



Oxidative bromination reaction using Cu²⁺-perfluorophthalocyanine-immobilized silica gel catalyst under mild reaction conditions

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ABSTRACT

A simplified, facile route has been applied for the grafting of copper(II) perfluorophthalocyanine complex onto functionalized silica gel. The resulting organic–inorganic hybrid material is used as an efficient and recyclable catalyst for the regioselective oxidative bromination of various aromatic substrates using KBr/H₂O₂ as the reagents, affording high yields under mild conditions. High catalytic activity efficiency could be attributed to the heterogenization of soluble metal complexes on the high surface area host.

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In recent years, considerable emphasis has been placed on improvement in the environmental impact of industrial chemical processes.¹ It is well recognized that solid catalysts can play a significant role in the development of cleaner technologies through their abilities to act as catalysts, support reagents, entrain by-products, avoid aqueous work-ups, and influence product selectivities, and several books on the applications of solids in organic synthesis have appeared.² Advances are particularly needed in the area of electrophilic aromatic substitutions,³ where traditional Lewis acid catalysts are a cause of considerable concern and where reactions are frequently unselective. Bromoaromatics are particularly versatile synthetic starting materials due to the possibility of their use in carbon–carbon bond formation reactions via Heck, Stille, and Suzuki transmetallation processes.⁴ Aromatic haloamines are used for the manufacture of polyurethanes, rubber chemicals, agricultural products, and drugs.^{5,6} The reported methods involve an electrophilic bromination of aromatic rings using brominating agents other than molecular bromine, such as *N*-bromosuccinimide,^{7,8} a hexamethylenetetraminebromine complex,⁹ and an alkyl bromide/sodium hydride/DMSO combination;¹⁰ whereas the others are based on oxidative bromination.^{11–19}

In oxidative halogenation, halide ions can be used as a halogen source together with a suitable oxidant; thus, this method represents more ecologically benign and economically attractive pathway to haloaromatics than the classical electrophilic substitutions. Main advantages of oxyhalogenation, which makes it safer

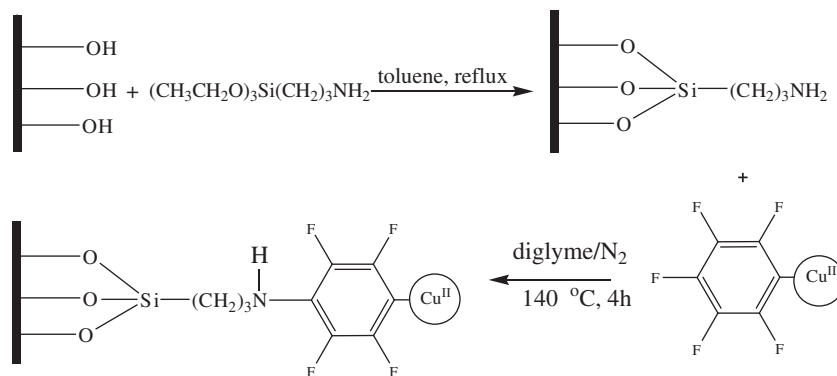
and greener, are the use of low-cost and easy-to-handle metal halides as halogenating agents and atom economy, that is, a full utilization of halogen atoms instead of using only half of the available amount. Only a few examples of the use of bromide or chloride salts as halogen source have appeared, all reporting low substrate conversions and/or low selectivities for individual products.^{20–22}

We have designed a novel heterogeneous catalytic system to generate electrophilic bromine in situ from easily available KBr as a bromine source and H₂O₂ as an oxidant for the oxidative bromination as a possible alternative to solve the disadvantages described in the earlier methods. Inorganic solids such as silica, particularly known for their mechanical and thermal stability and also for their chemical inertia, represent interesting supports for heterogenizing catalysts.^{23–25} In this context, the formation of organic–inorganic hybrids by the grafting method²⁶ is a convenient route to solid materials with catalytic properties. Present work deals with the preparation of hybrid organic–inorganic materials and the preliminary results of the activity and recyclability of this material in the oxidative bromination of aromatic substrates. Literature survey reveals that the oxidative bromination of aromatic substrates using covalently grafted silica gel as catalyst in the liquid phase and using H₂O₂ as the oxidizing agent has not been reported so far.

The synthesis of the organic–inorganic hybrid materials-immobilized copper catalyst is illustrated in Scheme 1. It was readily prepared through a two-step procedure. The activated silica gel (60–120 mesh, from Aldrich) was reacted with 3-aminopropyltriethoxy silane in dry toluene at 110 °C for 12 h to afford the 3-aminopropyl functionalized silica gel (APSG). The organic–inorganic

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Scheme 1. Preparation of silica-supported copper catalyst.

hybrid materials then reacted with copper(II) perfluorophthalocyanine complex in diglyme under nitrogen at 140 °C for 4 h to generate the silica-supported copper(II) catalyst. The catalyst characterized by surface area (BET), elemental analysis, FT-IR, diffuse reflectance UV–vis, and atomic absorption spectroscopy confirms the immobilization of CuPcF₁₆ onto APSG.

