Tetrahedron Letters 179 (2026) 156034

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Visible-light-induced photocatalytic intermolecular cyclization for synthesis of 2,2-diarylchromanes☆

Sakura Kodaki [a], Momo Kondo [b], Junta Minato [c], Shoko Itakura [b,d], Hiroyoshi Takamura [a], Makiya Nishikawa [b,d], Isao Kadota [a,*], Kosuke Kusamori [c,d,**], Kenta Tanaka [e,*]

[a] Graduate School of Environmental, Life, Natural Science and Technology, Okayama University, 3-1-1 Tsushima-Naka, Kitaku, Okayama 700-8530, Japan
[b] Laboratory of Biopharmaceutics, Faculty of Pharmaceutical Sciences, Tokyo University of Science, 6-3-1 Niijuku, Katsushika, Tokyo 125-8585, Japan
[c] Laboratory of Cellular Drug Discovery and Development, Faculty of Pharmaceutical Sciences, Tokyo University of Science, 6-3-1 Niijuku, Katsushika, Tokyo 125-8585, Japan
[d] Research Institute for Science & Technology, Tokyo University of Science, 2641 Yamazaki, Noda, Chiba 278-8510, Japan
[e] Research Institute for Interdisciplinary Science, Okayama University, 3-1-1 Tsushima-Naka, Kitaku, Okayama 700-8530, Japan

ARTICLE INFO

Keywords:
Chromane
Visible light
Photocatalysis
Chromene
Free-radical-scavenging activity

ABSTRACT

The photocatalytic cyclization of salicylaldehydes with 1,1-diarylalkenes for the synthesis of 2,2-diarylchromanes has been developed. The catalytic amount of Ir photocatalyst proceeds the cyclization to give the various 2,2-diaryl chromanes under irradiation with blue LEDs. The obtained 2,2-diarylchromanes exhibit noticeable free-radical-scavenging activities, which have been largely unexplored. Notably, the chromane can convert to 2,2-diaryl-2*H*-naphtho[1,2-*b*]pyran bearing strong electron withdrawing groups, which are found in various photochromic materials. Thus, the present reaction constitutes a promising tool for the synthesis of functional materials and biologically active compounds.

Introduction

2,2-Disubstituted chromanes are attractive synthetic targets due to their presence in functional materials and bioactive compounds (Fig. 1) 1. Among the various methods for their synthesis 2, photochemical approaches represent a sustainable strategy in organic chemistry 3. In 2011, UV-light irradiation of 3-(hydroxymethyl)-2-naphthols produces 2-napthoquinone-3-methide, which react with vinyl ethers via a hetero-Dies-Alder reaction to afford 2-alkoxybenzochromans (Scheme 1 (a)) 4. More recently, a photocatalytic selective radical cascade (4 + 2) annulation with olefins towards the synthesis of 2,2-dialkylchromanes under visible-light irradiation has been reported (Scheme 1 (b)) 5. While these reaction are attractive, only a few examples of photochemical syntheses of 2,2-disubstituted chromanes via intermolecular cyclization have been reported 6. Moreover, the reported methods are limited to introducing alkyl or alkoxy groups at the 2-position of chromanes. Therefore, the development of alternative strategies remains desirable to further expand the synthetic utility of 2,2-disubstituted chromanes. Meanwhile, we have developed a variety of visible-light-induced photochemical synthesis of chromanes 7. Based on this background, we herein report the visible-light-induced photocatalytic synthesis of 2,2-diarylchromanes from commercially available salicylaldehydes and 1,1-diarylalkenes (Scheme 1 (c)).

We initially investigated the reaction of salicylaldehyde (**1a**) with 1,1-diarylalkene (**2a**) in the presence of photocatalyst at room temperature under the irradiation of blue light (Table 1). The reaction did not proceed with typical organophotocatalysts (entries 1–2). In contrast, representative transition-metal photocatalysts with long excited-state lifetimes promoted the reaction to afford the desired product **3a** in moderate to good yields (entries 3–6). Furthermore, a variety of solvents were applicable to the reaction (entries 7–10). The shorter reaction time decreased the yield of the product (entry 11). Control experiments conducted in the absence of either the photocatalyst or light confirmed that both are essential for the reaction to proceed (entries 12–13).

