EurJOC
European Journal of Organic Chemistry

Research Article
doi.org/10.1002/ejoc.202201484

Chemistry Europe
European Chemical Societies Publishing

www.eurjoc.org

Oxidative Coupling of 4-Hydroxycoumarins with Quinoxalin-2(1*H*)-ones Induced by Visible Light under Aerobic Conditions

Loris Laze,[a] Paula Romero,[a] Irene Bosque,*[a] and Jose C. Gonzalez-Gomez*[a]

Direct and selective C(sp^2)–H/C(sp^2)–H cross-dehydrogenative coupling has become a promising strategy to increase molecular complexity with a high atom economy. This study describes an efficient and straightforward protocol for the regioselective C_3-H/C_3-H cross-coupling of 4-hydroxycoumarin derivatives with quinoxalin-2(1*H*)-ones, including late-stage modification of natural drugs, promoted by visible light under aerobic conditions at room temperature. With this approach, a wide range of hybrid drug-like molecules were prepared, using air as the terminal oxidant. Remarkably, the C_4-OH group at the coumarin ring is essential for the reaction and has been used as a handle for diverse functionalizations of the final products. Moreover, sunlight can promote the reaction under very mild and sustainable conditions, even on a gram scale. Qualitative and semi-quantitative tools were used to demonstrate the greenness advance of this methodology over previously reported ones. Several experiments were conducted to propose a plausible mechanism for this transformation.

Introduction

Derivatives of 4-hydroxycoumarin are produced by several plants, fungi, and bacteria, exhibiting outstanding bioactivities.[1] These heterocyclic compounds are versatile substrates[2] with several applications in medicinal chemistry,[3] material science,[4] food industry, and the cosmetic industry. In particular, some C_3- substituted derivatives are oral anticoagulants that function as vitamin K antagonists, exemplified by naturally occurring dicoumarol, warfarin, and coumatetralyl (Figure 1a).[5] On the other hand, quinoxaline-2(1*H*)-one is a privileged scaffold for discovering new drugs.[6] Among them, the C_3-substituted ones have attracted much attention due to their diverse bioactivities (Figure 1b). For example, natural Caroverine shows muscle relaxant activity.[7] Some derivatives have proved to be potent and selective aldose reductase inhibitors for the treatment of diabetes (e.g., compound A),[8] and others exhibit anticancer (e.g., compounds B/C)[9] or antimicrobial activity (e.g., compounds B/D),[10] among other pharmaceutical properties. Therefore, a wide range of synthetic methods has been reported for functionalizing this pharmacophore at C_3,[11] including photocatalytic methods.[12] Due to the relevant bioactivities displayed by C_3-substituted-4-hydroxycoumarins and C_3-substituted quinoxalinones, a hybrid molecule where both pharmacophores are connected at C_3-C_3 could be

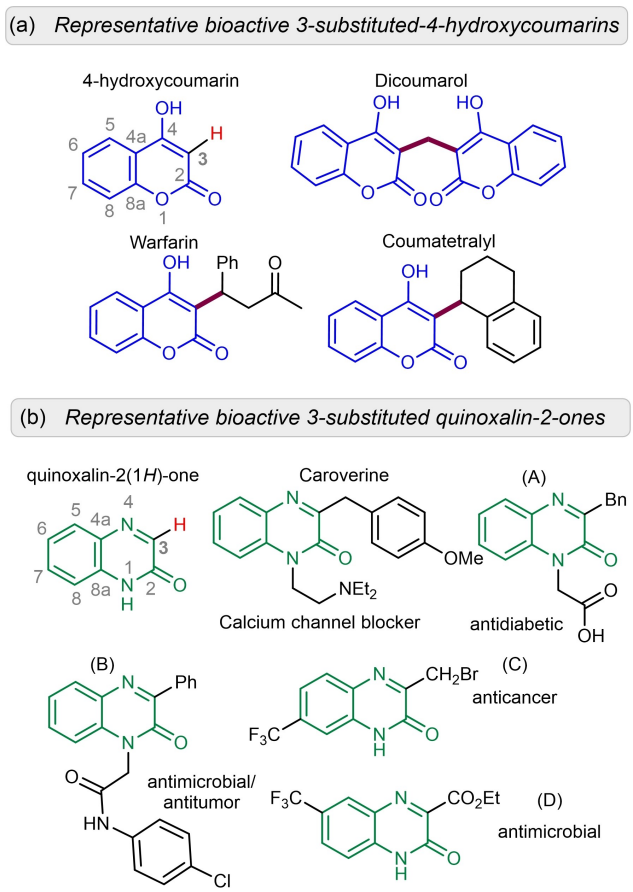


Figure 1. Representative bioactive 4-hydroxycoumarins and quinoxalin-2(1*H*)-ones.

[a] *L. Laze, P. Romero, Prof. Dr. I. Bosque, Prof. Dr. J. C. Gonzalez-Gomez*
Instituto de Síntesis Orgánica (ISO) and Departamento de Química Orgánica
Universidad de Alicante
Apdo. 99, 03080 Alicante (Spain)
E-mail: irene.bosque@ua.es
josecarlos.gonzalez@ua.es

Supporting information for this article is available on the WWW under https://doi.org/10.1002/ejoc.202201484

