U.D.C. 547.223

# The Ullmann Reaction

M.Goshaev, O.S.Otroshchenko, and A.S.Sadykov

The review describes data obtained in recent years on the synthesis of biaryls by treating aryl halides with powdered copper at an elevated temperature (the Ullmann reaction). The conditions governing the reaction, the limits of its applications at the present time, and its mechanism are discussed.
The bibliography includes 200 references.

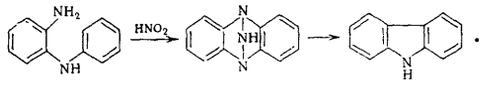
CONTENTS

1. Introduction 1046
2. Reaction conditions 1046
3. Reaction mechanism 1051

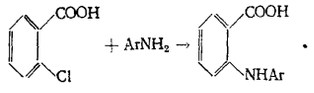
## I. INTRODUCTION

There are three reactions associated with Ullmann's name[1].

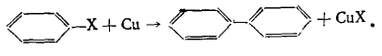
1. The Graebe–Ullmann synthesis of carbazole[2]:



2. The Ullmann condensation[3,4] which consists of the interaction of *o*-chlorobenzoic acid with phenols, thiophenols, arenesulphonic acids, and aromatic amines in the presence of catalytic amounts of copper with formation of diarylamines:



3. The Ullmann synthesis[5,6] of biaryls by the reaction of aryl halides with powdered copper at an elevated temperature:

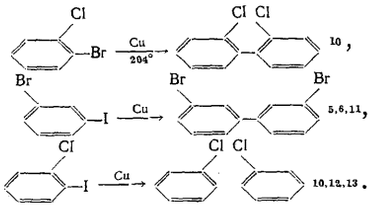


The last reaction is widely employed in organic chemistry and the number of studies dealing with it is continuously increasing. This review describes data for this reaction obtained from 1963, after the publication of Fanta's reviews[7,8], until 1971. The present limits of the applications of the Ullmann reaction (see, for example Nilsson[9]), the conditions governing its occurrence, and its mechanism are discussed.

## 2. REACTION CONDITIONS

### a. Synthesis of Symmetrical Biaryls

Depending on the nature of the halogen atom, aromatic halides behave differently under the conditions of the Ullmann reaction. The reactivity of the halides increases in the series Cl < Br < I. Aromatic fluoro-compounds do not enter into this reaction at all[10]:



In halogenonitrobenzenes, the activating effect of the nitro-group increases in the series $m < p < o$.[8,14]

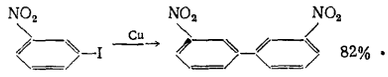
**Table 1.** Dependence of the yield of biaryls on the halogen and on the position of the nitro-group in the initial halogenonitrobenzene.

| Halogen | Yield of dinitrobiphenyl, % | | |
|---|---|---|---|
| | *ortho-* | *para-* | *meta-* |
| I | 65 | 54 | 36 |
| Br | 64 | 36 | 15 |
| Cl | 40 | 0 | 0 |

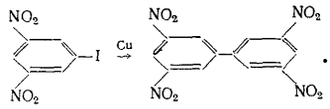
A defect of the results listed in Table 1 is that all the experiments carried out to establish the reactivity of the halogeno-derivatives were performed under severe conditions. To obtain valid data, experiments at a lower temperature using solvents are necessary. At any rate, in the synthesis of asymmetric biaryls exceptions from the rule formulated above are encountered[8]. Moreover, 2-iodopyridine is less reactive in the Ullmann reaction than 2-bromopyridine[15]. This problem will be discussed in greater detail in connection with the mechanism of the Ullmann reaction.

Highly electronegative groups such as the nitro-, carboxy-, and other groups have an activating effect when they are in the *ortho*-position relative to the halogen atom.

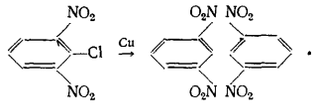
For the nitro-group, this effect decreases in the series $o > p > m$. For example, *o*-iodonitrobenzene is most reactive in the Ullmann reaction, while the *p*- and *m*-isomers are less reactive [16,17]. It has been found recently [11] that *m*-iodonitrobenzene forms under these conditions 3,3′-dinitrobiphenyl in 82% yield:



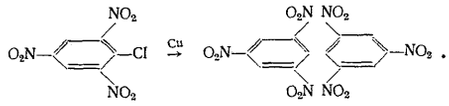
However, the presence of a further nitro-group in the *m*-position relative to the halogen greatly hinders the formation of the biaryl. Thus the yield of 3,3′,5,5′-tetranitrobiphenyl from 1-iodo-3,5-dinitrobenzene is only 15%:[18]



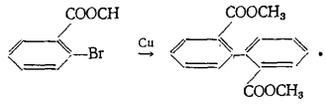
The nitro-group in the *o*-position relative to chlorine in the aromatic ring strongly activates it in this reaction; the yield of 2,2′-dinitrobiphenyl from *o*-chloronitrobenzene is 66%;[19–24] chlorobenzene is less reactive [8]. The introduction of a second nitro-group in the *o*-position relative to the halogen atom in *o*-chloronitrobenzene also reduces the yield of the biaryl; the yield of 2,2′,6,6′-tetranitrobiphenyl from 1-chloro-2,6-dinitrobenzene is 61%:[25,26]



On the other hand, the yield of the biaryl from picryl chloride is 55–58%:[19,27–29]

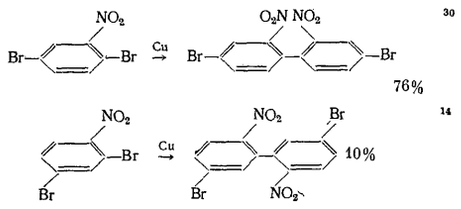


The effect of the alkoxy carbonyl group is approximately the same. Thus methyl *o*-bromobenzoate gives rise to 2,2′-dimethoxycarbonylbiphenyl in 80% yield [14]:



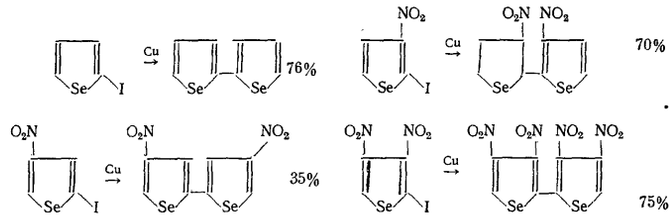
On the other hand, 3,3′- and 4,4′-dimethoxycarbonylbiphenyls are obtained from *m*- and *p*-iodobenzoate esters in yields of only 15 and 25% respectively [14].

The higher reactivity of the halogen in the *o*-position relative to the nitro-group compared with those in the *m*- and *p*-positions can be illustrated by the following examples:

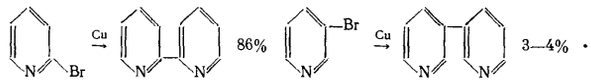


The phenyl substituent in the *p*-position relative to the halogen atom has a highly activating effect, while the same substituent in the *o*- and *m*-positions hinders the reaction. Thus, in the presence of copper at 225–260°C, *p*-, *o*-, and *m*-iodobiphenyls give rise to isomeric terphenyls in yields of 97, 50, and 16% respectively [31].

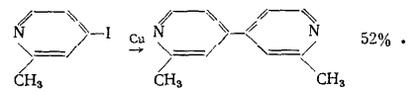
Interesting results were obtained for isomeric 2-iodoselenoles [32]:



An effect similar to that of the nitro-group is also shown by the nitrogen atom in the pyridine ring. It activates the halogen atom in the 2-position, as shown by the formation of 2,2′-bipyridyl from 2-bromopyridine (yield 87%).[33,34] 3-Halogenopyridines enter into this reaction with greater difficulty [35–37]:



A halogen in the 4-position of the pyridine ring is somewhat more reactive than in the 3-position [38]:

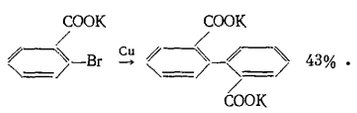


On the basis of literature data, Fanta [7] predicted that electropositive groups should deactivate the halogen in the Ullmann reaction. However, this hypothesis was disproved by later studies (see Table 2c in Ref. 8), in particular the work of Forrest [14].

The activating effect of the substituent depends both on its nature and its position relative to the halogen atom involved in the reaction.

A decrease of the yield of the biaryl is usually observed when the aromatic ring contains groups such as $NH_2$, $NHCOCH_3$, $NHCH_3$, $SO_2NH_2$, $SO_2NHC_6H_5$, COOH, and OH.[6,39] To obtain the required yields of products, the influence of the amino-group must be weakened by acylation and that of the hydroxy- and carboxy-groups by esterification (see Table 2c in Ref. 8).

Although *o*-bromobenzoic acid reacts with copper at 160°C with formation of copper benzoate and copper(I) bromide only, when the Ullmann reaction is performed with the potassium salt of this acid, it is possible to obtain a 43% yield of biphenyl-2,2′-dicarboxylic acid [40]:

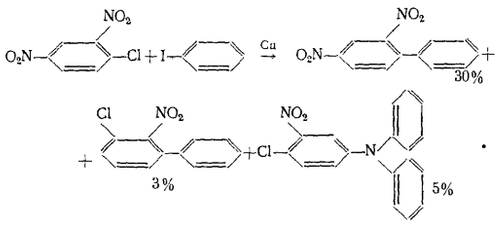


The methyl ester of this acid gives rise to the dimethyl ester of biphenyl-2,2′-dicarboxylic acid in 82% yield [6].

The yield of biaryls from aromatic compounds containing 2 or more halogen atoms is always lower than the yield from monohalogeno-derivatives [7,8].

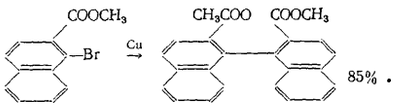
Certain halogenonitrobenzenes undergo side reactions, namely the reduction of the nitro-group. Thus when

1-chloro-2,4-dinitrobenzene reacts with iodobenzene, the following products are formed[14]:

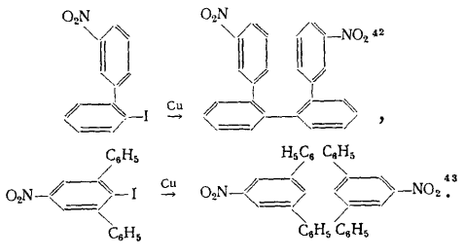


Steric factors have a definite influence on the course of the Ullmann reaction. Bulky substituents such as the nitro-, alkyl-, halogeno-, alkoxy-, and carboxy-groups do not hinder the Ullmann reaction. This is confirmed by the high yield of biaryls from 2,6-disubstituted halogenobenzene (Table 3, see also Table IIc in Ref. 8).

