



HAL
open science

Heterogenization of [Ru(bpy)₃].Cl₂ on ordered mesoporous silica materials for photocatalytic applications

Malik Sebbat, Anish Lazar, Claire Laurent, Christelle Despas, Neus Vilà, Alain Walcarius, Nathan D. Mcclenaghan, Emmanuel Oheix, Bénédicte Lebeau, Morgan Cormier, et al.

► **To cite this version:**

Malik Sebbat, Anish Lazar, Claire Laurent, Christelle Despas, Neus Vilà, et al.. Heterogenization of [Ru(bpy)₃].Cl₂ on ordered mesoporous silica materials for photocatalytic applications. SYNLETT, inPress, 10.1055/a-2317-3672 . hal-04567997

HAL Id: hal-04567997

<https://hal.science/hal-04567997v1>

Submitted on 3 May 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

Heterogenization of [Ru(bpy)₃].Cl₂ on ordered mesoporous silica materials for photocatalytic applications

Malik. Sebbat^a
Anish. Lazar^{b,c}
Claire. Laurent^a
Christelle. Despas^d
Neus. Vilà^d
Alain. Walcarius^d
Nathan. McClenaghan^e
Emmanuel. Oheix^{b,c}
Bénédicte. Lebeau^{*b,c}
Morgan. Cormier^{*a}
Jean-Philippe. Goddard^{*a}

^a Université de Haute-Alsace (UHA), Université de Strasbourg, CNRS, Laboratoire d'Innovation Moléculaire et Application (LIMA) UMR 7042, 68100 Mulhouse, France

morgan.cormier@uha.fr

jean-philippe.goddard@uha.fr

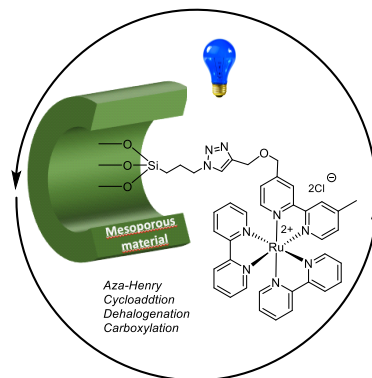
^b Université de Haute Alsace, CNRS, IS2M UMR 7361, 68100 Mulhouse, France

^c Université de Strasbourg, 6700 Strasbourg, France

benedicte.lebeau@uha.fr

^d Université de Lorraine, CNRS, Laboratoire de Chimie Physique et Microbiologie pour les Matériaux et l'Environnement (LCPME), Nancy F-54000, France

^e Université de Bordeaux, CNRS, Institut des Sciences des Moléculaires (ISM) UMR 5255, 33405 Talence, France
Mulhouse, France



Abstract Herein, the preparation and characterization of three Ru-based heterogeneous photocatalysts supported on ordered mesoporous silica materials are reported. The photocatalytic activity of these catalysts was evaluated through oxidation, reduction, cycloaddition and carboxylation reactions and their efficiencies are comparable to the parent [Ru(bpy)₃]Cl₂ in homogeneous conditions. These photocatalysts are efficiently recovered even after five reactions cycles offering new opportunities in sustainable chemistry.

Keywords Heterogeneous Photocatalysis, Ordered Mesoporous Silica, [Ru(bpy)₃]Cl₂, Sustainable Chemistry

Nowadays, sustainable, and environmentally-friendly processes allow chemists to move towards new methods adhering to green chemistry principles¹ including energy reduction, atom economy, catalysis, less chemical waste production and selective transformations in synthesis. A transition towards sustainable processes is thus required and the photocatalysis concept is considered as a valuable alternative.² Indeed, the activation of a photocatalyst (PCat) by UV-visible or near-infrared light³ allows conversion of these renewable sources of energy into chemical energy. The excited photocatalyst is capable of transferring electrons or energy to a substrate to form the key reactive intermediates, mandatory to initiate the transformation. The role of the photocatalyst is crucial but unfortunately these precious compounds are typically lost at the end of the reaction, during the work-up step. Thus, improving the photocatalyst recovery remains an important challenge in limiting waste production in this type of process. This is particularly important for expensive and potentially toxic PCat.

