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Recyclable, Bifunctional Metallaphotocatalysts for C–S Cross-Coupling Reactions

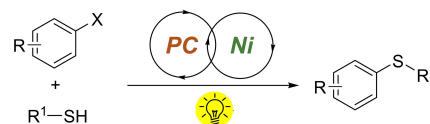
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Metallaphotocatalytic cross-coupling reactions are typically carried out by combining homogeneous or heterogeneous photocatalysts with a soluble nickel complex. Previous attempts to realize recyclable catalytic systems use immobilized iridium complexes to harvest light. We present bifunctional materials based on semiconductors for metallaphotocatalytic C–S cross-coupling reactions that can be reused without losing their catalytic activity. Key to the success is the permanent immobilization of a nickel complex on the surface of a heterogeneous semiconductor through phosphonic acid anchors. The optimized catalyst harvests a broad range of the visible light spectrum and requires a nickel loading of only ~0.1 mol%.

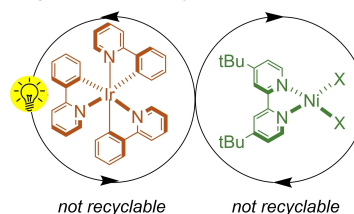
Visible light is a powerful reagent in organic synthesis.^[1] In particular, the merger of photo- and nickel catalysis (metallaphotocatalysis) has emerged as an attractive strategy to achieve carbon–carbon and carbon–heteroatom bond formations under mild conditions.^[2] The cross-coupling of thiols with (hetero)aryl halides, for example, was carried out by combining a nickel catalyst with an iridium, or ruthenium polypyridyl complex as photoredox catalyst (Figure 1, A).^[3] Similar C–S cross-couplings were also reported using an organic photocatalyst.^[4]

A semi-heterogeneous method using a carbon nitride material as photocatalyst was developed to partially recycle the catalytic system (Figure 1, B).^[5]

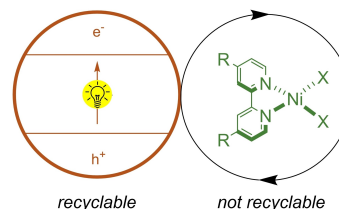
More recently, a bifunctional polymeric catalyst was prepared using building units that were functionalized with an iridium polypyridyl photocatalyst and a nickel complex.^[6] Metal leaching during recycling experiments resulted in a gradual decrease of the yield. Heterogeneous metal-organic frameworks that can be reused in C–S bond formations were



A Homogeneous dual catalysis [ref. 3]



B Semi-heterogeneous dual catalysis [ref. 5 & 9]



C This work: Heterogeneous dual catalysis

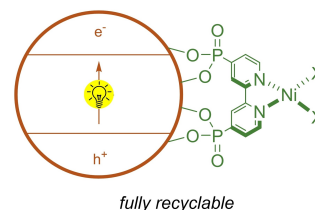


Figure 1. Catalytic systems for metallaphotocatalytic C–S cross-couplings.

synthesized by coordinating iridium- and nickel complexes to zirconium^[7] or hafnium clusters.^[8] However, these bifunctional catalysts are difficult to prepare and rely on immobilized noble-metal complexes as photocatalysts.

We recently developed a self-assembling catalyst system, in which a nickel complex and a dye adsorb to the surface of TiO₂ (dye-sensitized metallaphotocatalysts, DSMPs) that catalyzes several cross-couplings.^[9] Key to the success was that the nickel complex and the dye are equipped with carboxylic acid groups that bind to the semiconductor's surface. However, recycling studies suffered from a gradual decrease of the yield due to leaching of the nickel catalyst and the dye because of the weak interaction between carboxylic acid groups and TiO₂.^[10]

Various functional groups are known to bind to the surface of semiconducting materials and are intensively studied for dye-sensitized solar cells (DSSCs).^[11] Carboxylic acids are

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commonly used, because this functional group enables facile electron injection from the excited dye into the conduction band of the semiconductor.^[12] Phosphonic acid groups have a significantly higher adsorption strength than carboxylic acids,^[10,13] but their low electron injection rates make them often unsuitable for DSSCs.^[14]

Here we demonstrate that the strong interaction of phosphonic acid moieties with the surface of semiconducting materials accesses recyclable metallaphotocatalysts for C–S cross-coupling reactions (Figure 1, C).^[9]