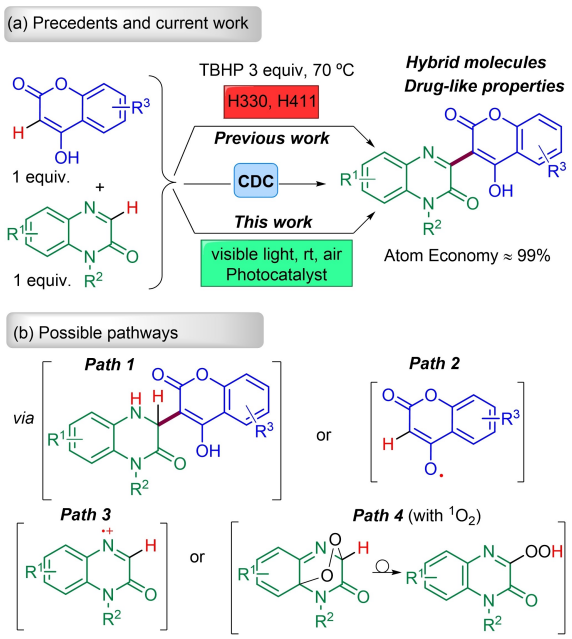
Research Article
doi.org/10.1002/ejoc.202201484

beneficial in the discovery of new drugs with the ability to address more than one target.[13]

In this context, a recent report describes a regioselective C_3-H/C_3-H cross-dehydrogenative coupling (CDC) of 4-hydroxycoumarins and quinoxalinones to obtain a wide range of hybrid molecules that follow Lipinski's rule of five and might display drug-like properties.[14] This simple and efficient protocol was also extended to cross-coupling quinoxalinones with 4-hydroxy-6-methyl-2-pyrone (triacetic acid lactone)[15] and hydroxynaphthoquinone (Lawsone),[16] also biologically relevant motifs. Inspired by this straightforward methodology and continuing with our interest in cross-dehydrogenative couplings,[17] we decided to develop a more sustainable protocol for this transformation with excellent atom economy (Scheme 1a).

Despite the advantages of the reported procedure, including the absence of toxic/expensive metals and the easy isolation/purification, the use of an excess of *tert*-butylhydroperoxide (TBHP) at 70 °C involves several physical- (H242), health- (H314, H330, H331), and environmental hazards (H411). More importantly, the fact that this reagent is fatally toxic (H330) and has severe environmental implications (H411) raises the red flag about the health and safety concerns of this methodology (Zero and First Pass).[18] Therefore, we decided to explore this oxidative C–C coupling at room temperature using visible light (including sunlight) in the presence of organic photocatalysts,[19] avoiding the presence of toxic/expensive metals, excess of reagents, and using air as the only terminal oxidant. Mechanistically, this transformation is intriguing since different plausible pathways can be proposed (Scheme 1b). A nucleophilic attack of the 4-hydroxycoumarin at the C3 position of the quinoxalinone followed by dehydrogenation (Path 1) has been previously considered for this oxidative coupling by other authors.[14] On the other hand, given the acidity of 4-hydroxycoumarins (pK_a 4.2),[20] the reaction could be initiated by deprotonation/single-electron oxidation of these substrates to obtain the corresponding radicals (Path 2) similarly to what occurs with carboxylic acids.[21] In addition, the photooxidation of the quinoxalinone moiety by excited organic dyes is documented and could also initiate this transformation (Path 3).[22] Finally, the formation of singlet oxygen is possible with photosensitizers in the presence of visible light under aerobic conditions.[23] Therefore, a Diels-Alder reaction of singlet oxygen with the quinoxalinone, followed by rearomatization, could afford a peroxide derivative where the C3 position of the quinoxalinone is activated for the addition/elimination of the 4-hydroxycoumarin (Path 4).

To our surprise, despite the outstanding properties of C_3-substituted 4-hydroxycoumarins, we have found only one reported example of visible-light-induced C_3-H functionalization of these bioactive heterocycles, where the CDC with thiols allowed the regioselective sulfenylation (C–S bond formation).[24] Remarkably, the yields obtained in the presence of an O_2 balloon were much higher than under open-to-air conditions. Therefore, photocatalytic methods for the C_3-H functionalization of 4-hydroxycoumarins are still scarce, and developing new CDC protocols for C–C bond formation under open-to-air conditions is pertinent. With the above-commented precedents, we wish to report the CDC of 4-hydroxycoumarins and quinoxalinones under very mild and sustainable conditions. Furthermore, the reaction mechanism and some synthetic modifications of the coumarin-quinoxalinone hybrids have been studied.



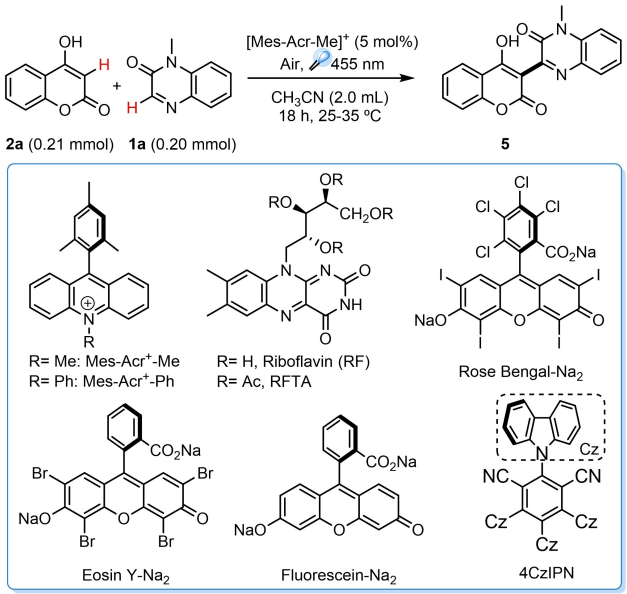
Scheme 1. (a) State of the art. (b) Possible pathways.