In this context, the use of heterogeneous photocatalysts⁴ prepared via the immobilization of the molecular photocatalyst onto a suitable solid material seems to be a valuable solution.⁵ The synthesis of a robust, stable support is determinant in reaching this goal. Usually, heterogeneous

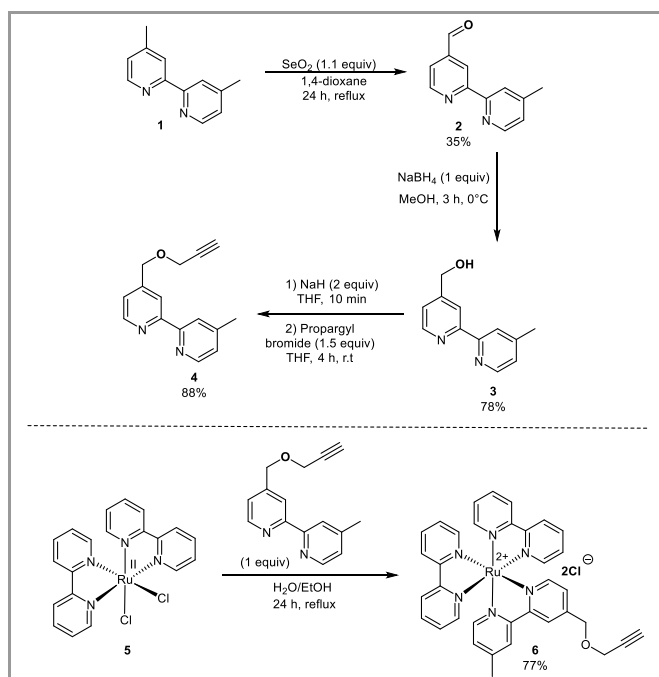
photoredox systems are composed of an insoluble support (metallic nanoparticles,⁶ polymer,⁷ silica⁸) bonded to a photocatalyst by an organic linker or simply by specific interactions between the two partners. Our previous results demonstrated that the heterogenization of two organic dyes Rose Bengal (**RB**)⁹ and Eosin Y (**EY**)¹⁰ on ordered mesoporous silica supports was possible and offered very interesting photocatalytic activities in oxidation and reduction.

Ordered mesoporous silica materials present interesting features such as availability, size-controlled porosity, stability, and facile functionalization.¹¹ Following on from our previous work, we sought to extend the strategy of conjugation of catalysts to supports to include successful metal complex redox photocatalyst [Ru(bpy)₃]Cl₂ (bpy = 2,2'-bipyridine). So far, the heterogenization of this complex has been achieved on polymer support or non-porous silica materials.^{7,8} Very few examples of derivatives of Ru(bpy)₃²⁺ grafted into porous material support are reported and their applications in organic synthesis are still undervalued.¹²

In this work, we performed the heterogenization of a [Ru(bpy)₂L]Cl₂ complex through a covalent grafting via functionalized bipyridyl ligand L into three mesoporous silica-based material with 2D hexagonal mesostructure and different pore sizes ranging from 2.6 to 6.1 nm after grafting. Covalent grafting of the complex into the material requires the slight modification of one of the 2,2'-bipyridine- ligands to anchor an alkyne motif, easily amenable to further functionalization via click-chemistry.

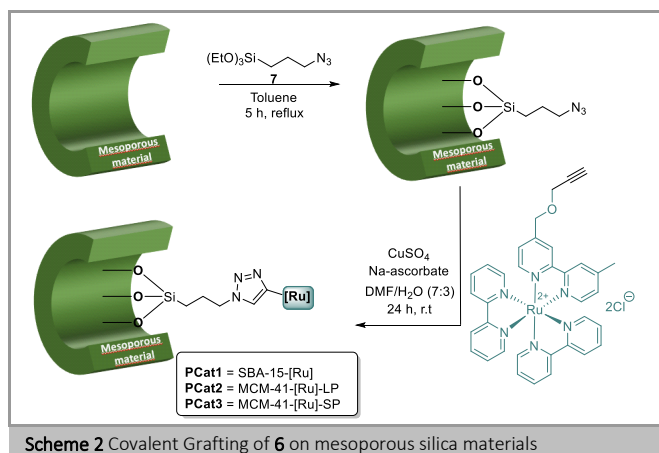
The study started with the preparation of this modified ligand.¹³ Benzylic oxidation of 4,4'-dimethyl-2,2'-dipyridyl **1** gave the corresponding monoaldehyde **2** in 35% yield. Undesired overoxidation was observed explaining the modest yield of this step (Scheme 1). Reducing this aldehyde **2** using NaBH₄ provided

