Eqs 4, 5). When a mixture of two different Grignard reagents was treated with thallium(I) bromide, all three possible biaryls were produced. Yield data for a typical crossover experiment are given in Eq 6, from which it can be seen that although, as expected, the unsymmetrical biaryl is the major constituent, the product distribution is not statistical. Efforts to improve significantly the yield of unsymmetrical biaryl in these reactions met with little success, and product distributions similar to those in Eq 6 were observed under a variety of experimental conditions.

$$\mathrm{2\text{-}C_6H_5C_6H_4MgBr + TlBr \rightarrow (2\text{-}C_6H_5C_6H_4)_2TlBr + C_6H_5C_6H_5} \tag{4}$$

$$\mathrm{2,4,6\text{-}(CH_3)_3C_6H_2MgBr + TlBr \rightarrow (2,4,6\text{-}(CH_3)_3C_6H_2)_2TlBr} \tag{5}$$

$$\mathrm{C_6H_5MgBr + 4\text{-}CH_3OC_6H_4MgBr + TlBr} \rightarrow \begin{array}{cr} & \% \\ \mathrm{4\text{-}CH_3OC_6H_4C_6H_5} & 46 \\ + & \\ \mathrm{C_6H_5C_6H_5} & 36 \\ + & \\ \mathrm{(4\text{-}CH_3OC_6H_4)_2} & 18 \end{array} \tag{6}$$

DISCUSSION

We should like to suggest the sequence of reactions shown in Eqs 7–12 for the coupling process (figures in parentheses refer to molar quantities):

$$\begin{array}{llllr}
\mathrm{ArMgBr} & \mathrm{+\ TlBr} & \mathrm{\rightarrow ArTl} & \mathrm{+\ MgBr_2} & (7) \\
(0{\cdot}5) & (0{\cdot}5) & (0{\cdot}5) & & \\
\mathrm{ArTl} & \mathrm{+\ 2TlBr} & \mathrm{\rightarrow ArTlBr_2} & \mathrm{+\ 2Tl} & (8) \\
(0{\cdot}5) & (1) & (0{\cdot}5) & & \\
\mathrm{ArTlBr_2} & \mathrm{+\ ArTl} & \mathrm{\rightarrow Ar\text{–}Ar} & \mathrm{+\ 2TlBr} & (9) \\
(0{\cdot}5) & (0{\cdot}5) & (1) & & \\
\mathrm{ArTlBr_2} & \mathrm{+\ ArMgBr} & \mathrm{\rightarrow Ar\text{–}Ar} & \mathrm{+\ TlBr + MgBr_2} & (10) \\
(0{\cdot}5) & (0{\cdot}5) & (1) & & \\
\mathrm{2ArTlBr_2} & & \mathrm{\rightarrow Ar_2TlBr} & \mathrm{+\ TlBr_3} & (11) \\
\mathrm{Ar_2TlBr} & \mathrm{+\ ArMgBr} & \mathrm{\rightarrow Ar\text{–}Ar} & \mathrm{+\ ArTl + MgBr_2} & (12)
\end{array}$$