Results and Discussion

We selected 4-hydroxycoumarin (**2a**) and 1-methylquinoxalin-2(*1H*)-one (**1a**) as model substrates to explore different conditions for their photocatalytic cross-dehydrogenative coupling. Furthermore, to minimize the waste, we used almost equimolar amounts of each reactant, making this intermolecular transformation more challenging in a relatively concentrated solution (0.10 M) of acetonitrile. Although acetonitrile is considered problematic for safety reasons, it is on the borderline with recommended solvents (Rank 4 from 1 to 10 in CHEM21 solvent guide, being solvents with rank 3 recommended) and has no health or environmental concerns.[25] When the reaction mixture was irradiated with blue LEDs in the presence of the Fukuzumi photocatalyst ($[Mes\text{-}Acr\text{-}Me]^+$, 5 mol%), we were pleased to observe the formation of a precipitate that resulted in the desired product **5** in almost quantitative yield (Table 1, entry 1). Control experiments revealed that air atmosphere, light irradiation, and the addition of the photocatalyst are necessary to furnish the desired product in good yield (Table 1, entries 2–4), while replacing the balloon of air with a balloon of O_2 did not improve the result (entry 5). Interestingly, when **1a** and **2a** were mixed in MeCN, a strong electron donor-acceptor (EDA) complex was observed by both the naked eye (yellow solutions) and the UV-Vis spectra (Figure S10 in Supporting Information). However, no effective coupling product was obtained (entry 4).

Research Article
doi.org/10.1002/ejoc.202201484

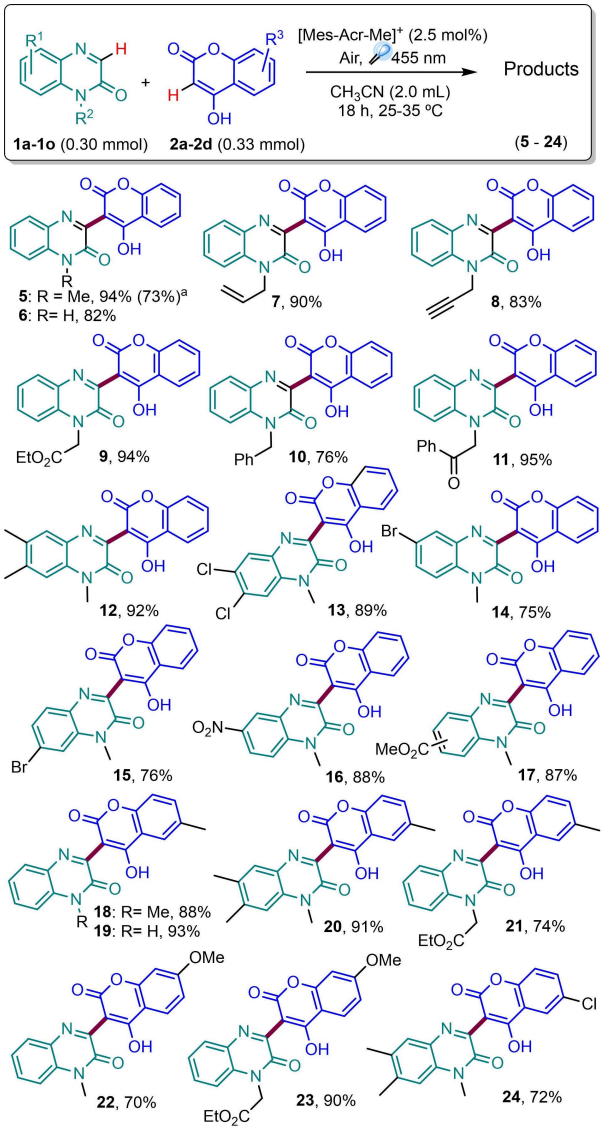
Table 1. Optimization of the CDC reaction conditions.



Entry	Variation from above	Yield [%][a]
1	None	98 (94)
2	Ar atmosphere	30
3	No irradiation	6
4	Without [Mes-Acr-Me]$^+$	10
5	O_2 atmosphere	95
6	5 mol% [Mes-Acr-Phe]$^+$	40
7	5 mol% Eosin Y-Na_2	32
8	5 mol% Fluorescein-Na_2	99
9	5 mol% Rose Bengal-Na_2	54
10	5 mol% RF	22
11	5 mol% RFTA	44
12	5 mol% 4CzIPN	99
13	2.5 mol% [Mes-Acr-Me]$^+$	98 (94)
14	2.5 mol% 4CzIPN	78
15	2.5 mol% Fluorescein-Na_2	50

[a] Yields determined by HPLC. Under brackets are the yields for pure isolated products.

Table 2. Reaction scope with 4-hydroxycoumarins.



[a] Sunlight irradiation over 7 h (see Supporting Information for details).

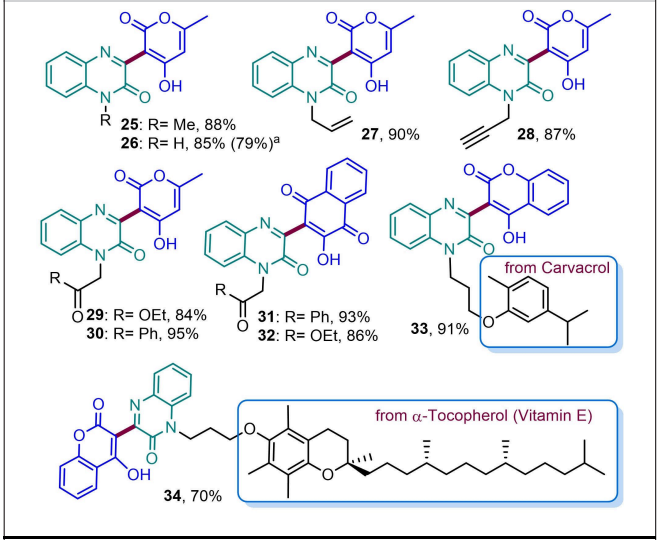
Seven other organic dyes were examined in this reaction (entries 7–12), getting equally excellent yields with Fluorescein-Na_2 (entry 8) and 4-CzIPN (entry 12). However, when the catalyst loading was decreased from 5 to 2.5 mol%, only the Fukuzumi photocatalyst retained a similar catalytic activity (entries 13–15). After this initial evaluation of the reaction, we selected the conditions of entry 13 to examine the scope of this photocatalytic CDC with different partners.