the alcohol **3** in 78% and finally the nucleophilic substitution of propargyl bromide afforded the desired ligand **4** in 88% yield. This ligand **4** was used in a ligand-exchange step with $[\text{Ru}(\text{bpy})_2]\text{Cl}_2$ to obtain the final modified complex $[\text{Ru}(\text{bpy})_2(\mathbf{4})]\text{Cl}_2$ (**6**). UV-visible absorption and emission spectra were recorded for **6** and no significant differences were observed with those measured for $[\text{Ru}(\text{bpy})_3]\text{Cl}_2$ in similar conditions (see ESI, Figure S3).



Scheme 1 Preparation of modified Ru-complex **6**

The next step consisted in the grafting of silica materials, with 3-azidopropyltriethoxysilane **7** playing the role of the covalent linker. The heterogeneous photocatalysts were finally obtained after a click reaction (CuAAC) step between the grafted material and **6** to afford **PCat1** = SBA-15-[Ru],¹⁴ **PCat2** = MCM-41-[Ru]-LP (Large Pores) and **PCat3** = MCM-41-[Ru]-SP (Small Pores).^{15, 16}



Scheme 2 Covalent Grafting of **6** on mesoporous silica materials

For each heterogeneous photocatalyst, the textural properties of the inorganic part were investigated. X-ray diffraction analysis was performed on the photocatalysts as well as the grafting intermediates (see ESI, Figure S.7). In all cases, the peaks associated with the mesopore organization are retained

upon Ru-complex grafting. The presence of azide was confirmed after the grafting by an intense IR band at 2100 cm^{-1} (stretching -N₃) in the FT-IR spectrum (see ESI, Figure S.6). In all cases, N₂ adsorption isotherms were recorded, from which specific surface area, pore diameters and mesoporous volumes were calculated, and we observed significant differences (Table 1). A larger pore diameter of 6.1 nm after grafting is obtained for **PCat1** compared to **PCat2** and **PCat3**, for which respective values of 3.8 nm and 2.6 nm were calculated from N₂ adsorption data. Interestingly, for each grafting step we observed a significant decrease of general textural data (diameter, mesoporous volume, and specific surface area) for all the materials which proves that the Ru-complex is mainly linked inside the pores (see ESI, Figure S10). Based on thermogravimetric analysis (TGA), loading values between 3 and 5 wt% were recorded and used for the rest of photocatalytic reactions. Interestingly, the same range of Ru-loading was achieved whatever the porous size of the material support. In addition, we also prepared a [Ru]-complex immobilized at the external surface of silica particles: Stöber silica, not porous enough (pore size of about 0.2 nm) to accommodate the photocatalyst.¹⁷ Thus, the specific surface area and the [Ru]-loading is strongly decreased compared to **PCat1-3**.

Table 1 Textural properties of heterogeneous photocatalyst and [Ru] loading

Entry	PCat	S _{BET} (m ² /g)	Pore diameter (nm)	Mesoporous volume (cm ³ /g)	[Ru] wt%
1	PCat1	440	6.1	0.57	5
2	PCat2	654	3.8	0.63	3
3	PCat3	628	2.6	0.41	4
4	Stöber-[Ru]	14	-	-	0.4

The evaluation of the photocatalytic activity of the heterogeneous catalysts started with the oxidation of the *N*-aryltetraisoquinoline **8** to form the aza-Henry product **9** in presence of MeNO₂ (Table 2).¹⁸ Regardless of the photocatalyst used, we measured almost full conversions (90 to 100%) for all the reactions performed in 24 h with the LED-420 nm. Similar isolated yields were obtained under these conditions (60 to 67%) which proved that the heterogenization did not impact the activity of the photocatalyst.¹⁹ It should be noted that the difference between the conversions and the isolated yield could arise from partial decomposition of compound **9** during the chromatography step.