Table 1 presents the literature precedents of copper-mediated oxidative bromination of various substrates under different reaction conditions and the results have been compared with those obtained by using CuPcF₁₆-APSG as catalyst (Table 3).²⁷ It is evident from the comparison of the two tables that conversion and selectivity of substrates obtained from the hybrid technique (Table 3) are far better than those obtained by copper phthalocyanine embedded in zeolite cavities (Table 2).²⁰ However, the use of homogeneous copper catalyst^{28–31} gave higher conversions of substrates but as expected, turnover numbers were low. Moreover, the catalyst could not be reutilized.

The salt effect was also studied for the given oxidative bromination reaction. The catalyst, CuPcF₁₆-APSG, was employed using

Table 2

Effect of different bromine source on the oxidative bromination of phenol and resorcinol using CuPcF₁₆-APSG as catalyst

Entry	Salt	Phenol ^a		Resorcinol ^a	
		Conv. ^b (%)	Selectivity ^{b,c}	Conv. ^b (%)	Selectivity ^{b,c}
1	LiBr	95	4-Bromophenol (76) + 4-bromophenyl acetate (24)	92	4-Bromo-1,3-dihydroxybenzene (100)
2	NaBr	85	2-Bromophenol (35) + 4-bromophenol (65)	92	2-Bromo-1,3-dihydroxybenzene (3) + 4-bromo-1,3-dihydroxybenzene (97)
3	KBr	>99	4-Bromophenol (100)	97	4-Bromo-1,3-dihydroxybenzene (100)

^a Conditions: substrate (2 mmol); MBr (2.2 mmol); glacial acetic acid (4 mL); 30% aq H₂O₂ (2.2 mmol), 50 mg catalyst at 60 °C.

^b Conversion and selectivity were determined by GC.

^c Products were characterized by GC–MS.

Table 1

Literature precedents of copper-catalyzed oxidative bromination reaction

Entry	Substrate	Catalytic conditions	Conv. (%)	Selectivity (wt %)		
				Mono-	Di-	Tri-
1	Phenol ²⁰	CuCl ₁₆ Pc-NaX; H ₂ O ₂ /KBr	24.1	40.0	33.5	26.5
2	Phenol ²⁸	CuBr ₂ /K ₂ Cr ₂ O ₇ /HOAc	90	—	—	100.0
3	Phenol ²⁹	Cu(OAc) ₂ /HBr/HOAc; O ₂ (1 atm)	75	97.0	—	—
4	Aniline ²⁰	CuCl ₁₆ Pc-NaX; H ₂ O ₂ /KBr	10.3	63.0	15.5	21.5
5	Aniline ²⁸	CuBr ₂ /K ₂ Cr ₂ O ₇ /HOAc	85	—	—	100.0
6	Aniline ³⁰	Cu(OAc) ₂ /HBr/HOAc; O ₂ (1 atm)	90	70.0	7.0	—
7	Benzene ²⁰	CuCl ₁₆ Pc-NaX; H ₂ O ₂ /KBr	11.5	58.0	34.0	8.0
8	Benzene ²⁸	CuBr ₂ /K ₂ Cr ₂ O ₇ /HOAc	65	100.0	—	—
9	Resorcinol ²⁰	CuCl ₁₆ Pc-NaX; H ₂ O ₂ /KBr	31.6	54.1	26.5	19.0
10	Acetanilide ²⁸	CuBr ₂ /K ₂ Cr ₂ O ₇ /HOAc	70	100.0	—	—
11	2-Naphthol ³¹	CuBr ₂ /K ₂ Cr ₂ O ₇ /HOAc	80	100.0	—	—
12	Naphthalene ²⁸	CuBr ₂ /K ₂ Cr ₂ O ₇ /HOAc	88	100.0	—	—
13	Naphthalene ³¹	CuBr ₂ /NaBiO ₃ /HOAc	72	100.0	—	—
14	Anthracene ²⁸	CuBr ₂ /K ₂ Cr ₂ O ₇ /HOAc	90	100.0	—	—

H₂O₂ as an oxidant and MBr (M = Li, Na, K) as a bromine source (Table 2) (Scheme 2). Among the three salts, KBr has been found to be the most efficient bromine source and a monoselective product is obtained. This could be well explained by the proposed mechanism where the generation of Br₂ is much easier in this case. The use of sodium bromide did not produce regioselective products. LiBr, though efficient, is less selective than KBr.

