

**1136.** *Organometallic Compounds of the Alkali Metals. Part VII.<sup>1</sup> Orientation in Protophilic Aromatic Metallation by Ethylsodium and Ethyl-lithium-potassium Reagents: Factors Influencing the Reactivity of Metallating Reagents.*

By D. BRYCE-SMITH.

An extension of previous work on the metallation of isopropylbenzene by alkylsodiums and an ethyl-lithium-potassium complex is described. The isomer ratios for metallation of isopropylbenzene by ethylsodium are similar at 20° and 85° and very similar to those given by n-pentylsodium at 20°: *meta*-substitution predominates in each case. The total rate factors for nuclear metallation of isopropylbenzene by ethylsodium and an ethyl-lithium-potassium complex are closely similar, and show that the isopropyl group behaves as a deactivating substituent, in agreement with previous work. Little or no rearrangement appears to occur in the conditions employed, in contrast with the recently reported behaviour of related lithium-free systems. Phenyl-lithium-potassium is less reactive than phenylpotassium towards toluene and chlorobenzene. It is suggested that metallations of the present type may occur in homogeneous solution, notwithstanding the apparent heterogeneity of the reaction systems.

ALKALI-METALLATION of aromatic compounds is here defined as replacement, by an alkali metal, of hydrogen attached to an aromatic ring, *e.g.*, by the reaction  $C_6H_6 + C_2H_5Na \longrightarrow C_6H_5Na + C_2H_6$ .<sup>\*</sup> Metallation at saturated carbon can also occur. Mechanistically, the reaction falls into none of the three most common types of aromatic substitution, and was termed protophilic substitution (nucleophilic attack on hydrogen being rate-determining) in view of the evidence from substituent effects,<sup>2</sup> and the demonstration of a kinetic hydrogen-isotope effect.<sup>3</sup> Similar isotope effects were later found by Gronowitz and Halvorsen for  $\alpha$ -metallation of thiophen by n-butyl-lithium:<sup>4</sup> Grignard reagents will not readily metallate aromatic rings, but their related metallation of acetylenes is subject to considerable hydrogen-isotope effects.<sup>5</sup> There seems no reason to doubt that nucleophilic attack on hydrogen is a kinetically important stage in these types of metallation.† (For reviews covering metallation see refs. 8—13.) Benkeser and Liston<sup>14</sup> confirmed the finding<sup>2</sup> that metallation of isopropylbenzene by n-pentylsodium leads

<sup>\*</sup> Replacement of atoms other than hydrogen (*e.g.*, halogen), and addition reactions, are excluded from this definition because of probable dissimilarities in mechanism.

† Mercuration, although formally analogous to alkali-metallation, undoubtedly operates by different mechanisms, which depend on the conditions.<sup>6</sup> Alkali-metallating reagents are, in general, strong nucleophiles. Metallation and base-catalysed hydrogen-isotope exchange are closely related. They differ mechanistically from acid-catalysed hydrogen-exchange which is known to involve electrophilic attack on the aromatic ring.<sup>7</sup>

<sup>1</sup> Part VI, Bryce-Smith, *J.*, 1956, 1603.

<sup>2</sup> Bryce-Smith, *J.*, 1954, 1079.

<sup>3</sup> Bryce-Smith, Gold, and Satchell, *J.*, 1954, 2743.

<sup>4</sup> Gronowitz and Halvorsen, *Arkiv Kemi*, 1955, **8**, 343.

<sup>5</sup> Dessy and Hollingworth, *J. Amer. Chem. Soc.*, 1957, **79**, 358.

<sup>6</sup> Klapproth and Westheimer, *J. Amer. Chem. Soc.*, 1950, **72**, 4461.

<sup>7</sup> Gold, Lambert, and Satchell, *J.*, 1960, 2461, and references therein.

<sup>8</sup> Gilman and Morton, *Org. Reactions*, 1954, **8**, 258.

<sup>9</sup> Benkeser, Foster, and Sauve, *Chem. Rev.*, 1957, **57**, 867.

<sup>10</sup> Shatenshtein, *Tetrahedron*, 1962, **18**, 95 (hydrogen-isotope exchange catalysed by potassamide).

<sup>11</sup> Hall, Piccolini, and Roberts, *J. Amer. Chem. Soc.*, 1955, **77**, 4540 (subject as ref. 10).

<sup>12</sup> Hart and Crocker, *J. Amer. Chem. Soc.*, 1960, **82**, 418 (hydrogen-isotope exchange catalysed by potassium).

<sup>13</sup> Streitwieser, van Sickle, and Reif, *J. Amer. Chem. Soc.*, p. 1513 (hydrogen-isotope exchange catalysed by lithium cyclohexylamide).

