A Directed, General Synthesis of Azoxy-compounds containing Alkyl, Aryl, Ester, Acyl, and Amide groups

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Summary A wide variety of unsymmetrically substituted azoxy-compounds can be synthesized regiospecifically in high yield by condensation of nitroso-compounds with *NN*-dichloro-substrates in the presence of copper(I) chloride.

UNTIL recently, there were only two useful methods for the directed synthesis of unsymmetrical azoxyalkanes and alkylazoxyarenes, namely, combination of arylazoxy tosylates with alkyl Grignard reagents,[1] and reaction of alkyl diazotates with alkyl halides.[2] Other approaches[2,3] often generate mixtures of the two possible isomers or are not convenient for the production of azoxy-compounds containing electron-withdrawing groups.[4]

Recently we described the regiospecific synthesis of azoxyalkanes and alkylazoxyarenes by condensation of an *NN*-dichloramine with a nitroso-compound in the presence of base,[5] but this route is not useful for base-sensitive products. Thus, primary and secondary alkyl dichloroamines give relatively low yields of product, presumably owing to dehydrohalogenation.

$$\mathrm{RNCl_2 + R'NO \rightarrow RN{=}N(O)R'}$$

We report a modified synthesis of isomerically pure unsymmetrical azoxy-compounds which is not base-sensitive. An *NN*-dichloro-compound is condensed with an aryl nitroso-substrate in the presence of CuCl. Yields are higher and the scope of the reaction, *e.g.* preparation of compound (**3**) is possible, is broader than in the original system.

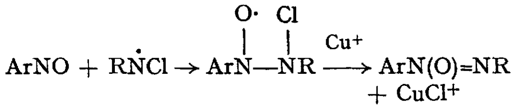
The *NN*-dichloro-compound (1 mol), from chlorination of the precursor with calcium hypochlorite,[6] is stirred with nitrosobenzene (1 mol) in acetonitrile, followed by addition of crude CuCl (2 mol). The mixture is stirred overnight at room temperature, poured into water, and extracted with ether. Chromatography on silica gel with light petroleum followed by benzene–light petroleum (30:70) as eluent yields the pure azoxy-compound. All products gave satisfactory elemental analyses after crystallization or distillation. The n.m.r. spectra were consistent with the assigned structures, and i.r. spectra exhibited characteristic azoxy-absorption in the 1300—1500 cm^{-1} region. Yields of the pure, isolated products are shown in the Table where the benefits of using CuCl as catalyst are evident. The moderate yield of (**5**) probably reflects the instability of the *NN*-dichloro-precursor.

TABLE. Azoxy products

Product	R	PhN(O)=NR yield/%	M.p./°C
(**1**)	Bu^n	83	—
(**2**)	C_6H_{11}	58	—
(**3**)	CO_2Et	65	37
(**4**)	PhCO	75	53
(**5**)	Me_2NCO	51	44

The reaction mechanism may involve homolytic cleavage[5] of the N–Cl bond with concomitant oxidation of Cu$^+$ followed by addition of the nitrogen-centred radical to the N=O group [reactions (1) and (2)]. This scheme is analogous to that proposed for addition of R_2NCl to olefins in the presence of redox salts, Cu^{I} or Fe^{II}, in which dialkylamino-radicals appear to participate.[7]

$$\mathrm{RNCl_2 + Cu^+ \rightarrow R\dot{N}Cl + CuCl^+} \qquad (1)$$



$$\mathrm{ArNO + R\dot{N}Cl \rightarrow Ar\overset{O\cdot}{\overset{|}{N}}{-}\overset{Cl}{\overset{|}{N}}R \xrightarrow{Cu^+} ArN(O){=}NR + CuCl^+} \qquad (2)$$

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