On the other hand, 1-bromo-2-methylnaphthalene[41] is completely inert, which is probably not caused solely by the steric influence of the methyl group. Alkyl and other electropositive groups in any position relative to the halogen atom in the naphthalene ring are known to deactivate the halogen, while electronegative (electrophilic) groups ($NO_2$, COOR) activate it[41]. This is also confirmed by the high yield of the dimethyl ester of 1,1′-binaphthyl-2,2′-dicarboxylic acid from the methyl ester of 1-bromo-2-naphthoic acid[41]:



Steric hindrance becomes appreciable when substituents such as the phenyl and naphthyl groups are introduced in the 2,6-positions relative to the halogen atom in the benzene ring:

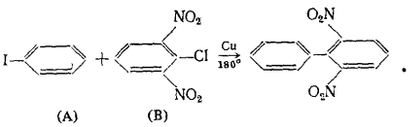


The yields of biaryls in such cases are very low.

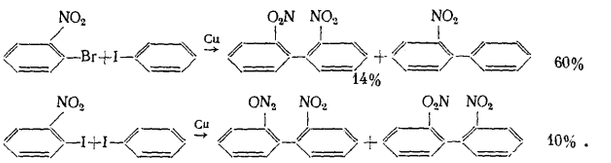
b. Synthesis of Asymmetric Biaryls

Examples of the use of the Ullmann reaction for the synthesis of symmetrical biaryls were described above (Table 4 on p. 1053; see also Table IIc in Ref. 8 and Table 1c in Ref. 7). At the same time, the reaction has been successfully used also for the synthesis of asymmetric biaryls. The results of latest syntheses of asymmetric biaryls by the Ullmann reaction are presented in Table 5 on p. 1055. For earlier results, see Table IIIc in Ref. 8 and Table 2c in Ref. 7.

Forrest[14] showed that optimal yields of asymmetric biaryls are obtained when one of the aryl halides (A) is more reactive than the other (B):



Component (B) should contain at least one electronegative group ($NO_2$, COOR) in the 2-position and better still two such groups in the 2- and 6-positions relative to the halogen atom. Best yields of asymmetric biaryls are obtained when component (A) contains iodine and component (B) contains bromine or chlorine, as can be seen from the following examples:

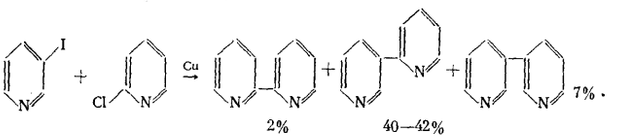


As was to be expected, the reaction of aryl halides with similar reactivities gives a mixture of three biaryls in approximately equal proportions[44-47].

When mixtures of aryl halides (A) and (B) are used, the reaction can be carried out at a much lower temperature than with component (B) alone.

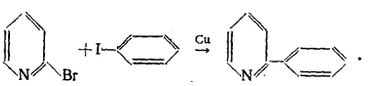
The degree of reaction increases when the reaction is performed in the presence of an excess of component (A) with simultaneous increase of the amount of asymmetric biaryls[14].

It has been established[48] that, when an inactive component (A) is heated with copper for a specific time with subsequent addition of an active component (B) in portions, the yield of the asymmetric biaryl increases sharply. In such cases component (B) is taken in an excess:



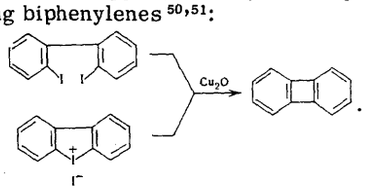
Under the usual conditions, i.e. on simultaneous heating of a mixture of components (A) and (B) in the presence of copper, 2,3′-bipyridyl is formed in a yield of only 7%.[48]

2-Bromopyridine reacts with iodobenzene, forming 2-phenylpyridine in a yield of 50–55%:[49]



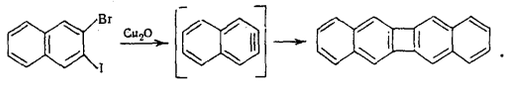
c. Synthesis of Biphenylenes

By heating 2,2′-dihalogenobiphenyls or 2,2′-biphenyliodonium iodide with copper(I) oxide, Lothrop succeeded in synthesising biphenylenes[50,51]:

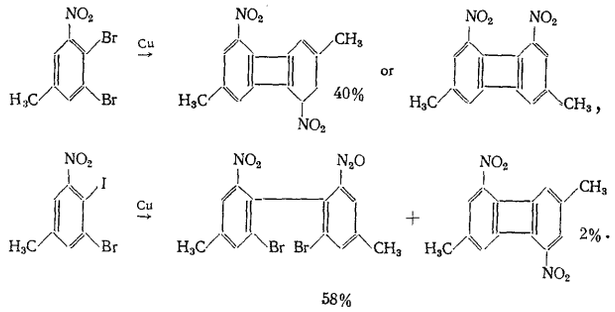


Subsequently this method was used to synthesise also many other biphenylenes [8]. In most cases the reaction is carried out in the presence of copper(I) oxide, the yields of biphenylenes depending significantly on its quality [52-54].

In view of the formation of dibenzobiphenylene on heating 2-bromo-3-iodonaphthalene with copper bronze in dimethylformamide, it was suggested that the reaction proceeds via the formation of dehydronaphthalene with its subsequent dimerisation [56]:



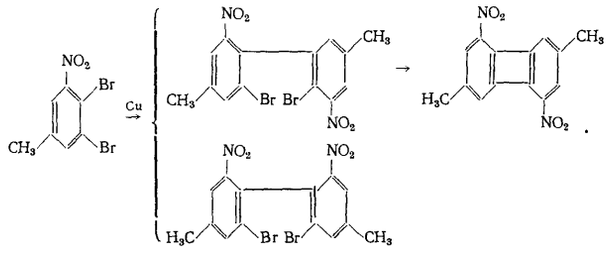
On the other hand, dihalogenonitrotoluenes yield the following products [57]:



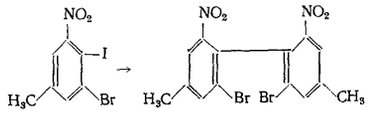
58%

According to Corbett and Holt [57], biaryls cannot serve as intermediates in the formation of biphenylenes. A more detailed examination of these investigations and the studies of recent years [58-60] reveals certain other features of the reaction. Thus contrary to Lothrop's data [50, 51], Salfeld and Baume [58] established that metallic copper can also be employed in the synthesis of biphenylenes instead of copper(I) oxide. The yield of biphenylenes is then considerably higher.

The structure of biphenylenes synthesised by the method of Corbett and Holt [57] was investigated by Harrison et al. [59], who found that the product obtained under these conditions is 3,7-dimethyl-1,5-dinitrobiphenylene. Together with the main product, 2,2′-dibromo-4,4′-dimethyl-6,6′-dinitrobiphenyl is also formed in this reaction with a yield of 20%. Probably the process proceeds via the following mechanism:

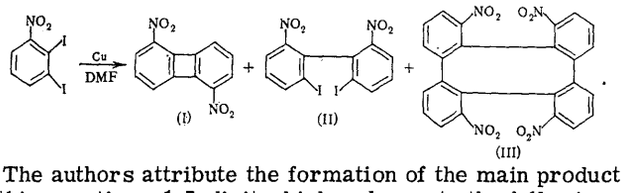


The above scheme shows that the formation of biphenylene involves the formation of a biaryl as an intermediate. Therefore it is easy to account for the formation of a biaryl and not a biphenylene from 3-bromo-4-iodo-5-nitrotoluene:

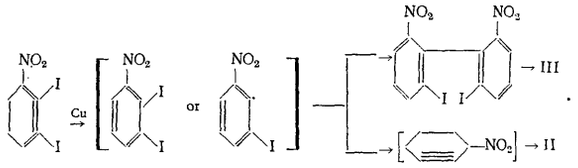


The 2,2′-dibromo-6,6′-bitolyl obtained does not enter into subsequent reactions owing to the presence of the nitro-group in the *m*-position relative to the halogen.

The reaction of 2,3-di-iodo-1-nitrobenzene with copper yielded 1,5-dinitrobiphenylene, 2,2′-di-iodo-6,6′-dinitrobiphenyl, and 4,5,12,13-tetranitroquaterphenylene [60]:

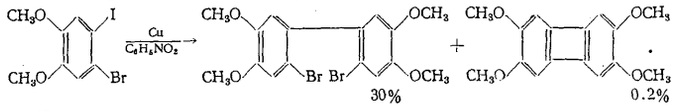


The authors attribute the formation of the main product of this reaction—1,5-dinitrobiphenylene—to the following sequence of steps:



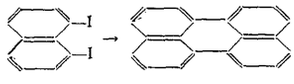
According to this scheme, biphenyl is obtained from dehydrobenzene. However, the absence of 1,2-dinitrobiphenylene (II) from the mixture is evidence against the formation of dehydrobenzene, since in this case the formation of both 1,2- and 1,5-dinitrobiphenylene (I) would be equally probable.

In addition, it has been shown [61] that, when 4-bromo-5-iodoveratrol reacts with copper bronze in nitrobenzene, biphenylene is formed in an insignificant yield (0.2%) and the main product is a biaryl:

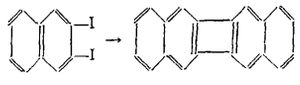


Thus a more detailed examination of the available literature data reveals a similarity of the Ullmann and Lothrop reactions. It is likely that an intermediate aryne is not in fact formed in the Lothrop reaction. The formation of intermediates of this type is usually coupled [62] with an increase in the complexity of the mixture of products obtained. Under the conditions described, this did not occur.

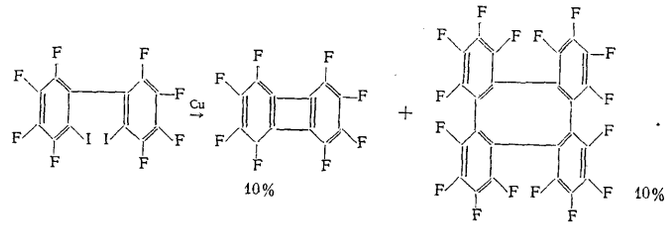
Apart from biphenylenes, other cyclic polyaryls were obtained from aryl dihalides. Thus perylene was synthesised from 1,8-di-iodonaphthalene [63]:



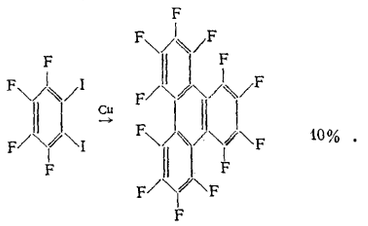
and 2,3-di-iodonaphthalene yielded dibenzobiphenylene [64]:



Octafluorobiphenylene and polyfluoroquaterphenylene were obtained from octafluoro-2,2′-di-iodophenylene [65]:

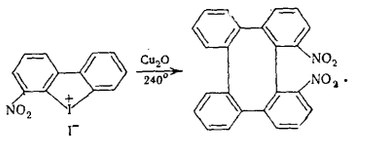


3,4,5,6-Tetrafluoro-1,2-di-iodobenzene forms a trimer:

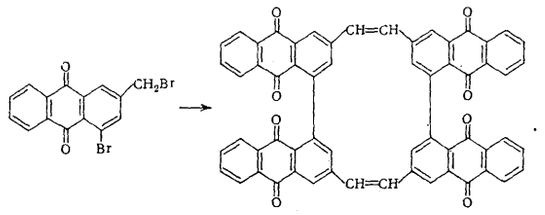


10%.