Our investigations started by studying different semiconductors as photocatalysts in the metallaphotocatalytic cross-coupling of methyl 4-iodobenzoate and 2-mercaptoethanol in presence of catalytic amounts of NiBr₂·3H₂O, a bipyridine ligand that is equipped with phosphonic acid groups (dpbpy = [2,2'-bipyridine]-4,4'-diylidiphosphonic acid), and a base (Table 1). Using blue light (440 nm), two carbon nitride materials (CN-OA-m^[15] and mpg-CN^[16]), TiO₂ P25, dye-sensitized TiO₂ P25 (pre-functionalized with a ruthenium dye that contains a phosphonic acid anchoring group (Ru(bpy)₂(dpbpy)-TiO₂^[17]), and CdS resulted in the formation of the desired coupling product (Entry 1–5). Bismuth oxide was unsuitable as photocatalyst (Entry 6–7).

We also studied this reaction at longer wavelengths (Entry 8–14), because the high energy of blue light potentially causes deactivation of nickel catalysts through the formation of nickel black,^[18] and can lead to undesired side reactions.^[9,19] Quantitative product formation was observed at 525 nm using CN-OA-m, (Entry 8). In addition, Ru(bpy)₂(dpbpy)-TiO₂ also catalysed the desired reaction and resulted in 69% of the desired coupling product (Entry 11). All other tested semiconductors showed low catalytic activities using green light.

Next, we sought to optimize the two most promising catalytic systems. In case of CN-OA-m, a careful investigation of

all reaction parameters showed that 1.67 mg/mL of the semiconductor in combination with 5 mol% of NiBr₂·3H₂O and dpbpy are sufficient to quantitatively form the desired product within 17 h using 525 nm LEDs (Table 2, Entry 1). Under the same conditions, methyl 4-bromobenzoate resulted in low amounts of **1** (Table 2, Entry 2). When Ru(bpy)₂(dpbpy)-TiO₂ was used as photocatalyst, a longer reaction time in combination with a higher loading of the nickel complex was necessary, but the high selectivity towards the desired product was maintained (Entry 3). Control studies showed that no reaction occurred in the absence of CN-OA-m, dpbpy, the base, or light (Entry 4–7). Only small amounts of the coupling product were formed without the Ni^{II} salt, or in the presence of oxygen (Entry 8–9). Using a 440 nm irradiation source, full conversion was obtained after 3 h (Entry 10).

The optimized conditions were evaluated for a small set of thiols and aryl iodides using blue and green light irradiation (Table 3). When 2-mercaptoethanol was used, a selective C–S bond formation (**2**), with no detectable amount of the corresponding C–O coupling product was obtained. The catalytic cocktail was also applicable for selective couplings of secondary, tertiary and aromatic thiols with methyl 4-iodobenzoate (**3–6**). Moreover, the protocol is not limited to electron-rich aryl iodides, and excellent yields were obtained for iodobenzene (**7**) and 4-iodoanisole (**8**) were used.

Similar to the previously reported DSMPs, in which the nickel complex and a dye were equipped with carboxylic acid groups,^[9] the catalytic system reported herein self-assembles *in situ*. To characterize the functional heterogeneous catalysts, an *ex situ* preparation was carried out (Figure 2). Therefore, the respective semiconductor material was dispersed in MeCN,

Table 1. Semiconductor screening for C–S cross-coupling reactions using a nickel complex that contains phosphonic acid groups.^[a]

Entry	Semiconductor	1 [%] ^[b]	Entry	Semiconductor	1 [%] ^[b]
1	CN-OA-m	99	8	CN-OA-m	99
2	mpg-CN	99	9	mpg-CN	4
3	TiO ₂	38	10	TiO ₂	5
4	Ru(bpy) ₂ (dpbpy)-TiO ₂	99	11	Ru(bpy) ₂ (dpbpy)-TiO ₂	69
5	CdS	45	12	CdS	20
6	Bi ₂ O ₃	n.d.	13	Bi ₂ O ₃	n.d.
7	Bi ₂ O ₃ nanopowder	n.d.	14	Bi ₂ O ₃ nanopowder	n.d.