With the optimal conditions in hand, we screened various salicylaldehydes and diarylalkenes (Table 2). A variety of alkyl groups such as

---

☆ This article is part of a Special issue entitled: 'Heterocycles' published in Tetrahedron Letters.
* Corresponding authors.
** Corresponding author at: Laboratory of Cellular Drug Discovery and Development, Faculty of Pharmaceutical Sciences, Tokyo University of Science, 6-3-1 Niijuku, Katsushika, Tokyo 125-8585, Japan.
E-mail address: ktanaka@okayama-u.ac.jp (K. Tanaka).

https://doi.org/10.1016/j.tetlet.2026.156034
Received 4 December 2025; Received in revised form 28 February 2026; Accepted 7 March 2026

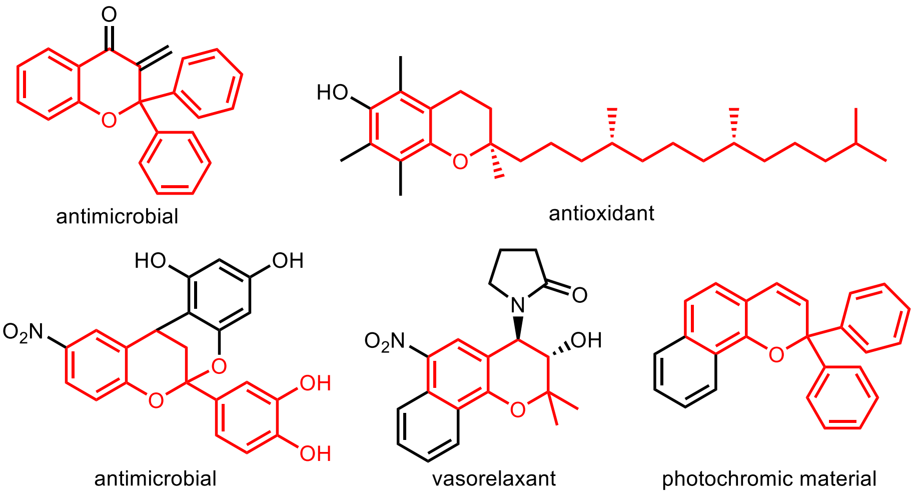
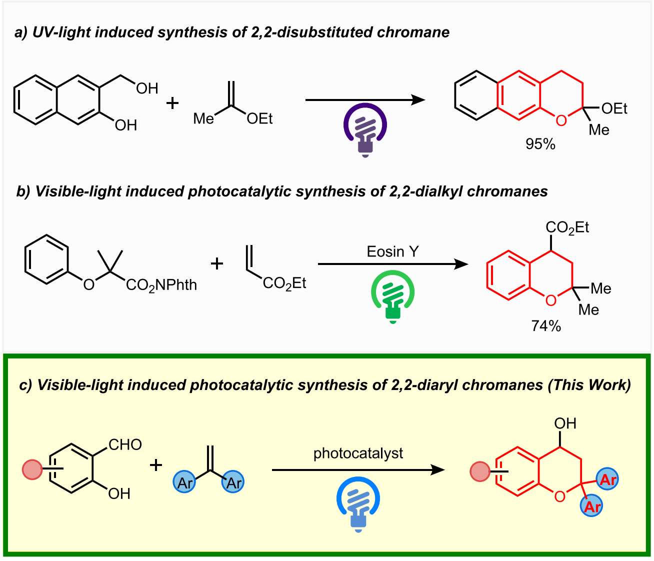


Fig. 1. Representative examples of 2,2-disubstituted chromanes and chromene.

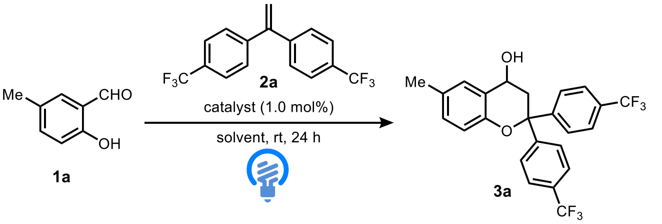


Scheme 1. Photocatalytic synthesis of 2,2-disubstituted chromanes.

methyl and *tert*-butyl groups could be applied to the reaction (**1a**-**1f**). In contrast, salicylaldehydes bearing electron-withdrawing group did not proceed to the reaction (**3g**-**3i**). the π-extended salicylaldehydes, furnished the corresponding product in moderate yield (**3j**-**3k**). 1,1-Diarylalkenes with electron-withdrawing groups proved suitable substrates (**1l**-**1m**), while methyl and *tert*-butyl-substituted diarylalkenes decreased the reactivity (**3n**-**3o**). The structure of chromane **3n** was determined by 2D NMR, as shown in the Supporting Information. Furthermore, 1,1-diphenylethylene furnished the product in moderate yield (**3p**). In contrast, trisubstituted alkenes, α-methylstyrene, and monosubstituted alkenes exhibited poor reactivity (**1q**–**1t**), indicating that a 1,1-diarylalkene scaffold is particularly well suited for this transformation.