Table 1. Coupling of aromatic Grignard reagents with thallium(I) bromide

No	Starting material Grignard reagent from	Product Biaryl	Yield, %[a]	Extraction Solvent[b]	Chromatography Solvent[b]	m.p. °C	Lit. m.p. °C
1	Bromobenzene	Biphenyl	92	E	B	70	70·5[c]
2	3-Bromotoluene	3,3′-Dimethylbiphenyl	97	E	B	b.p. 97/0·04 mm	b.p. 130/1 mm[d]
3	4-Bromotoluene	4,4′-Dimethylbiphenyl	90	B	B	121–122	121[c]
4	3-Ethylbromobenzene	3,3′-Diethylbiphenyl	80	E	B	b.p. 160/10 mm	b.p. 154/10 mm[e]
5	3-n-Propylbromobenzene	3,3′-Di-n-propylbiphenyl	65	E	B	b.p. 155–160/15 mm	[f]
6	4-Bromo-1,2-dimethylbenzene	3,3′,4,4′-Tetramethylbiphenyl	82	E	B	76	76[g]
7	4-Bromobiphenyl	4,4′-Quaterphenyl	91	N(hot)	[h]	320	320[i]
8	(4-Bromophenylethynyl)trimethylsilane	4,4′-Di(bis-trimethylsilyl)-ethynylbiphenyl	100	E	B	165–166	[j]
9	3-Bromoanisole	3,3′-Dimethoxybiphenyl	81	C	C	35–36	36[k]
10	4-Bromoanisole	4,4′-Dimethoxybiphenyl	99	C	C	176–178	174[l]
11	4-Bromofluorobenzene	4,4′-Difluorobiphenyl	77[m]	E	B	91–92	94–95[n]
12	3-Bromochlorobenzene	3,3′-Dichlorobiphenyl	74	E	B	b.p. 316–318	b.p. 320[p]
13	4-Bromochlorobenzene	4,4′-Dichlorobiphenyl	73[q]	E	B	146–147	148[r]
14	4-Bromo-N,N-dimethylaniline	N,N,N′,N′-Tetramethylbenzidine	76	[s]	B	195–196	198[t]
15	2-Bromonaphthalene	2,2′-Binaphthyl	84	B(hot)	[h]	184	184[i]
16	2-Bromo-6-methoxynaphthalene	6,6′-Dimethoxy-2,2′-binaphthyl	72	N(hot)	[h]	290–291	289[u]

[a] Calculated on pure recrystallized or redistilled material. [b] E = ether; B = benzene; C = chloroform; N = nitrobenzene. [c] E. Sakellarios and T. Kyrimis, *Chem. Ber.* **57B**, 322 (1924). [d] O. S. Mills, *Nature, Lond.* **167**, 726 (1951). [e] P. M. Everitt, D. M. Hall and E. E. Turner, *J. Chem. Soc.* 2286 (1956). [f] Found: C, 90·40; H, 9·40. $C_{18}H_{22}$ requires: C, 90·69; H, 9·31%. [g] A. W. Crossley and C. H. Hampshire, *J. Chem. Soc.* **99**, 721 (1911). [h] Biaryl not sufficiently soluble for chromatography. [i] S. T. Bowden, *J. Chem. Soc.* 1111 (1931). [j] Recrystallized from methanol. Found: C, 75·70; H, 7·70. $C_{22}H_{26}Si_2$ requires: C, 76·22; H, 7·56%. [k] H. Gottlieb-Billroth, *J. Am. Chem. Soc.* **49**, 482 (1927). [l] G. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.* 1404 (1955). [m] Accompanied by 7% di(4-fluorophenyl)thallium bromide. [n] G. Balz and G. Schiemann, *Chem. Ber.* **60**, 1186 (1927). [p] L. Mascarelli and D. Gatti, *Gazz. Chim. Ital.* **59**, 867 (1929). [q] Accompanied by 5% di(4-chlorophenyl)thallium bromide. [r] F. R. Shaw and E. E. Turner, *J. Chem. Soc.* 285 (1932). [s] Isolated initially as the bis-hydrochloride; free base obtained by treatment of the salt with aqueous sodium hydroxide solution. [t] P. Rumpf, *Bull. Soc. Chim. Fr.*, **7**, 634 (1940). [u] K. W. Bentley, *J. Chem. Soc.* 2398 (1955).

Formation of an unstable arylthallium(I) derivative (Eq 7) is a logical assumption, and while such compounds have never been isolated, the generation of organothallium(I) species has previously been postulated in the reactions of thallium(I) halides both with Grignard[7,11] and organolithium reagents.[12] Conversion of the initially formed, highly reactive ArTl intermediate into $ArTlBr_2$ by the action of thallium(I) bromide (Eq 8) is a reaction for which, as far as we are aware, there is no experimental precedent. Previous workers who have invoked the intermediacy of RTl and ArTl species assumed that rapid disproportionation to a trialkyl- or triaryl-thallium derivative occurred (Eq 13).[13] In this latter context it is significant that Gilman and his

$$3ArTl \rightarrow Ar_3Tl + 2Tl \qquad (13)$$

co-workers have demonstrated that triphenylthallium undergoes decomposition to biphenyl when heated under reflux in xylene.[12,14] That such a process was not operative in the present coupling reaction was easily proved by the following control reactions. Triphenylthallium[12] was recovered unchanged in virtually quantitative yield after being heated under reflux in tetrahydrofuran/benzene (a) for 12 hr; (b) for 5 hr in the presence of thallium(I) bromide; and (c) for 5 hr in the presence of anhydrous magnesium bromide. The yield of biphenyl formed in each of these reactions was $< 1\%$.