[a] Reaction conditions: methyl 4-iodobenzoate (190.3 μmol), methyl 3-mercaptoacetate (380.5 μmol), Ru(bpy)₂(dpbpy) (2.4 μmol), NiBr₂·3H₂O (19.0 μmol), dpbpy (19.0 μmol), semiconductor (30 mg) and BIPA (951.5 μmol) in MeCN (3 mL). [b] Determined by ¹H-NMR using 1,3,5-trimethoxybenzene as internal standard. dpbpy = [2,2'-bipyridine]-4,4'-diylidiphosphonic acid, BIPA = *N*-tert-butylisopropylamine, bpy = 2,2'-bipyridine, n.d. = not detected.

Table 2. Optimized conditions and control studies.^[a]

Entry	Conditions	1 [%] ^[b]
1	As shown	99 (94) ^[c]
2	methyl 4-bromobenzoate	11
3	Ru(bpy) ₂ (dpbpy)-TiO ₂ instead of CN-OA-m ^[d]	99
4	No CN-OA-m	n.d.
5	No dpbpy	n.d.
6	No BIPA	n.d.
7	No light	n.d.
8	No NiBr ₂ ·3H ₂ O	10
9	no degassing	4
10	440 nm, 3 h	99

[a] Reaction conditions: methyl 4-iodobenzoate (190.3 μmol), methyl 3-mercaptoacetate (380.5 μmol), NiBr₂·3H₂O (9.5 μmol), dpbpy (9.5 μmol), CN-OA-m (5 mg) and BIPA (951.5 μmol) in MeCN (3 mL). [b] Determined by ¹H-NMR using 1,3,5-trimethoxybenzene as internal standard. [c] Isolated yield in parentheses. [d] Carried out with 10 mg/mL TiO₂ P25, Ru(bpy)₂(dpbpy) (2.4 μmol), NiBr₂·3H₂O (19 μmol), dpbpy (19 μmol), BIPA (951.5 μmol) in MeCN (3 mL) within 24 h. dpbpy = [2,2'-bipyridine]-4,4'-diylidiphosphonic acid, BIPA = *N*-tert-Butylisopropylamine, bpy = 2,2'-bipyridine, n.d. = not detected.

followed by addition of dpbpy, the nickel salt and the dye (optional) (Figure 2, A). The mixture was stirred overnight and the resulting material was isolated by centrifugation, washing and lyophilization (see SI for details). Inductive coupled plasma - optical emission spectroscopy (ICP-OES) was used to study the amount of nickel, phosphorus and ruthenium. In case of the functionalized carbon nitride material (**Cat 1**), a nickel loading of 21.1 mg g^{-1} (corresponding to 1 mol% $\text{NiBr}_2 \cdot 3\text{H}_2\text{O}$) and a phosphorus content of 71.2 mg g^{-1} (corresponding to 3 mol% dpbpy) was determined. For the variant using dye-sensitized TiO_2 (**Cat 2**), a nickel loading of 4.18 mg g^{-1} (corresponding to 1 mol% $\text{NiBr}_2 \cdot 3\text{H}_2\text{O}$), a Ru loading of

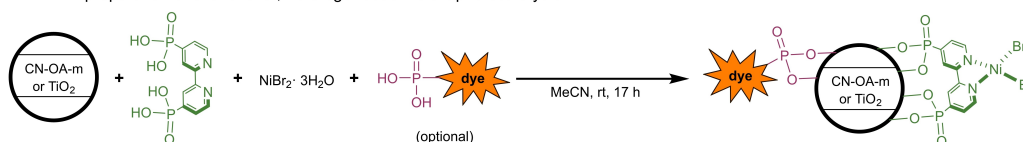
4.59 mg g^{-1} (corresponding to 0.7 mol% $\text{Ru}(\text{bpy})_2(\text{dpbpy})$) and a phosphorus content of 32.2 mg g^{-1} (corresponds to 8.2 mol% dpbpy as ligand in the nickel salt and $\text{Ru}(\text{bpy})_2(\text{dpbpy})$) was measured. The significant difference in the nickel loadings was further confirmed by energy-dispersive X-ray spectroscopy (EDX) analysis (Table S11 and S13), and is likely responsible for the different catalytic activity of the functionalized materials in the model reaction. The UV-Vis spectrum of the functionalized carbon nitride confirms its absorption up to $\sim 700 \text{ nm}$ (Figure 2, B), which is similar to the non-functionalized CN-OA-m (Figure S6).^[15] TiO_2 functionalized with the ruthenium dye and the nickel complex broadly absorbs across the visible light spectrum (Figure 2, C). Scanning electron microscopy (SEM) analysis of both materials showed that the porous surface of CN-OA-m and TiO_2 P25 was not altered during the immobilization (Figure S7 and S10).