<sup>14</sup> Benkeser and Liston, *J. Amer. Chem. Soc.*, 1960, **82**, 3221.

principally to *meta*-substitution, although earlier results of Morton and his co-workers<sup>15</sup> appeared to show that this reaction gives a mixture of *o*- and *p*-sodioisopropylbenzene. These latter researches supported Morton's proposal<sup>16</sup> that alkali-metallation is an electrophilic substitution, giving an orientation comparable with that of electrophilic nitration (for observations on the theoretical and experimental basis of Morton's metallation mechanism see refs. 1—3, 9, 14, 17). Both the subsequent groups of investigators<sup>2,14</sup> concluded that Morton and his co-workers<sup>15</sup> had not recognised the *meta*-isomer as the major nuclear substitution product.\* An important but potentially confusing new factor was introduced by Benkeser and Liston's observation that the nuclear potassioisopropylbenzenes formed from isopropylbenzene by *n*-pentylpotassium tended in time to rearrange to the *l'*-isomer (*i.e.*, Ph·CMe<sub>2</sub>K) in the presence of isopropylbenzene:<sup>14</sup> analogous rearrangements of *o*-, *m*-, and *p*-sodioethylbenzene have recently been described,<sup>24</sup> and the rearrangement of *o*-, *m*-, and *p*-sodiotoluene to benzylsodium has long been known.<sup>25</sup> It might be inferred that the earlier values for isomer ratios and rate factors are liable to be suspect if appreciable rearrangement of the initial products had taken place before termination of the reactions by carboxylation. Some further results for the metallation of isopropylbenzene are now presented; they are considered to show that the present and previous<sup>2</sup> results are not significantly complicated by rearrangement in the conditions employed. The new results of determinations of isomer ratios and total (T.R.F) and total nuclear (T.N.R.F) rate factors for the metallation of isopropylbenzene are given in the Table. Some previously reported results, and also some of Benkeser and Liston's data,<sup>14</sup> are included for comparison.†

The following conclusions can be drawn. First, in the reactions with ethyl- and *n*-pentyl-sodium, little or no *l'*-substituted products are formed either by direct substitution or by rearrangement of nuclear isomers under the conditions employed (nos. 1—5). The proportions of nuclear isomers fall broadly within the ranges *ortho* 0—2, *meta* 50—55, *para* 42—46%. The measure of agreement between Benkeser and Liston's figures<sup>14</sup> (*e.g.*, no. 4) and those now reported is noteworthy in view of the different analytical procedures employed: Benkeser and Liston analysed the derived methyl esters by vapour-phase chromatography, whereas the present procedure has been a gravimetric one based on quantitative isolation of the derived acid after selective oxidation with alkaline permanganate, and oxidation by chromic acid of the isomeric nuclear isopropylbenzoic

\* In the light of this conclusion, Morton and Little's report<sup>18</sup> that metallation of isopropylbenzene by an *n*-pentylsodium-sodium isopropoxide complex, followed by carboxylation, gives a mixture containing 88.5% of *p*- and 11.5% of *o*-isopropylbenzoic acid should probably be viewed with reserve pending confirmation (*cf.* Morton and Ward<sup>19</sup>). In recent years Morton and his co-workers have advanced a "radical pair" hypothesis to explain metallation and related reactions on a homolytic basis.<sup>20</sup> It seems that the further hypothesis is intended to supplement in some way the earlier proposal that organoalkali-metal compounds function as electrophiles; but it may be noted that Morton and Cluff's supposed evidence for homolytic dissociation of *n*-pentylsodium<sup>21</sup> has been questioned,<sup>22</sup> and was recently withdrawn by Morton and Ward.<sup>23</sup> On the other hand, reactions between alkali-metal alkyls and alkyl halides have been shown to have a homolytic component.<sup>1</sup>

† Ethylmetal reagents have been generally used in this work in preference to the commonly employed corresponding *n*-pentyl derivatives because, as previously shown,<sup>17</sup> they cause much less dimetallation. Thus, ambiguities which might arise from the selective consumption of the monometallated isomers are largely avoided.

<sup>15</sup> Morton, Massengale, and Brown, *J. Amer. Chem. Soc.*, 1945, **67**, 1620; Morton and Cluff, Abs. 119th Meeting Amer. Chem. Soc., Boston, Mass., 1951, p. 11M.

<sup>16</sup> Morton, *Chem. Rev.*, 1944, **35**, 1; *J. Amer. Chem. Soc.*, 1947, **69**, 969.

<sup>17</sup> Bryce-Smith and Turner, *J.*, 1953, 861.

<sup>18</sup> Morton and Little, *J. Amer. Chem. Soc.*, 1949, **71**, 487.

<sup>19</sup> Morton and Ward, *J. Org. Chem.*, 1959, **24**, 1571.

<sup>20</sup> Morton and Lanpher, *J. Org. Chem.*, 1956, **21**, 93.

<sup>21</sup> Morton and Cluff, *J. Amer. Chem. Soc.*, 1953, **75**, 134.

<sup>22</sup> Bryce-Smith, *J.*, 1955, 1712.

<sup>23</sup> Morton and Ward, *J. Org. Chem.*, 1960, **25**, 120.

<sup>24</sup> Benkeser, Trevillyan, and Hooz, *J. Amer. Chem. Soc.*, 1962, **84**, 4971.