Formation of an arylthallium dibromide as shown in Eq 8 is, we believe, the controlling reaction in the overall sequence resulting in coupled product.[14] It also leads to a rational explanation both for the difference observed in the reactions of aromatic and primary aliphatic Grignard reagents and for the formation of small amounts of diarylthallium bromides in some of the reactions. Arylthallium dibromides are a relatively well known, if unstable, class of compound, and symmetrisation to the corresponding diarylthallium bromides is known to occur with great ease (Eq 11).[15] Simple alkylthallium dibromides, on the other hand, have yet to be prepared; all attempts to synthesise these compounds have been uniformly unsuccessful, and have resulted in formation of dialkylthallium bromides.*

It is impossible to say at present which, if either, of the two major product-forming reactions (Eqs 9, 10) is dominant. If the rate of arylthallium(I) formation (Eq 7) is much faster than that of conversion of the same species to the arylthallium dibromide (Eq 8), biaryl formation should occur as shown in Eq 9. Conversely, product formation as shown in Eq 10 will be the more important reaction if the relative rates of reactions 7 and 8 are $8 \gg 7$. The overall stoichiometry of the reaction, however, is independent of the route by which the biaryls are ultimately derived. A particularly important feature of the stoichiometry of Eqs 7–10 is the regeneration of thallium(I) bromide in the product-forming reactions, and this is discussed more fully below.

The reactions shown in Eqs 9 and 10 are unusual. Preparation of diarylthallium halides by treatment of a thallium(III) halide with either an organolithium or Grignard reagent has long been regarded as a routine organometallic reaction in which the intermediacy of an arylthallium dihalide has been tacitly assumed.[4] Evidence to show that not only is such an assumption unwarranted, but also that Eqs 9 and 10 are

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* The preparation and isolation of alkylthallium dihalides by reaction of thallium(III) bromide with dialkylthallium halides has been claimed (N. N. Mel'nikov and G. P. Gracheva, *Zh. Obshch. Khim.* **5**, 1787 (1935)). This claim has since been shown to be specious (C. R. Hart and C. K. Ingold, *J. Chem. Soc.* 4372 (1964); D. Sarrach, *Z. Anorg. Allg. Chem.* **319**, 16 (1962)). Although alkylthallium dihalides were indeed formed *in situ*, they were shown to undergo spontaneous disproportionation to dialkylthallium halides, the species actually isolated.

justifiably included in the above reaction scheme, was obtained in the following manner.

Attempts to isolate arylthallium dibromides from the reactions of thallium(I) bromide with aromatic Grignard reagents were unsuccessful. The alternative approach of employing independently prepared arylthallium dibromides in the coupling reaction was, however, more informative. Thus treatment of phenylthallium dibromide with 4-methoxyphenylmagnesium bromide under the standard reaction conditions resulted in smooth reaction and production of the three biaryls shown in Eq 14. It is significant that, following from the general reaction shown in Eq 10, this reaction proceeded without deposition of any black solid, and no metallic thallium was formed.

$$\mathrm{4\text{-}CH_3OC_6H_4MgBr + C_6H_5TlBr_2} \rightarrow \begin{array}{cr} & \% \\ \mathrm{C_6H_5C_6H_5} & 19 \\ + & \\ \mathrm{(4\text{-}CH_3OC_6H_4)_2} & 37 \\ + & \\ \mathrm{4\text{-}CH_3OC_6H_4C_6H_5} & 44 \end{array} \qquad (14)$$

In control reactions, phenylthallium dibromide was heated under reflux in tetrahydrofuran/benzene, both in the presence and absence of thallium(I) bromide. Only traces of biphenyl ($<1\%$) were formed, and the products consisted of the expected decomposition products of phenylthallium dibromide, namely diphenylthallium bromide, bromobenzene and thallium(I) bromide.

