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FUNCTIONALIZATION REACTIONS OF N-NONSUBSTITUTED, N-SUBSTITUTED AND N,N-DISUBSTITUTED HYDRAZONES IN THE PRESENCE OF CuCl CATALYST

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Abstract. The paper represents polyfunctionalization reactions of N-nonsubstituted, N-substituted and N,N-disubstitutedhydrazones with polyhalogenalkanes in the presence of CuCI catalyst in recent years. Wide utilization of synthesized compounds in organic synthesis as effective syntons, especially various heterocyclic compounds, arylhydrazones of α-keto acide ethers and also synthesis of 4-azodio-1,2,3-tiazole derivatives should be specified.

Keywords: *hydrazones, CuCl catalyst, dihalogenalkenes, dihalogendiazadienes, 4-azido-1,2,3-triazole.*

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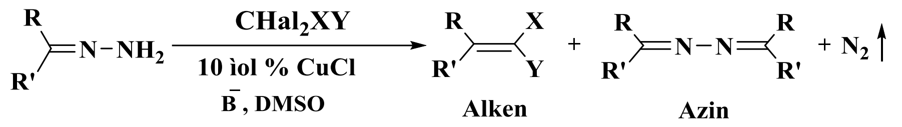
1. Introduction

There are a number of papers in the literature dedicated to the utilization of hydrazones and their activity. The presented work especially focuses on carbon with imine and functionalization of C(sp^2)-H hydrogen atom. Here we investigate the polyfunctionalization reactions of N-non substituted, N-substituted and N,N-disubstitutedhydrazonesCuCl catalyst that is ecologically efficient. The use of these compounds as a suitable synton has been expanding in recent years (Tsyrenova *et al.*, 2020, 2021; Shikhaliyev *et al.*, 2021). All these indicate that the reaction of hydrazones with polyhalogenalkanes in the presence of a CuCI catalyst is an important reaction in terms of organic synthesis.

2. Discussion

Reactions of hydrazones with polyhalogenalkanes in the presence of CuCI

Reaction between N-unsubstituted hydrazones and polyhalogen alkanes in a basic state with CuCl catalyst resultes in proper alkenes. (Shastin *et al.*, 2000, 2001; Korotchenko *et al.*, 2001, 2002, 2003, 2001; Nenajdenko *et al.*, 2003). As an olefinated agent various polyhalogenmetanes- $CBrCl_3$, CBr_4, $CFBr_3$, etanes- CF_3CCl_3, CF_3-CBr_3, CF_3-$CFBr_2$, also derivatives of trichloro vinegar acid-ethyl chloroacetate and trichloroacetonitrile were used (Scheme 1). During a reaction only symmetric azines are formed as extra compounds and nitrogen evaporates.

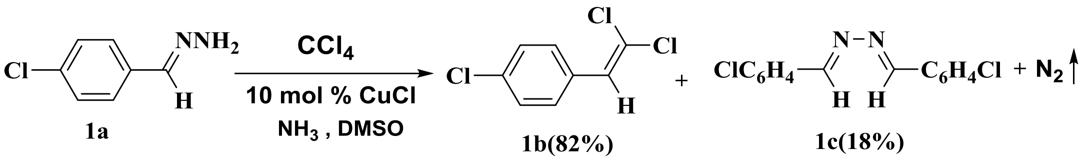


$CXYHal_2$ CCl_4 , CBr_4 , $CHBr_3$, $CFBr_3$,$CFCl_3$, CCl_3CF_3 , CF_3CBr_3 , CCl_3CN , CCl_3O_2Et

B^- NH_3 , Et_3N , $NH_2CH_2CH_2NH_2$

Scheme 1. Synthesis of dichloroalkenes from N-non substituted hydrazones in the presence of CuCl catalyst

Catalytic activity of many transition metals was investigated before the reaction of 4-chlorobenzaldehyde with 1a CCl_4 in which CuCl was chosen as a catalyst (Scheme 2) (Nenajdenko *et al.,* 2003).



1-chloro-4-(2,2-dichlorovinyl)benzene

Scheme 2. Synthesis 1-chloro-4-(2,2-dichlorovinyl)benzene

Reaction between hydrazone and 1a CCl_4 was taken place in a presence of catalytic amount (10 mol.%) of transition metal chlorides. As a catalyst IB-VIII group metal chlorides were used (Shikhaliyev, 2015). In that case, metal chlorides which have a high oxidation level were used and all the reactions were taken place in a presence of DMSO in ammonia solution (Table 1).