<sup>25</sup> (a) Bachmann and Clarke, *J. Amer. Chem. Soc.*, 1927, **49**, 2089; (b) Gilman and Pacevitz, *ibid.*, 1940, **62**, 673; (c) Gilman, Pacevitz, and Baine, *ibid.*, p. 1514.

## Metallation of isopropylbenzene: isomer ratios and rate factors.

No.	Reagent	Temp.	Ratios of isomers (%)				Partial rate factors					
			1'	<i>o</i>	<i>m</i>	<i>p</i>	T.R.F.†	T.N.R.F.†	$\alpha$	<i>o</i>	<i>m</i>	<i>p</i>
1	Ethylsodium	20°	1.8	0	54.6	43.6	—	—				
2	Ethylsodium	85	0	1.8	55.6	42.6	—	—				
3	Ethylsodium	20	0.2	0	54.4	45.4	0.24	0.24	0.003	0	0.39 (0.44)	0.65 <sub>s</sub> (0.55)
4	n-Pentylsodium	" room temp "	2.6	0	55.6	41.8	—	—				
5	n-Pentylsodium	20	1.0	3.0	49.5	46.5	—	—				
6	Ethyl-lithium- potassium	20	13.0	9.0	48.5	29.5	0.28	0.245	0.22	0.08	0.41	0.49 <sub>s</sub>
7	Ethyl-lithium- potassium	85	19.0	11.5	44.5	25.0	0.28	0.23	0.32	0.10	0.38	0.43
8	Ethyl-potassium	20	45	7	23	25	—	—				

† See text.

Nos. 1 and 2: Direct reaction of diethylmercury with sodium in isopropylbenzene. No. 3: Ethylsodium prepared from diethylmercury in heptane before addition of isopropylbenzene. No. 4: Data from ref. 14. Nos. 5 and 7 and isomer ratios from no. 6: From ref. 2. Nos. 6 and 7: Direct reaction of ethyl-lithium with potassium in isopropylbenzene. No. 8: Direct reaction of diethylmercury with potassium in isopropylbenzene during 10 hr. at 20°; the mixture was evidently undergoing rearrangement (cf. ref. 14). Values in the last two columns in parentheses are based on the isomer ratios measured in the competition experiment which differed slightly from those found in the absence of benzene, apparently because of secondary metallation of benzene; no such difference was found in the corresponding metallations by ethyl-lithium-potassium (Nos. 6 and 7).

acids to phthalic acids which were then separated through the dithallic salts.<sup>2,26</sup> The virtual absence of products derived from *ortho*-sodium-metallation is a surprising feature, and obviously not explicable on the basis of rearrangement to the 1'-isomer. According to a previous discussion<sup>2</sup> of the effect of alkyl groups on nuclear metallation, the proportion of *ortho*-isomers would be expected to be smaller than that of *meta*- and *para*-isomers, but finite: this is in fact the case in some circumstances (nos. 6 and 7). It is possible that *o*-sodioisopropylbenzene is thermally unstable, for attempts to obtain it directly from *o*-bromoisopropylbenzene and sodium in conditions normally suited to such preparations gave no organosodium product. Be that as it may, the general substitution pattern is more selective with ethylsodium than with ethyl-lithium-potassium, and suggests that ethyl carbanions are more fully developed in the latter reagent.

Comparison of nos. 1 and 2 in the Table shows that the ratios of isomers in the metallation by ethylsodium at 20° are very similar to those at 85°. The small difference in the proportions of 1'-metallated products is believed to be real, for the procedure for isolating pure  $\alpha$ -methyl- $\alpha$ -phenylpropionic acid from the mixture of isomeric carboxylation products was carefully standardised and was effective even when the proportion was only 0.2% (as in no. 3 of the Table): reproducibility of the analyses was good (see Experimental section).

Comparison of nos. 1 and 3 in the Table shows that the result is essentially the same when ethylsodium is formed *in situ* (the Schorigin reaction<sup>27</sup>) as when it is prepared separately in an inert medium (heptane) and treated subsequently with isopropylbenzene. It is interesting that a little 2,3-dimethyl-2,3-diphenylbutane was isolated after two of the present Schorigin-type reactions (Table, nos. 2 and 8) although none of this compound was obtained at 20° in either the one- or the two-step reaction with sodium (nos. 1 and 3) or in the reactions which involved the ethyl-lithium-potassium reagent (nos. 6 and 7, and ref. 2), despite a careful search. The formation of this hydrocarbon in such reactions implies the production of a small proportion of free radicals, presumably ethyl radicals, which with isopropylbenzene would give  $\alpha\alpha$ -dimethylbenzyl radicals: the dimerisation

<sup>26</sup> Bryce-Smith, *Chem. and Ind.*, 1953, 244.<sup>27</sup> Schorigin, *Ber.*, 1910, **43**, 1938.