With the optimized conditions in hand, we examined the reaction of 4-hydroxycoumarin (**2a**) with various N_1-substituted quinoxalinones (**1a**–**1o**). As shown in Table 2, the absence of substituents at N_1 was well tolerated. More importantly, substrates with functionalities sensitive to oxidation, such as alkyl groups, double bonds, triple bonds, and benzyl moieties, also afforded the corresponding products in good-to-excellent yields (76–95% for products **5**–**11**). In addition, the presence of an ester functionality was also compatible with this protocol (product **9**), as well as an aromatic ketone (product **11**) which might be sensitive under UV irradiation. The tolerance to different groups attached to the benzene ring of the quinoxalinone was also evaluated. As a result, it was observed that regardless of the electronic nature of the groups attached to C_6/C_7 of the quinoxalinone, including –Me, –Cl, –Br, $–NO_2$ and –COOMe, the corresponding products were obtained in uniformly good-to-excellent yields (75–92%, for products **12**–**17**). Similarly, 4-hydroxycoumarins with a –Me at C_6 (**2b**), a MeO– at C_7 (**2c**), or a –Cl at C_6 (**2d**) were suitable substrates, providing the products **18**–**24** in good-to-excellent yields (70–93%).

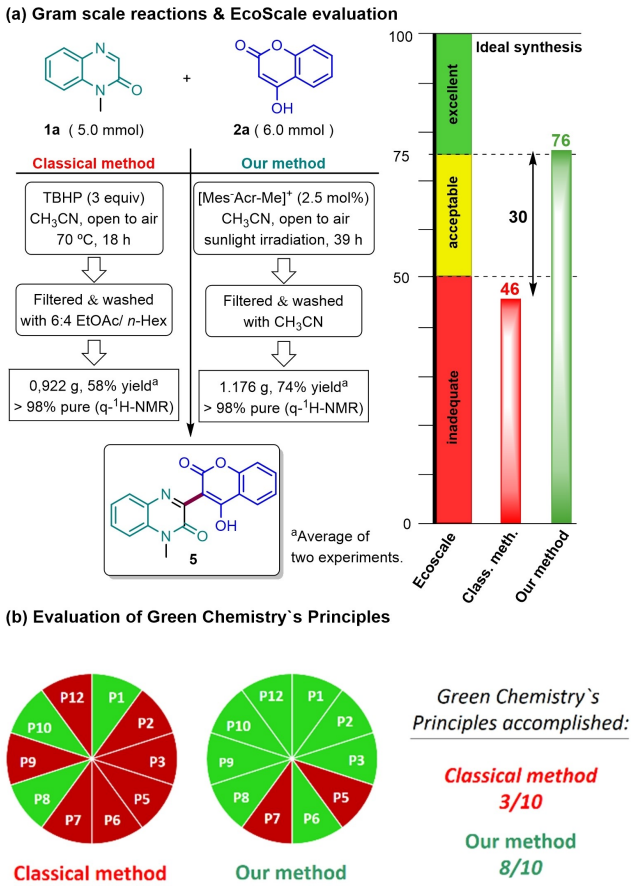
Next, when 4-hydroxy-6-methyl-2-pyrone (**3**) was examined in the reaction with quinoxaline-2-ones under the optimized conditions, products **25**–**30** were obtained in excellent yields (84–95%, Table 3). Furthermore, Lawsone (**4**) was also a suitable reaction partner, giving products **31** and **32** in 93% and 86% yield, respectively. Remarkably, compounds **5** and **26** formed

Research Article
doi.org/10.1002/ejoc.202201484

Table 3. Reaction scope with 4-hydroxy-6-methyl-2-pyrone (3), Lawsone (4) and late-stage functionalizations.



[a] Sunlight irradiation over 7 h (see Supporting Information for details).

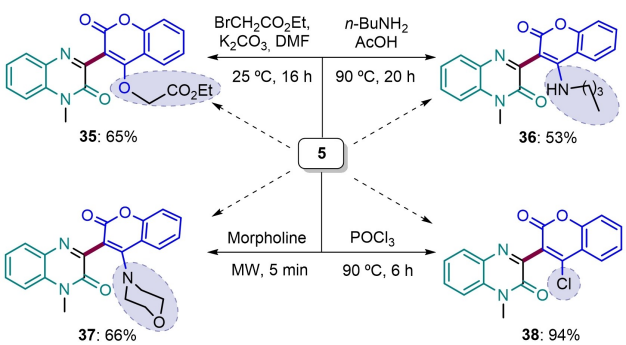


Scheme 2. (a) Gram-scale reaction with sunlight irradiation and with TBHP at 70 °C and semi-quantitative evaluation using the Ecoscale. (b) Qualitative evaluation of the accomplishment of Green Chemistry's principles (P1-P12).

successfully with sunlight irradiation in open-to-air vials (see page S22 in Supporting Information). Finally, continuing with the idea of developing hybrid drug-like molecules, we decided to explore the performance of our CDC protocol in late-stage functionalization, using quinoxalinones linked to natural molecule fragments at N_1 in the reaction with **2a**. To our delight, substrates with Carvacrol and Vitamin E frameworks furnished the corresponding products **33** and **34** in good-to-excellent yields. Given that these examples contain three bioactive moieties, this protocol is attractive for the modular synthesis of bioactive hybrid molecules.