Substrates like phenol, aniline, and acetanilide showed excellent *para*-selectivity. The activated aromatics, such as phenol, resorcinol, naphthol, cresol, and aniline, have shown the regioselective conversion into their respective monobrominated products in high turnover numbers, while inactive ones such as benzene, naphthalene, and anthracene showed very low conversion, though monoselective. The deactivated substrates did not show any conversion at all. In case of styrene, the oxidative bromination of aromatic nucleus does not take place, though side chain leads to oxidation as well as oxidative bromination products. We also examined the behavior of aniline under both oxidative bromination as well as oxychlorination conditions that is, using KBr and KCl, respectively, as a halogen source. Surprisingly, the conversion of aniline with KCl was slower than in the presence of KBr and the corresponding chlorinated derivative, that is, 2-chloroaniline appeared only as a minor product as identified by GC/MS.

Further, GC/MS identification of the reaction mixture, experiment 7 (see Table 3), has shown that a main transformation of aniline, which competes with the oxidative bromination, is *N*-acetylation giving *N*-phenylacetamide. At the end of the reaction, monobrominated acetamide (major) and monobrominated aniline

Table 3
Silica-supported copper-catalyzed oxidative bromination of various aromatic substrates

Entry	Substrate ^a	Conv. ^b (%)	TON ^d × 10 ³ (time/h)	Product selectivity ^{b,c}
1 ^e	Phenol	>99, 99, 98, 98, 98, 95	440 (1.5)	4-Bromophenol (100%)
2	Resorcinol	97	431 (1.5)	4-Bromo-1,3-dihydroxybenzene (100)
3	2-Naphthol	75	333 (2.0)	1-Bromo-2-naphthol (100%)
4	4-Methylphenol	97	431 (1.5)	2-Bromo-4-methylphenol (100%)
5.	Salicylaldehyde	94	418 (3.0)	5-Bromo-2-hydroxy benzaldehyde
6	2-Methoxynaphthalene	85	377 (2.5)	1-Bromo-2-methoxynaphthalene (100%)
7	Styrene	100	444 (2.0)	Styrene dibromide + styrene glycol + 1-phenylethanol (50:25:25)
8	Acetanilide	87	386 (2.2)	4-Bromoacetanilide (100%)
9	Aniline	100	444 (1.0)	<i>N</i> -Phenylacetamide: 4-bromoaniline: 4-bromo- <i>N</i> -phenylacetamide (4:6:90)
10	Anthracene	30	133 (6.0)	9-Bromoanthracene: anthra-9,10-quinone (85:15)
11	Naphthalene	18	80 (6.0)	1-Bromonaphthalene (100%)
12	Benzene	12	53 (6.0)	Bromobenzene (100%)
13	Benzoic acid	—	—	—
14	Nitrobenzene	—	—	—

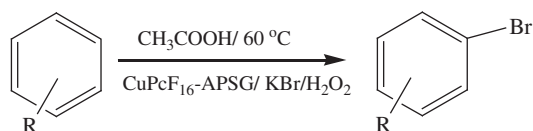
^a Conditions: substrate (2 mmol); KBr (2.2 mmol); glacial acetic acid (4 mL); 30% aq H₂O₂ (2.2 mmol), 50 mg catalyst at 60 °C.

^b Conversion and selectivity were determined by GC.

^c Products were characterized by GC-MS.

^d Turnover number (TON) = mole of product formed/mole of metal present in the catalyst.

^e Catalytic runs to test recyclability.

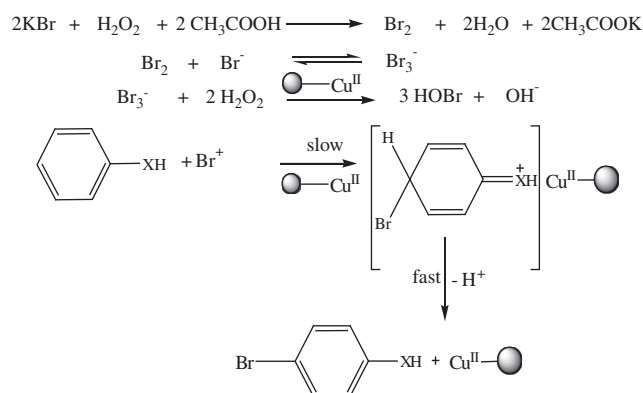


Scheme 2. Oxidative bromination of aromatics.