of these to give 2,3-dimethyl-2,3-diphenylbutane is well known.\* The reaction of diethylmercury with sodium seems likely to follow the course  $\text{Et}_2\text{Hg} + 2\text{Na} \longrightarrow \text{EtNa} + \text{EtHgNa} \xrightarrow{\text{Na} (?)}$   $\text{EtNa} + \text{Hg}/\text{Na}$ . In view of the ready homolysis of carbon-mercury bonds, free ethyl radicals might be formed by a side reaction  $\text{EtHgNa} \longrightarrow \text{Et}\cdot + \text{Hg}/\text{Na}$ .† That the Schorigin procedure<sup>27</sup> (Table. no. 1) appeared to give no 2,3-dimethyl-2,3-diphenylbutane but gave more 1'-metallated product than the comparable two-stage reaction (no. 3) could be attributed to the reaction  $\text{PhMe}_2\text{C}\cdot + \text{Na} \longrightarrow \text{PhMe}_2\text{CNa}$ . However, the extent of such a reaction was evidently very small, and dimerisation of the  $\alpha\alpha$ -dimethylbenzyl radicals seems to be preferred at 85°.

The total rate factor of 0.24 for metallation of isopropylbenzene by ethylsodium (no. 3) is virtually the same as for metallation by ethyl-lithium-potassium (nos. 6 and 7). In conjunction with the partial rate factors, these results show the behaviour of the isopropyl group as a deactivating substituent in sodium-metallation, in accord with previous results obtained with related systems.<sup>2</sup>

Experiments 6 and 7 in the Table involved treating a solution of ethyl-lithium in isopropylbenzene with potassium.‡ The reagents involved were earlier<sup>17</sup> shown to be complexes of the type  $(\text{RLi})_x(\text{RK})_y$ . Little emphasis was given to the possible influence of the lithium component on the chemical reactivity,<sup>2</sup> as has been pointed out by Morton and Lanpher.<sup>28</sup> Further work has shown that the general reactivity of these complexes is intermediate between that of the corresponding separate potassium and lithium compounds. Potassium has now been found to react with up to two equivalents of phenyl-lithium in toluene, to give the apparently insoluble complex  $\text{C}_6\text{H}_5\text{Li}, \text{C}_6\text{H}_5\text{K}$ , probably highly associated (exact reproducibility has been difficult, and products have sometimes contained less lithium than is required by this formula). All these complexes, and those related ones prepared by reaction of benzene with a mixture of ethyl-lithium and potassium, are approximately as reactive to toluene (giving the benzyl-metal derivative) or chlorobenzene (giving biphenyl and a complex mixture of hydrocarbons, possibly through "benzyne") as is phenylsodium,<sup>29</sup> and much less reactive than phenylpotassium prepared from potassium and diphenylmercury or *in situ* from potassium and chlorobenzene.<sup>25c</sup> Thus, the phenyl-lithium-potassium complex may even be prepared in toluene from phenyl-lithium and potassium at 20° without attack on the solvent, whereas chlorobenzene reacts with potassium in toluene at 20° to give benzylpotassium free from phenylpotassium.

These observations assist understanding of the fact, noted by Benkeser and Liston,<sup>14</sup> that, whereas nuclear isomeric potassioisopropylbenzenes (the initial products of metallation of isopropylbenzene by n-pentylpotassium) rearrange to the 1'-isomer when stirred with isopropylbenzene for 20 hours at room temperature, the corresponding materials formed by use of the alkyl-lithium-potassium reagent rearrange very little, if at all (see the Table and ref. 2). It appears that complex-formation with an organolithium compound stabilises the nuclear isomers against rearrangement. The complex from *p*-tolyl-lithium and potassium in benzene has already<sup>2</sup> been shown not to rearrange to the benzyl derivative. It has now been confirmed that reaction of di-*p*-tolylmercury with potassium, followed by carboxylation, gives phenylacetic acid free from *p*-toluic acid (cf. ref. 25c).

\* Photolysis of a solution of tetraethyl-lead in isopropylbenzene gave 2,3-dimethyl-2,3-diphenylbutane (39%), together with ethane (51%) and traces of ethylene and butane.

† There is some cause to suspect that the corresponding reactions with potassium can stop at the stage  $\text{R}_2\text{Hg} + 2\text{K} \longrightarrow \text{RK} + \text{RHgK}$ . Carboxylation of the products of several reactions of diphenylmercury and potassium gave only *ca.* 50% of the phenyl groups as benzoic acid, and only traces of other materials less volatile than benzene were found.

‡ Ethyl-lithium alone is insufficiently reactive to metallate isopropylbenzene at an appreciable rate, although at 95° a slow reaction was detected and carboxylation gave a trace of mixed acids including  $\alpha$ -methyl- $\alpha$ -phenylpropionic acid and isopropylbenzoic acids: accurate analysis of the mixture has not yet proved feasible.

<sup>28</sup> Morton and Lanpher, *J. Org. Chem.*, 1958, **23**, 1636.

<sup>29</sup> Bryce-Smith and Turner, *J.*, 1950, 1975, and references therein.