To examine the practicability of our methodology, the reaction of **1a** with **2a** was conducted on a gram scale, using sunlight as the only energy source and open to the air (terminal oxidant). We also performed the reaction at the same scale but using TBHP at 70 °C,[17] to evaluate the greenness advance of our method over the previously reported conditions. As shown in Scheme 2, both protocols afforded product **5** with a purity >98% after simple filtration, according to q-^{1}H NMR (Supporting Information, page S23–24). A quick qualitative evaluation of the accomplishment of ten principles of green chemistry by each method is illustrated in Scheme 2 (Green color for the accomplished principle and red for the not accomplished ones, see tables S1 and S2 in Supporting Information). This analysis shows that while under our photochemical conditions, eight principles were accomplished, only three were followed using TBHP at 70 °C. Then we compared the results of both methods using the Ecoscale. This semi-quantitative tool considers parameters such as yield, cost, safety, conditions and ease of workup/purification.[26] After careful evaluation of these parameters (see Supporting Information, page S25), the total score of our method is 30 points superior to the classical conditions (Scheme 2). Therefore, according to this tool, our methodology can be considered an excellent approach to compound **5**, while using TBHP at 70 °C is inadequate.

To further increase our protocol's synthetic usefulness, we decided to examine some derivatizations of the hydroxycoumarin moiety using compound **5** as starting material (Scheme 3). As illustrated with the formation of product **35**, the alkylation of the hydroxyl group can be conveniently carried out under conventional conditions. Moreover, the hydroxyl

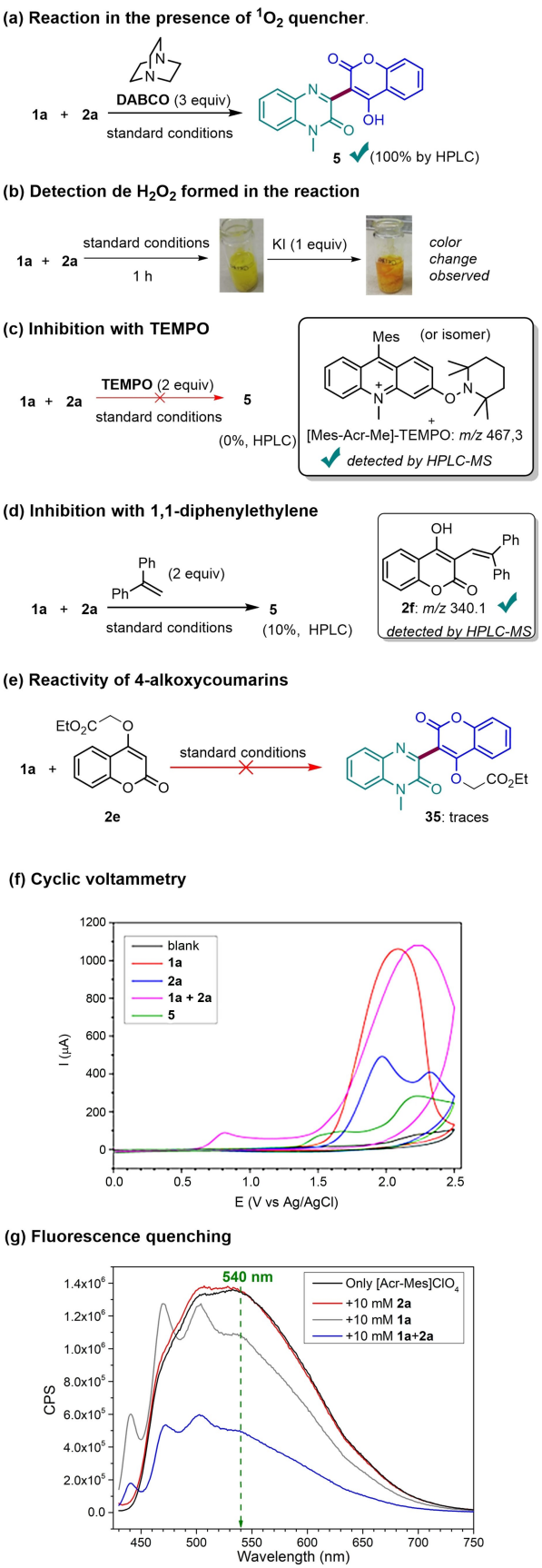


Scheme 3. Modifications of the hydroxycoumarin moiety.

Research Article
doi.org/10.1002/ejoc.202201484

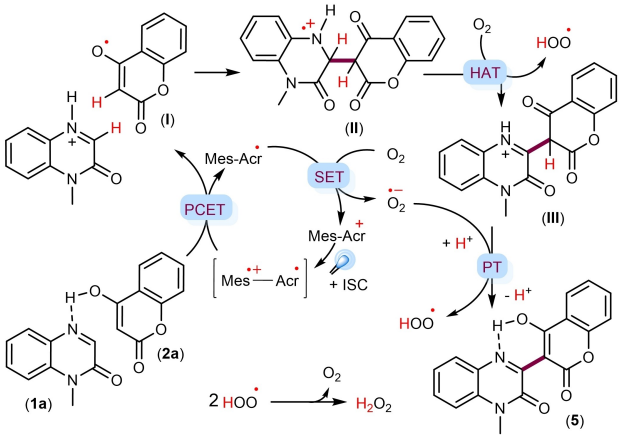
group can be selectively replaced by the amino group of primary and secondary amines, as illustrated in the syntheses of compounds **36** and **37** under previously reported conditions.[27] It is worth mentioning that 4-aminocoumarins exhibit outstanding bioactivities.[28] Finally, the reaction of **5** with $POCl_3$ furnished 4-chlorocoumarin **38** in excellent yield. The latter compound is ready for further elaboration at C_4 by the addition/elimination of nucleophiles or using Pd-catalyzed transformations.

