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Formation of Diazoketones and Azines by Improved Oxidation of Ketohydrazones using Cu(acac)$_2$ as a Catalyst

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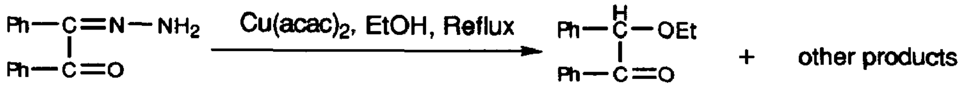
Key words: Ketohydrazone, Cu(acac)$_2$, oxidation, diazoketone, azine.

Abstract: An efficient Cu(acac)$_2$-catalyzed oxidation of ketohydrazones afforded the corresponding α-diazoketones or ketazines in high yields depending on the reaction conditions. However, the reaction of benzophenone hydrazone gave benzophenone azine without affording diphenyldiazomethane. The formation of azines is explained by the intermediacy of carbenoid generated by the Cu(acac)$_2$-catalyzed decomposition of diazo compounds.

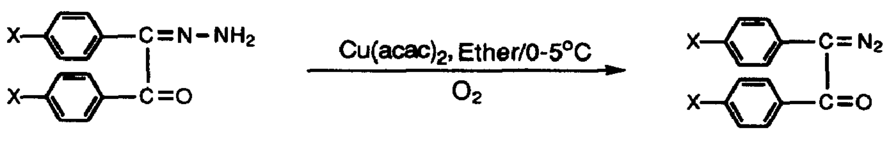
Recent years have witnessed extensive investigations of the chemistry of transition metal salts and complexes to explore their potentiality for many types of oxidative reactions of organic substrates.[1-7] On the other hand, several such salts and complexes including Cu(acac)$_2$ have frequently been used as a catalyst to decompose diazo compounds and generate transient carbenoid intermediate.[8,9] During some ongoing studies on copper ketocarbenoids in our laboratory, we observed an extremely fast reaction of benzil monohydrazone (**1a**) in the presence of Cu(acac)$_2$ indicated by striking color change of the reaction mixture from blue to dark brown. Therefore, we decided to investigate their reaction expecting isolation of copper complex of **1a**. Although the structure of resulting complex was not quite certain the two main possibilities addressed by literature were (i) a weak coordination of imino carbon of **1a** with copper as proposed in case of diazo compounds,[8,9] and (ii) coordination of amino nitrogen and carbonyl oxygen of **1a** with copper due to exchange of one or both acetylacetonate legands.[10] The reaction of **1a** with nickel acetate has been reported to give a complex with molecular formula [PhCOC(Ph):N.NH]$_2$Ni without an elucidation of exact structure.[11] The preliminary spectroscopic analysis (IR and ^{1}H NMR) of the product mixture obtained from an equimolar reaction of **1a** with Cu(acac)$_2$ in ethanol at reflux temperature, however, showed the presence of *O*-ethylbenzoin in trace amount (together with other products) which was formed by the reaction of benzoylphenyl carbene with ethanol.[12]



1a

An indication of the involvement of carbenoid and so azibenzil (**2a**) in the reaction prompted us to optimize the reaction conditions to isolate **2a** and investigate the generality of the reaction which we wish to report in the present communication. The preparation of **2a** has been reported earlier by oxidation of **1a** with mercuric oxide, and iodine in the presence of strong bases,[13,14] triflation of **1a** with $(CF_3SO_2)_2O$ at -78°C,[15] and some other methods.[16] The only precedence of copper catalyzed oxidation of **1a** leading to **2a** requires vigorous O_2 bubbling in pyridine solution of ten molar equivalents of CuCl followed by addition of **1a**.[17] A case of oxidation of **1a** by Ag_2O has been reported to give benzil (82%) as a sole product.[18]

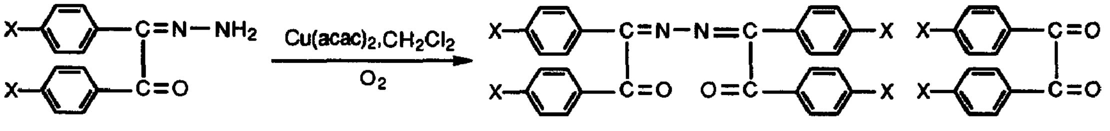
The treatment of benzil monohydrazone (**1a**) with 0.1 equivalent of Cu(acac)$_2$ in ether[19a,b] under atmosphere of air afforded azibenzil (**2a**) in 82% yield. The structure of **2a** was characterized on the basis of satisfactory elemental analysis, spectral data, and comparison with an authentic sample.[13]