The plausible reaction mechanism is shown in Scheme 2 8. The excitation of an iridium catalyst enables a one-electron reduction of salicylaldehyde **1**, generating the ketyl radical **B**. The radical **B** reacts with 1,1-diarylalkene to form the stable dibenzyl radical **D**. Finally, one-electron oxidation of intermediate **D** by the reduced catalyst and cyclization yields the corresponding product **3**. When the reaction was carried out in the presence of TEMPO, product formation was not observed, suggesting that the reaction could proceed via a radical pathway (Scheme 3). Furthermore, Stern–Volmer quenching experiments revealed that the excited-state photocatalyst is quenched by both substrates, with the alkene displaying more efficient quenching than salicylaldehyde (Fig. 2). Styrenes are often excited by Ir photocatalysts to undergo [2 + 2] cycloadditions for the synthesis of cyclobutanes 9. However, no cyclobutane products were observed when 1,1-diarylalkenes were employed under the present reaction conditions. This result indicates that 1,1-diarylalkenes are significantly less reactive in [2 + 2] cycloaddition processes, presumably due to steric hindrance. Based on the substrate scope, salicylaldehydes bearing alkyl substituents or π-extended frameworks proved to be more suitable substrates for this reaction. In contrast, substrates bearing electron-withdrawing groups did not undergo the reaction. Although the detailed reaction mechanism remains unclear, the cyclization step, likely involving nucleophilic

Table 1
Photocatalytic synthesis of 2,2-diarylchlormane.[a]



Entry	Catalyst	Solvent	Yield (%)
1	Eosin Y	MeOH	0
2	4CzIPN	MeOH	0
3	Ir(bpy)$_2$(dtbbpy)PF$_6$	MeOH	39
4[b]	Ir(ppy)$_3$	MeOH	40
5	[Ir(dF(Me)ppy)$_2$(dtbbpy)]PF$_6$	MeOH	67
6	[Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]PF$_6$	MeOH	71
7	[Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]PF$_6$	DCM	50
8	[Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]PF$_6$	toluene	60
9	[Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]PF$_6$	DMF	64
10	[Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]PF$_6$	CH_3CN	61
11[c]	[Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]PF$_6$	MeOH	36
12[d]	[Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]PF$_6$	MeOH	0
13[e]	[Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)]PF$_6$	MeOH	0

[a] All reactions were carried out with **1a** (0.8 mmol), **2a** (0.4 mmol), photocatalyst (1.0 mol%) in solvent (2.0 mL) at room temperature for 24 h under irradiation with blue LED (λ_{ex} = 425 nm).

[b] λ_{ex} = 405 nm LEDs were used.

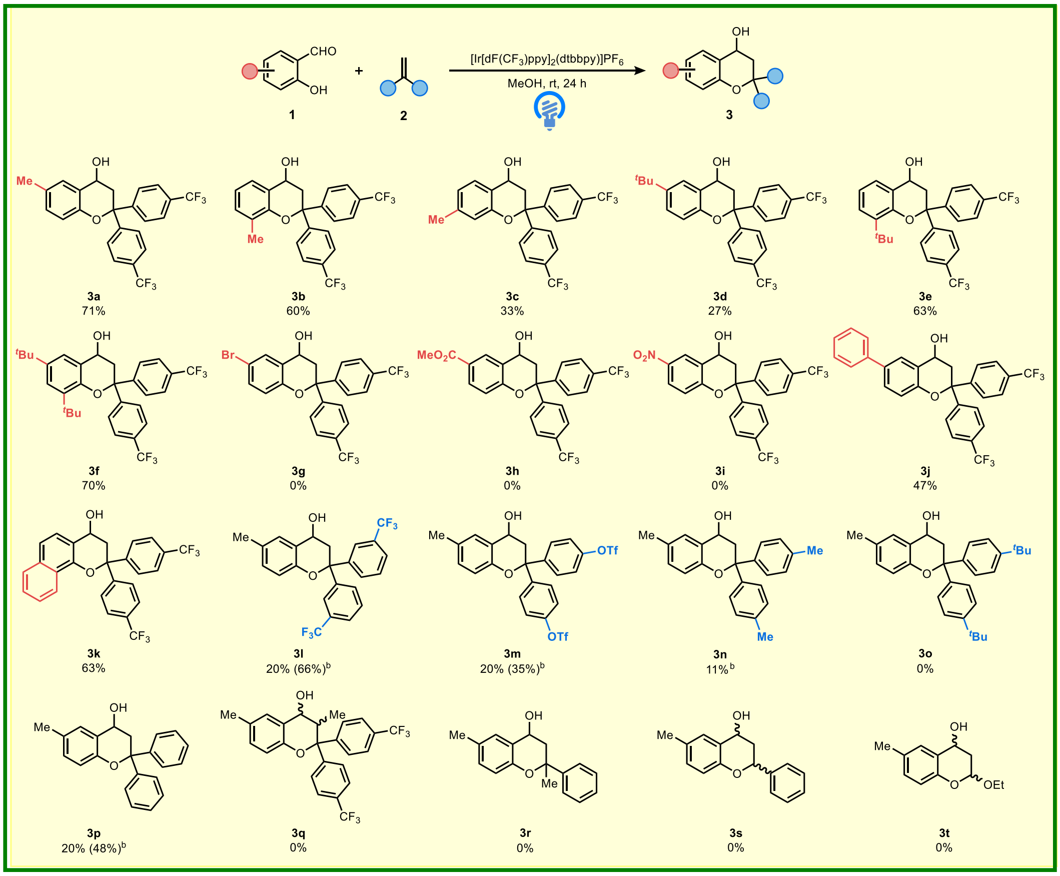
[c] 12 h.

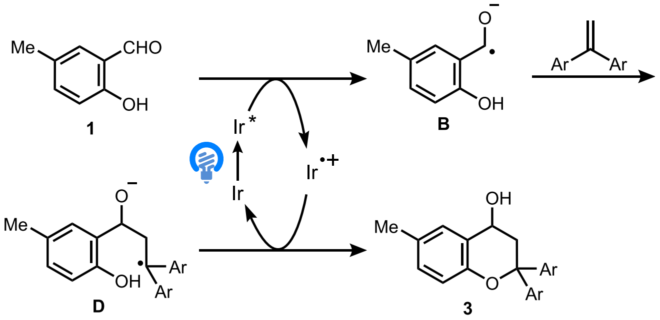
[d] No catalyst.

[e] No light.

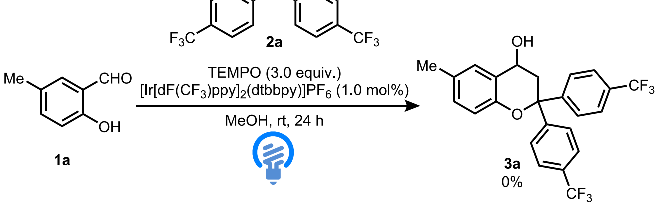
Table 2

Scope of the salicylaldehydes with alkenes.[a] All reactions were carried out with **1** (0.8 mmol), **2** (0.4 mmol), Ir photocatalyst (1.0 mol%) in MeOH (2.0 mL) at room temperature for 24 h under irradiation with blue LED (λ_{ex} = 425 nm). [b]CH_3CN was used as a solvent.





Scheme 2. Proposed reaction mechanism.



Scheme 3. Examination of the use of the radical scavenger.

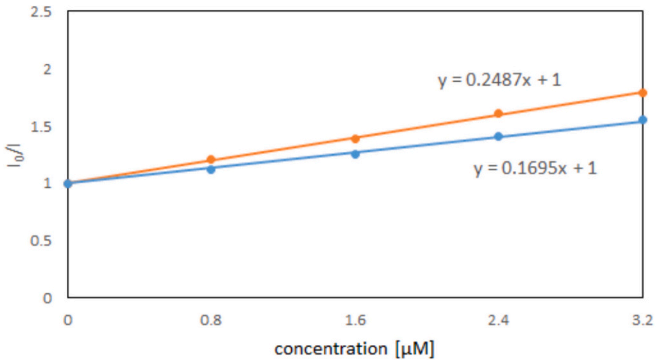
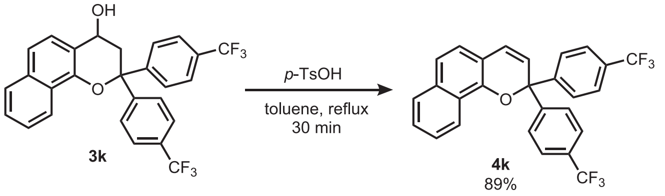


Fig. 2. Stern-Volmer plot. Orange line: alkene **2a**, Blue line: salicylaldehyde **1a**. **(For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)**



Scheme 4. Transformation of chromane to 2,2-diaryl-2*H*-naphtho[1,2-*b*]pyran.

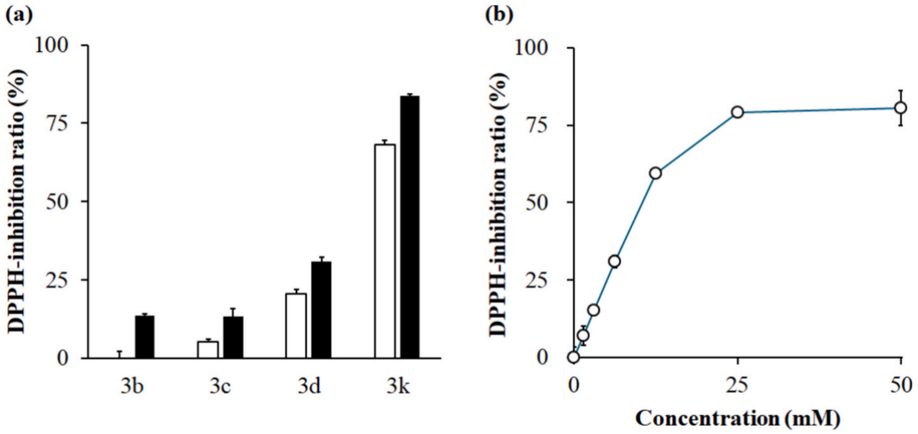


Fig. 3. Free-radical-scavenging activity of the chromanes. (a) Radical-scavenging activity of the chromanes (**3b**, **3c**, **3d**, and **3k**) at concentrations of 10 (white bar) and 50 mM (black bar). (b) Concentration-dependent radical-scavenging activity of **3k** at 1.56, 3.12, 6.25, 12.5, 25, and 50 mM. Results are expressed as mean values ± SD (*n* = 3).

attack of the phenol moiety on a benzyl cation, appears to be inhibited in the presence of electron-withdrawing substituents due to their reduced nucleophilicity. Furthermore, because ketyl radicals is nucleophilic 10, 1,1-diarylalkenes bearing electron-withdrawing groups are more suitable reaction partners in this transformation. The detailed reaction mechanism will be reported elsewhere in due course.

The further transformation of chromane is shown in Scheme 4. When the chromane **3k** was treated with *p*-TsOH, the desire 2,2-diaryl-2*H*-naphtho[1,2-*b*]pyran **4k** was obtained in high yield 11. Since 2,2-diaryl-2*H*-naphtho[1,2-*b*]pyrans are important structural motifs in photochromic materials 12, this transformation provides a promising tool for the synthesis of such functional compounds. Notably, as methods for introducing strong electron-withdrawing groups into 2,2-diaryl-2*H*-naphtho[1,2-*b*]pyrans remain largely unexplored 13, the present reaction offers a valuable strategy for the development of advanced photochemical materials.

Although 2,2-dialkylchromanes show useful biological activities, 2,2-diarylchromanes have been largely unexplored, especially regarding their free-radical-scavenging activities.[1]In our preliminary screening, **3b**, **3c**, **3d**, and **3k** exhibited measurable free-radical-scavenging activity, as evaluated by DPPH inhibition assays in comparison with standard antioxidants (Fig. 3) 14. Therefore, their free-radical-scavenging activities were further evaluated by performing DPPH-inhibition experiments.

In summary, we have developed a photocatalytic cyclization of salicylaldehydes with 1,1-diarylalkenes. In the presence of $[Ir[dF(CF_3)ppy]_2(dtbbpy)]PF_6$ catalyst and under blue LED irradiation, salicylaldehydes undergo cyclization with diarylalkenes to afford 2,2-diarylchromanes. The obtained 2,2-diarylchromanes exhibit noticeable free-radical-scavenging activities, a feature that has been largely unexplored. Furthermore, treatment of 2,2-diarylchromane with *p*-TsOH furnished the desired 2,2-diaryl-2*H*-naphtho[1,2-*b*]pyran in high yield. Since only a few examples of the synthesis of 2,2-diaryl-2*H*-naphtho[1,2-*b*]pyrans bearing strong electron-withdrawing groups have been reported, the present method provides a promising tool for accessing photochromic materials. Therefore, the present reaction represents a promising tool for the synthesis of functional materials and biologically active compounds.

CRediT authorship contribution statement

Sakura Kodaki: Writing – review & editing, Writing – original draft, Investigation. **Momo Kondo:** Writing – review & editing, Investigation. **Junta Minato:** Investigation, Writing – review & editing. **Shoko Itakura:** Writing – review & editing. **Hiroyoshi Takamura:** Writing – review & editing. **Makiya Nishikawa:** Writing – review & editing. **Isao Kadota:** Writing – review & editing. **Kosuke Kusamori:** Writing – review & editing, Writing – original draft. **Kenta Tanaka:** Writing – review & editing, Writing – original draft, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was supported by the JGC-Saneyoshi Scholarship Foundation, the TOSOH Award in Synthetic Organic Chemistry, Japan, and the Wesco Scientific Promotion Foundation. We appreciate the assistance of the Division of Instrumental Analysis at Okayama University with NMR spectroscopy and high-resolution mass spectrometry.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2026.156034.

Data availability

Data will be made available on request.

References

[1] (a) M. Eggersdorfer, D. Laudert, U. Létinois, T. McClymont, J. Medlock, T. Netscher, W. Bonrath, Angew. Chem. Int. Ed. 51 (2012) 12960–12990; (b)McFadden ME, Barber RW, Overholts AC, Robb MJ. Chem. Sci. 2023; 14: 10041–10067. (c) F.E. Ward, D.L. Garling, R.T. Buckler, D.M. Lawler, D. P. Cummings, J. Med. Chem. 24 (1981) 1073–1077; (d) R. Bergmann, R. Gericke, J. Med. Chem. 33 (1990) 492–504; (e) A. Alejo-Armijo, N. Glibota, M.P. Frías, J. Altarejos, A. Gálvez, S. Salido, E. Ortega-Morente, J. Agric. Food Chem. 66 (2018) 2151–2158.(f)McFadden ME, Barber RW, Overholts AC, Robb MJ. Chem. Sci. 2023; 14: 10041–10067.

[2] Representative synthesis of 2,2-disubstituted chromanes see: (a) Liang Z, Liu C, Fan J, Wang M, Yan X, Huang M, Cai S. Green Chem. 2022; 24: 7442–7447. (a) Y. Qiu, Y. Ye, X. Song, X. Zhu, F. Yang, B. Song, J. Wang, H. Hua, Y. He, Y. Han, X. Liu, Y. Liang, Chem. Eur. J. 21 (2015) 3480–3487; b T. Aoyama, T. Furukawa, M. Hayakawa, T. Takido, M. Kodomari, Synlett 26 (2015) 1875–1879; (c) A. Jha, P. Jimmy Huang, J. Heterocycl. Chem. 46 (2009) 1098–1106.

[3] Representative photochemical synthesis of chromanes see: (a) Zhang W, Chen Z, Jiang Y-X, Liao L-L, Wang W, Ye J-H, Yu D-G. Nat Commun. 2023; 14: 3529. a Y. Wang, J. Miao, H. Dong, D. Zhang, B. Chen, M. Guan, G. Zhang, Q. Zhang, Chem. Sci. 16 (2025) 5640–5650;

(b)Betori RC, McDonald BR, Scheidt KA. Chem. Sci. 2019; 10: 3353–3359. c Y.-W. Zheng, P. Ye, B. Chen, Q.-Y. Meng, K. Feng, W. Wang, L.-Z. Wu, C.-H. Tung, Org. Lett. 19 (2017) 2206–2209;
d S. Han, L. Liu, J. Meng, M. Li, Q. Cao, Z. Shen, J. Org. Chem. 90 (2025) 7062–7069.

[4] S. Arumugam, V.V. Popik, J. Am. Chem. Soc. 133 (2011) 5573–5579.

[5] Z. Guan, X. Zhong, Y. Ye, X. Li, H. Cong, H. Yi, H. