A General and Useful Copper(II)-promoted Iodofunctionalization of Unsaturated Systems

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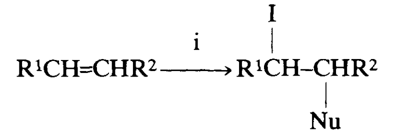
A mixture of iodine and CuO·HBF$_4$ reacts stereospecifically with olefins in the presence of a wide variety of nucleophiles (NaNO$_2$, NaSO$_2$Ar, NaI, Et$_3$SiH, MeOPh and H$_2$O) to give the corresponding 2-functionalized iodo compounds; the same reagents also cause iodofunctionalization of 1,3-dienes and acetylenes.

The organic chemistry of copper has been widely studied,[1] and Cu^{II} salts are important reagents in organic synthesis.[2] Copper(II) ions are commonly used as oxidants of halogen or halide anions in electrophilic halogenations.[3] When olefins[4] or acetylenes[5] are the substrates of these halogenations the scope of these reactions is limited by the addition of the counter ion of the Cu^{II} salt (Cl$^-$ or Br$^-$) as nucleophile to the unsaturated substrate; only one process with different functionality has been described.[6] In connection with our research on 1,2-functionalization of unsaturated systems promoted by mercury salts[7] and by bis(pyridine)iodine(I) tetrafluoroborate,[8] we report here a general method for 1,2-iodofunctionalization of olefins, dienes, and acetylenes with a mixture of iodine and CuO·HBF$_4$. The low nucleophility of the BF$_4$$^-$ anion allows a wide variety of charged as well as uncharged nucleophiles to be added to the unsaturated substrate.



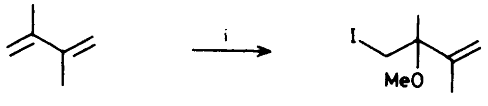
$$\mathrm{R^1CH{=}CHR^2} \xrightarrow{\text{i}} \mathrm{R^1}\overset{\displaystyle\mathrm{I}}{\mathrm{CH}}\text{–}\underset{\displaystyle\mathrm{Nu}}{\mathrm{CHR^2}}$$

(1) $R^1R^2 = [CH_2]_4$ (3) $R^1R^2 = [CH_2]_4$
(2) $R^1 = H, R^2 = Ph$ (4) $R^1 = H, R^2 = Ph$

Scheme 1. *Reagents:* i, CuO·HBF$_4$, I$_2$, NuH or Nu$^-$.

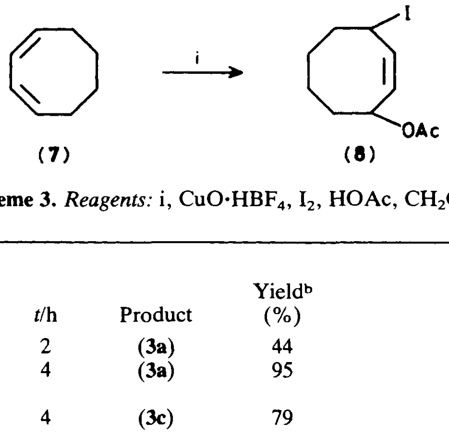
The reaction of an olefin with a mixture of iodine and CuO·HBF$_4$ in the presence of various nucleophiles gives, in a clean 'one-pot' single-step process, the corresponding *trans*-1,2-iodofunctionalized product stereoselectively (Scheme 1). At the end of the transformation, copper may be quantitatively recovered as copper(I) iodide. The stereochemistry of the products (3) derived from cyclohexene was determined by comparison of their spectral data with our previous data,[7,8] and by measurement of ^{1}H coupling constants.

Under the same reaction conditions, 2,3-dimethylbuta-1,3-diene (5) undergoes specific 1,2-addition (Scheme 2); in



(5) (6)

Scheme 2. *Reagents:* i, CuO·HBF$_4$, I$_2$, MeOH.



(7) (8)

Scheme 3. *Reagents:* i, CuO·HBF$_4$, I$_2$, HOAc, CH$_2$Cl$_2$.

Table 1. Iodofunctionalization reactions.