Table 1. Influence of the catalyst on yields of 1a substance

Catalyst	Inadditiontothe periodictablesubgroup	Yield of theproducts,%		
		Dichlorstyrol 1b	Azine 1c	Total, 1b+1c
CuCl	IB	82	18	100
AgCl	IB	20	76	96
$HAuCl_4$	IB	11	86	97
$ZnCl_2$	IIB	20	47	67
$CdCl_2$	IIB	13	80	93
$HgCl_2$	IIB	5	87	92
$LaCl_3$	IIIB	22	69	91
$Ce(NO_3)_3 \times 6H_2O$	IIIB	15	73	88
$TiCl_3 \times 3THF$	IVB	17	37	54
$ZrCl_4$	IVB	6	84	90
$NbCl_5$	VB	8	87	95
$TaCl_5$	VB	10	90	100
$CrCl_2$	VIB	-	73	73
$MoCl_5$	VIB	-	76	76
WCl_6	VIB	-	92	92
$MnCl_2 \times 4H_2O$	VIIB	20	73	93
$FeCl_3$	VIII	25	58	83
$CoCl_2 \times 6H_2O$	VIII	22	62	84
$NiCl_2 \times 6H_2O$	VIII	10	62	72
$RuCl_3 \times 3H_2O$	VIII	15	80	95
$RhCl_3 \times 3H_2O$	VIII	5	29	34
$PdCl_2$	VIII	17	66	83
H_3IrCl_6	VIII	-	95	95
K_2PtCl_4	VIII	25	73	98

It is observed that all the investigated transition metal chlorides had a catalytic effect on an interaction between hydrazone and 1a CCl_4. In all cases former hydrazone was fully converted. 1a conversion yields of hydrazone are only alkene 1b and azine 1c and mostly total yield of reaction products is near to 100%.Similar products are obtained when different transition metals are used as catalysts which explains the general characteristic of a reaction. As shown in the table, proper catalyst for synthesis of dichloroalekenes is Cu (I) chloride.

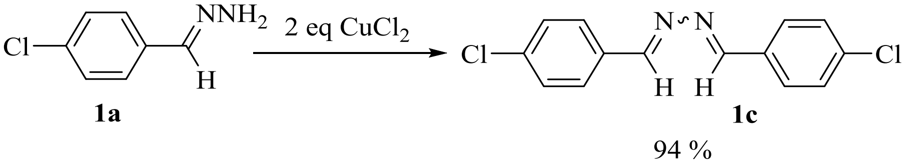
Dependence of 1b yield of dichloroalkene and 1c yield of azine on oxidation number of salt and Cu and vice versa makes the results considerable. For such purpose, both one and two valenced cupric salts of hydrazone with 1a CCl_4 were used (Table 2).

Table 2. Influence of the nature of anion and oxidation number of Cu on the yield of a reaction of hydrazone with 1a CCl_4

Catalyst	Yield of the products,%		
	Dichlorstyrol 1b	Azine 1c	Total, 1b+1c
CuCl	82	18	100
$CuCl_2$	73	27	100
$CuSO_4 \times 5H_2O$	68	19	87
$Cu(OAc)_2 \times 2H_2O$	75	20	95
$Cu(OTf)_2$	74	22	96
CuCN	20	65	85

It is observed that in both cases similar products are obtained for 1b and 1c in olefination reaction and yield of reaction products is near to 100%.

Thus, both Cu^I andCu^{II} compounds may be used as catalysts. However, CuCl is more convenient, because it is observed that oxydation results in hydrazone to transform into azine when $CuCl_2$ is used. Whereas this does not happen when Cu has one valency for instance when Cu^{II} is used ($CuCl_2$ was used in DMSO in a presence of liquid ammonia without CCl_4) as oxidator only 1c azine has found with 94% of yield (Scheme 3).

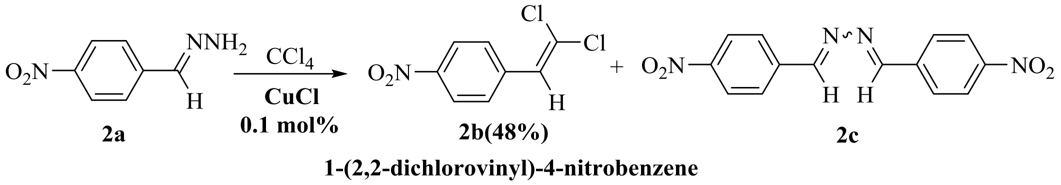


Scheme 3. Synthesis of azine (1c) in the presence of $CuCl_2$ catalyst

Other salts of Cu^{II} show the catalytic activity but does not affect a ratio of the products. But in a reaction 1b yield of alkene reduced 20% when Cu (I) sianide was used and 1c azine have gotton as a main product.

This is proablybecause of a strong complex forming ability of sianideione which dissosiates easily with cuprus atom (dissociation constant of a complex $[Cu(CN)_2]^-$ K = 1×10^{-16}), to prevent alken to be formed. Aniones which have weaker complex forming ability- halogenide, sulphat, acetat and triphtal ions make salts which easily solve in solvent. Thus, if there are opposite iones which have weak interactions with cuprus atom, reaction depends less on catalyst and oxidation of oppositeione. Based on this information, only CuCl was used by authors as a catalyst afterwards. Influence of the amount of CuCl catalyst on the yield of compounds which were synthesized from hydrazone 2a was investigated. Reactions take place between hydrazone 2a and 5 mmole CCl_4 in DMSO in a presence of liquid ammonia.

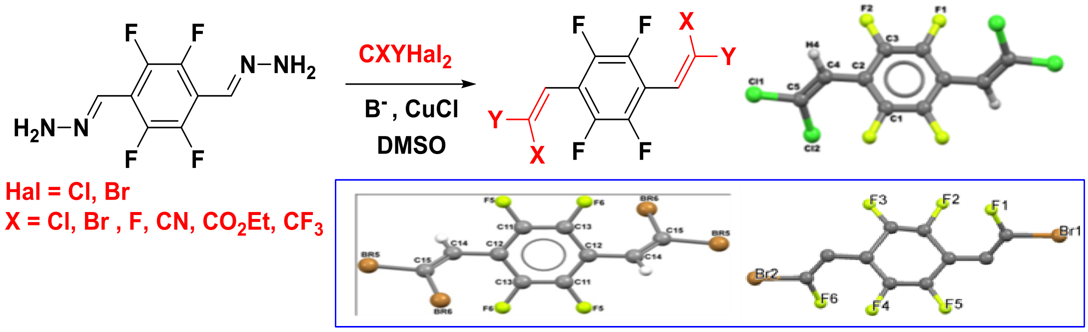
It is observed that when 0.1 mole % CuCl is used, the yield of dichloroalkene 2b is 48%. In a conversion of hydrazone 2a,additionally, azine 2c have formed (Scheme 4).



Scheme 4. Synthesis of 1-(2,2-dichlorovinyl)-4-nitrobenzene

When catalyst was used 1 mol%, the yield of alkene 2b increased to 75%. When the amount of catalyst was increased to10 mol%, the yield of alkene 2b also increased to 79%, furthermore, yield of extra compounds reduced. That is why, in the following analysis 10 mol% catalyst was taken.

Reactions have general characteristic and aliphatic, aromatic, heterocyclic aldehyde and ketones attend in these reactions. Additionally, reactions about bis-aldehydes have studied and the structure of reaction products was proved by X-Ray Structural Analysis method (Scheme 5).

