The Substitution of Aryl Iodides with Cuprous Acetylides. A Synthesis of Tolanes and Heterocycles

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Diarylacetylenes are prepared conveniently in good yields by treating aryl iodides with cuprous acetylides in refluxing pyridine under a nitrogen atmosphere. Under these conditions, aryl iodides bearing an ortho nucleophilic substituent are converted exclusively to the corresponding heterocycle in high yields.

Diarylacetylenes have been prepared by the dehydrohalogenation of dihalodibenzyls, oxidation of the benzil dilydroazones with mercuric oxide, rearrangement of 1,1-diaryl-2-haloethenes upon treatment with base, and by the action of base upon 5,5-diaryl-3-nitroso-2-oxazolidones.

In the course of studies of the reduction of multiple bonds by low valent transition metal ions, we have had occasion to prepare a variety of tolanes. We have found that these substances are readily obtained in good yield by exposing aryl iodides to cuprous acetylides in refluxing pyridine. Reaction 1 is carried out in a nitrogen atmosphere to prevent coupling to the diacetylene.

The results portrayed in Table II are indicative of the scope and usefulness of this reaction.

![Chemical structure](image)

**TABLE I**

<table>
<thead>
<tr>
<th>Aryl halide</th>
<th>Product</th>
<th>Yield,%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodobenzene</td>
<td>Diphenylacetylene</td>
<td>87</td>
</tr>
<tr>
<td>p-Methoxyiodobenzene</td>
<td>4-Methoxydiphenylacetylene</td>
<td>99</td>
</tr>
<tr>
<td>o-Methiodiiodobenzene</td>
<td>2-Methiodiiodobenzene</td>
<td>91</td>
</tr>
<tr>
<td>p-Iodosalicyl</td>
<td>4-Iodosalicyl</td>
<td>78</td>
</tr>
<tr>
<td>p-Iodosalicylic acid</td>
<td>4-Iodosalicylic acid</td>
<td>85</td>
</tr>
<tr>
<td>p-Iodonaphthalene</td>
<td>4-Iodonaphthalene</td>
<td>76</td>
</tr>
<tr>
<td>o-Iodobiphenyl</td>
<td>2-Iodobiphenyl</td>
<td>84</td>
</tr>
</tbody>
</table>

Yields reported here and in Table II are for the purified product. Not previously described.

When the aryl iodide bears an ortho nucleophilic substituent, tolane is not obtained, but rather cyclization to the corresponding heterocycle occurs exclusively under the same reaction conditions (see eq. 2).

The reactions are similar to a series of transformations (eq. 3) that resemble the Rosenmund-von Braun nitrile synthesis. Thus, the solvolysis of allylic halides has been shown to be catalyzed by cuprous salts. Alkyl alcohols, alkyl halides, and alkyl bromides have been converted to the corresponding cyanides through the action of cuprous cyanide. Aryl and alkyl halides have been converted to thio ethers with cuprous mercaptides. The exchange of aromatic halides has been effected with Cu(I) halides, and the Cu(I)-catalyzed alkylation of acetylenic halides with acetylides has been noted.

It is noteworthy that the following path has been proposed for the Rosenmund-von Braun nitrile synthesis (eq. 4) conducted in the absence of solvent. A somewhat related sequence has been advanced to...
Cuprous Phenacylidyne.\(^{(19)}\) An aqueous ammonium solution of 20.0 g (0.105 mole) of cuprous iodide\(^{(15)}\) was poured with stirring into a solution of 10.7 g (0.105 mole) of phenacylidencyne in 500 ml of ethanol. The reaction mixture was allowed to stand for 15 min. The bright charrote precipitate was filtered off and washed five times each with water, ethanol, and ether. The bright canary yellow solid thus obtained was dried in a rotary evaporator at 50° (20 mm) for 2 hr.; yield, 13.4 g (77%).\(^{(16)}\)

Cuprous \(\alpha\)-Propenacylidyne.\(^{(17)}\) In a manner entirely analogous to that described previously for cuprous phenacylidyne, 19.4 g (0.102 mole) of cuprous iodide and 6.95 g (0.098 mole) of 1-phenylpropane provided after warming and drying 11.2 g (0.086 mole, 58%) of bright yellow cuprous \(\alpha\)-propanacylidyne.

\(-p\)-Methoxyphenacylidencyne.\(^{(18)}\) In a 300-ml round-bottomed flask equipped with a magnetic stirring bar, nitrogen inlet, and a reflux condenser fitted to a mercury trap was placed 7.1 g (0.098 mole) of \(p\)-iodobenzene and 100 ml of dry pyridine. The flask was purged with nitrogen while stirring and 5.0 g (0.090 mole) of cuprous phenacylindyne was added during the nitrogen flush. The contents were warmed in an oil bath at 120° for 10 hr. with stirring. Upon addition of the cuprous phenacylidencyne a yellow slurry was formed which, after warming, slowly dissolived to give a yellow solution. As the reaction progressed, the color of the solution changed from a bright yellow to a clear reddish amber. Upon completion of the reaction the solution was cooled and diluted with 500 ml of water. The mixture was extracted three times with ether, and the combined ether extracts were washed successively three times each with dilute hydrochloric acid, 5% sodium bicarbonate, and water, and dried over magnesium sulfate. The dried ethereal solution was concentrated in vacuo and the residue crystallized to yield an amber solid having m.p. 81–82°. This substance was decolorized with Norit in hot methanol and crystallized. There was obtained 6.2 g (0.0298 mole, 98.5%) of small white plates of \(-p\)-methoxyphenacylidencyne with m.p. 58–59° (lit. m.p. 58–61°).\(^{(19)}\) The infrared spectrum of this substance was identical with that of an authentic sample.

**Experimental**

**Diphenacylidencyne.** In the manner described for \(-p\)-methoxyphenacylidencyne, 6.40 g (0.099 mole) of cuprous phenacylidencyne reacted with 7.94 g (0.089 mole) of iodobenzene in 100 ml of pyridine. The crude product was recrystallized from ethanol to yield 6.0 g (0.084 mole, 87%) of long white needles of diphenacylidencyne having m.p. 50–52°. The infrared spectrum of this product was identical with that of an authentic sample.

\(-o\)-Methoxyphenacylidencyne.\(^{(19)}\) In similar fashion 6.5 g (0.036 mole) of \(-o\)-iodobenzene and 6.0 g (0.036 mole) of phenacylidencyne in 100 ml of pyridine provided 10.3 g (87%) of brown oil giving upon fractionalization through a small Vigreux column 7.5 g (0.033 mole, 91%) of \(-o\)-methoxyphenacylidencyne. The clear colorless oil had b.p. 144–145° (0.2 mm.), \(\nu \text{max} 1.6567, \text{C} = \text{C} \text{ at } 4.56 \mu\).

Anal. Caled. for \(\text{C}_{13}\text{H}_{18}\text{O}:\) C, 86.54; H, 5.77; mol. wt., 208. Found: C, 86.46; H, 5.80; mol. wt. (Melcherlomrometer), 206.

**P-Nitrophenacylidencyne.** A mixture of 7.0 g (0.028 mole) of \(p\)-nitrobromobenzene, 4.7 g (0.028 mole) of cuprous phenacylidencyne, and 100 ml of pyridine warmed at 85° for 10 hr. afforded 5.0 g of crude tolane. The material was recrystallized from petroleum ether to yield 4.8 g (0.021 mole, 75%) of long amber needles of \(p\)-nitrophenacylidencyne having m.p. 119–120°.

Anal. Caled. for \(\text{C}_{14}\text{H}_{12}\text{NO}:\) C, 75.33; H, 4.04; N, 6.28; mol. wt., 223. Found: C 75.45; H, 4.10; N, 6.29; mol. wt., 228.

**\(-o\)-Nitrophenacylidencyne.** A mixture of 4.0 g (0.017 mole) of \(o\)-nitrobenzene, 2.74 g (0.016 mole) of cuprous phenacylidencyne, and 100 ml of pyridine warmed at 100° for 8 hr. yielded a brown oil.

\(\text{Cu} \cdot \text{ArX} + \text{Cu}^+ \rightarrow [\text{ArXCu}]^+ \rightarrow \text{Cu}^+ + [\text{ArXCu}]^+[\text{ArXCu}]^+ \rightarrow \text{Ar}^+ + \text{CuX} \rightarrow \text{Ar}^+ + \text{CuCN} \) (4)

In the present work the ease of reaction of para substituted iodobenzenes with cuprous phenacylidencyne is in the order \(p\)-NO2 > \(p\)-H > \(p\)-CH3O. A similar order of reactivity has been observed for the halogen exchange brought about by the action of \(\text{Cu}(1)\) halides on \(p\)-substituted aryl halides.\(^{(15)}\) Moreover, the kinetics for this latter process are reported to be first order in both aryl halide and \(\text{Cu}(1)\) halide.\(^{(16)}\) These findings are suggestive of a homolytic process (eq. 7).

In the heterocyclic synthesis both the substitution and cyclization would seem to occur within the same copper complex, since 2-aminodiphenylacetylene was not cyclized upon exposure to cuprous iodide and cuprous phenyl acetylide in refluxing pyridine.\(^{(22)}\)
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SYNTHESIS OF UNSYMMETRICAL DIARYLPHOSPHINOUS CHLORIDES

Institute, Public Health Service.

needles of p-carboxydiphenylacetylene having m.p. 221-222° treated with 50 ml. of petroleum ether to give 3.4 g. (0.0153 mole, 85%) of white needles having m.p. 83-84°. C, 83.57; H, 5.03. Found: C, 83.57; H, 4.95.

In suitable melting point and mixture melting point with an authentic sample. The infrared spectrum of the product was very similar to

Anal. Calcd. for ClsHloOz: C, 81.09; H, 4.50; mol. wt., 221-222° (lit.3 p. 220.5-222°, C, 83.57; H, 4.95.).


2-Phenylbenzofuran.- A mixture of 5.35 g. (0.025 mole) of p-methoxytolane except that the red oil was recovered after work-up. The substance was decolorized with Norit in methanol and recrystallized from petroleum ether to yield 3.8 g. of a reddish crystalline solid which was recrystallized from methanol-water to yield 3.8 g. of colorless 3-phenylisocoumarin with m.p. 90-91° (lit.31 m.p. 91-92°), C, 87.02; H, 5.85; N, 7.14.

Anal. Calcd. for C14H10O2: C, 81.09; H, 4.50; mol. wt., 221-222° (lit.3 p. 220.5-222°, C, 83.57; H, 4.95.).

Anal. Calcd. for C19H18O: C, 82.90; H, 8.18; N, 8.80. Found: C, 82.90; H, 8.18; N, 8.80.

(30) The work-up in these solvents was the same as that described for p-methoxytolane except that before extraction the solution was diluted with 400 ml. of water and the ether extracts were washed with water only.

(31) S. Gabriel, Ber., 18, 2445 (1885).


The reduction with aluminum of six aryldiazonium fluoroborate-arylphosphonous dichloride reaction products (presumably Ar=PH2:BF4- has produced diarylphosphinous chlorides in roughly 30-50% yield. This reaction offers a new route to unsymmetrical diarylphosphinous chlorides, which have remained relatively obscure up to the present study. It also was found that the phosphinous chlorides can be hydrolyzed on addition to water to produce diarylphosphine oxides in good yield and purity. Unsymmetrical diaryl phosphine oxides have not hitherto been available.

Recent reports from this laboratory3 have described a new synthesis of arylphosphinous dichlorides, based on reactions 1 and 2. Reaction 1, conducted in dry solvents, was first observed by Doak and Freedman.4

Structure I has been suggested, but not established, for the product. This intermediate, which is not isolated, has been widely used as a precursor of phosphonic acids which are formed on hydrolysis. The occurrence of reaction 2 was anticipated because of the resemblance of I to other structures capable of undergo-

(1) A portion of this work was presented at the 112nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962.

(2) Supported by Research Grant CY-5007 from the National Cancer Institute, Public Health Service.


Synthesis of Unsymmetrical Diarylphosphinous Chlorides and Their Conversion to Secondary Phosphine Oxides1,2

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The reduction with aluminum of six aryldiazonium fluoroborate-arylphosphonous dichloride reaction products (presumably Ar=PH2:BF4- has produced diarylphosphinous chlorides in roughly 30-50% yield. This reaction offers a new route to unsymmetrical diarylphosphinous chlorides, which have remained relatively obscure up to the present study. It also was found that the phosphinous chlorides can be hydrolyzed on addition to water to produce diarylphosphine oxides in good yield and purity. Unsymmetrical diaryl phosphine oxides have not hitherto been available.

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