Pyrolysis of 3-nitrobiphenylene-2,2′-iodonium iodide at 340°C in the presence of copper(I) oxide yields dinitroquaterphenylene; biphenylene was not detected in the reaction products [66]:



Another interesting product was obtained from 4-bromo-2-bromomethylanthraquinone [67]:



Numerous other studies on biphenylenes have been made [68–78].

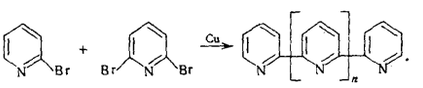
Reactions of aryl dihalides with aryl monohalides yield various polyaromatic compounds.

### d. Reactions of Bifunctional Aryl Halides

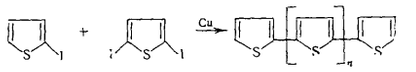
The reactions of bifunctional aryl halides can be divided into two groups: (1) synthesis of cyclic condensation products from two aryl dihalide molecules and (2) synthesis of linear products from a mixture of an aryl dihalide and an aryl monohalide.

The reactions of the first group were largely considered in the discussion of the synthesis of biphenylenes. Those of the second group give rise to a mixture of ter-, quater-, and poly-phenyls; this is best regarded as a special case of the synthesis of asymmetric biaryls. The results obtained are compiled in Table 6 (see also Table IVc in Ref. 8).

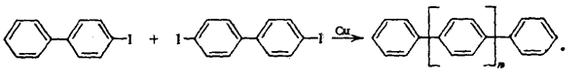
The reaction of 2-bromopyridine with 2,6-dibromopyridine yields bi-, ter-, quater-, quinque-, and sexipyridyls [79]:



Polythienyls have also been synthesised [80,81]:



as well as polyphenyls [82]:



Arylation products are formed in high yields when one of the aryl halides is reactive and the reactivity of the other is somewhat lower [83,84].

### e. Experimental Conditions

In most cases copper powder is gradually added to the aryl halide at a specified temperature. An excess of copper, usually a threefold excess, is almost always employed. Sometimes a tenfold excess of copper is used [14,17]. With the exception of certain cases [41], special purification of the aryl halide is not required for the Ullmann reaction. The yield of the biaryl very often depends on the quality of the copper employed. The question of the effect of the quality of the copper used in the reaction still remains controversial. Frequently commercial copper powder, known as copper bronze, is employed [14]. A special form of copper bronze, "Naturcupfer-C", is also used [6,85].

Commercial copper bronze contains traces of oil but these impurities are readily removed by washing with alcohol or ether. According to Ullmann and Bielecki [19], preliminary treatment of the copper is not needed for the synthesis of biaryls. However, the use of commercial copper powder precludes reproducible yields of 2,2′-dinitrobiphenyl [16] and 2,2′-bipyridyl [86,87]. In such cases freshly prepared copper has been used for a long time [88].

Kleiderer and Adams [89] and Vogel [90] suggest that activated copper be used in the Ullmann reaction. The activation involves treatment of the copper bronze with iodine in acetone and subsequent washing with a mixture of acetone and hydrochloric acid and then pure acetone. When a tenfold excess of copper bronze activated in this way was used, 2,2′-dinitrobiphenyl was obtained from *o*-iodonitrobenzene in almost quantitative yield [17].

In some studies [19,91], it was stated that sometimes mechanically contaminated copper gives better results than freshly precipitated copper. Thus "lithographic copper", containing 0.2–0.5% of long-chain fatty acids (mainly stearic, palmitic, oleic, etc. [13]) is effective. Electrolytic copper treated with stearic acid has also been used [92].

Lothrop [50,51] found that in the synthesis of biphenylenes from 2,2′-dihalogenobiphenyls or from biphenylene-2,2′-iodonium iodide, copper(I) oxide gives very satisfactory results, while copper powder is completely inactive. Contrary to these results, it has been established [93,94] that freshly precipitated copper gives entirely satisfactory yields of biphenylenes. "Gatterman's precipitated copper powder" gives even better results [95].

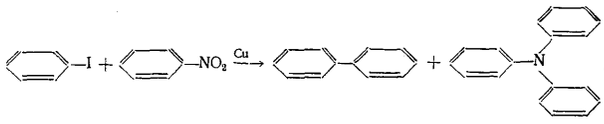
The study of the synthesis of biphenylenes in the presence of copper(I) oxide, commercial copper powder, and copper prepared by the method of Brady and McHugh [88] showed [58] that in the last case best results are obtained.

Apart from those mentioned above, one of the decisive factors governing the success of the Ullmann reaction is reaction temperature. The Ullmann reaction is carried out over a very wide range of temperatures, between 60° [17] and 360°. [96] In most cases the range is between 150° and 280°C (see Tables 4 and 5 on pp.1053 and 1055 and also the Tables in Refs. 7 and 8). Sometimes high temperature may cause the formation of side products. For example, for compounds containing the nitro-groups, the reaction temperature should not be raised above 200°C, since this promotes oxidation-reduction processes [13,14].

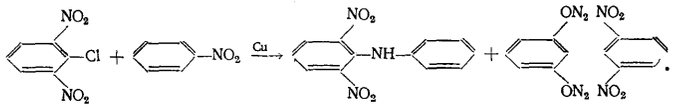
The Ullmann reaction is frequently carried out in solution. Under these conditions, side reactions, which

may occur in the case of labile aryl halides, are to some extent suppressed. The solvents employed are nitrobenzene, toluene, naphthalene, *p*-cymene, biphenyl, anthracene, dimethylformamide (DMF), and others.

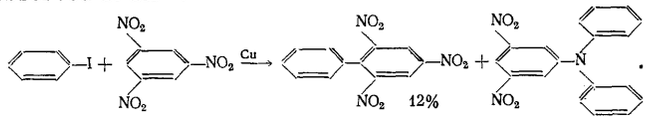
Forrest[14], who used nitrobenzene as a solvent, found that in the presence of copper iodobenzene enters into the following reaction:



When 1-chloro-2,6-dinitrobenzene was allowed to react in boiling nitrobenzene, a product corresponding to the reduction of the nitro-group and a biaryl were obtained in a very low yield[96]:



When a mixture of iodobenzene and 1,3,5-trinitrobenzene was treated with copper, the formation of a biaryl was not observed at all[14]:



Thus nitrobenzene cannot be regarded as an inert solvent in the Ullmann reaction. More suitable solvents are high-boiling hydrocarbons—biphenyl, *p*-cymene, naphthalene, and others.

Recently DMF has been employed with increasing frequency[97]. One of its advantages is its miscibility with water, which facilitates the isolation of reaction products. Moreover, certain aryl halides, which are relatively unreactive in other solvents, give high yields of biaryls in DMF.[11,33,34,41,97] For example, 3,3′-dinitrobiphenyl was obtained in a yield of 82% from the relatively unreactive *m*-iodonitrobenzene[11] (see p. 1046). 3,3′-Dimethyl-5,5′-dinitrobiphenyl was prepared in 71% yield from 3-iodo-5-nitrotoluene[98]. Bipyrrolyls[99-102], bifuryls[103], and bithienyls[104,105] have been obtained in satisfactory yields. Aryl halides containing the formyl[106], keto-[107,108], and carbamoyl[109] groups give satisfactory yields of biaryls in DMF.

Only a few studies in which DMF was used to synthesise asymmetric biaryls have been published[30,37,110,111] and the yields were relatively low. The disadvantages of DMF include its capacity to promote dehalogenation reactions[26,108,112] and halogen exchange reactions[13].

Apart from these solvents, toluene[28], benzene[102,113,114], decane, decalin, pseudocumene, tetralin[33,115-118], xylene[32,118], phenyl ether[119], bitolyl[73], pyridine[120], quinoline[121], etc. have been used in the Ullmann reaction. Sand[19,20,23] has also been employed as an inert diluent and heat exchanger. In some cases common salt has been used instead of sand, which facilitates the isolation of the product from the sintered mass[87].

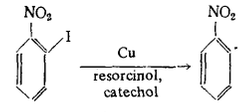
The Ullmann reaction is usually performed in air and in some cases a stream of hydrogen or nitrogen is employed[122]. Some investigators claim[123] that these precautions are superfluous when the initial and final reaction products are not sensitive to atmospheric oxygen. However, it is very likely that an inert atmosphere promotes a satisfactory yield of products, protecting the copper powder, particularly the activated powder, from oxidation[89,90].

## 3. REACTION MECHANISM

The mechanism of the Ullmann reaction, like those of certain other organic reactions, is still the subject of controversy and discussion[8,14]. There are several views concerning the mechanism but none is entirely convincing.

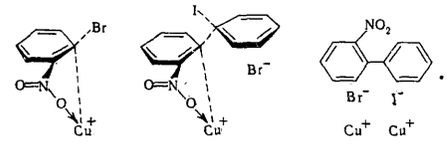
By treating halogenobenzenes with copper or sodium, Rapson and Shuttleworth[124,125] obtained the corresponding dehalogenated products. They suggested that these products are formed owing to the abstraction of hydrogen atoms from the solvent by the free radical produced in the reaction. To confirm this hypothesis, halogenobenzenes were treated with copper bronze in an excess of ethyl benzoate in a sealed tube; 2-carboxybiphenyl and 4-carboxybiphenyl were isolated from the reaction mixture. The authors concluded that a biaryl is formed in the Ullmann reaction as a result of the coupling of free phenyl radicals. Bell and Morgan[126] also believe that the Ullmann reaction has a free-radical mechanism.

To solve the problem of the intermediate in the Ullmann reaction (the aryl radical or aryl anion), the behaviour of *o*- and *p*-iodonitrobenzenes and of *o*-bromonitrobenzenes in an excess of resorcinol and catechol was examined[127]. It was shown that the yield of the dehalogenated product (nitrobenzene) in the experiments with catechol is higher than with resorcinol, although the critical oxidation constant for resorcinol (1.043) is higher than for catechol (0.742). The authors believe[127] that these results confirm a free-radical mechanism of the Ullmann reaction:



Despite these conclusions, Fanta[7,8] concluded on the basis of literature data (he examined about 500 studies) that this reaction has a clearly ionic mechanism. He believes that the reaction consists mainly of two stages, the first of which includes nucleophilic attack by metallic copper on the carbon–halogen bond as a result of which an arylcopper complex is formed on the surface of the metal. He also believes that the success of this stage depends strongly on the sensitivity of aromatic halides to nucleophilic attack in general.