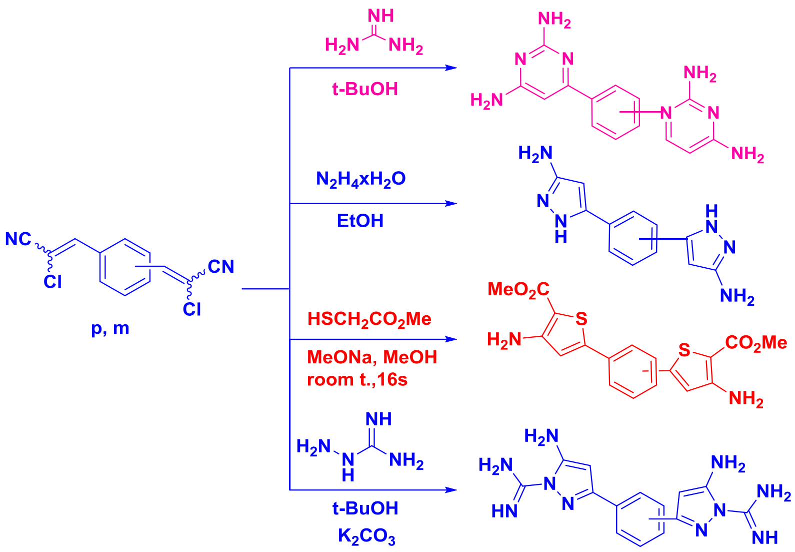


Scheme 5. Synthesis of 1,4-Bis(2,2-dihalogen)-2,3,5,6-tetrafluorbenzenes

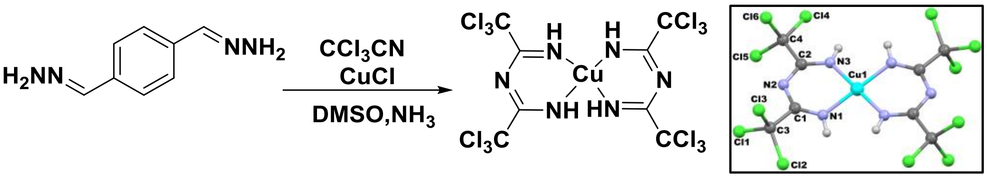
From the reaction of binucleophile reagents 1,3- and 1,4-bis-(2-chloro-2-sianovinyl)benzenes have synthesized which are used as effective syntons in the synthesis of heterocyclic compounds (Muzalevskiy *et al.*, 2013) and this shows the importance of the reaction which took place in the presence of CuCl (Scheme 6).

In the synthesis of dichloroalkenes from N-nonsubstitutedhydrazones with CuCl catalyst (Scheme 3),when trichloroasetonitryl CCl_3CN was used as a polyhalogenated reagent, NH_3 was used as an alkali bis-(2.4-bis(trichloromethyl))1,3,5-triazapentadienato Cu^{II}complex has synthesized as a product (Shikhaliyev, 2012) (Scheme 7). The structure of the complex was proved by X-Ray Structural Analysis method.

When CuCN is used as a catalyst, the yield of a reaction product decreases to 20%. This boosts assumpion about corresponding complex between nitrile and Cu. However, synthesized alkene was not observed.

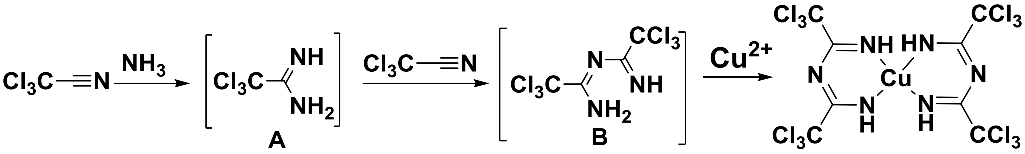


Scheme 6. Reactions of 1,3 və 1,4-Bis(2-chlorine-2-sianovinyl)benzenewith binucleophilic reagents



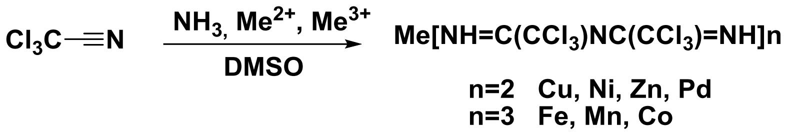
Scheme 7. Synthesis of bis-(2.4-bis(trichloromethyl))1,3,5-triazapentadienato Cu^{II}complex

It is explained below how complexes are formed. C atom in CN group of trichloroasetonitryl shows high electrophilicity because of CCl_3 group which shows ability of strong - J induction effect and makes nucleophilic attack of ammonia easier. As a result,firstly, amidine (A) has formed as an intermediate compound. Then amidine as a nucleophile has a reaction with the second molecule of trichloroasetonitrile and turnes into a corresponding ligand B. The corresponding complex is formed by the latest product and metal. Although CuCl was first seen, during a reaction $Cu^{1+} \rightarrow Cu^{2+}$ oxydized which shows the oxydation effect of the system (Scheme 8).