The most obvious explanation of this is that *p*-tolylpotassium, formed initially, rearranges to benzylpotassium; but there is no proof of the intermediate formation of *p*-tolylpotassium and the reaction appears to be somewhat more complex than is normally considered, for an unidentified mercury-containing acid, of the probable empirical formula  $C_8H_8HgO_2$ , was obtained as a by-product, evidently from an organometallic precursor containing mercury and potassium (cf. an earlier footnote referring to the possible existence of PhHgK).

The diminished reactivity of organopotassium compounds when present as complexes with organolithium compounds\* seems to provide an example of a more general phenomenon: namely, that organometallic compounds having a tendency to associate have also a tendency to form "mixed" associated complexes with compounds of the same or other metals, the chemical properties of which are not those to be expected of a mixture of the components but tend rather to be as of an intermediate individual type. Thus the present alkyl-lithium-potassium complexes resemble chemically the corresponding organosodium compounds. Their reactivity does not seem to depend critically on the precise lithium : potassium ratio, although some dependence is to be expected on general grounds. Other apparent instances of the phenomenon are the discovery by Wittig *et al.*<sup>30</sup> that phenylsodium does not cleave diethyl ether in the presence of small proportions of phenyl-lithium, Morton's "associated salts" phenomena (references in ref. 28). Kollonitsch's report<sup>31</sup> that the chemical properties of dialkylcadmium compounds are strongly influenced by the presence of, *e.g.*, magnesium halides, and Blues and Bryce-Smith's observation<sup>32</sup> that stable alcoholic solutions containing methylmagnesium iodide can be prepared in the presence of certain light-metal alkoxides.

*Comparison of Homogeneous and Heterogeneous Systems.*—The reaction systems employed in the metallation of hydrocarbons by alkyl-sodium and -potassium compounds are heterogeneous, for no solvents are known which resist attack by these reagents. A quantitative approach to metallation might be of uncertain value if the reactions occur at the surface of the solid phase, as there would be difficulty in establishing whether all positions in the hydrocarbon substrate have equal access to the active surface sites.† At one time, the widely varying isomer ratios reported by different workers for the metallation of isopropylbenzene appeared to support such a view (cf. ref. 28). The present results, which apply to conditions where rearrangement is negligible, are essentially independent of the procedures used to prepare the reagents and are internally consistent (see Table). Where comparison is appropriate they agree with Benkeser and Liston's results<sup>14</sup> obtained with somewhat different systems. This consistency would not be expected if the orientation were dependent on the physical nature of the surface of an insoluble reagent or, as has been suggested,<sup>14</sup> on the rate of stirring of the reaction mixtures. A study of the metallation of ethylbenzene has recently led Benkeser *et al.*<sup>24</sup> to a similar conclusion, namely, that the observed *meta-para*-substitution occurs in kinetically-controlled steps which are independent of the mode of preparation of the metallating agents. The present substitution pattern broadly resembles that found by Hall, Piccolini, and Roberts<sup>11</sup> for some potassamide-catalysed hydrogen-isotope exchange reactions carried out under homogeneous conditions in liquid ammonia. It becomes, in fact, increasingly evident that heterogeneity plays little or no part in determining isomer

\* Likewise, the reactivity of phenyl-lithium is enhanced by complexing with phenylpotassium. In illustration, a phenyl-lithium-potassium complex was found to metallate toluene at 105°, and carboxylation gave phenylacetic acid *free from benzoic acid*. Under the same conditions, uncomplexed phenyl-lithium did not react with toluene, and carboxylation gave benzoic acid free from phenylacetic acid.

† Similar uncertainty could in principle apply to metallation by bulky associated aggregates of organolithium compounds in solution. Stereospecific polymerisation catalysed by organolithium compounds in solution may be a pseudo-homogeneous process.

<sup>30</sup> Wittig, Ludwig, and Polster, *Chem. Ber.*, 1955, **88**, 294.

<sup>31</sup> Kollonitsch, *Nature*, 1960, **188**, 140.

<sup>32</sup> Blues and Bryce-Smith, *Chem. and Ind.*, 1960, 1533.

ratios in the metallation of alkylbenzenes by alkyl-sodium and -potassium compounds.\* Indeed, certain observations suggest that these reactions may occur in homogeneous solution, notwithstanding the apparent heterogeneity of the systems. Thus, Morton *et al.* found that the reactivity of alkylsodiums in metallation decreases markedly with decreasing chain length of the alkyl group. For example, *n*-propylsodium was virtually inert to toluene in conditions where *n*-butylsodium readily afforded benzylsodium.<sup>33</sup> Although this effect could in principle be due to differing surface areas, it parallels the decrease in microsolubility to be expected for these reagents and is not accompanied by appreciable orientation effects (see nos. 1 and 3—5 in the Table); no comparable effect has been reported for the freely soluble ethyl- and higher alkyl-lithium compounds (although irregular and solvent-dependent variations in reactivity sometimes occur<sup>34</sup>). It seems to require a physical rather than a chemical explanation. Further, the partial rate factors found by Shatenstein<sup>10</sup> for protophilic nuclear deuterium-protium exchange in deuterated toluene under homogeneous conditions ( $f_o$  0.2;  $f_m$  0.4;  $f_p$  0.4) can be correlated well with those for the apparently heterogeneous metallation of isopropylbenzene given in our Table. The orientation in each case seems to be governed mainly by the inductive effects of the substituents, as has been earlier proposed.<sup>2,11,35</sup> Finally, the study by Williams, Laakso, and Dalmage<sup>36</sup> of the polymerisation of styrene by triphenylmethylpotassium led them to suggest that this apparently insoluble reagent reacts homogeneously in benzene and heterogeneously in hexane.<sup>36</sup>