Various control experiments were conducted to elucidate the reaction mechanism. When the cross-coupling of **1a** with **2a** was carried out under our optimized conditions but in the presence of DABCO (Scheme 4a), a known inhibitor of $^1O_2$,[29] the formation of compound **5** was not affected. This result suggests that the involvement of $^1O_2$ is not plausible (Path 4 from Scheme 1b). On the other hand, the formation of H_2O_2 in the model reaction was observed by the color change of the reaction mixture upon the addition of KI (Scheme 4b and page S32 in Supporting Information). In addition, the formation of compound **5** was suppressed entirely in the presence of TEMPO (Scheme 4c), pointing to a radical pathway. In this experiment (Scheme 4c), we could not detect any product related to **1a** or **2a**. Still, we identified the adduct [Acr^+•-TEMPO] by HPLC-MS, which explains the reaction inhibition. In addition, the model reaction was also inhibited in the presence of 1,1-diphenylethylene (Scheme 4d). In this case, the formation of adduct **2f** was observed by HPLC-MS, indicating that a radical derived from **2a** must be involved in the reaction pathway (Path 2, Scheme 1b). Furthermore, when coumarin **2e** was used as the substrate under standard conditions, only traces of compound **35** (previously obtained by functionalization of **5**) were detected by TLC (Scheme 4e). This result emphasizes the importance of the C_4-OH group at the coumarin ring for the success of the reaction. On the other hand, the quantum yield obtained for product **5** (2.28%, page S32 in Supporting Information) supports a closed photocatalytic cycle instead of a radical chain propagation process.[30] The cyclic voltammograms (Scheme 4f) of compounds **1a** and **2a** show that their oxidation starts around +1.50 V (vs. Ag/AgCl), being feasible for the photoexcited catalyst [E_{red} (Mes-Acr^+-Me)* = +1.93 V vs. Ag/AgCl].[19b] Remarkably, the CV of an equimolar mixture of **1a** and **2a** shows a first oxidation peak around +0.75 V and a second oxidation peak with an onset potential below the ones of each reactant. The appearance of these peaks could be explained by single-electron oxidation of the 4-hydroxycoumarin (**2a**) followed by fast deprotonation (Nernstian shift).[31] Although quinoxalinone **1a** (pKa ~ −1)[32] is not basic enough to significantly deprotonate **2a** (pKa ~ 4),[20] we presume that the acidity of radical cation **2a**•+ should be enough for fast deprotonation. This easier oxidation of the reaction mixture (**1a** + **2a**) can be considered a proton-coupled electron transfer (PCET), acting **1a** as a base. Upon studying the fluorescence quenching of the Fukuzumi catalyst, we also observed that adding a 1:1 mixture of **1a**/**2a** produced a much more pronounced effect than adding each reactant alone (Scheme 4g and page S34 in Supporting Information).[33]



Scheme 4. Mechanistic studies.

Research Article
doi.org/10.1002/ejoc.202201484



Scheme 5. Plausible mechanism.

We proposed a plausible mechanism for the model reaction based on all the above-mentioned investigations and literature precedents (Scheme 5). A complex of substrates **1a** and **2a** (likely by H-bond interaction) is oxidized by the photoexcited catalyst, obtaining radical **I** and protonated **1a**. Similarly, the single-electron oxidation of **2a** might be facilitated by subsequent proton transfer to **1a** via a proton-couple electron transfer (PCET) mechanism. The radical addition to the protonated heteroaromatic base takes place to obtain intermediate **II** with regioselective C–C bond formation, following a Minisci-like pathway.[34] Triplet oxygen (from the air) might abstract a hydrogen atom (HAT) from **II** to furnish intermediate **III**, which yields the final product **5** after deprotonation. Notably, according to the redox potentials of the involved species [$E°(O_2/O_2^{\bullet})=-0.35$ V vs. SCE;[35] E (Mes-Acr$^+$/Mes-Acr$^{\bullet}$) = 0.57 V vs. SCE[19b]] and literature precedents,[36] the turnover of the photocatalyst by $^3O_2$ is feasible. The disproportionation of intermediate radical hydroperoxide provides H_2O_2, the only by-product of the reaction detected in control experiments (Scheme 4b). Remarkably, this mechanism is conceptually different from the one suggested for the C_3-H sulfenylation of 4-hydroxycoumarins, where $^1O_2$ is involved, and independent oxidation of each CDC partner is proposed with final radical recombination.[24] Moreover, a photocatalytic method involving $^1O_2$ does not seem suitable for selective CDC of 4-hydroxycoumarins because it may lead to modifications of this heterocyclic scaffold.[37]

Conclusion

We have demonstrated that the cross-dehydrogenative coupling of quinoxalin-2(1*H*)-ones with 4-hydroxycoumarins and related compounds can be efficiently photocatalyzed by the Fukuzumi catalyst in the presence of visible light under aerobic conditions. As shown in 30 examples, this methodology exhibits high functional group tolerance and enables the preparation of hybrid drug-like molecules in uniformly good-to-excellent yields (72–95%). Furthermore, the synthetic usefulness of the products was illustrated with four diverse derivatizations at the C_4-OH group of the coumarin moiety. In terms of sustainability, salient features of this protocol are: (a) the absence of toxic reagents; (b) heating is not required; (c) almost equimolar amounts of reaction partners are used; (d) air is used as terminal oxidant; (e) the reaction can be promoted by sunlight; even at gram scale, and the desired product is obtained pure after simple filtration. The qualitative and semi-quantitative analysis (Ecoscale) of the results obtained in gram-scale indicates that this methodology represents a significant greenness advance over classical CDC conditions (e.g., excess of TBHP at 70 °C). Furthermore, mechanistic studies, including radical trap experiments, and electrochemical and photochemical investigations, support a closed photocatalytic cycle involving the photooxidation of the 4-hydroxycoumarin assisted by protonation of the quinoxalinone (PCET).