Theoretically Eqs 7–10 are consistent with the stoichiometry and experimental data available for the coupling reaction. We feel, however, that an additional, if minor, pathway leading to the generation of biaryl, and summarized in Eqs 11 and 12, must be included. Analogous with the reactions shown in Eqs 9 and 10, formation of biaryls on treatment of diarylthallium bromides with Grignard reagents was both unexpected and unprecedented. Diphenylthallium bromide was recovered unchanged after being heated under reflux in tetrahydrofuran/benzene both in the presence and absence of thallium(I) bromide; only minute amounts of biphenyl were formed in these reactions ($<1\%$). When the same compound was added to a solution of 4-methoxyphenylmagnesium bromide, however, the three possible biaryls were produced in high yield (Eq 15), although the relative proportions differed substantially from those observed in the corresponding reaction with phenylthallium dibromide (Eq 14).

$$\mathrm{4\text{-}CH_3OC_6H_4MgBr + (C_6H_5)_2TlBr} \rightarrow \begin{array}{cr} & \% \\ \mathrm{(4\text{-}CH_3OC_6H_4)_2} & 5 \\ + & \\ \mathrm{4\text{-}CH_3OC_6H_4C_6H_5} & 29 \\ + & \\ \mathrm{C_6H_5C_6H_5} & 66 \end{array} \qquad (15)$$

Having established an overall reaction sequence which adequately accounted for the experimental observations, it was necessary to eliminate two further reactions which might reasonably be expected to have contributed to the scheme. The first of these, a Kharasch-type reaction (Eq 16), was not observed, although the presence

$$\mathrm{ArMgBr + TlBr \rightarrow ArTl + MgBr_2} \tag{7}$$

$$\mathrm{ArTl + Ar'Br \rightarrow ArAr' + TlBr} \tag{16}$$

of aromatic bromide in the reaction mixture is possible (from decomposition of the arylthallium dibromide). Addition of thallium(I) bromide to a solution containing a mixture of an aromatic Grignard reagent and an aliphatic bromide resulted only in the standard coupling reaction leading to formation of the biaryl. No alkylated aromatic compounds, coupled aliphatic products, or saturated or olefinic hydrocarbons could be detected in the reaction mixture. Similarly, treatment of a mixture of 4-methoxyphenylmagnesium bromide and bromobenzene with thallium(I) bromide gave a mixture of biphenyl (5·4%), 4-methoxybiphenyl (7·2%) and 4,4′-dimethoxybiphenyl (87·4%). It is unlikely that the formation of small amounts of biphenyl and 4-methoxybiphenyl in this instance is indicative of either a Kharasch-type reaction or of a radical process. A more plausible explanation is participation of a cross-metallation reaction (Eq 17). Such processes have been observed previously,

$$\mathrm{ArMgBr + Ar'X \rightarrow Ar'MgBr + ArX} \tag{17}$$

and are known to be catalysed by metal salts.[16,17] The relative proportions of biphenyl and 4-methoxybiphenyl are thus an approximate estimate of the extent to which cross-metallation had taken place.

The second feasible route to biaryls, an Ullmann-type reaction (Eq 18), was also shown to be untenable. Reaction in this manner might well be expected were the

$$\mathrm{2ArBr + 2Tl \rightarrow Ar{-}Ar + 2TlBr} \tag{18}$$

aromatic bromide to be generated in the presence of finely divided thallium. Treatment of aromatic bromides with both massive and pyrophoric[18] thallium, however, yielded only small amounts of biaryls (< 5%) under the standard reaction conditions.

There remain two features of the reaction scheme which deserve comment, namely the regeneration of thallium(I) bromide in the product-forming reactions, and the failure of *ortho* substituted Grignard reagents to give biaryls. From stoichiometric considerations, one third of the thallium(I) bromide originally employed should be regnerated *in situ* during the course of the biaryl synthesis; this conclusion was confirmed by actual isolation of thallium(I) bromide after reaction was complete. From the preparative point of view, however, this observation suggested that addition of further Grignard reagent at the end of the reaction cycle should again result in biaryl formation. This recycling technique is illustrated as follows: 4-methoxyphenylmagnesium bromide was allowed to react with thallium(I) bromide under standard conditions. At the end of the normal reaction period the mixture was allowed to cool. A further portion of 4-methoxyphenylmagnesium bromide was then added, the amount of Grignard reagent being two-thirds of the calculated amount of thallium(I) bromide produced in the first reaction cycle. Formation of a second black precipitate was instantaneous. Work-up of the reaction mixture (after allowing the appropriate time interval for the second reaction cycle to take place) gave 4,4′-dimethoxybiphenyl in "110%" yield, based only on the initial amount of Grignard reagent added

Sequential addition of Grignard reagent in this way is thus an attractive and simple procedure which, especially in large scale reactions, ensures maximum utilisation of the inorganic halide.