Table 2 Photocatalytic aza-Henry reaction

Entry	Conditions ^a	Isolated yield (%)
1	$[\text{Ru}(\text{bpy})_3]\text{Cl}_2$	67
2	Ru-complex 6	62
3	PCat1	60
4	PCat2	67
5	PCat3	62
6	Stöber-Ru	40

^a Reactions were run on 0.25 mmol scale with 1 mL of MeNO₂ under air.

However, with Stöber-[Ru] photocatalyst, the reaction is much slower (78% of conversion and 40% of yield), demonstrating the advantage of grafting [Ru] onto porous silica materials.

Then, we explored the recyclability of the heterogeneous photocatalyst (Figure 1). To do so, we selected **PCat2** which gave a slightly higher yield for the aza-Henry reaction. Under the same reaction conditions, we obtained consistent conversion in the range 85 - 95% over 5 cycles and consistent isolated yields (49-67%). Although the **PCat2** was still active and efficient, a darkening color change was observed suggesting a partial and slow degradation of the [Ru]-complex.

To demonstrate the robustness of our heterogeneous photocatalysts we explored a series of organic transformations involving different type of intermediates.

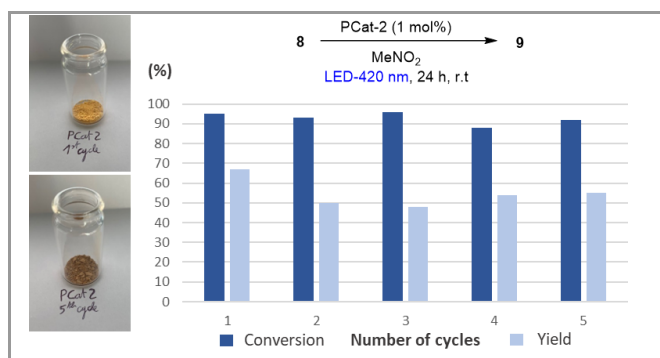
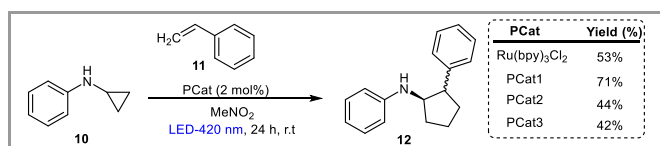


Figure 1 Recyclability of the heterogeneous photocatalyst **PCat2**

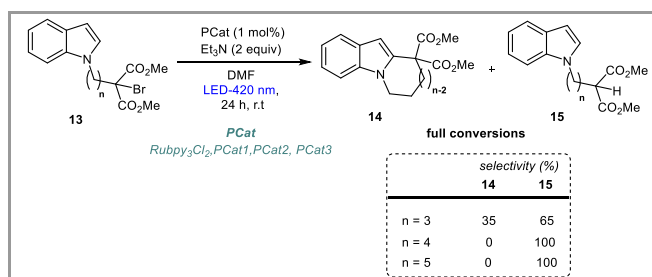
First, we started to explore the intermolecular [3+2] cycloaddition between the cyclopropylamine **10** and the styrene **11** to form the cyclopentane **12**. This reaction has been developed by Zheng *et al* in a homogeneous phase using $[\text{Ru}(\text{bpy})_3](\text{PF}_6)_2$ ($\text{bpy} = 2,2'$ -bipyrazine).²⁰ We adapted the previously reported conditions to our heterogeneous photocatalysts, and we observed 71% yield for **PCat1**, 44% yield for **PCat2** and 42% yield for **PCat3** (Scheme 3).²¹ These results were compared to the homogeneous $\text{Ru}(\text{bpy})_3\text{Cl}_2$, which provided 53% of **12**. This value is slightly lower than the reaction catalyzed by [Ru]-supported in SBA-15 (**PCat1**). It should be noted that the impact of the material support on the diastereoselectivity was not observed since the same diastereomeric ratio ($d.r = 60:40$) was measured for each photocatalyst.