1a-d **2a-d**

a, X = H; b, X = CH_3; c, X = Cl; d, X = CH_3O

The reaction was extremely fast in CH_2Cl_2 solution as just after five minutes the hydrazone **1a** disappeared completely and the presence of **2a** and two other products was detected by IR spectrum [absorption bands at 2075 (CN_2), 1677 (CO), 1660 (CO), 1615 (diazocarbonyl) and 1600 (azine) cm^{-1}] and TLC of the reaction mixture. Finally, the reaction[19c] afforded benzil azine (**3a**)[20] and benzil (**4a**)[21] (Table 1).



1a-d **3** **4**

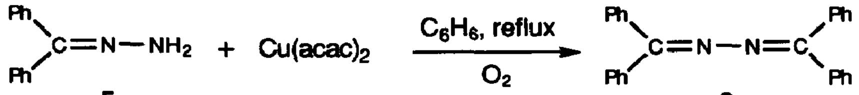
Table 1. Yield (%) of the Oxidation Products of Benzil Monohydrazones (**1**).

Run	X	Diazoketones[a]	Ketazines[b]	Benzil[b]
		2	**3**	**4**
a	H	82	86	7
b	CH_3	77	75	3
c	Cl	76	81	4
d	CH_3O	73	76	3

a) reaction in ether at 0 - 5°C.
b) reaction in CH_2Cl_2 at 20°C.

Similar reactions of 4,4'-dimethylbenzil monohydrazone (**1b**), 4,4'-dichlorobenzil monohydrazone (**1c**) and 4,4'-dimethoxybenzil monohydrazone (**1d**)[19d] also gave the corresponding α-diazoketones (**2b-d**) or azines (**3b-d**)[20] and diketones (**4b-d**) depending upon the reaction conditions (Table 1). A carbene dimer, *trans*-1,2-bis(4-chlorobenzoyl)-1,2-bis(4-chlorophenyl)ethylene (5% yield) was isolated in the reaction of **1c**.

The treatment of benzophenone hydrazone (**5**) by Cu(acac)$_2$ under the condition used for isolation of **2a-d** did not afford the corresponding diazoalkane, diphenyldiazomethane recovering **5** in quantitative yield. However, treatment of **5** with an equimolar amount of Cu(acac)$_2$ in benzene at reflux temperature for four hrs afforded benzophenone azine (**6**)[22] in 84% yield.



5 **6**

From the mechanistic rationale it seems that a copper-hydrazone complex was formed initially, as reported in case of nickel,[11] and underwent air oxidation to lead to α-diazoketones **2a-d** which decomposed and reacted in the usual way as copper-carbenoids do with another molecule of diazo compound and with water to give the ketazines **3a-d** and benzils **4a-d**, respectively.

In conclusion, this preparative method of α-diazoketones **2a-d** which appears to be the first application of Cu(acac)$_2$ as a catalyst of oxidation of hydrazone is a clean and convenient method under extremely mild condition avoiding the use of strong bases and toxic mercury reagent as in conventional methods.[13-17] Moreover, an easy treatment by Cu(acac)$_2$ in comparison to other reagents specially moisture sensitive $(CF_3SO_2)_2O$ is an added advantage to the method. With the viewpoint of ketazines formation (**3a-d** and **6**) it is also the most simplest method of the previously reported ones which require either formation of diazo compound followed by the catalytic decomposition or condensation and treatment of hydrazones with ketones and some acids, respectively for several hours.[22]

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19. a) In a typical reaction procedure 1 mmol of hydrazone and 0.1 mmol of Cu(acac)$_2$ were stirred in 30 ml of dry ether at 0-5°C till the complete disappearance of hydrazone (20-45 min.). The reaction mixture was separated by a silica gel column (20 X 10 cm^2) using hexane as an eluent.

    b) Since the reaction does not stop at the step of diazoketone formation, the reaction mixture must be transferred to column quickly without evaporating the solvent.

    c) Although reaction time depends on temperature (ice, room temp., reflux) no marked variation in yield was observed.

    d) Benzene-ether (1:1) mixture was used as a solvent.
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