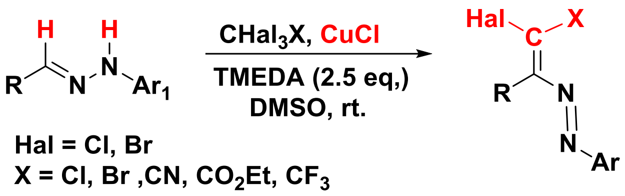
Scheme 8. Probable general scheme of formation of the complex

This mechanism explainswhy hydrazone did not completely participiated in the reaction. Besides CuCl participiated as an effective catalyst in catalytic olefination reaction to be formed dichloroalkenes, it also showed a new synthesis of halogenated triazapentadien complexes from a simple reaction. Especially from this reaction bis and tris-(2,4-bis(trichlorometyl))-1,3,5-triazapentadienato Me(II), Me(III) complexes of other transition metals (Ni, Zn, Pd, Fe, Mn, Co) were synthesized (Shikhaliyev *et al.*, 2013) (Scheme 9).



Scheme 9. Synthesis of bis and tris-(2,4-bis(trichlorometyl))-1,3,5-triazapentadienato Me(II), Me(III) complexes

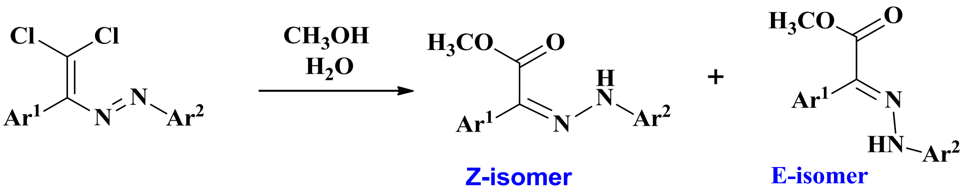
Reaction of N-substituted hydrazones resulted in synthesis of dichlorodiazabutanies in Scheme 1. Unlike a standart condition (DMSO, NH_3, CuCl), TMEDA was used as an alkali instead of ammonia and arylhydrazones turned into heterodienes which keep RN=N-RC=CCl_2 fragment. Different polyhalogenmetals-$CBrCl_3$, CBr_4, $CFBr_3$, etanes-CF_3CCl_3, CF_3-CBr_3, CF_3-$CFBr_2$, also derivatives of trichloro vinegar acid-etyltrichloroasetate and trichloroasetonitryl were used in this reaction and corresponding diazadienes were synthesized (Nenajdenko *et al.*, 2017) (Scheme 10).



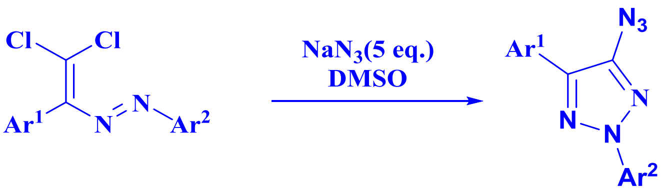
Scheme 10. Synthesis of dichlorodiazadienes from N-substituted hydrazones

Relevant reactions of arylhydrazones of various derivatives of benzyaldehyde (4-OCH_3; 2-NO_2; 3-NO_2; 4-NO_2; 4-Br) (Nenajdenko *et al.*, 2020), as well as bis-aldehydes were carried out in this direction. The role of non-covalent bonds in crystal design in these compounds has been studied. Hishfeld surface analysis of many diazediens was performed (Akkurt *et al.*, 2019; Atioglu *et al.* 2021).

Synthesized dichlorodiazadienes were used in many synthesis of compounds especially synthesis of arylhydrazones (Shikhaliev *et al.*, 2021) of α-ketoacid ether and 4-azido-1,2,3-triazol derivatives (Tsyrenova *et al.*, 2020, 2021) can be shown as follows (Scheme 11-12).

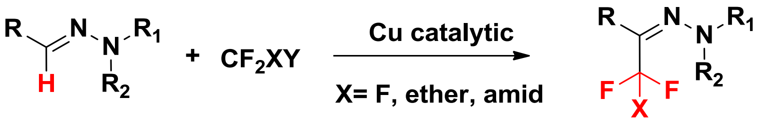


Scheme 11. Synthesis of Z/E isomers of arylhydrazones of α-ketoether



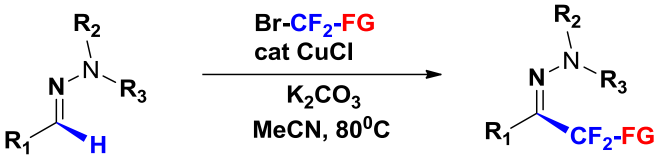
Scheme 12. 4-azido-1,2,3-triazol derivatives

There is information about new methods of trifluoromethylation and difluoroalkylation (Prieto *et al.*, 2016) of N-substituted hydrazones with CuCl in the literature of chemistry (Scheme 13).