Experimental Section

General procedure for photochemical CDC: The corresponding quinoxalin-2(1*H*)-one (**1**, 0.30 mmol) and 4-hydroxycoumarin (**2**, 54 mg, 0.33 mmol), 4-hydroxy-2-pyrone (**3**, 42 mg, 0.33 mmol) or 2-hydroxy-1,4-naphthoquinone (**4**, 58 mg, 0.33 mmol) were added to a 4 mL vial, followed by the catalyst, 9-mesityl-10-methylacridinium perchlorate (3.1 mg, 0.0075 mmol) and MeCN (3 mL). The vial was closed with a septum and connected to an air balloon through a needle before being inserted into the PhotoRedOx Box Duo reactor and irradiated with blue LEDs for 16–18 h, maintaining the stirring at room temperature (25–35 °C) controlled by a fan in the photoreactor. Once this time had elapsed, the reaction mixture was concentrated in vacuo, and the residue was purified by column chromatography on silica gel (1:1 *n*-hexane: EtOAc, followed by 100% EtOAc, then EtOAc: EtOH 9:1).

CDC of 1a with 2a with sunlight irradiation on gram scale: The reaction was placed in a Kitasato flask (250 mL) connected to an open-air reflux condenser and loaded with the acridinium catalyst (52 mg, 0.13 mmol, 2.5 mol%), compound **2a** (891 mg, 5.50 mmol) and substrate **1a** (800 mg, 5.00 mmol), followed by MeCN (50 mL). The reaction mixture (set up in Figure S3) was exposed to sunlight for 18 h (9 h × 2 days). After this time, the reaction mixture was cool down in the fridge to ca. 5 °C, and the precipitate was filtered *in vacuo* and washed with cold MeCN (5 mL). The orange crystalline solid obtained (**5**: 915 mg, 2.86 mmol, 57%) was pure by TLC (4:1 EtOAc/EtOH, R_f 0.35) and ^{1}H NMR. Since the TLC of the filtrate showed some unreacted **1a**, a small portion of **2a** was added (81 mg, 0.50 mmol, 10 mol%), and the reaction mixture was exposed again to sunlight for 21 h (7 h × 3 days). More orange precipitate was obtained then, and the reaction mixture was stored in the fridge (ca. 5 °C) for 2 h. Then, the precipitate was filtered out *in vacuo* and washed with cold MeCN (3 mL), obtaining a pure crystalline orange solid (**5**: 275 mg, 0.86 mmol, 17%), identical to the first crop, according to TLC and ^{1}H NMR. Therefore, the desired product **5** was obtained with an overall 74% yield (1.190 g, 3.72 mmol) and pure after filtration. The purity of the combined solids was evaluated by q-H NMR using ethylene carbonate as the internal standard and resulting > 99% pure (page S24). *This result is the average of two experiments.*

Acknowledgements

This work was financially supported by the Spanish Ministerio de Ciencia e Innovación (grant no. CTQ2017-88171-P), Generalitat Valenciana (SEJIGENT/2021/005, granted to I. B.), and the University of Alicante (GRE20-03-A granted to I. B.). We thank Dr. Francisco Montilla for giving us access to the spectrofluorometer of his research group at the University of Alicante. We thank Dr. Teresa Lana-Villarreal for a helpful discussion of the photo- and electrochemical studies.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: 4-hydroxycoumarins · oxidative coupling · photocatalysis · quinoxalin-2(1*H*)-ones · sustainable chemistry

