The Use of Complexing Agents in the Activation of Copper for the Ullmann Biaryl Synthesis

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IN our study[1] of the Ullmann biaryl synthesis,[2] we have found that commercial copper powder can be substantially activated toward this reaction by pretreating it with a solution of a suitable complexing agent. Thus, in a given time interval, considerably increased conversions into bitolyl are obtained when *p*-iodotoluene is heated with activated copper as compared with the analogous reaction in which untreated metal is used. Some typical results are shown in the Table.

The activation procedure consists of stirring *ca.* 0·5 g. of the copper powder with 50 ml. of the complexing solution, washing by decantation twice with water and twice with methanol, and drying in a vacuum dessicator for 1—2 hr.* Such treatment of different commercial copper bronzes, with wide variations in activity, causes comparable activation (runs 1—3), with the relative reactivity order remaining the same as before treatment.† Neither extending the treatment period nor increasing the concentration of complexing agent is effective in further enhancing the activity of the copper powders. This activity is preserved when the copper is stored under water (runs 5—7) although the physical appearance of the metal changes. Whereas the freshly treated copper is light salmon coloured and quite shiny, the preserved copper develops a black, carbon-like coating.

Control tests showed that treatment of commercial copper with various solvents either fails to cause substantial activation (water, aqueous acetic acid) or actually causes the metal to become deactivated (methanol, dioxan, and chloroform). Trace amounts of EDTA added directly to the reaction mixture have no catalytic effect.

In another test of the activation process, it was found that treatment of copper powder with an aqueous solution, 0·02M in EDTA, greatly

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* The methanol wash is not an absolute requirement, but rapid drying of the powder with minimum exposure to air is essential.

† Freshly precipitated copper, which is sometimes recommended (ref. 2), is considerably less effective than the most active commercial brand studied, Engelhard 1107. Even a less active brand such as Fisher copper, when treated with a complexing agent, compares favourably with the freshy prepared material in terms of activity reproducibility, ease of preparation, and preservation.

TABLE

Catalysis of the Ullmann coupling of p-*iodotoluene*[a]

Run	Source of Cu	Treatment	Temp.	Time (hr.)	% Bitolyl	
					Control	Treated
1	Fisher[b]	EDTA[c]	175	2	9	24
2	B and A[d]	,,	190	18	10	28
3	MC and B[e]	,,	192	2	10	34
4[f]	Fisher[b]	,,	190	1	29	28
5	From run 3	Preserved 48 hr.[g]	190	2	9	38
6	,,	,, 1 wk.[g]	190	2	10	31
7	,,	,, 6 wk[g].	190	2	6	27
8	MC and B[e]	Ethylenediamine[h]	195	2	7	17
9	,,	Ethylenediamine[i]	191	2	7	23
10	,,	Biquinolyl[i]	191	2	7	17
11	,,	NH_3[j]	190	2	8	31
12	,,	NaOAc[j]	192	2	7	27
13	,,	NaBr[k]	191	2	9	8

[a] Performed by heating 0·5 g. *p*-iodotoluene with 0·5 g. of copper powder (under nitrogen except in run 4). Analyses by v.p.c. [b] Fisher C-431. [c] 0·02 M-Aqueous solution of disodium salt of ethylenediaminetetracetic acid. [d] Baker and Adamson 1618. [e] Matheson, Coleman and Bell, CX-1925. [f] Nitrogen not used. [g] Under water. [h] 0·06 M-Aqueous solution. [i] 0·06 M-Solution in tetrahydrofuran. [j] 0·24 M-Aqueous solution. [k] 2·4 M-Aqueous solution.

enhances its effectiveness in catalyzing the decomposition of an arenediazonium tetrafluoroborate.‡§ We have previously found[3] that cuprous copper is a much more effective catalyst in this decomposition than copper powder and it therefore seems possible that the activation process essentially consists of cleaning the copper surface (conceivably of cupric salts) by means of a complexing agent; this might be followed by subsequent rapid oxidation to form some cuprous copper (perhaps an oxide) on this surface. The "new" cuprous species might well be the active agent.¶ This hypothesis is supported by the fact that freshly activated copper turns aqueous ammonia blue as does cuprous oxide. On the other hand, ammonia water turns blue quite slowly when it is mixed with either unactivated copper or cupric oxide. It is also of interest in this connection that the enhanced reactivity of the treated copper is only manifested when the Ullmann coupling is carried out with the exclusion of air (compare runs 1—3 with run 4). However, addition of either cuprous or cupric oxide to the reaction mixture has no catalytic effect.

It thus appears to us that we are dealing with a surface phenomenon in which the disruption of the surface of the catalyst through removal of some ionic species from it by complexation enhances the reactivity. It is possible that such an activation process might be useful in other copper-promoted reactions and might also be applicable to other metals.

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‡ The salt used in this experiment was derived from *o*-amino-*NN*-dimethylbenzamide.

§ The relative reactivity order of commercial copper powder towards diazonium decomposition is reversed from that in the biaryl synthesis.

¶ This explanation is consistent at least in the Ullmann case with the recent finding (T. Cohen and A. H. Lewin, *J. Amer. Chem. Soc.*, 1966, **88**, 4521) that organocopper species, thought (ref. 1) to be intermediates in this reaction, are readily produced by the action of cuprous benzoate on aryl halides.

[1] A. H. Lewin and T. Cohen, *Tetrahedron Letters*, 1965, 4531.

[2] P. E. Fanta, *Chem. Rev.*, 1964, **64**, 613.

[3] A. H. Lewin, A. H. Dinwoodie, and T. Cohen, *Tetrahedron*, 1966, **22**, 1527.