Scheme 3 Photocatalytic and intermolecular [3+2] cycloaddition of cyclopropylamines with styrene

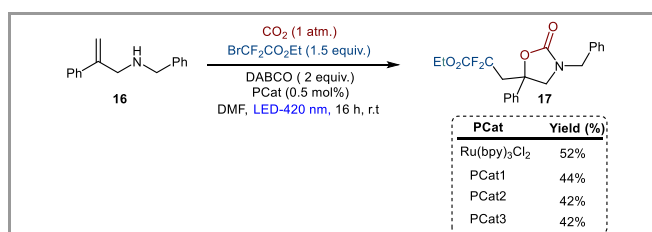
Next, we explored another type of reaction which involves the reduction of carbon-bromine bond by the photocatalytic system. To do so, a reaction developed by Stephenson was selected which involves the photocatalytic reduction of bromomalonate derivatives followed by radical addition into an indole ring (Scheme 4).²² This reaction is usually in competition between the formation of cyclized products **14** or the reduced compounds **15**. Additionally, reactants with different lengths of carbon chains ($n=3, 4, 5$) were prepared to check if changing selectivity could be observed. The efficiencies of the reactions were similar for all photocatalysts ($[\text{Ru}(\text{bpy})_3]\text{Cl}_2$,

PCat1, **PCat2**, **PCat3**) and surprisingly the selectivity seems to be independent of the material support. Using only 1 mol% of photocatalyst in DMF in the presence of 2 equivalents of triethylamine, full conversion was observed for each reaction.²³ The selectivity between **14** and **15** is only driven by the substrate (selectivity determined by $^1\text{H NMR}$ on the crude mixture). When the carbon chain is short, formation of the six-member ring containing **14** can be observed (35%), otherwise the reductive product **15**^{24, 25} (without cyclization) is obtained as the exclusive product.



Scheme 4 Photocatalytic reduction of bromomalonates

Then, we tried more complex conditions to perform oxy-difluoroalkylation of allylamine **16** (Scheme 5). Using the conditions of Yu *et al*, the ability of the heterogeneous photocatalysts to be efficient under triphasic conditions (solid-liquid-gas) was investigated.²⁶ In our hands, the homogeneous conditions with 2 equivalents of DABCO (1,4-diazabicyclo[2.2.2]octane) and 1 atmosphere of CO_2 gave the final product **17** in 52% isolated yield.²⁷ Switching to heterogeneous conditions (**PCa1**, **PCat2**, **PCat3**), the same product **17** was obtained, with a minor alteration of the yields ($\sim 42\%$) suggesting that the heterogenization did not strongly influence the efficacy of the photocatalyst. This last result opens the door to a sustainable approach to recycle CO_2 using heterogeneous photocatalysis.²⁸



Scheme 5 Photocatalytic oxy-difluoroalkylation of **16**

In conclusion, the preparation of three ordered mesoporous silica-based [Ru]-containing heterogeneous photocatalysts has been achieved using a covalent grafting route. These new photocatalysts were fully characterized and evaluated through various reactions. Thanks to the ordered mesoporous support, the [Ru]-complex is rather accessible, and the photocatalytic activities of such heterogeneous photocatalysts are comparable to the homogeneous version. Recyclability experiments confirm that these sustainable photocatalysts can be reused more than five times in aza-Henry reactions. The versatility of the catalysts is still conserved since they are efficient in oxidation, reduction and CO_2 trapping. More material-supports are currently under investigation to study their impact on organic transformations.

Funding Information

This study was supported by a public grant from the French "Agence Nationale de la Recherche" (ANR-21-CE07-044, PHOTOMATON2).

Acknowledgment

The authors thank UHA (Université de Haute-Alsace) for providing facilities.

Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

NO.

Conflict of Interest

The authors declare no conflict of interest.