The second stage involves the reaction of the arylcopper complex with a second molecule of the initial aryl halide to form the biaryl and copper halide. This stage depends mainly on steric factors.

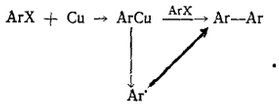


Thus Fanta rules out the formation of free radicals in the Ullmann reaction.

On the basis of a vast number of experimental data and literature results, Forrest[14] also postulates an ionic mechanism for the Ullmann reaction.

Other workers[128] formulate the mechanism of the Ullmann reaction in a somewhat different way. They believe that the reaction consists of two stages: the first involves the formation of an organocopper compound and the second, involving the formation of a biaryl, can occur in two ways, i.e. the biaryl can be formed either as a result of the attack by the initial aryl halide on the organocopper compound or as a result of the coupling of

two free radicals formed owing to the disproportionation of the organocopper compound. They believe that more than half of the biaryl is formed due to the attack by the initial aryl halide on the organocopper compound.

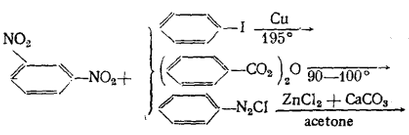


The foregoing statements clearly show that the question of the mechanism of the Ullmann reaction remains controversial.

The formation of anomalous products such as biphenyl-2-carboxylic and biphenyl-4-carboxylic acids from iodobenzene and methyl benzoate [125], 2,6-dinitrobiphenyl from iodobenzene and *m*-dinitrobenzene, and 2,4,6-trinitrobiphenyl from iodobenzene and *sym*-trinitrobenzene [11] is quoted as an argument in support of the free-radical reaction mechanism. In view of the formation of carbon dioxide in 2.6% yield on heating a mixture of benzoic acid and copper in *o*-iodonitrobenzene at 201–208 °C, Nursten concluded [127] that the dehalogenation observed in previous studies [129–131] involves the formation of intermediate free radicals. However, Forrest showed [14] that the formation of such side products is observed for highly hindered aryl halides and is virtually absent for simple halides.

Fanta [8] showed that the interaction of iodobenzene with *m*-dinitrobenzene under the conditions of the Ullmann reaction yields somewhat different proportions of products than on treatment of *m*-dinitrobenzene with benzoyl peroxide at 100 °C (a free-radical reaction) or on decomposition of diazonium chloride in *m*-dinitrobenzene (a Gomberg–Bachmann free-radical reaction) (Table 2).

**Table 2.**

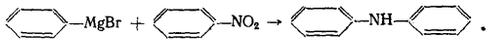
| Starting materials and reaction conditions | Relative yields (%) of products (isomeric dinitrobiphenyls) | |
|---|---|---|
| | 2,4- | 2,6- |
|  | 0 | 8 |
| | 8 | 1 |
| | 2 | 0.2 |

Supporters of the ionic mechanism believe that the Ullmann reaction involves the formation of an organocopper complex or compound as an intermediate stage. Therefore their attention was attracted to the question of the synthesis and reactivity of arylcopper derivatives.

Organocopper compounds of this type were synthesised for the first time by Reich [132] and then Gilmann and Straley [133], Starkey and coworkers [134], and Costa et al. [135] In the last study, the optimal conditions for the formation of phenylcopper were established. Recently Lewin and Cohen [128,136,137] and other investigators [138–147] carried out several studies on the synthesis and properties of organocopper compounds.

Diphenylcopper and dimethyl copper were also obtained [148] and it was shown that they are stable at the boiling point of tetrahydrofuran (THF) (64 °C).

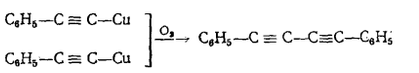
On hydrolysis, diphenylcopper yields benzene and not biphenyl. It has been shown that phenylcopper reacts with aldehydes as a typical Grignard reagent: for example, it reacts with benzaldehyde to form diphenylmethanol in 24% yield [133]. Forrest showed [14] that the addition of nitrocompounds, aldehydes, and ketones to the reaction mixture suppresses the main Ullmann reaction. The formation of triphenylamine when the reaction of iodobenzene and copper is carried out in nitrobenzene may be attributed to typical reactions of organometallic compounds with nitrobenzenes, although phenylmagnesium bromide reacts with nitrobenzene to form only diphenylamine and not triphenylamine [149]:



The thermal decomposition of phenylcopper, *p*-tolylcopper, phenylsilver, and *p*-tolylsilver has been investigated [150,151] and it has been established that the process proceeds via the formation of free radicals, since biaryls and benzenes are the products of this reaction. When a free-radical acceptor (*p*-benzoquinone) is added to the mixture, the yield of products falls sharply. The formation of free radicals is observed also when methylcopper is decomposed [150]. Other workers claim that the thermal decomposition involves a bimolecular mechanism in which a dimer is formed via an organocopper compound [151].

The thermal decomposition of *cis*- and *trans*-ethylenecopper compounds has been studied and the possibility of their dimerisation has been demonstrated [151].

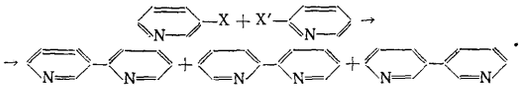
A necessary condition for the synthesis of biaryls from arylcopper is the presence of oxidising agents in the mixture. Gilmann and Straley [133] showed that phenylcopper is oxidised in air over a period of 2 h with formation of biphenyl. On the other hand, in an inert atmosphere phenylcopper is stable over a period of 36 h but the product is again biphenyl. This is also consistent with the following synthesis of diacetylenes [152]:



which has been known for a long time. Furthermore the presence of free radicals in the reaction mixture leads to the formation of side products. Lewin and Cohen [128] claim that, when the reaction of *p*-iodotoluene with copper is performed in quinoline, 8-methylquinoline, or 1-methylnaphthalene, about half of the biaryl is formed from free radicals which are generated owing to the disproportionation of phenylcopper. They did not observe the formation of side products. However, the free radicals produced in the decomposition of benzoyl peroxide in quinoline [153] and in 2-methylnaphthalene [154] gave various phenyl-substituted quinolines and 2-methylnaphthalenes. The decomposition of benzoyl peroxide in chloro- and bromo-benzenes [155] results in the formation of 2-, 3-, and 4-chloro- and 2-, 3-, and 4-bromo-biphenyls, dihydrobiphenyls, diphenyl-, chloro-, and bromo-benzoic acids, dichloro- and dibromotetrahydroquarterphenyls, etc. On the other hand, the decomposition of phenyldiazonium chloride in pyridine gives an almost 80% yield of 2-, 3-, and 4-phenylpyridines [156].

The absence of these products in the experiments of Lewin and Cohen [128] casts doubt on the hypothesis of a radical mechanism of the Ullmann reaction.

The studies by the authors of this review are useful for the estimation of the reactivities of halogen atoms [37,48,49,157–159]. Using the synthesis of 2,3′-bipyridyl as an example, a new method of synthesising asymmetric biaryls was proposed. When 3-iodopyridine was heated with copper in boiling DMF and 2-chloropyridine was added dropwise, 2,3′-bipyridyl was formed in 40–42% yield. On the other hand, when the mixture of all the reactants was heated simultaneously, 2,3′-bipyridyl was formed in a yield of only 7%: [157]



When 3-iodopyridine was replaced by 3-chloropyridine and 2-chloropyridine was replaced by 2-iodopyridine in this reaction, 2,3′-bipyridyl was not obtained. Other halogenopyridines were also employed (Table 3).

**Table 3.**

| X in 3-X-pyridine | X′ in 2-X′-pyridine | Yield of 2,3′-bipyridyl, % of 3-bromopyridine | Yield of 2,2′-bipyridyl, % of 3-bromopyridine | Yield of 3,3′-bipyridyl, % of 3-bromopyridine |
|---|---|---|---|---|
| Cl | Cl | 2—4 | 3 | 0 |
| Cl | Br | Следы | 70 | 0 |
| Br | Cl | 35 | 2.5 | 3—4 |
| Br | Br | 28—30 | 45 | 4 |
| I | Cl | 40—42 | 2 | 8 |
| I | Br | 32—35 | 45—47 | 7—8 |

**Table 4.** Compilation of symmetrical biaryls synthesised by the Ullmann reaction:

$$2ArX \xrightarrow{Cu} Ar\text{–}Ar.$$

| Ar | X | Reaction temp., °C | Reaction conditions | Yield of biaryl, % | Refs. |
|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 |
| 2,3,4,5,6-Pentafluorophenyl | Cl | 320—360 | — | 73 | 170 |
| 3-Bromophenyl | I | — | DMF | 30 | 11 |
| 2-Nitrophenyl | Cl | 315—325 | — | 66 | 24 |
| " " | I | 190—240 | — | 96 | 17 |
| 3-Nitrophenyl | I | — | DMF | — | 11 |
| 3,4,5,6-Tetrafluoro-2-nitrophenyl | Br | — | ditto | — | 171 |
| 3,4,5,6-Tetrafluoro-2-methylphenyl | Br | — | ditto | — | 171 |
| 2-Cyano-3,4,5,6-tetrafluorophenyl | Br | — | ditto | — | 171 |
| 2-Iodo-6-nitrophenyl | I | — | ditto | 6.46 | 172 |
| 3-Methylphenyl | I | — | — | — | 84 |
| 4-Methylphenyl | I | — | — | 16 | 167 |
| 5-Methyl-3-nitrophenyl | I | — | DMF, stream of $N_2$ | 71 | 98 |
| 4-Methoxyphenyl | I | — | — | 12 | 167 |
| 3-Methoxy-2-methylphenyl | I | — | — | — | 173 |
| 3-Bromo-4-methyl-6-nitrophenyl | I | 70 | DMF | 77 | 174 |
| 2,6-Dimethyl-4-nitrophenyl | I | — | DMF, stream of $N_2$ | 60 | 98 |
| 4-Methoxy-2-methyl-6-nitrophenyl | Br | 200—230 | — | 65 | 175 |
| " " | Br | 190 | nitrobenzene | 59 | 175 |
| 2-Formyl-6-nitrophenyl | I | — | — | — | 176 |
| 2,3-Dimethoxyphenyl | I | 250 | — | 70—83 | 177 |
| 2,4-Dimethoxyphenyl | I | 220 | — | — | 177, 178 |
| | — | — | — | 73 | 59 |
| 2,5-Dimethoxyphenyl | I | 220 | — | — | 178 |
| 3,4-Dimethoxyphenyl | I | 220—250 | — | — | 179 |
| 3,4-Dimethoxy-2,3-dimethylphenyl | I | 260 | — | 13 | 180 |
| 2-Chloro-4,5-dimethoxyphenyl | Cl | 230—250 | — | 31—36 | 177 |
| 5,6-Dimethoxy-3-methylphenyl | Br | 300 | — | 18.5—20 | 177 |
| 5,6-Dimethoxy-2,3-dimethylphenyl | Br | 280—300 | — | 17—20 | 177 |
| 2,5-Dimethoxy-3,4-dimethylphenyl | I | 220 | — | — | 181 |
| 2,4,5-Trimethoxyphenyl | I | — | — | — | 177 |
| 3-Formyl-4-methoxyphenyl | I | — | — | — | 182 |
| 2-Bromo-4-carboxymethyl-5-nitrophenyl | I | 150—225 | — | 40 | 174 |
| 2-Biphenylyl | I | — | — | — | 31 |
| 3-Biphenylyl | I | 225—260 | — | 16 | 31 |
| 4-Biphenylyl | I | 225—260 | — | 97 | 31 |
| 3-Methyl-4-(*o*-tolyl)phenyl | I | 200—240 | *m*-bitolyl | | 83 |
| 2-(*p*-Terphenylyl) | I | 230—290 | — | 49.5 | 24 |
| 2-(*o*-Terphenylyl) | I | 215—225 | — | 28 | 24 |
| 4-(*m*-Terphenylyl) | I | 320 | — | 10 | 24 |
| 2-(2-Azo-1-hydroxy-4-methylphenyl)-3-chlorophenyl | Cl | 30 | pyridine + toluene | 92 | 183, 184 |
| 2-(2-Azo-1-hydroxy-4-methylphenyl)-3-bromophenyl | Br | — | — | — | 183, 184 |
| 2-(1-Azo-2-hydroxynaphthyl)phenyl | Br | — | — | 45 | 183, 184 |
| 2-(1-Azo-2-hydroxynaphthyl)-3-chlorophenyl | Cl | — | — | — | 183, 184 |
| 2-(1-Azo-2-hydroxynaphthyl)-3-bromophenyl | Br | — | — | — | 150, 184 |
| 2-Phenanthryl- | I | — | — | — | 84 |
| 9,10-Dihydro-2-phenanthryl | I | — | — | — | 84 |
| 3-Phenanthryl | I | 250 | biphenyl | | 172 |
| " " | I | 200—240 | — | 39 | 176 |
| 6-Nitro-3-phenanthryl | I | — | DMF | 22 | 176 |
| 10,11-Dihydro-5-*n*-dibenzo (*a*, *b*)cycloheptane* | Cl | — | benzene | — | 113 |
| 9-Methyl-9-fluorenyl | Cl | — | benzene | — | 114 |