Next, we studied the recyclability of the bifunctional materials using blue (440 nm) and green (525 nm) light (Figure 3, A). In all cases, the first experiment was carried out through *in situ* catalyst formation using the conditions reported in Table 2. After the respective reaction time, the heterogeneous catalyst was separated, washed and reused without adding additional nickel salt or ligand. To our delight, both catalytic systems could be recycled multiple times without losing their activity using both wavelengths. This provides evidence that the ligand binds permanently to the surface of the semiconductor, and that the nickel atoms strongly coordinate to the ligand.

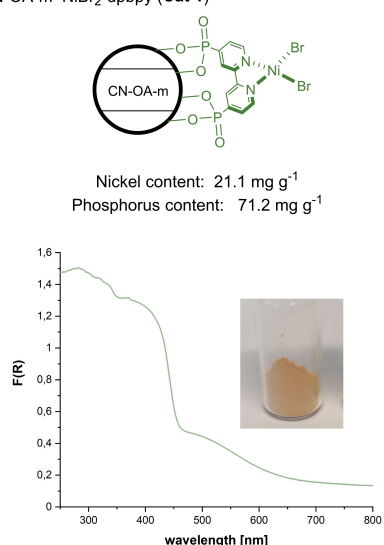
Table 3. Scope.^[a]

 440 nm, 3 h, 99% (63%) ^b 525 nm, 20 h, 98%	 440 nm, 18 h, 91% (64%) ^b 525 nm, 48 h, 99%	 440 nm, 18 h, 91% (59%) ^b 525 nm, 80 h, 96%
 440 nm, 18 h, 99% (82%) ^b 525 nm, 80 h, 97%	 440 nm, 3 h, 90% (73%) ^b 525 nm, 18 h, 99%	 440 nm, 18 h, 99% (70%) ^b 525 nm, 48 h, 99%
 440 nm, 18 h, 99% (78%) ^b 525 nm, 48 h, 98%		
<p>[a] Reaction conditions: methyl 4-iodobenzoate (190.3 μmol), methyl 3-mercaptopropionate (380.5 μmol), $\text{NiBr}_2 \cdot 3\text{H}_2\text{O}$ (9.5 μmol), dpbpy (9.5 μmol), CN-OA-m (5 mg) and BIPA (951.5 μmol) in MeCN (3 mL). Yields were determined by ¹H-NMR using 1,3,5-trimethoxybenzene as internal standard. [b] Isolated yield in parantheses. dpbpy = [2,2'-bipyridine]-4,4'-diylidiphosphonic acid, BIPA = <i>N</i>-tert-Butylisopropylamine.</p>		

A *Ex situ* preparation of bifunctional, heterogeneous metallaphotocatalysts



B CN-OA-m-NiBr₂-dpbpy (**Cat 1**)



C $\text{Ru}(\text{bpy})_2(\text{dpbpy})\text{-TiO}_2\text{-NiBr}_2\text{-dpbpy}$ (**Cat 2**)

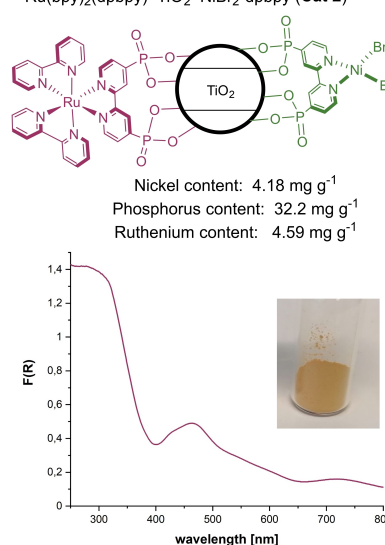


Figure 2. Preparation (A) and characterization (B,C) of fully heterogeneous metallaphotocatalysts.