References and Notes

- (1) Anastas, P. T. *Chem. Rev.* **2007**, *107*, 2167.
- (2) (a) Candish, L.; Collins, K. D.; Cook, C. G.; Douglas, J. J.; Gomez-Suarez, A.; Jolit, A.; S. Keess, S. *Chem. Rev.* **2022**, *122*, 2907. (b) McAtee, C.; McClain, E. J.; Stephenson, C. R. J. *Trends Chem.* **2019**, *1*, 111. (c) Shaw, M. H.; Twilton, J.; Macmillan, D. W. C. *J. Org. Chem.* **2016**, *81*, 6898. (d) Goddard, J. -P.; Ollivier, C.; Fensterbank, L. *Acc. Chem. Res.* **2016**, *49*, 1924. (e) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322.
- (3) Sellet, N.; Cormier, M.; Goddard, J. -P. *Org. Chem. Front.* **2021**, *8*, 6783.
- (4) (a) Savateev, A.; Antonietti, M.; *ACS Catal.* **2018**, *8*, 9790. (b) Lang, X.; Chen, X.; Zhao, J. *Chem. Soc. Rev.*, **2014**, *43*, 473.
- (5) (a) Rana, P.; Kaushik, B.; Solanki, K.; Mohan Saini, K.; Sharla, R. K. *Chem. Commun.* **2022**, *58*, 11354. (b) Yakushev, A. A.; Abel, A. S.; Averin, A. D.; Beletskaya, I. P.; Cheprakov, A. V.; Ziankou, I. S.; Bonneviot, L.; Bessmertnykh-Lemeune, A. *Coord. Chem. Rev.* **2022**, *458*, 214331. (c) Hong Mak, C.; Han, X.; Du, M.; Kai, J. -J.; Fung Tsang, K.; Jia, G.; Cheng, K. -C.; Shen, H. -H.; Hsu, H. -Y. *J. Mater. Chem. A* **2021**, *9*, 4454.
- (6) Santiago-Portillo, A.; Baldovi, H. G.; Carbonell, E.; Navalon, S.; Alvaro, M.; Garcia, H.; Ferrer, B. J. *Phys. Chem. C* **2018**, *122*, 29190.
- (7) (a) Peng, H.; Romero, T.; Papaefthimiou, V.; Bertani, P.; Ritleng, V. *Mol. Catal.* **2023**, *545*, 113183. (b) Wang, C.-A.; Han, Y.-F.; Nie, K.; Li, Y.-W. *Mater. Chem. Front.* **2019**, *3*, 1909. (c) Zhang, X.; Li, Y.; Hao, X.; Jin, K.; Zhang, R.; Duan, C. *Tetrahedron*, **2018**, *74*, 1742. (d) Liang, Y.; Bergbreiter, D. E. *Catal. Sci. Technol.* **2016**, *6*, 215. (e) Priyadarshani, N.; Liang, Y.; Suriboot, J.; Bazzi, H. S.; Bergbreiter, D. E. *ACS Macro Lett.* **2013**, *2*, 571. (f) Wang, J.-L.; Wang, C.; deKrafft, K. E.; Lin, W. *ACS Catal.* **2012**, *2*, 417.
- (8) (a) Blanchard, V.; Asbai, Z.; Cottet, K.; Boissonnat, G.; Port, M.; Amara, Z. *Org. Process Res. Dev.* **2020**, *24*, 822. (b) Teixeira, R. I.; de Lucas, N. C.; Garden, S. J.; Lanterna, A. E.; Scaiano, J. C. *Catal. Sci. Technol.* **2020**, *10*, 1273. (c) Tambosco, B.; Segura, K.; Seyrig, C.; Cabrera, D.; Port, M.; Ferroud, C.; Amara, Z. *ACS Catal.* **2018**, *8*, 4383.
- (9) Soria-Castro, S. M.; Lebeau, B.; Cormier, M.; Neunlist, S.; Daou, J.; Goddard, J. -P.; *Eur. J. Org. Chem.* **2020**, *2020*, 1572.
- (10) Mahmoud, N.; Awassa, J.; Toufaily, J.; Lebeau, B.; Daou, T. J.; Cormier, M.; Goddard, J. -P.; *Molecules*. **2023**, *28*, 549.
- (11) (a) Wang, Y.; Zhao, D. *Chem. Rev.* **2007**, *107*, 2821 (b) Hoffmann, F.; Cornelius, M.; Morelle, J.; Fröba, M. *Angew. Chem. Int. Ed.* **2006**, *45*, 3216.
- (12) (a) Roja-Luna, R.; Castillo-Rodriguez, M.; Ruiz, J. R.; Jiménez-Sanchidrián, C.; Esquivel, D.; Romero-Salguero F. J. *Dalton Trans.* **2022**, *51*, 18708. (b) Waki, M. Shirai, S.; Yamanaka, K. -I.; Maegawa, Y.; Inagaki, S. *RSC Adv.* **2020**, *10*, 13960. (c) Takeda, H.; Ohashi, M.; Goto, Y.; Ohsuna, T.; Tani, T.; Inagaki, S. *Adv. Funct. Mater.* **2016**, *26*, 5068. (d) Jana, A.; Mondal, J.; Borah, P.; Mondal, S.; Bhaumik, A.; Zhao, Y.; *Chem. Commun.* **2015**, *51*, 10746.
- (13) Walcarius, A.; Nasraoui, R.; Wang, Z.; Qu, F.; Urganova, V.; Etienne, M.; Göllü, M.; Demir, A. S.; Gajdzik, J.; Hempelmann, R. *Bioelectrochemistry* **2011**, *82*, 46.
- (14) Zhao, D.; Huo, Q.; Feng, J.; Chmelka, B. F.; Stucky, G. D. *J. Am. Chem. Soc.* **1998**, *120*, 6024.