(minor) were also detected. This major product seems to be a result of *N*-acetylation of the primarily formed 4-bromoaniline rather than bromination of *N*-phenylacetamide, as at lower conversions, higher selectivities for 4-bromoaniline were observed as identified by GC/MS. Whereas, at longer reaction times 4-bromoaniline decreased and 4-bromo-*N*-phenylacetamide increased. This product, 4-bromo-*N*-phenylacetamide, could be easily hydrolyzed by aqueous base back to 4-bromoaniline, if desired. The only by-product of this reaction is *N*-phenylacetamide, also a valuable chemical, making the method synthetically useful.

Oxidative bromination of the substrates by dissolved copper complex leached out from the solid catalyst is negligible since no copper was detected in the filtrate (atomic absorption spectroscopy). Also, in the absence of the catalyst, H₂O₂ alone is unable to oxyhalogenate the substrate to any significant extent. It is worth mentioning here that unsubstituted copper phthalocyanine has a low activity; only oxidation reactions by H₂O₂ were observed. No halogenated products were obtained.²⁰ The reaction could also be carried out with homogeneous catalyst, that is, CuPcF₁₆, but the catalyst cannot be recovered or reused and the turnover numbers for the conversions were also low. The probable mechanism has been illustrated in **Scheme 3**. Apparently the nucleophilic halide ions, when present, coordinate with the copper ions and suppress the formation of intermediates (like dioxygen complexes) that lead to nuclear hydroxylation. Since the liberation of Br₂ from KBr by H₂O₂ in the presence of homogeneous and enzyme catalysts is well known, it was expected that the same situation may prevail in the present case also. Probably, the catalyst enhances the oxidation of Br⁻ (Br₃⁻) to Br⁺ (HOBr), which reacts in the presence of acidic centers of catalyst including lewis acid metal site with the substrate to give brominated compounds.

The recyclability of the silica-supported copper was also surveyed. After reaction, the solution was vacuum filtered using a sintered glass funnel and the catalyst (50 mg) was washed with CH₂Cl₂ (5 mL), Et₂O (5 mL), C₂H₅OH (5 mL), and hexane (5 mL),



Scheme 3. Plausible rationale for oxidative bromination of aromatics.

respectively. After being dried, it was reused directly without further purification. The silica-supported copper was recovered, recycled, and used for 6 consecutive trials without loss of activity (**Table 3**).

The catalyst has been prepared by following the slightly modified method of Mansuy et al.^{32,33} The decrease in the surface area of catalyst is indicative of the grafting of the complex onto silica gel.³⁴ Chemical analyses of CuPcF₁₆-APSG (Anal. Found: C: 7.139, H: 1.273, N: 1.739) revealed the presence of organic matter with a C/N ratio roughly similar to that of phthalocyanine. The IR spectrum of catalyst shows band at 1637 cm⁻¹ that is due to C=N stretching vibration of the imine bond. The diffuse reflectance (DR)-UV-vis spectra of silica gel do not have any absorption band in the region 250–850 nm. The curve of CuPcF₁₆ exhibits two shoulders around 300 nm and a broad absorption band in the region of 550–800 nm due to ligand π-π* electronic transitions (**Fig. 1**). The two shoulders in CuPcF₁₆-APSG and the shifting of band maximum from ~730 to ~715 nm (blue shift) is indicative of an increased π overlap on immobilization/grafting of the complex molecule.³⁵

In conclusion, the application of an organic-inorganic hybrid copper catalyst has been demonstrated for the first time for the oxidative bromination of aromatics. The method has been found to offer additional advantages such as commercial availability of the reagents, simple reaction conditions, no evolution of hydrogen

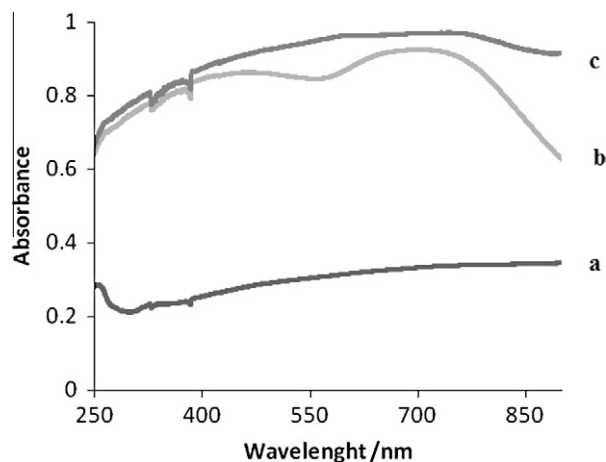


Figure 1. DR-UV-vis spectra of (a) silica gel; (b) CuPcF₁₆-APSG (after grafting); (c) CuPcF₁₆.

bromide, high yield, economical, easy setup and workup, selective mono-bromination, inexpensive, and greener synthesis.

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Supplementary data

Supplementary data (¹³C NMR solid state spectrum, FT-IR analysis, BET and elemental analysis) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.06.067.

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