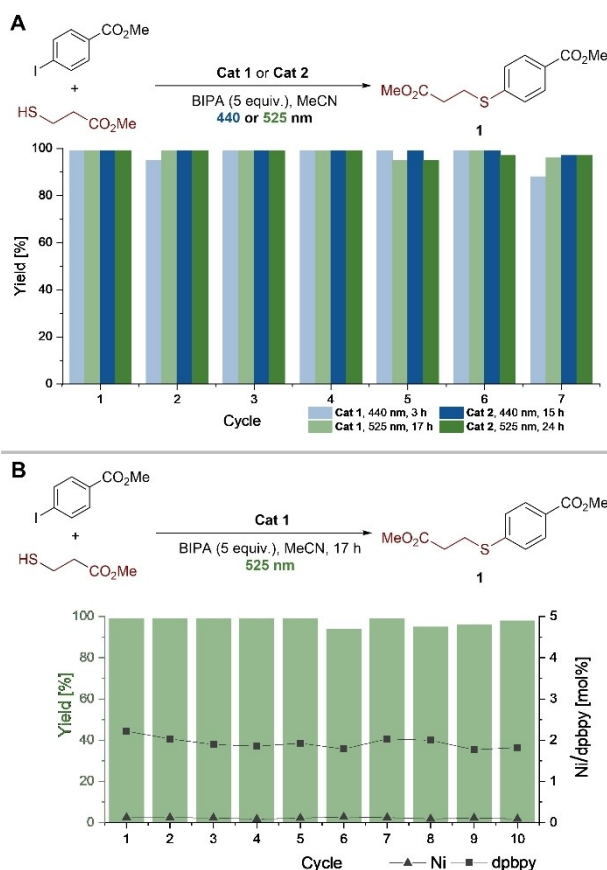


Figure 3. Recycling studies of Cat 1 and Cat 2 with blue and green light irradiation (A) and recycling studies including ICP-OES analysis using Cat 1 with green light irradiation (B).

A more detailed investigation was carried out using the functionalized carbon nitride material (Figure 3, B). The heterogeneous catalyst was reused ten times and analyzed after each experiment by ICP-OES. After the first experiment, a nickel loading of 2.65 mg g^{-1} and a phosphorus content of 52.2 mg g^{-1} was determined, which indicates that 2.2 mol% of the ligand and 0.1 mol% of the nickel salt that were initially added to the reaction mixture were still immobilized (for details, see Table S21). The amount of nickel and phosphorus did not further decrease during the subsequent cycles, and the catalytic activity was maintained. This shows that both species are permanently immobilized on the surface of the semiconductor and that the catalytic system only requires $\sim 0.1 \text{ mol\%}$ of the nickel salt and $\sim 1.9 \text{ mol\%}$ of the ligand. Indeed, a control experiment using this nickel and ligand loading through the *in situ* method gave quantitative product formation within 17 h (Table S23).

Unfortunately, the heterogeneous materials was not applicable for the metallaphotocatalytic C–O cross-coupling of carboxylic acids with aryl halides,^[20] or the C–C coupling of α -silylamines with aryl halides (Table S24 and S25).^[21] Control experiments using iridium polypyridyl complexes instead of the heterogeneous semiconductor also gave no product formation in these reactions, which indicates a detrimental effect of the phosphonic acid groups of the nickel complex in these trans-

formations. Product formation (25 %) was observed for the C–C cross-coupling reaction of potassium benzyltrifluoroborates with aryl halides using mpg-CN^[22] in combination with NiBr₂·3H₂O and dpbbp (Table S26), but attempts to optimize the reaction or to recycle the catalyst failed, presumably due to the formation of nickel black.^[18]

In conclusion, we have shown that a self-assembling heterogeneous material for metallaphotocatalytic C–S cross-couplings can be obtained by mixing a carbon nitride material or dye-sensitized TiO₂ with a nickel complex that is functionalized with phosphonic acid groups. The final catalyst shows high activity even though the nickel content is only 0.1 mol% and absorbs broadly across the visible light spectrum. The catalyst can be recycled at least ten times maintaining its catalytic activity. Improved ligand designs to expand the applicability of this concept to other cross-coupling reactions are currently evaluated in our laboratory.

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Conflict of Interest

The authors declare no conflict of interest.

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