Table 4 (contd.)

| Ar | X | Reaction temp., °C | Reaction conditions | Yield of biaryl, % | Refs. |
|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 |
| 2-Perylenyl | I | 250 | — | — | 185 |
| 3-Benzanthronyl | Cl | 280—300 | — | 4.3 | 186 |
| " " | Br | 250—270 | — | 6.3 | 186 |
| " " | I | 280—300 | — | 12.7 | 186 |
| " " | I | 300—320 | — | 11.3 | 186 |
| 2-Dibenzofuryl | I | 200—220 | — | 58 | 187 |
| 2-Dibenzofuryl-3-methoxy- | I | 180—220 | — | 65 | 187 |
| 2-Methoxy-5-flavonyl | I | 250—260 | — | — | 182 |
| 4-Methoxy-3-flavonyl | I | 250—260 | — | — | 182 |
| 5-Nitro-2-furyl | I | — | DMF | 76 | 103 |
| 5-Formyl-2-furyl | I | — | ditto | 50 | 103 |
| 5-Methoxycarbonyl-2-furyl | Br | — | " | 68 | 103 |
| 5-Benzoyl-2-furyl | Br | — | " | | 103 |
| 5-Methoxycarbonyl-2-furyl 3-methyl | Br | — | " | 62 | 103 |
| 5,5-Diethoxycarbonyl-3,4-dimethyl-2-pyrrolyl | I | — | " | 31.6 | 101 |
| 4-Ethoxycarbonyl-3,5-dimethyl-2-pyrrolyl | I | — | " | 17.6 | 101 |
| 3-Ethoxy-5-ethoxycarbonyl-4-methyl-2-pyrrolyl | I | — | " | 28.6 | 101 |
| 4-Ethoxycarbonyl-1,3,5-trimethyl-2-pyrrolyl | I | 160—225 | in a sealed tube | 58.6 | 188 |
| 3-Ethoxy-5-ethoxycarbonyl-4-methyl-2-pyrrolyl | I | — | DMF | 30 | 101 |
| 3,5-Dimethoxycarbonyl-4-methyl-2-pyrrolyl | I | — | ditto | 60 | 102 |
| 5-Ethoxycarbonyl-4-methoxycarbonyl-3-methyl-2-pyrrolyl | I | — | " | 21 | 102 |
| 3,5-Diethoxycarbonyl-4-methyl-2-pyrrolyl | I | — | " | 61—65 | 101, 102 |
| " " | I | — | benzene | 77 | 102 |
| " " | I | — | nitrobenzene | 38.4 | 102 |
| " " | Br | 180—210 | in a sealed tube | 54 | 99 |
| 5-Carboxyphenyl-3-ethoxycarbonyl-4-methyl--2-pyrrolyl | I | — | DMF | 77 | 101 |
| 5-Carboxyethyl-3-carboxyphenyl-4-methyl-2-pyrrolyl | I | — | ditto | 27 | 101 |
| 3,5-Dicarboxyphenyl-4-methyl-2-pyrrolyl | I | — | " | 56 | 101 |
| 5-Carboxyethyl-2,4-dimethyl-3-pyrrolyl- | I | — | " | 25 | 102 |
| | Br | — | — | 72—74 | 189 |
| 2-Pyridyl | Br | — | DMF | 86 | 33, 34 |
| " " | Br | — | tetralin | 25 | 33 |
| " " | Br | — | decane | 50.6 | 33 |
| " " | Br | — | decalin | 60.7 | 33 |
| " " | Br | — | *p*-cymene | 63.4 | 33 |
| " " | Br | — | pseudocumene | 65.4 | 33 |
| " " | Br | — | biphenyl | 72 | 33 |
| 3-Pyridyl | Br | — | ditto | 3—4 | 159 |
| " " | I | — | " | 7—8 | 48 |
| 4-Pyridyl | Cl | — | " | — | 157, 158 |
| 2-Quinolinyl | X | — | DMF | — | 34 |
| 4,5-Dimethyl-2-pyrimidinyl | Br | — | DMF | 26 | 190 |
| 4-Phenyl-2-pyrimidinyl | Br | — | DMF | 20 | 191 |
| 6-Methyl-2-phenyl-4-pyrimidinyl | I | — | *p*-cymene | 28 | 192 |
| 2-Carboxymethyl-4-nitro-3-thienyl | Br | — | DMF | 73 | 105 |
| 3-Nitro-2-selenolyl | | — | xylene | 76 | 193 |
| 5-Cyano-2-selenolyl | I | — | ditto | 70 | 193 |
| 3,5-Dinitro-2-selenolyl | I | — | " | 35 | 193 |
| 5-Acetyl-2-selenolyl | I | — | " | 75 | 193 |
| 10(12)-*o*-Carboranyl | I | — | " | 55 | 193 |
| 9(10)-*m*-Carboranyl | I | — | THF | — | 194 |
| Ferrocenyl | I | — | THF | — | 194 |
| " " | I | — | — | 52 | 195 |
| " " | Br | — | — | 35 | 195 |
| " " | Cl | — | — | 7.1 | 195 |

*The condensation of 5,5-dibromo-10,11-dihydro-5*H*-dibenzo[*a*, *d*]cycloheptene to 5,5′-bi-(10,11-dihydro-5*H*-dibenzo[*a*, *d*]cycloheptenylidene) in the presence of alkyllithium [113] is apparently meant here (Ed. of Translation).

Thus the reactivity of halogens in the first stage, involving the formation of an arylcopper compound, increases from chlorine to iodine and that in the second stage, involving the decomposition of the arylcopper compound, increases from iodine to chlorine. The arylcopper compound is evidently formed via a free radical.

The following mechanism was proposed for the Ullmann reaction as the most probable:

$$\begin{array}{l} ArX + Cu \rightarrow Ar^{\cdot} + CuX \\ \qquad\quad \downarrow Cu \\ \qquad\quad ArCu \\ ArX + ArCu \rightarrow Ar{-}Ar + CuX \end{array}$$

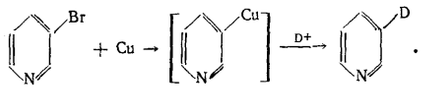
**Table 5.** Compilation of asymmetric biaryls synthesised by the reaction

$$ArX + Ar'X' \xrightarrow{Cu} Ar-Ar'.$$

| Ar | Ar' | X | X' | Reaction temp., °C | Reaction conditions | Yield of biaryl, % | Refs. |
|---|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| 2-Methoxyphenyl | 2,3,5,6-tetrafluoro-phenyl | Br | Br | 252 | in a sealed tube | — | 196 |
| 3,4-Dimethoxyphenyl | 4-nitrophenyl | I | I | 200—250 | — | 14—16 | 179 |
| 2-Methoxycarbonylphenyl | 3,4-dimethoxyphenyl | Br | I | — | — | — | 179 |
| 5-Carboxymethyl-2-methoxyphenyl | 2,6-dimethoxyphenyl | I | I | 220 | — | — | 197 |
| " " | 2,3,6-trimethoxyphenyl | I | I | 220 | — | — | 197 |
| " " | 2,4,5-trimethoxyphenyl | I | I | 220 | — | — | 197 |
| 5-Carboxymethyl-3,4-dimethoxyphenyl | 2-methoxyphenyl | I | I | 220 | — | — | 197 |
| 5-Carboxymethyl-2,3,4-trimethoxy-phenyl | 4-nitrophenyl | Br | I | — | — | 18 | 119 |
| " " | 4-methoxy-2-nitrophenyl | Br | I | 250—265 | | 11 | 119 |
| 4-*p*-Biphenylyl | without substituent | I | I | 300 | in a sealed tube | 65—69 | 198 |
| 4-(*p*-Biphenylyl)- | 2-methylphenyl | I | I | 190—260 | — | 34 | 199 |
| " " | 3-methylphenyl | I | I | 190—260 | — | 37 | 199 |
| " " | 4-methylphenyl | I | I | 190—260 | — | 17 | 199 |
| 2-Fluorenyl | without substituent | I | I | — | — | 53 | 84 |
| | 2-methyl-4-(*m*-tolyl)phenyl | I | I | — | biphenyl | 44 | 83 |
| 9,10-Dihydro-2-phenanthryl | without substituent | I | I | — | — | 50 | 84 |
| 2-Dibenzofuryl | ditto | I | I | 180—220 | — | 58 | 187 |
| " " | 2-methoxyphenyl | I | I | 180—220 | — | 57 | 187 |
| " " | 3-methoxyphenyl | I | I | 180—220 | — | 60 | 187 |
| 3-Methoxy-2-dibenzofuryl | without substituent | I | I | 180—260 | — | 60 | 187 |
| 2-Thienyl | ditto | I | I | 160 | quinoline | 50 | 121 |
| 2-Pyridyl | " " | Br | I | — | — | 50—55 | 49 |
| " " | 3-pyridyl | I | Cl | — | — | 40—42 | 48 |
| " " | 4-pyridyl | Br | Cl | — | — | 14.5—20 | 157, 158 |

According to this mechanism, the first reaction stage involves the cleavage of the carbon–halogen bond with formation of a free aryl radical. The latter then forms an organocopper compound. This is followed by the second reaction stage—the formation of a biaryl as a result of nucleophilic attack by the organocopper compound on the initial aryl halide.

The formation of an organocopper compound in the Ullmann reaction is consistent with the observed dehalogenation of the starting material [129,130,160–162] and also with the formation of pyridine from 3-bromopyridine in the presence of copper at a high temperature [35–37]. In the last case pyridine is formed owing to the decomposition by acid agents of the organocopper compound formed in the course of the reaction. When the reaction mixture obtained in the Ullmann reaction with 3-bromopyridine was decomposed with a solution of DCl in $D_2O$, [3-D]pyridine was obtained [163]:



The reactivities of aryl halides can also be estimated from the yields of dehalogenation products. Such dehalogenation was first observed by Ullmann [160] in the reaction of 2-chloro-3,5-dinitrobenzoic acid with copper; the main product was 3,5-dinitrobenzoic acid. Dehalogenation is observed also when the reaction is carried out in the presence of tetrahydronaphthalene [161], alcohol [162], and benzoic acid [129,130]. The last method has been used to debrominate various bromonitronaphthalenes [131]. The dehalogenation process proceeds via the mechanism

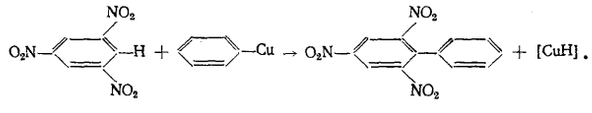
$$ArX + Cu \rightarrow ArCu \xrightarrow{H^+} ArH + Cu^+.$$

Smidt established [129] that the interaction of picryl chloride with copper in the presence of benzoic acid results in the formation of 1,3,5-trinitrobenzene in a yield of only 20%, while the reaction of 1-chloro-2,4-dinitrobenzene and *o*-chloronitrobenzene gives 1,3-dinitro- and nitro-benzenes in yields of 52 and 59% respectively. Consequently an increase of the number of electronegative constituents (in the present case nitro-groups) in the *ortho*-position relative to the halogen atom deactivates the aryl halide in the first stage of the Ullmann reaction. However, this should promote the second reaction stage, since electronegative groups in the *ortho*-position relative to the halogen should activate the carbon–halogen bond in relation to nucleophilic attack.

Indeed the interaction of iodobenzene, picryl chloride, and copper at 135°C is explosive and leads to an asymmetric biaryl [164,165].

The formation of 2,6-dinitrobiphenyl and 2,4,6-trinitrobiphenyl in the reaction of iodobenzene with *m*-dinitrobenzene and *sym*-trinitrobenzene [14] can be accounted for by the following processes:

$$C_6H_5I + Cu \rightarrow C_6H_5Cu,$$



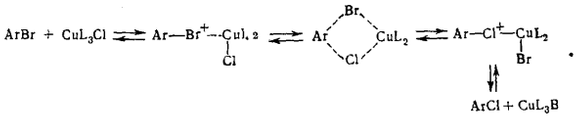
A number of 2,6-dinitrobiphenyls have been synthesised according to this scheme [167].

The reaction of *o*-bromonitrobenzene with α-iodonaphthalene gave α-bromonaphthalene (yield 40%). [14,168]

**Table 6. Products obtained from bifunctional and monofunctional aryl halides.**

| Bifunctional aryl halide | Monofunctional aryl halide | Reaction product | Reaction temp., °C | Reaction conditions | Yield of product, % | Refs. |
|---|---|---|---|---|---|---|
| 1,4-Di-iodobenzene | *o*-iodotoluene | 1,3-dimethyl-*p*-terphenyl | 220–240 | bitolyl | 38 | 83 |
| " " | *m*-iodotoluene | 1,3-dimethyl-*p*-terphenyl | – | *m*-bitolyl | 33 | 83 |
| " " | 4-iodo-1,2-dimethoxybenzene | 3,4,3",4"-tetramethoxy-*p*-terphenyl | 220–250 | – | – | 179 |
| " " | 4-iodo-3,3'-dimethylbiphenyl | 2,3,2"',3""-tetramethyl-*p*-quinquephenyl | – | – | – | 83 |
| 1,3-Di-iodo-2,5-dimethoxybenzene | 1-iodo-2,4-dimethoxybenzene | 2,4,2',5',2",4"-hexamethoxy-*m*-terphenyl | – | *m*-bitolyl | 50 | 178 |
| 1,3-Di-iodo-4,6-dimethoxybenzene | 1-iodo-2,5-dimethoxybenzene | 2,5,4,6,2",5"-hexamethoxy-*m*-terphenyl | 220 | – | 41 | 83 |
| 1,3-Dibromo-2,5-dinitrobenzene | [2,4,6-$D_3$] iodobenzene | 2,4-dinitro-*m*-[2,4,6,2",4",6"-$D_6$] terphenyl | 190–200 | in a stream of $N_2$ | 35 | 200 |
| 4,4-Di-iodobiphenyl | *o*-iodotoluene | 2,2"'-dimethyl-*o*-quaterphenyl | 200–240 | *m*-bitolyl | 45 | 83 |
| " " | *m*-iodotoluene | 3,3"'-dimethyl-*p*-quaterphenyl | – | " | 42 | 83 |
| " " | 4-iodo-3,3'-dimethylbiphenyl | 3,3"',2"",3""'-tetramethyl-*p*-sexiphenyl | – | " | 43 | 83 |
| 4,4'-Di-iodo-3,3'-dimethylbiphenyl | iodobenzene | 2',3"-dimethyl-*p*-quaterphenyl | 200–240 | biphenyl, in a stream of $N_2$ | – | 83 |
| " " | *o*-iodotoluene | 2,2,3",2"'-tetramethyl-*p*-quaterphenyl | – | *m*-bitolyl | 39 | 83 |
| " " | *m*-iodotoluene | 3,2',3",3"'-tetramethyl-*p*-quaterphenyl | – | " | 40 | 83 |
| 4,4-Di-iodo-2,2'-dimethylbiphenyl | *o*-iodotoluene | 2,3,2",2"'-tetramethyl-*p*-quaterphenyl | – | – | 65 | 83 |
| 4,4-Di-iodo-*p*-terphenyl | iodobenzene | *p*-quinquephenyl | 200–240 | biphenyl, in a stream of $N_2$ | 52 | 83 |
| " " | *o*-iodotoluene | 2,2""-dimethyl-*p*-quinquephenyl | 200–240 | biphenyl | 47 | 83 |
| " " | *m*-iodotoluene | 3,3""-dimethyl-*p*-quinquephenyl | – | *m*-bitolyl | 49 | 83 |
| " " | 4-iodo-3,3'-dimethylbiphenyl | 3,3,2"",3""'-tetramethyl-*p*-septiphenyl | – | " | 37 | 83 |
| 4,4-Di-iodo-3,3-dimethyl-*p*-terphenyl | iodobenzene | 3,3"'-dimethyl-*p*-quinquephenyl | 200–240 | biphenyl, in a stream of $N_2$ | 42 | 83 |
| 2,7-Di-iodofluorene | iodobenzene | 2,7-diphenylfluorene | – | biphenyl | 42 | 83 |
| " " | *o*-iodotoluene | 2,7-di-(*o*-tolyl)-fluorene | – | *m*-bitolyl | 39 | 83 |
| " " | *m*-iodotoluene | 2,7-di-(*m*-tolyl)-fluorene | – | " | 34 | 83 |
| 3,6-Di-iodophenanthrene | 3-iodophenanthrene | 3,6-di-(3-phenanthryl)-phenanthrene | – | – | – | 172,176 |
| 2,7-Di-iodo-9,10-dihydrophenanthrene | iodobenzene | 2,7-diphenyl-9,10-dihydrophenanthrene | – | – | 49 | 84 |
| " " | *o*-iodotoluene | 2,7-di-(*o*-tolyl)-9,10-dihydrophenanthrene | – | – | 52 | 84 |
| " " | *m*-iodotoluene | 2,7-di-(*m*-tolyl)-9,10-dihydrophenanthrene | – | – | 50 | 84 |
| 2,7-Di-iododibenzofuran | iodobenzene | 2,7-diphenyldibenzofuran | – | – | 30 | 187 |
| " " | *m*-iodotoluene | 2,7-di(*m*-tolyl)dibenzofuran | – | – | 27 | 187 |

Thus there is an exchange of halogen atoms. This process can be accounted for by the following mechanism [169]:




We may note that, according to this mechanism, halogen exchange involves an organocopper halide formed in the Ullmann reaction.

The mechanism proposed above for the Ullmann reaction, involving the intermediate formation of organocopper compounds, accounts for the following typical features: (1) the Ullmann reaction takes place only with aromatic halogeno-derivatives; (2) dehalogenated products may be formed in the course of the reaction [124,125]; (3) asymmetric biaryls may be formed in high yields by the reaction of activated and non-activated aryl halides below the temperature required for the synthesis of the symmetrical biaryl from the non-activated aryl halide [14,165]; (4) the Ullmann reaction may be suppressed by the addition of proton donors [14,129–131,160]; (5) exchange of halogen atoms between the starting materials is possible in the course of the Ullmann reaction [168].

The mechanism discussed above is also consistent with the following findings: electronegative groups in the *ortho*-position relative to the halogen atom in aryl halides activate it in relation to the Ullmann reaction; the reaction of iodobenzene with copper in the presence of nitrobenzene results in the formation of triphenylamine [14]; when iodobenzene reacts with copper in the presence of *m*-dinitrobenzene and *sym*-trinitrobenzene, 1,3-dinitrobiphenyl and 1,3,5-trinitrobiphenyl are formed [14].

It is noteworthy that certain aspects of this reaction, for example the effect of solvents on the yield of product, the influence of the amount and quality of the copper on the main and side reactions, and the nature of the stabilisation of the intermediate arylcopper compound, still remain obscure. The use of new effective methods for the analysis and separation of reaction products (ultraviolet, infrared, NMR, and mass spectroscopy, gas–liquid chromatography, etc.) may and should extend significantly our knowledge in this field.

## REFERENCES

1. K. H. Meuer, Helv. Chim. Acta, **23**, 93 (1940).
2. C. Graebe and F. Ullmann, Annalen, **291**, 16 (1896).
3. F. Ullmann, Ber., **36**, 2382 (1903).
4. F. Ullmann, Ber., **37**, 2001 (104).
5. F. Ullmann, Ber., **29**, 1878 (1896).
6. F. Ullmann, Annalen, **332**, 38 (1904).

7. P. E. Fanta, Chem. Rev., 38, 139 (1946).
8. P. E. Fanta, Chem. Rev., 64, 613 (1964).
9. M. Nilsson, Svensk. kem. Tidskr., 73, 447 (1961); Chem. Abs., 61, 2110b (1966).
10. L. Mascarelli, B. Longo, and A. Ravera, Gazzetta, 68 (1938); Chem. Abs., 32, 4565 (1938).
11. H. A. Staab and F. Binning, Ber., 100, 293 (1967).
12. J. von Alphen, Rec. Trav. chim., 51, 453 (1932).
13. M. Nilsson, Acta. Chem. Scand., 12, 537 (1958).
14. J. Forrest, J. Chem. Soc., 594 (1960).
15. J. P. Wibaut and J. Overhoff, Rec. Trav. chim., 47, 761 (1928).
16. P. H. Core and G. K. Hughes, J. Chem. Soc., 1615 (1959).
17. M. D. Rausch, J. Org. Chem., 26, 1802 (1961).
18. F. H. Case, J. Amer. Chem. Soc., 64, 1848 (1942).
19. F. Ullmann and J. Bielecki, Ber., 34, 2174 (1901).
20. R. J. W. LeFèvre, J. Chem. Soc., 733 (1929).
21. G. Schiemann and W. Roselius, Ber., 65, 737 (1932).
22. R. J. W. LeFèvre and H. Vine, J. Chem. Soc., 967 (1938).
23. R. C. Fuson and E. A. Cleveland, "Organic Syntheses", John Wiley, New York, 1940, Vol. 20, p. 45.
24. J. A. Cade and A. Pilbeam, J. Chem. Soc., 114 (1964).
25. H. Stetter and M. Schwartz, Ber., 90, 1349 (1957).
26. R. S. W. Braithwaite and P. F. Holt, J. Chem. Soc., 3025 (1959).
27. A. M. von Arendonk, M. E. Cupery, and R. Adams, J. Amer. Chem. Soc., 55, 4225 (1958).
28. B. P. 18 333 (1914); Chem. Abs., 10, 392 (1916).
29. C. E. Castro, L. J. Andrews, and R. M. Keefer, J. Amer. Chem. Soc., 80, 2322 (1958).
30. J. F. Corbett and P. F. Holt, J. Chem. Soc., 3646 (1960).
31. J. A. Cade and A. Pilbeam, Tetrahedron, 20, 519 (1964).
32. L. Chierici, C. Dellèrba, A. Guareschi, and D. Spinelli, Ricerca sci., A8, 1537 (1965).
33. W. Karminski and L. Kulicki, Chem. Stosowana, A9, 129 (1965).
34. L. Kulicki and W. Karminski, Polish P. 52038; Ref. Zhur. Khim., 24P249(1967).
35. J. Forrest, J. Chem. Soc., 574 (1960).
36. R. Frank and J. Crowford, Bull. Soc. chim. France, 419 (1958).
37. M. Goshaev, Candidate'sThesis, Tashkent State University, Tashkent, 1970.
38. E. Proft and H. Richter, J. prakt. Chem., 281(9), 164 (1959).
39. R. Pummerer, H. Puttfarcken, and P. Schopfelcher, Ber., 58, 1808 (1925).
40. W. R. H. Hurtley, J. Chem. Soc., 1870 (1929).
41. R. G. R. Bacon and R. Bankhead, J. Chem. Soc., 839 (1963).
42. S. Sako, Bull. Chem. Soc. Japan, 11, 144 (1936); Chem. Abs., 30, 5984 (1936).
43. C. K. Bradsher and S. T. Amore, J. Amer. Chem. Soc., 66, 1283 (1944).
44. A. Critchlow, R. D. Haworth, and P. L. Pauson, J. Chem. Soc., 1318 (1951).
45. R. B. Carlin and G. E. Foltz, J. Amer. Chem. Soc., 78, 1997 (1956).
46. W. Baker, J. W. Borton, and J. F. W. McOmie, J. Chem. Soc., 2658 (1958).
47. H. Erdtmann, F. Haglid, and N. E. Stjernstroem, Acta. Chem. Scand., 15, 1761 (1961).
48. M. Goshaev, L. S. Otroshchenko, and A. S. Sadykov, Trudy Samarkand. Gos. Univ., 1, No. 167, 95 (1969).
49. M. Goshaev, L. S. Otroshchenko, and A. S. Sadykov, "Tezisy Dokladov Simposiuma po Modifikatsii Struktur Prirodnykh Fiziologicheski Aktivnykh Soedinenii. Erevan, 1969" (Abstracts of Reports at the Symposium on the Modification of the Structures of Natural Physiologically Active Compounds, Erevan, 1969), p. 56.
50. W. C. Lothrop, J. Amer. Chem. Soc., 63, 1187 (1941).
51. W. C. Lothrop, J. Amer. Chem. Soc., 64, 1698 (1942).
52. M. P. Cava and J. F. Stucker, J. Amer. Chem. Soc., 77, 6022 (1955).
53. R. F. Curtis and G. Wiswanat, J. Chem. Soc., 1960 (1959).
54. E. R. Ward and B. D. Pearson, J. Chem. Soc., 1676 (1959).
55. W. Baker, M. P. V. Boarland, and J. F. W. McOmie, J. Chem. Soc., 1476 (1954).
56. E. R. Ward and B. D. Pearson, J. Chem. Soc., 515 (1961).
57. J. E. Corbett and P. F. Holt, J. Chem. Soc., 4261 (1961).
58. J. C. Salfeld and E. Baume, Tetrahedron Letters, 3365 (1966).
59. Ch. R. Harrison, J. F. W. McOmie, J. B. Searle, J. O. Jenkins, and J. W. Smith, J. Chem. Soc., 1769 (1966C).
60. K. Iqbal and R. C. Wilson, J. Chem. Soc., 1690 (1967C).
61. W. Baker, J. W. Barton, J. F. W. McOmie, R. J. Penneck, and M. L. Watts, J. Chem. Soc., 3986 (1961).
62. H. Günther, Ber., 96, 1801 (1963).
63. R. Scholl, C. Seer, and R. Weitzenböck, Ber., 43, 2202 (1910).
64. E. R. Ward and J. E. Marriott, J. Chem. Soc., 4999 (1963).
65. S. C. Cohen and A. G. Massey, Tetrahedron Letters, 4393 (1966).
66. J. W. Barton and K. E. Whitaker, J. Chem. Soc., 2097 (1967C).
67. P. Ruggli and E. Merz, Helv. Chim. Acta, 12, 71 (1929).
68. J. J. Dobbie, J. J. Fox, and A. J. H. Gamge, J. Chem. Soc., 36 (1913).
69. L. Maskarelli, D. Gatti, and B. Longo, Gazzetta, 63, 661 (1933); Chem. Abs., 28, 1686 (1934).
70. J. F. W. McOmie, Rev. Chim. (Acad. R. P. R.), 7, 1071 (1962); Ref. Zhur. Khim., 2ZH138 (1965).
71. J. W. Barton, J. Chem. Soc., 5161 (1964).
72. N. Campbell and A. H. Scott, J. Chem. Soc., 1050 (1966C).
73. P. R. Constantine, G. E. Hall, C. R. Harrison, J. F. W. McOmie, and R. J. G. Searle, J. Chem. Soc., 1767 (1966C).
74. R. F. C. Brown, D. V. Gardner, J. F. McOmie, and R. K. Solly, Chem. Comm., 407 (1966).
75. J. W. Reiyendam, Chem. Weekblad., 62, 21 (1966).
76. R. G. R. Bacon, S. G. Seeterram, and O. J. Stewart, Tetrahedron Letters, 2003 (1967).
77. D. W. Lawson, J. F. W. McOmie, D. E. West, J. Chem. Soc., 2414 (1968C).
78. M. Nilsson, Acta. Chem. Scand., 10, 1377 (1956).
79. F. H. Burstall, J. Chem. Soc., 1662 (1938).
80. W. Steinkopf, R. Leitsmann, and K. H. Hoffmann, Annalen, 546, 180 (1941).
81. W. Steinkopf, H. J. von Petersdorf, and R. Gording, Annalen, 527, 272 (1937).
82. R. Pummerer and L. Seligsberger, Ber., 64, 2477 (1931).
83. H. O. Wirth, K. H. Gönner and W. Kern, Makromol. Chem., 63, 30 (1963).

84. H. O. Wirth, K. H. Gönner, and W. Kern, Makromol. Chem., 63, 53 (1963).
85. E. Mülkr and E. Tietz, Ber., 74, 807 (1941).
86. O. S. Otroshchenko, Yu. V. Kurbatov, and A. S. Sadykov, Nauch. Trudy Tashkent. Gos. Univ., No. 263, 33 (1964).
87. G. I. Mikhailov, Zhur. Prikl. Khim., 28, 114 (1955).
88. O. L. Brady and G. P. McHugh, J. Chem. Soc., 2047 (1923).
89. E. C. Kleiderer and R. Adams, J. Amer. Chem. Soc., 55, 4219 (1933).
90. See Ref. 234 in Ref. 8.
91. E. Schreiner, J. prakt. Chem., 81, 422 (1910).
92. L. J. Hughes and L. J. Weaver, US P. 2907799.
93. R. B. Carlin, J. Amer. Chem. Soc., 67, 928 (1945).
94. H. R. Frank, P. E. Fanta, and D. E. Tarbell, J. Amer. Chem. Soc., 70, 2314 (1948),
95. H. G. Rule, W. Pursell, and A. J. G. Barnett, J. Chem. Soc., 571 (1935).
96. W. Borsche and D. Rahtscheff, Annalen, 379, 152 (1911).
97. W. Kornblum and D. L. Kendall, J. Amer. Chem. Soc., 74, 5782 (1952).
98. H. Braunling, F. Binnig, and A. H. Staal, Ber., 100, 880 (1967).
99. L. A. Webb James and R. Pobert, J. Chem. Soc., 1406 (1960) [wrong Ref. (Ed. of Translation)].
100. L. A. Webb James, J. Chem. Soc., 1413 (1960) [wrong Ref. (Ed. of Translation)].
101. R. Grigg, A. W. Johnson, and J. W. Wasby, J. Chem. Soc., 1359 (1963).
102. R. Grigg and A. W. Johnson, J. Chem. Soc., 3315 (1964).
103. R. Grigg, J. A. Knight, and M. V. Sargent, J. Chem. Soc., 976 (1966).
104. H. Wynberg and A. Logothetis, J. Amer. Chem. Soc., 78, 1958 (1956).
105. S. Gronowitz and K. Dahlgren, Arkiv. Kemi., 21, 201 (1963).
106. R. G. R. Bacon and W. S. Lindsay, J. Chem. Soc., 1375 (1958).
107. R. G. Bacon and W. S. Lindsay, J. Chem. Soc., 1382 (1958).
108. J. Gardent, Bull. Soc. chim. France, 1049 (1962).
109. B. P. 889746 (1961); Chem. Abs., 57, 7202 (1962).
110. T. F. Corbett and P. F. Holt, J. Chem. Soc., 5029 (1961).
111. W. M. Whaley, M. Meadlow, and C. N. Robinson, J. Org. Chem., 19, 973 (1954).
112. D. E. Hathway, J. Chem. Soc., 519 (1957).
113. I. Moritani, S.-I. Murahashi, K. Yoshinaga, and H. Ashitaka, Bull. Chem. Soc. Japan, 40, 1506 (1967); Ref. Zhur. Khim., 6Zh182 (1968).
114. S.-I. Murahashi and I. Moritani, Tetrahedron, 23, 3631 (1967).
115. R. W. Hardacre and A. G. Perkin, J. Chem. Soc., 180 (1929).
116. M. S. Lesslie and E. E. Turner, J. Chem. Soc., 281 (1932).
117. E. D. Bergmann, Bull. Soc. chim. France, 1070 (1968).
118. C. Carpanelli and G. Leandri, Ann. Chim. (Italy), 51, 181 (1961).
119. K. P. Sarbhai and K. B. L. Mathur, Indian. J. Chem., 4, 81 (1966).
120. T. Nozol, K. Doi, and K. Kitihara, Proc. Japan Acad., 32, 480 (1956).
121. M. Nilsson, Tetrahedron Letters, 679 (1966).
122. J. Harley-Mason and F. G. Mann, J. Chem. Soc., 1379 (1940).
123. R. B. Carlin and E. A. Swakon, J. Amer. Chem. Soc., 77, 966 (1955).
124. W. S. Rapson and R. G. Shuttleworth, J. Chem. Soc., 487 (1941).
125. W. S. Rapson and R. G. Shuttleworth, Nature, 147, 675 (1941).
126. F. Bell and W. H. D. Morgan, J. Chem. Soc., 1716 (1954).
127. H. E. Nursten, J. Chem. Soc., 3081 (1955).
128. A. K. Lewin and T. Cohen, Tetrahedron Letters, 4531 (1965).
129. W. T. Smidt, J. Amer. Chem. Soc., 71, 2855 (1949).
130. W. T. Smidt and L. Campazano, J. Amer. Chem. Soc., 75, 3602 (1953).
131. N. Campell and N. M. Hasan, Chem. Ind. (London), 2026 (1966).
132. P. Reich, Compt. rend., 177, 322 (1923) (Quoted after Ref. 128).
133. H. Gilmann, J. M. Straley, Rec. Trav. chim., 55, 821 (1936); Chem. Abs., 1015 (1937).
134. F. A. Bolth, W. M. Whaley, and E. B. Starkey, J. Amer. Chem. Soc., 65, 1456 (1943).
135. G. Costa, A. Camus, L. Catti, and N. Morsich, J. Organometal. Chem., 5, 568 (1966).
136. A. H. Lewin, M. J. Zovko, W. H. Rosewater, and T. Cohen, Chem. Comm., 80 (1967).
137. T. Cohen and A. H. Lewin, J. Amer. Chem. Soc., 88, 4521 (1966).
138. K. H. Thiele and J. Köhler, J. Organometal. Chem., 12, 225 (1968).
139. E. J. Corey and G. H. Posner, J. Amer. Chem. Soc., 90, 5615 (1968).
140. S. S. Dua, A. Lukes, and H. Gilman, J. Organometal. Chem., 12, 24 (1968).
141. O. P. Vig, S. D. Sharma, and J. C. Kapur, J. Indian Chem. Soc., 46, 167 (1969).
142. R. W. Herr, D. M. Wieland, and C. R. Johnson, J. Amer. Chem. Soc., 92, 3813 (1970).
143. A. E. Lukes, S. S. Dua, and H. Gilman, J. Organometal. Chem., 12, 44 (1968).
144. O. P. Vig, J. C. Kapur, and S. D. Sharma, J. Indian Chem. Soc., 45, 734 (1968).
145. G. V. Koten, A. J. Lensink, and J. G. Noltes, Chem. Comm., 1107 (1970).
146. A. P. Terent'ev, I. G. Il'ina, K. G. Rukhadze, and I. G. Vorontsov, Zhur. Obshch. Khim., 40, 1516 (1970).
147. F. A. Cotton and T. J. Marks, J. Amer. Chem. Soc., 92, 5114 (1970).
148. M. Tsutsui, Ann. N. Y. Acad. Sci., 93, 133 (1961).
149. H. Gilmann and R. McCraken, J. Amer. Chem. Soc., 51, 821 (1929).
150. H. Hasimoto and T. Nakano, J. Org. Chem., 31, 891 (1966).
151. G. M. Whitesides and C. P. Casey, J. Amer. Chem. Soc., 88, 4541 (1961).
152. C. Glaser, Annalen, 154, 159 (1870).
153. J. M. don Henri and M. L. Brian, Compt. rend., C262, 1537 (1966).
154. J. M. Bonnier, M. Gelus, and J. Rinando, Tetrahedron Letters, 627 (1967).
155. C. B. Gill and G. K. Williams, J. Chem. Soc., 7127 (1965).
156. J. W. Haworth, M. Heilbron, and D. H. Hey, J. Chem. Soc., 349 (1940).
157. O. S. Otroshchenko, M. Goshaev, A. S. Sadykov, and M. Kuznetsova, USSR P. 253066; Byul. Izobret., No. 30 (1969).

158. M. Goshaev, O. S. Otroshchenko, A. S. Sadykov, and M. Kuznetsova, Izv. Akad. Nauk Tadzh. SSR, Ser. Fiz.-tekh. Khim. i Geol. Nauk, No. 5, 114 (1970).
159. Yu. V. Kurbatov, O. S. Otroshchenko, A. S. Sadykov, and M. Goshaev, Trudy Samarkand. Gos. Univ., 1, No. 167, 85 (1969).
160. F. Ullmann and H. Engi, Annalen, 366, 88 (1909).
161. J. Forrest, J. Chem. Soc., 589 (1960).
162. H. Meyer, German P. 234726; Chem. Zentr., 82, 1767 (1911).
163. M. Goshaev, O. S. Otroshchenko, and A. S. Sadykov, Zhur. Org. Khim. (in the Press).
164. H. C. Gall and E. E. Tyrner, J. Chem. Soc., 491 (1929).
165. H. G. Rull and F. R. Smith, J. Chem. Soc., 1096 (1937).
166. H. M. L. Dieteren and C. Köningsberger, Rec. Trav. chim., 82, 5 (1963).
167. Ch. Björklund, M. Nilsson, Acta. Chem. Scand., 22, 2338 (1968).
168. H. Longo and A. Pirone, Gazzetta, 77, 117 (1947).
169. R. G. R. Bacon and H. D. O. Hill, J. Chem. Soc., 1097 (1964).
170. G. G. Yakobson, V. D. Shteingarts, A. I. Miroshnikov, and N. N. Vorozhtsov, Dokl. Akad. Nauk SSSR, 159, 1109 (1964).
171. L. J. Belf, M. W. Buxton, and J. F. Tilney-Basset, Tetrahedron, 23, 4719 (1967).
172. H. A. Staab and H. Bräunling, Tetrahedron Letters, 45 (1965).
173. M. Lounasmaa, Acta, Chem. Scand., 22, 2388 (1968).
174. R. E. Carter and L. Dahlgren, Arkiv. Kemi., 27, 257 (1967).
175. H. Musso and W. Steckelberg, Annalen, 693, 187 (1966).
176. H. A. Staal and H. Bräunling, K. Schneider, Ber., 101, 879 (1968).
177. L. Horner and K. H. Weber, Ber., 96, 1568 (1963).
178. N. E. Stjernström, Arkiv. Kemi., 21, 57 (1963).
179. L. Horner and K. H. Weber, Ber., 100, 1842 (1967).
180. D. W. Lawson, J. F. W. McOmie, and D. E. West, J. Chem. Soc., 2414 (1968C).
181. N. E. Stjernström, Arkiv. Kemi., 21, 73 (1963).
182. K. P. Mathai and S. Sethna, J. Indian. Chem. Soc., 41, 347 (1964).
183. L. M. Legon'kova and B. I. Stepanov, Trudy. Moskov. Khim.-tekhnol. Inst. im. Mendeleeva, No. 48, 120 (1965).
184. S. V. Mikheeva, M. A. Andreeva, and B. I. Stepanov, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 11, 114 (1966).
185. N. Goto and I. Koga, Monthly J. Inst. Ind. Sci. Univ. Tokyo, 19, 175 (1967); Ref. Zhur. Khim., 4Zh235 (1968).
186. I. Nagai and K. Nagasawa, J. Chem. Soc. Japan, 69, 666 (1966); Ref. Zhur. Khim., 2Zh257 (1967).
187. U. O. Wirth, G. Wasse, and W. Keru, Makromol. Chem., 86, 139 (1965).
188. J. L. A. Webl, J. Chem. Soc., 1413 (1960).
189. Z. Kulicki, and W. Karminsky, Zeszyty Nauk Politechn. Slask. Chem., 16 (85), 11 (1963); Chem. Abs., 62, 4001C (1965).
190. D. Bly-Donald, J. Org. chem., 29, 943 (1964).
191. J. J. Lafferty and F. H. Case, J. Org. chem., 32, 1591 (1967).
192. M. P. L. Caton, D. T. Hurst, J. F. W. McOmie, and R. R. Huht, J. Chem. Soc., 1204 (1967C).
193. Ch. Luigi, D. Carlo, G. Alessandro, and S. Domenico, Ricerca Sci., A8, 1537 (1965).
194. V. I. Stanko, Yu. V. Gol'tyapin, and V. A. Brattsev, Zhur. Obshch. Khim., 37, 2360 (1967).
195. M. D. Rausch, P. V. Roling, and A. Siegel, Chem. Comm., 502 (1970).
196. P. J. Brown, R. Stephens, and J. C. Tatlow, Tetrahedron, 23, 4041 (1967).
197. E. Pettersson and N. E. Stjernstöm, Arkiv. Kemi., 21, 49 (1963).
198. K. Bujimoto, S. Arima, and K. Taeshita [tentative spelling (Ed. of Translation)], J. Soc. Org. Synth. Chem. Japan, 22, 390 (1964); Ref. Zhur. Khim., 14Zh147 (1965).
199. D. Günther and W. Klaus, J. prakt. Chem., 28, 242 (1965).
200. H. L. Otto, L. Stein, and G. Juppe, J. Labelled Comp., 4, 205 (1968).

Tashkent State University