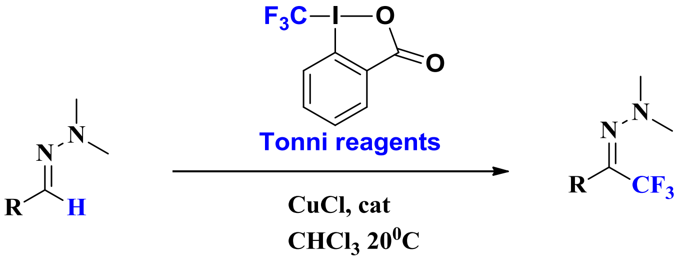
Scheme 13. PerfluoroalkylationofN,N-substituted hydrazones with CuCl catalyst

In a functionalization reaction aldehyde hydrazonesdifluoroalkylated with difluoromethylbromide in a presence of CuCl catalyst and α,α-difluoro-β-ketohydrazones were synthesized. Stereoselectivity of the process provide it to be used practically and widely (Prieto *et al.*, 2016).

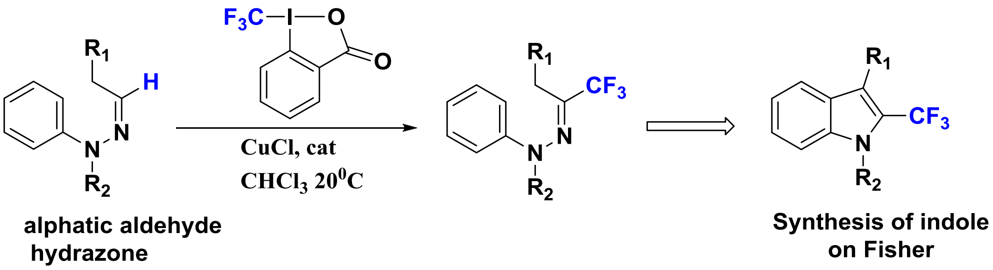


FG = ether, amid, heterocycle

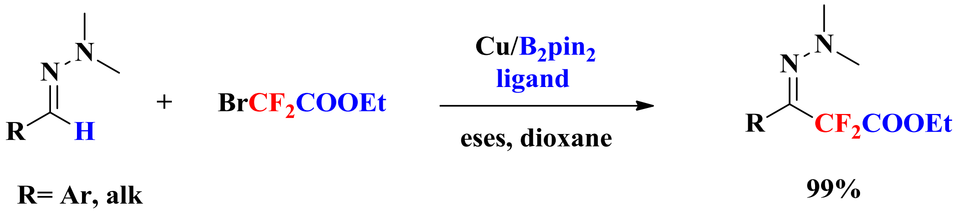
In a room temperature, in a presence of CuCl catalyst trifluoromethylation of N,N-dialkylhydrazones of aromatic aldehydes with Tony reagent was resulted in useful trifluoromethylated constructor blocks (Pair *et al.*, 2013).



C-H (sp^2) trifluoromethylation of N,N-disubstitutedhydrazones in a presence of CuCl catalyst with Tony reagent is more effective for substances which are synthesized from aliphatic aldehydes. Beside this, for Fisher trifluoromethylated N-arylhydrazones are ideal substances in indole synthesis. They support 3 staged process in which 2-trifluoromethylindol derivatives are formed from simple aldehydes (Prieto *et al.*, 2015).

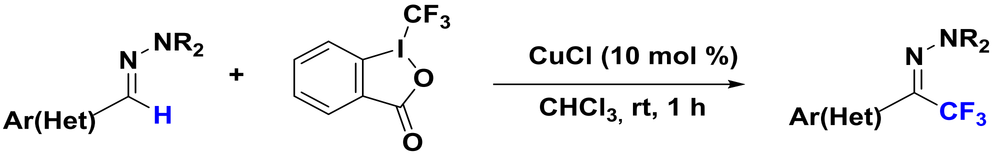


Next, effective general method ofdifluoroalkylation of C-H (sp^2) bonding of aldehyde based hydrazones in a presence of Cu catalyst was prepared (Ke *et al.*, 2016).