It can be concluded at the present stage that the results of metallation in non-isomerising conditions are comparable with those of homogeneous base-catalysed hydrogen-isotope exchange. The effect of heterogeneity in aromatic metallation may be more apparent than real, and in no case is there evidence that it significantly influences the isomer ratios or rate factors.

#### EXPERIMENTAL

The general procedure and analytical techniques were similar to those described in Parts II<sup>16</sup> and III.<sup>2</sup> A thermostat-bath at  $20^\circ \pm 0.01^\circ$  was used except where otherwise indicated. Reactions were carried out under dry nitrogen.

*Metallation of Isopropylbenzene by Ethylsodium.*—(a) *Two-stage procedure at 20°.* Ethylsodium was prepared from diethylmercury (10 g., 0.0385 mole) and sodium wire (3.0 g., 0.13 g.-atom) in *n*-pentane (50 ml.). Pentane was removed at 20—25° under reduced pressure of nitrogen. The residue was stirred with isopropylbenzene (60 ml.) at 20° for 7 days, and the product was carboxylated with solid carbon dioxide. Duplicate analysis of the resulting mixture of isopropylbenzoic acids (8.8 g., 70%) showed: *ortho*, nil, 0.05; *meta*, 54.2, 54.7; *para*, 45.6, 45.1; and  $\alpha$ -methyl- $\alpha$ -phenylpropionic acid, 0.2, 0.15%. The last-mentioned acid was isolated, and had m. p. and mixed m. p. 78°. No dicarboxylic acid was found, and no 2,3-dimethyl-2,3-diphenylbutane.

(b) *One-stage procedure at 20°.* Diethylmercury (10 g., 0.0385 mole) was added to sodium wire (3.0 g., 0.13 g.-atom) in isopropylbenzene (60 ml.) in 1 hr. with stirring at 20°. Slight cooling was necessary. The black product was stirred at 20° for 7 days. Carboxylation gave monocarboxylic acids, b. p. 142—144°/4 mm. (7.0 g., 55%), and no dicarboxylic acids. The isomeric composition was: 1', 1.8; *ortho*, nil; *meta*, 54.4, 54.9; *para*, 43.9, 43.4%. No 2,3-dimethyl-2,3-diphenylbutane was found. Gilman *et al.*<sup>25c</sup> reported a red product and 41% of 1'-substitution from a reaction of this type, but did not state the reaction temperature.

(c) *One-stage procedure at 85°.* A solution of diethylmercury (10 g., 0.0385 mole) in isopropylbenzene (10 ml.) was added in 1 hr. with stirring to sodium wire (3.0 g., 0.13 g.-atom) in

\* This statement is almost certainly not applicable to dimetallation, for reasons discussed in ref. 17.

<sup>33</sup> Morton, Richardson, and Hollowell, *J. Amer. Chem. Soc.*, 1941, **63**, 327.

<sup>34</sup> Gilman, Moore, and Baine, *J. Amer. Chem. Soc.*, 1941, **63**, 2479.

<sup>35</sup> Roberts and Curtin, *J. Amer. Chem. Soc.*, 1946, **68**, 1658.

<sup>36</sup> Williams, Laakso, and Dulmage, *J. Org. Chem.*, 1958, **23**, 638.

isopropylbenzene (50 ml.) at 85°, and the mixture was stirred at this temperature for a further 30 min. Carboxylation of the chocolate-coloured product gave a mixture of monocarboxylic acids (5.0 g., 40%) and no dicarboxylic acids. The isomeric composition was: 1'-, nil; *ortho*, 1.8; *meta*, 55.4, 55.9; *para*, 42.8, 42.4%. 2,3-Dimethyl-2,3-diphenylbutane (0.05 g.), m. p. and mixed m. p. 117°, was isolated from the neutral products.