- (15) Kresge, C. T.; Leonowicz, M. E.; Roth, W. J.; Vartuli, J. C.; Beck, J. S. *Nature*, **1992**, *359*, 710.
- (16) Vilà, N.; Ghanbaja, J.; Aubert, E.; A. Walcarius, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 2945.
- (17) Despas, C.; Walcarius, A.; Bessière, J. *Langmuire* **1999**, *15*, 3186.
- (18) Condie, A. G.; González-Gómez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, *132*, 1464.
- (19) **General procedure for photocatalyzed Aza-Henry reaction** : 2-(4-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline **8** (59.83 mg, 0.25 mmol, 1 equiv) PCat (0.0025 mmol, 1 mol%) were added in 1 mL of freshly distilled MeNO₂ in a flask equipped with a magnetic stir bar. The mixture was stirred at room temperature and irradiated with a blue LED (420 nm) at 5 cm for 24 h under air. The mixture was evaporated under vacuum and purified by column chromatography on silica gel (pentane/Ether, 80 : 20, v/v) to afford **9** as an yellow oil.
- (20) Maity, S.; Zhu, M.; Shinabery, R. S.; Zheng, N. *Angew. Chem. Int. Ed.* **2012**, *51*, 222.
- (21) **General procedure for the photocatalyzed [3+2] cycloaddition**: N-Cyclopropylaniline **10** (26.64 mg, 0.2 mmol, 1 equiv), PCat (0.004 mmol, 0.02 equiv), styrene **11** (0.11 mL, 1 mmol, 5 equiv) and 1.12 mL of distilled and degassed MeNO₂ were added in a flask. The mixture was stirred at room temperature and irradiated with a blue LED (420 nm) at 5 cm for 24 h under air. The mixture was filtered over a Celite® pad with ether and the filtrate was evaporated under vacuum. The mixture was purified by column chromatography on silica gel (PE/AcOEt, 95:5, v/v) to afford **12** as a yellow oil (d.r = 60:40).
- (22) Tucker, J. W.; Narayanam, J. M. R.; Krabbe, S. W.; Stephenson, C. R. J.; *Org. Lett.* **2010**, *12*, 368.
- (23) **General procedure for photocatalytic reduction of bromomalonate**: The corresponding substrate **13** (0.076 mmol, 1 equiv) and PCat (0.0008 mmol, 1 mol%) was added in a flask equipped with magnetic stir bar evacuated and back filled with nitrogen (N₂) with 1 mL of freshly degassed DMF. Et₃N (0.021 mL, 0.15 mmol, 2 equiv) was added dropwise. The mixture was stirred at room temperature and irradiated with blue LED (420 nm) placed at 5 cm for 24 h. 25 mL of water were added and the aqueous layer was extracted with ether (3 x 25 mL). The organic layers were combined, dried over MgSO₄ and evaporated under vacuum. Full conversions were observed for all the substrates and the ratio of **14**:**15** were determined by ¹H NMR one the crude reaction.
- (24) **Analytical data for 15b (n = 4), Dimethyl 2-(4-(1H-indol-1-yl)butyl)malonate**: ¹H NMR (400 MHz, CDCl₃) δ 7.66 (d, J = 7.9 Hz, 1H), 7.39 - 7.32 (m, 1H), 7.24 (d, J = 1.1 Hz, 1H), 7.18 - 7.07 (m, 2H), 6.52 (dd, J = 3.1, 0.6 Hz, 1H), 4.13 (t, J = 7.0 Hz, 2H), 3.73 (s, 6H), 3.35 (t, J = 7.4 Hz 1H), 2.01 - 1.84 (m, 4H), 1.36 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 169.7, 135.8, 128.6, 127.8, 121.4, 121.0, 119.2, 109.3, 101.0, 52.5, 51.4, 45.9, 29.7, 28.3, 24.6. **FT-IR (neat)** : 3026, 2951, 2865, 1730, 1511, 1462, 1434, 1335, 1313, 1243, 1226, 1195, 1148, 1010, 739 cm⁻¹. **HRMS (ESI)** : [M+Na]⁺, calculated for C₁₇H₂₁NaO₄Na 326.1363; found 326.1357.
- (25) **Analytical data for 15c (n = 5), Dimethyl 2-(5-(1H-indol-1-yl)pentyl)malonate**: ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, J = 7.9 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.30 - 7.20 (m, 1H), 7.19 - 7.08 (m, 2H), 6.54 (d, J = 3.1 Hz, 1H), 4.12 (t, J = 7.0 Hz, 2H),