We have not yet been able to account satisfactorily for the anomalous behaviour of *ortho* substituted Grignard reagents in the coupling reactions. Even if the first reaction (Eq 7) in the overall scheme were inhibited by steric effects, treatment of an independently prepared arylthallium dibromide with an *ortho* substituted Grignard reagent might reasonably be expected to yield a mixture of biaryls (c.f. Eq 14). As can be seen from the resulted summarized in Eqs 19 and 20, however, only two of the three possible biaryls were obtained in experiments designed to test this hypothesis.

$$
\begin{array}{llrr}
 & & \% & \\
C_6H_5TlBr_2 + 2{,}4{,}6\text{-}(CH_3)_3C_6H_2MgBr \rightarrow & & & \\
 & 2{,}4{,}6\text{-}(CH_3)_3C_6H_3 & 20 & \\
 & + & & \\
 & C_6H_5C_6H_5 & 40 & (19) \\
 & + & & \\
 & 2{,}4{,}6\text{-}(CH_3)_3C_6H_2C_6H_5 & 40 & \\
2{,}4{,}6\text{-}(CH_3)_3C_6H_2TlBr_2 + C_6H_5MgBr \rightarrow & & & \\
 & 2{,}4{,}6\text{-}(CH_3)_3C_6H_3 & 9 & \\
 & + & & \\
 & 2{,}4{,}6\text{-}(CH_3)_3C_6H_2Br & 12 & \\
 & + & & (20) \\
 & C_6H_5C_6H_5 & 34 & \\
 & + & & \\
 & 2{,}4{,}6\text{-}(CH_3)_3C_6H_2C_6H_5 & 45 &
\end{array}
$$

None of the symmetrical *ortho* substituted biaryl was formed.

In summary, the reactions outlined in Eqs 7–12 account satisfactorily for the majority of the experimental observations on the thallium(I) bromide/Grignard reagent coupling reaction. The limitations are threefold: (a) the reaction is unsuccessful with *ortho* substituted Grignard reagents; (b) the preparation of unsymmetrical biaryls by this method is only moderately successful; and (c) the range of possible aromatic nuclear substituents is limited to those groups compatible with formation of a Grignard reagent. Within these limitations, however, the present technique compares very favourably with more classical procedures such as the Ullmann and Gomberg reactions for the synthesis of biaryls.

EXPERIMENTAL

M.ps were determined on a Kofler hot stage apparatus and are uncorrected. Microanalyses were performed by Mr. A. R. Saunders of the University of East Anglia. Where appropriate, identity of compounds was confirmed by comparison of IR spectra determined by the normal Nujol mull or liquid film techniques on a Perkin–Elmer Model 257 Grating Infrared Spectrophotometer. GLC analyses were carried out on a Perkin–Elmer Model 452 Gas Chromatogram using a 2m Apiezon column.

Aromatic bromides. Compounds **1–3**, **6**, **7**, **9–14** were commercially available samples and were purified prior to use. The remaining aromatic bromides were prepared by literature procedures: **4**,[19] **5**,[20] **8**,[21] **15**,[22] **16**.[23]

Preparation of Grignard reagents. All preparations were carried out under an atmosphere of dry N_2. A soln of 0·07 mole of the aromatic bromide in 30 ml THF was added dropwise to a stirred suspension of 1·70 g (0·07 mole) Mg in 5 ml THF. Stirring and slight warming were sufficient to initiate reaction. After addition of the aromatic bromide was completed the soln was heated under reflux for a further hr and then allowed to cool. The volume of the soln was adjusted to 50 ml by addition of anhyd benzene and the concentration of Grignard reagent determined titrimetrically by the method of Gilman.[24]

General procedure for the preparation of biaryls. A soln of 0·042 mole Grignard reagent was added to a stirred suspension of 17·9 g (0·063 mole) thallium(I) bromide in 20 ml anhyd benzene. A black solid formed immediately, and the resulting mixture was stirred and heated under reflux for 3–4 hr and then cooled. In the majority of cases the biaryl crystallized from soln at this stage. The reaction mixture was filtered and the residual solids extracted with the appropriate solvent (Table 1). The resulting soln of biaryl was added to the filtrate and the combined organic solvents washed with HCl and water, and then dried over Na_2SO_4. Removal of the solvents by evaporation under reduced press gave the crude biaryl which was dissolved in the appropriate solvent (Table 1) and the soln passed through a short column of alumina to remove traces of inorganic thallium salts. Concentration of the eluate followed by crystallization or distillation gave the pure biaryl.