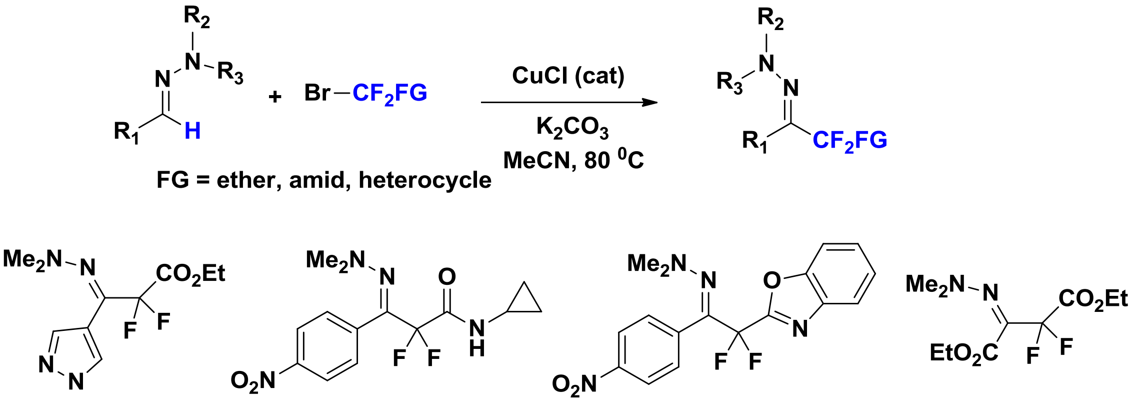


It is possible to add difluoroasethat into both aromatic and aliphatic aldehydesas a result of this reaction. Beside this, diboran as a catalytic reagent plays a significant role in this process.

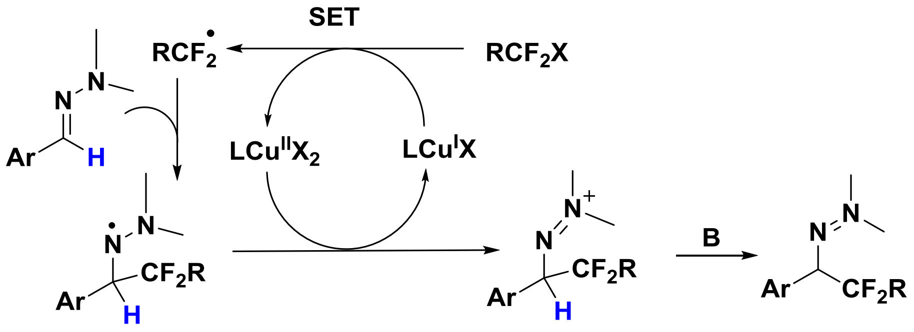
Trifluoromethylation of aromatic aldehyde N,N-dialkylhydrazones was represented in a presence of CuCl catalyst (Scheme 3). In a room temperature Tony reagent was used as trifluoromethy source (Pair *et al.*, 2013). Former hydrazones keep different functional groups as nitro, cyano, ester and hydroxyl groups.



In another work, information was prepresented about dialkylation of hydrazones with functionalized difluoromethylbromide with CuCl catalyst (Prierto *et al.*., 2015). In a room temperature stereofunctionalized α,α-difluoro-β-ketohydrazones were obtained (Scheme 13). It is interesting that, hydrazones attended in a reaction which keep cyano, ester and hydroxyl functional groups. They have an importance for future investigations.



Presumably, in a reaction of fluoroalkyle radical with hydrazone transit difluoroalkylatedaminyl radicals were gotton. Next oxydation and deprotonation reactions reduces functional groups of hydrazone.



3. Conclusion

In recent years,in the literature one can meet an information about compounds which were obtained as a result of polyfunctionalization of N-nonsubstituted, N-substituted and N,N-disubstitutedhydrazones with polyhalogenalkanes in a presence of ecologically efficient CuCl catalyst and importance of these compounds as effective syntones in organic chemistry was emphasized. Especially synthesis of different heterocyclic compounds, arylhydrazones of α-ketoacid ethers and 4-azido-1,2,3-triazole derivatives should be specifically considered and this show how important the application of CuCl catalyst is in the listed reactions.

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