*Competitive Metallation of Benzene and Isopropylbenzene by Ethylsodium.*—Ethylsodium was prepared as in experiment (a) above, and after removal of pentane, a mixture of isopropylbenzene (60.0 g., 0.5 mole) and benzene (39.0 g., 0.5 mole) was added. Evolution of ethane ceased after 5 days' stirring at 20°, and the product was carboxylated after a total reaction period of 7 days. The monocarboxylic acids were separated as a solution in light petroleum (950 ml.; b. p. 40—60°) from phthalic (0.26 g.) and isopropylphthalic acids (0.025 g.). The ratio of acids from benzene and isopropylbenzene was determined by the oxidation procedure described in Part III.<sup>2</sup> Three determinations of  $F_{\text{PhH}}^{\text{PhPr}}$  gave the values 0.23, 0.245, and 0.255 after correction for the slight dimetallation. Measurement of acid equivalent gave values 0.22 and 0.25. A mean value of 0.24 has been used in the calculation of partial rate factors. Values of the ratios of *m*- to *p*-isopropylbenzoic acid in the mixture were 1.58, 1.55, and 1.71 (mean 1.61). These were appreciably different from the value 1.19 found in the non-competitive experiment (a) above. The reason for this is not wholly clear, but some metallation of benzene by *p*-sodioisopropylbenzene may be assumed. The discrepancy is absent in the metallation of isopropylbenzene by ethyl-lithium-potassium.

*Metallation of Isopropylbenzene by Ethylpotassium (from Diethylmercury) at 20°.*—Diethylmercury (5.2 g., 0.02 mole) was stirred with a dispersion of potassium (2.75 g., 0.07 g.-atom) in isopropylbenzene (50 ml.) at 20° for 10 hr., by which time evolution of ethane had almost ceased. Carboxylation of the black product gave monocarboxylic acids (2.7 g., 42%) and less than 0.1 g. of crude isopropylphthalic acids. The isomeric composition was 1'-, 45; *ortho*, 7; *meta*, 23; *para*, 25%. 2,3-Dimethyl-2,3-diphenylbutane (0.036 g.), m. p. and mixed m. p. 117—118° was also isolated.

*Competitive Metallation of Benzene and Isopropylbenzene by Ethyl-lithium-Potassium at 20°.*—A solution of ethyl-lithium (0.19 mole) in a mixture of benzene (46.8 g., 0.6 mole) and isopropylbenzene (72.0 g., 0.6 mole) was stirred with an alloy of potassium (14.8 g., 0.38 g.-atom) and sodium (3 g.) at 20° for 7 days, by which time evolution of ethane had ceased. Carboxylation gave acids which were not isolated but were used as a colourless solution in light petroleum (890 ml.; b. p. 40°). Phthalic acids (0.37 g., mainly the 1,3- and 1,4-acid) and isopropylphthalic acids (0.1 g.) were also obtained. Oxidation by chromium trioxide gave  $F_{\text{PhH}}^{\text{PhPr}} = 0.28, 0.285$  in duplicate runs. The figure 0.28 has been used in calculation of partial rate factors. Determination of the ratio *m*- to *p*-isopropylbenzoic acid 1.67, 1.66 which agreed well with the value 1.64 calculated from the isomer ratios in a previous non-competitive experiment.<sup>2</sup> As in the similar experiment at 85°,<sup>2</sup> the orientation in the metallation of isopropylbenzene was virtually unaffected by the presence of benzene (contrast ethylsodium above).

*Attempted Metallation of Biphenyl.*—Addition of potassium to a solution of ethyl-lithium in a pentane-biphenyl mixture at 60° led to almost immediate formation of a bulky blue solid, but no ethane was evolved. It was subsequently found that most samples of potassium or sodium-potassium alloy rapidly reacted with biphenyl, evidently by addition, in benzene or pentane solution even at room temperature. Sodium reacted at *ca.* 250°. No substitutive metallation was detected. One sample of potassium (from British Drug Houses) could not be made to add to biphenyl: the success of the addition may depend on the presence or absence of some impurity, as is the case with certain reactions of lithium<sup>37</sup> and calcium.<sup>38</sup>

*Formation of Phenyl-lithium-Potassium Complexes.*—An ethereal solution of phenyl-lithium was prepared from bromobenzene (16 g.), lithium wire (1.5 g.), and ether (75 ml.). After removal of ether, the solid residue was heated at 60—65° under reduced pressure of nitrogen for 30 min. Toluene was then added to give a 0.965N-solution. Control experiments showed that this solution was unchanged after 1½ hr. at 65°; and although a brown solid separated at

<sup>37</sup> West and Glaze, *J. Org. Chem.*, 1961, **26**, 2096, and references therein.

<sup>38</sup> Bryce-Smith and Skinner, *J.*, 1963, 577.

105° during 1½ hr. no metallation of the solvent toluene occurred, as judged by carboxylation to benzoic acid free from phenylacetic acid.

25 Ml. (0.0245 mole) of the solution of phenyl-lithium in toluene was stirred with potassium (0.409 g., 0.0105 g.-atom) for 2½ hr. at 65°. Titration of hydrolysed aliquot parts of the supernatant liquid showed that 0.0208 mole of phenyl-lithium had been consumed, *i.e.*, converted into insoluble material. No further reaction occurred during 1 hr. more at 65°. The reactant ratio  $C_6H_5Li : K = 1.98$ . This closely corresponds to formation of the complex  $C_6H_5Li \cdot C_6H_5K$ ,

Two attempts at duplication of this experiment led to reactant ratios  $C_6H_5Li : K = 1.38$  and 1.59. It is possible that the ratio is sensitive to variation in the overall rates of reaction which could result from almost unavoidable variations in the degree of dispersion of liquid potassium. Carboxylation of each of the three complexes gave benzoic acid free from phenylacetic acid.