Reaction of 2-biphenylylmagnesium bromide with thallium(I) bromide. A soln of 0·025 mole 2-biphenylylmagnesium bromide was added to a stirred suspension of 14·2 g (0·05 mole) thallium(I) bromide in 25 ml anhyd benzene. The soln turned black on warming, and the mixture was stirred and heated under reflux for 12 hr. The reaction mixture was filtered free of solids, which were washed with 20 ml benzene. The combined filtrates were then washed with dil HCl, at which point a colourless solid precipitated. This was removed by filtration and recrystallized from pyridine to give 1·2 g (16%) di(2-biphenylyl)thallium bromide as colourless needles, m.p. > 300°. (Found: C, 48·86; H, 3·75. $C_{24}H_{18}BrTl$ requires: C, 48·79; H, 3·07%). Concentration of the residual filtrate gave 1·9 g (50%) biphenyl.

Reaction of mesitylmagnesium bromide with thallium(I) bromide. A soln of 0·025 mole mesitylmagnesium bromide was added to a stirred suspension of 14·2 g (0·05 mole) thallium(I) bromide in 30 ml of anhyd benzene. A black solid began to precipitate in a few mins, and the mixture was stirred and heated under reflux for 5 hr. The cooled reaction mixture was poured into 50 ml dil HCl and the resulting mixture extracted with ether (2 × 20 ml) and benzene (2 × 20 ml). The combined extracts were dried over Na_2SO_4, concentrated, and the crude product purified by chromatography over alumina using chloroform as eluent. This gave 1·5 g (23%) dimesitylthallium bromide as colourless needles, m.p. 207° (dec), from chloroform. (Found: C, 41·55; H, 4·50. $C_{18}H_{22}BrTl$ requires: C, 41·36; H, 4·24%).

Reaction of a mixture of phenylmagnesium bromide and 4-methoxyphenylmagnesium bromide with thallium(I) bromide. A mixture of solns of the two Grignard reagents was allowed to react with thallium(I) bromide in the usual manner. Isolation of the products by the general procedure gave a mixture of solids which was analysed by GLC using genuine samples of each component as reference standards. The constitution of the mixture was: 4,4′-dimethoxybiphenyl, 18%; biphenyl, 36%; and 4-methoxybiphenyl, 46%.

The relative proportions of the three biphenyls formed in this reaction varied only slightly with alteration of the reaction conditions. Thus sequential addition of the two Grignard reagent solns to the thallium(I) bromide gave the product distribution: 4,4′-dimethoxybiphenyl, 25% biphenyl, 29%; and 4-methoxybiphenyl, 46%.

Reaction of phenylthallium dibromide with 4-methoxyphenylmagnesium bromide and mesitylmagnesium bromide. A soln of 0·0058 mole 4-methoxyphenylmagnesium bromide was added to a stirred suspension of 2·56 g (0·0058 mole) phenylthallium dibromide in 20 ml anhyd benzene, and the resulting soln heated under reflux for 20 hr. Isolation of the organic products in the usual manner gave 0·3 g of a solid consisting of (GLC) biphenyl, 19%; 4,4′-dimethoxybiphenyl, 37%; and 4-methoxybiphenyl, 44%.

Under similar conditions, reaction of phenylthallium dibromide with mesitylmagnesium bromide gave a mixture of bromomesitylene, < 1%; mesitylene, 20%; biphenyl, 40%; and 2,4,6-trimethylbiphenyl, 40%.

Reaction of diphenylthallium bromide with 4-methoxyphenylmagnesium bromide. A soln of 0·0025 mole 4-methoxyphenylmagnesium bromide was added to a stirred suspension of 1·1 g (0·0025 mole) diphenylthallium bromide[26] in 20 ml anhyd benzene, and the resulting mixture heated under reflux for 16 hr. The diphenylthallium bromide gradually dissolved, and metallic thallium separated as a fine black solid. Isolation of the organic products in the usual manner gave 0·5 g of a solid consisting of (GLC) 4,4′-dimethoxybiphenyl, 5%; 4-methoxybiphenyl, 29%; and biphenyl, 66%.

Reaction of mesitylthallium dibromide with phenylmagnesium bromide. A soln of 0·00596 mole phenylmagnesium bromide was added to a stirred suspension of 2·88 g (0·00596 mole) mesitylthallium dibromide[27] in 15 ml anhyd benzene, and the resulting soln heated under reflux for 8 hr. No thallium was deposited and work up of the reaction mixture in the usual manner gave 0·14 g pale yellow oil consisting of (GLC) mesitylene, 9%; bromomesitylene, 12%; biphenyl, 34%; and 2,4,6-trimethylbiphenyl, 45%.

REFERENCES

[1] Part XVI: A. McKillop, B. P. Swann and E. C. Taylor, *Tetrahedron* **26**, 4031 (1970)

[2] We gratefully acknowledge the financial support of this work by the Smith Kline and French Laboratories, Philadelphia, Pa

[3] Certain aspects of this work were reported in preliminary form: A. McKillop, L. F. Elsom and E. C. Taylor, *J. Am. Chem. Soc.* **90**, 2423 (1968)

[4] A. N. Nesmeyanov and R. A. Sokolik, *Methods of Elemento-Organic Chemistry* Vol. 1. *The Organic Compounds of Boron, Aluminium, Gallium, Indium and Thallium* pp. 552–554. North Holland, Amsterdam (1967)

[5] R. J. Meyer and A. Bertheim, *Chem. Ber.* **37**, 2051 (1904)

[6] D. Goddard and A. E. Goddard, *J. Chem. Soc.* 256 (1922)

[7] R. C. Menzies and I. S. Cope, *Ibid.* 2862 (1932)

[8] H. Gilman, R. G. Jones and L. A. Woods, *J. Am. Chem. Soc.* **76**, 3615 (1954)

[9] O. Yu. Okhlobystin, K. A. Bilevitch and L. I. Zakharkin, *J. Organometal. Chem.* **2**, 281 (1964)

[10] For a detailed description see: A. McKillop, L. F. Elsom and E. C. Taylor, *Ibid.*, **15**, 500 (1969)

[11] F. Hein and F. A. Segitz, *Z. Anorg. Allg. Chem.* **158**, 162 (1927)

[12] H. Gilman and R. G. Jones, *J. Am. Chem. Soc.* **62**, 2357 (1940)

[13] Ref. 4, pp. 547–549

[14] H. Gilman and I. Haiduc, *J. Am. Chem. Soc.* **90**, 5912 (1968)

[15] Ref. 4, pp. 556–557, 561–562, 567–568, 571–574, 581–582

[16] M. S. Kharasch and C. Fuchs, *J. Org. Chem.* **10**, 292 (1945)

[17] L. H. Slaugh, *J. Am. Chem. Soc.* **83**, 2734 (1961)

[18] L. P. McHatton and M. J. Soulal, *J. Chem. Soc.* 4095 (1953)

[19] J. H. Brown and C. S. Marvel, *J. Am. Chem. Soc.* **59**, 1175 (1937)

[20] M. Crawford and F. H. C. Stewart, *J. Chem. Soc.* 4443 (1952)

[21] C. Eaborn, A. R. Thompson and D. R. M. Walton, *J. Chem. Soc.* (C), 1364 (1967)

[22] A. I. Vogel, *Practical Organic Chemistry* p. 604. Longmans, London (1966)

[23] G. W. Gray and B. Jones, *J. Chem. Soc.* 678 (1954)

[24] H. Gilman, E. A. Zoellner and J. B. Dickey, *J. Am. Chem. Soc.* **51**, 1576 (1929)

[25] F. Challenger and B. Parker, *J. Chem. Soc.* 1462 (1931)

[26] E. Krause and A. v. Grosse, *Chem. Ber.* **58**, 1933 (1925)

[27] A. McKillop, J. D. Hunt and E. C. Taylor, *J. Organometal. Chem.*, in press.