[1] F. Borges, F. Roleira, N. Milhazes, L. Santana, E. Uriarte, *Curr. Med. Chem.* **2005**, *12*, 887–916.
[2] B. Borah, K. Dhar Dwivedi, L. R. Chowhan, *Asian J. Org. Chem.* **2021**, *10*, 3101–3126.
[3] a) S. Emami, S. Dadashpour, *Eur. J. Med. Chem.* **2015**, *102*, 611–630; b) F. Annunziata, C. Pinna, S. Dallavalle, L. Tamborini, A. Pinto, *Int. J. Mol. Sci.* **2020**, *21*, 4618.
[4] Y. Chen, X.-R. Wei, R. Sun, Y.-J. Xu, J.-F. Ge, *Org. Biomol. Chem.* **2018**, *16*, 7619–7625.
[5] N. Au, A. E. Rettie, *Drug Metab. Rev.* **2008**, *40*, 355–375.
[6] a) A. Carta, S. Piras, G. Loriga, G. Paglietti, *Mini-Rev. Med. Chem.* **2006**, *6*, 1179–1200; b) L. Shi, W. Hu, J. Wu, H. Zhou, H. Zhou, X. Li, *Mini-Rev. Med. Chem.* **2018**, *18*, 392–413.
[7] Y. Kudo, S. Shibata, *Br. J. Pharmacol.* **1984**, *83*, 813–820.
[8] B. Wu, Y. Yang, X. Qin, S. Zhang, C. Jing, C. Zhu, B. Ma, *ChemMedChem* **2013**, *8*, 1913–1917.
[9] P. Sanna, A. Carta, M. Loriga, S. Zanetti, L. Sechi, *Il Farmaco* **1999**, *54*, 169–177.
[10] S. A. M. El-Hawash, N. S. Habib, M. A. Kassem, *Arch. Pharm. Chem. Life Sci.* **2006**, *339*, 564–571.
[11] a) Q. Ke, G. Yan, J. Yu, X. Wu, *Org. Biomol. Chem.* **2019**, *17*, 5863–5881; b) Kiran, P. Rani, S. Chahal, J. Sindhu, S. Kumar, R. S. Varma, R. Singh, *New J. Chem.* **2021**, *45*, 18722–18763.
[12] J. Rostoll-Berenguer, G. Blay, J. R. Pedro, C. Vila, *Eur. J. Org. Chem.* **2020**, *2020*, 6148–6172.
[13] B. Meunier, *Acc. Chem. Res.* **2008**, *41*, 69–77.
[14] S. Sharma, N. B. Dutta, M. Bhuyan, B. Das, G. Baishya, *Org. Biomol. Chem.* **2020**, *18*, 6537–6548.
[15] a) J. Zhu, M. Majikina, S. Tawata, *Biosci. Biotechnol. Biochem.* **2001**, *65*, 161–163; b) Y. Wang, S.-Y. Mo, S.-J. Wang, S. Li, Y.-C. Yang, J.-G. Shi, *Org. Lett.* **2005**, *7*, 1675–1678.
[16] S. Spyroudis, *Molecules* **2000**, *5*, 1291–1330.
[17] I. Bosque, R. Chinchilla, J. C. Gonzalez-Gomez, D. Guijarro, F. Alonso, *Org. Chem. Front.* **2020**, *7*, 1717–1742.
[18] C. R. McElroy, A. Constantinou, L. C. Jones, L. Summerton, J. H. Clark, *Green Chem.* **2015**, *17*, 3111–3121.
[19] a) N. Holmberg-Douglas, D. A. Nicewicz, *Chem. Rev.* **2022**, *122*, 1925–2016; b) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075–10166.
[20] P. M. Nowak, M. Woźniakiewicz, M. Piwowarska, P. Kościelniak, *J. Chromatogr. A* **2016**, *1446*, 149–157.
[21] a) J. C. Gonzalez-Gomez, N. P. Ramirez, T. Lana-Villarreal, P. Bonete, *Org. Biomol. Chem.* **2017**, *15*, 9680–9684; b) M. Estruch-Blasco, I. Bosque, D. Guijarro, J. C. Gonzalez-Gomez, *Org. Chem. Front.* **2021**, *8*, 5130–5138.
[22] a) J. Zhou, P. Zhou, T. Zhao, Q. Ren, J. Li, *Adv. Synth. Catal.* **2019**, *361*, 5371–5382; b) X. Xu, C. Xia, X. Li, J. Sun, L. Hao, *RSC Adv.* **2020**, *10*, 2016–2026; c) L. Zhao, L. Wang, Y. Gao, Z. Wang, P. Li, *Adv. Synth. Catal.* **2019**, *361*, 5363–5370; d) K. C. C. Aganda, B. Hong, A. Lee, *Adv. Synth. Catal.* **2021**, *363*, 1443–1448.
[23] A. A. Ghogare, A. Greer, *Chem. Rev.* **2016**, *116*, 9994–10034.
[24] G. Brahmachari, A. Bhowmick, I. Karmakar, *J. Org. Chem.* **2021**, *86*, 9658–9669.
[25] D. Prat, A. Wells, J. Hayler, H. Sneddon, C. R. McElroy, S. Abou-Shehada, P. J. Dunn, *Green Chem.* **2016**, *18*, 288–296.
[26] K. Van Aken, L. Strekowski, L. Patiny, *Beilstein J. Org. Chem.* **2006**, *2*, 3.
[27] E. V. Stoyanov, I. C. Ivanov, *Molecules* **2004**, *9*, 627–631.
[28] M. Sadeghpour, A. Olyaei, A. Adl, *New J. Chem.* **2021**, *45*, 5744–5763.
[29] a) C. Ouannes, T. Wilson, *J. Am. Chem. Soc.* **1968**, *90*, 6527–6528; b) P. Bao, F. Liu, Y. Lv, H. Yue, J.-S. Li, W. Wei, *Org. Chem. Front.* **2020**, *7*, 492–498.
[30] M. A. Cismesia, T. P. Yoon, *Chem. Sci.* **2015**, *6*, 5426–5434.
[31] R. D. Little, *J. Org. Chem.* **2020**, *85*, 13375–13390.
[32] G. H. W. Cheeseman, *J. Chem. Soc.* **1961**, 1246–1251.
[33] J. Rostoll-Berenguer, M. Martín-López, G. Blay, J. R. Pedro, C. Vila, *J. Org. Chem.* **2022**, *87*, 9343–9356.
[34] M. A. J. Duncton, *MedChemComm* **2011**, *2*, 1135–1161.
[35] W. H. Koppenol, D. M. Stanbury, P. L. Bounds, *Free Radical Biol. Med.* **2010**, *49*, 317–322.
[36] S. Fukuzumi, K. Ohkubo, *Chem. Sci.* **2013**, *4*, 561–574.
[37] a) G. Brahmachari, I. Karmakar, *J. Org. Chem.* **2020**, *85*, 8851–8864; b) G. Brahmachari, I. Karmakar, *Asian J. Org. Chem.* **2022**, *11*, e202100800.

Manuscript received: December 20, 2022
Revised manuscript received: December 22, 2022
Accepted manuscript online: December 23, 2022