Attempts to prepare analogous complexes of the unknown 1-naphthylpotassium were not successful, apparently owing to the thermal instability of the products. 1-Naphthyl-lithium itself is evidently less stable than phenyl-lithium, and had completely decomposed after 1 hr. at 70°.

*Metallation of Toluene by Phenyl-lithium-Potassium.*—As indicated above, these complexes showed no tendency to metallate toluene at 65°, even when formed *in situ*; but the following two experiments indicated fairly rapid formation of a benzyl-lithium-potassium complex in toluene at 105°.

(i) 20 Ml. of a 1.0N-solution of phenyl-lithium in toluene was stirred for 36 hr. at room temperature with an alloy of potassium (1.55 g.) and sodium (0.4 g.). Carboxylation of a small portion of the dark brown product gave benzoic acid free from phenylacetic acid. The main part was heated at 105–110° with stirring for 1½ hr. and then carboxylated. The crude product was heated under reflux for 1 hr. with concentrated hydrochloric acid in order to decarboxylate any phenylmalonic acid, and the cooled solution deposited crystals of phenylacetic acid, m. p. 73° (4-bromophenacyl ester, m. p. and mixed m. p. 89°). Little or no benzoic acid was formed.

(ii) 45 Ml. of a 1.04N-solution of phenyl-lithium in toluene was stirred with potassium (2.75 g.) at 105° for 45 min. Carboxylation, etc., as in (i) gave phenylacetic acid free from benzoic acid.

*Metallation of Toluene by Phenylpotassium Prepared from Diphenylmercury.*—A solution of diphenylmercury (9.0 g., 0.025 mole) in toluene (50 ml.) was shaken with dispersed potassium (3.9 g., 0.1 g.-atom) at room temperature in an evacuated flask for 20 hr. The temperature was kept below 30°. Carboxylation gave an acidic product, m. p. 50–52° (2 g.), and repeated recrystallisation of this from water gave phenylacetic acid, m. p. 74–75° and mixed m. p. 75–76°. No benzoic acid was isolated, but may have been formed in small amount.

In a similar experiment, the mixture was stirred for 8 hr. but was then set aside for a further 12 hr. Carboxylation gave benzoic (2 g.) and phenylacetic acid (*ca.* 0.1 g.).

*Stability of Phenyl-lithium-Potassium towards Chlorobenzene.*—50 Ml. (0.053 mole) of a 1.06N-solution of phenyl-lithium in toluene was stirred with a dispersion of potassium (1.35 g., 0.035 g.-atom) in toluene (10 ml.) for 105 min. at 65°. These conditions were chosen to ensure that no free potassium should remain. 10 Ml. of the supernatant liquid gave, after hydrolysis, a titre of 9.0 ml. of 0.02N-hydrochloric acid. This is consistent with formation of a complex  $(C_6H_5K)_5 \cdot C_6H_5Li$ . Chlorobenzene (4.5 g., 0.04 mole) was then added at 65°. No reaction occurred during 15 min. at 65°.

*Reaction between Chlorobenzene and Potassium in Benzene.*—Chlorobenzene (4.5 g.) was added in 1 hr. at 30–35° to a stirred dispersion of potassium (3.9 g.) in benzene. Reaction commenced readily, and the final product was black. Carboxylation gave no benzoic acid or other acidic product. Biphenyl (1.1 g., 36%) was obtained, together with high-boiling tar. In corresponding conditions, sodium gives phenylsodium in high yield.

*Reaction of Di-*p*-tolylmercury with Potassium* (cf. ref. 25c).—Di-*p*-tolylmercury (3.83 g., 0.01 mole) was stirred with a dispersion of potassium (1.95 g., 0.05 g.-atom) in benzene (30 ml.) at room temperature (*ca.* 20°). A dark brown solid separated but there was no noticeable evolution of heat until the reaction had been continuing for 23 hr., whereupon the reaction temperature spontaneously rose to *ca.* 50° (the cause of this is unknown). The mixture was stirred at *ca.* 20° for a further 4 hr. Carboxylation gave phenylacetic acid (0.4 g., 15%), m. p. and mixed m. p. 76°, but no trace of *p*-toluic acid. There was also obtained a colourless,



unidentified acid (0.55 g.), almost insoluble in boiling water, which sublimed above 300° without melting (Found: C, 26.6; H, 2.0%). This acid gave mercury when heated with sodium carbonate.

The stability of a *p*-tolyl-lithium-potassium complex towards rearrangement has been described in Part III.<sup>2</sup>

CHEMISTRY DEPARTMENT, THE UNIVERSITY,  
READING, BERKS.

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