Substrate	Nucleophile (Nu)	Method[a]	Solvent	*t*/h	Product	Yield[b] (%)
(1)	NaNO$_2$(NO$_2$)	A	Dioxane	2	**(3a)**	44
(1)	*p*-MeC$_6$H$_4$SO$_2$Na (*p*-MeC$_6$H$_4$SO$_2$)	A	MeCN	4	**(3a)**	95
(1)	NaI(I)	B	CH$_2$Cl$_2$	4	**(3c)**	79
(1)	Et$_3$SiH(H)	B	CH$_2$Cl$_2$	3	**(3d)**	95
(1)	MeOPh (*p*-MeOC$_6$H$_4$)	B[c]	CH$_2$Cl$_2$	13	**(3e)**	30
(2)	H$_2$O(HO)	A	MeCN	5	**(4)**	65
(5)	MeOH(MeO)	B	MeOH	2	**(6)**	75
(7)	AcOH(AcO)	B	CH$_2$Cl$_2$–AcOH (5:1)	2	**(8)**	40
(9)	KSCN(NCS)	A	MeCN	15	**(11)**	40
(10)	LiBr(Br)	A	MeCN	84	**(12)**	40

[a] Typical procedures are as follows. *Method A*. To a solution of copper(II) tetrafluoroborate [1.62 ml of aq. 35% HBF$_4$ and 4 mmol of CuO] were added the solvent (20 ml) and the nucleophile (20 mmol). After 2 min stirring, iodine (6 mmol) and the substrate (8 mmol) were introduced and the mixture was stirred at room temperature. The precipitated copper(I) iodide was filtered off, and the solution extracted with CH$_2$Cl$_2$; the usual work-up procedure gave the product. *Method B*. A similar aqueous solution of copper(II) tetrafluoroborate was evaporated at 10^{-2} Torr and 50–60 °C to constant weight, to yield a pale blue solid. This was added to a mixture of solvent (20 ml), nucleophile (20 mmol), iodine (6 mmol), and substrate (8 mmol), at room temperature under argon. After stirring, the solution was hydrolysed, and treated as in method A. [b] Yields of isolated products, relative to starting substrate; not optimized. The resulting crude materials were essentially pure compounds (g.l.c. purity > 90%). Only (3e) was purified by column chromatography (silica gel; hexane ether, 98:2). [c] Silica gel 60 (Merck, 2 g) was added to prepare the copper(II) reagent.

$$\mathrm{R^3C{\equiv}CR^4} \xrightarrow{\text{i}} \mathrm{R^3CI{=}CNuR^4}$$

(**9**) $R^3 = R^4 = \mathrm{Et}$ (**11**) $R^3 = R^4 = \mathrm{Et}$
(**10**) $R^3 = \mathrm{Me}, R^4 = \mathrm{Ph}$ (**12**) $R^3 = \mathrm{Me}, R^4 = \mathrm{Ph}$

Scheme 4. *Reagents:* i, $\mathrm{CuO{\cdot}HBF_4}$, $\mathrm{I_2}$, $\mathrm{Nu^-}$.

contrast, cyclo-octa-1,3-diene (**7**) yields the 1,4-addition product in acetic acid–dichloromethane as solvent (Scheme 3).

Treatment of an acetylene with a solution of $\mathrm{Cu^{II}}$ tetrafluoroborate in acetonitrile–water, iodine, and a salt with nucleophilic anion gives the corresponding 1,2-iodofunctionalized olefin (**11**) or (**12**) (Scheme 4).

Selected examples of copper-promoted iodofunctionalization of olefins, dienes, and acetylenes are summarized in Table 1. All compounds reported show ^{1}H and ^{13}C n.m.r., i.r., and mass spectra as expected for the given structures, and the products (**3a**), (**3b**), (**3d**), (**4**), (**6**), and (**11**) have spectral data identical with those of the products obtained by other iodofunctionalizations.[7,8]

Our method allows the generalization of the use of $\mathrm{Cu^{II}}$ salts in the functionalization of unsaturated systems and is applicable to a range of nucleophiles; furthermore the reagents employed are common and safe.

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