3.76 (s, 6H), 3.38 (t, $J = 7.5$ Hz, 1H), 1.89 (ddd, $J = 20.1, 8.8, 5.5$ Hz, 4H), 1.44 - 1.30 (m, 4H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 169.7, 135.8, 128.5, 127.7, 121.3, 120.9, 119.1, 109.3, 100.9, 52.4, 51.5, 46.0, 29.8, 28.6, 26.8, 26.5. **FT-IR (neat)** : 3023, 2952, 2862, 1731, 1511, 1484, 1462, 1435, 1313, 1253, 1200, 1153, 1047, 1012, 740 cm^{-1} . **HRMS (ESI)** : $[\text{M}+\text{Na}]^+$, calculated for $\text{C}_{18}\text{H}_{23}\text{NO}_4\text{Na}$ 340.1519; found 340.1516.

- (26) Yin, Z. -B.; Ye, J. -H.; Zhou, W. -J.; Zhang, Y. -H.; Ding, L.; Gui, Y. -Y.; Yan, S. -S.; Li, J.; Yu, D. -G.; *Org. Lett.* **2018**, *20*, 190.
- (27) **General procedure for photocatalytic for oxydifluoroalkylation** : **16** (45 mg, 0.20 mmol, 1 equiv), **PCat** (0.001 mmol, 0.5 mol%) and DABCO (0.039 mL, 0.4 mmol, 2 equiv) were added in 2.2 mL of anhydrous DMF (previously degassed with CO_2) into a Schlenk tube equipped with magnetic stir bar evacuated and backfilled with nitrogen (N_2). Then $\text{BrCF}_2\text{CO}_2\text{Et}$ (0.038 mL, 0.3 mmol, 1.5 equiv) was added dropwise then CO_2 was bubbled into the solution. The mixture was stirred at room temperature and irradiated with a blue LED (420 nm) placed at 5 cm for 16 h. 25 mL of brine were added and the aqueous layer was extracted with AcOEt (3 x 25 mL). The organic layers were combined, dried over MgSO_4 and evaporated under vacuum. The mixture was purified by column chromatography on silica gel (PE/AcOEt, 80 : 20, v/v) to afford **17** as a white solid.
- (28) Yeung, C. S. *Angew. Chem. Int. Ed.* **2019**, *58*, 5492.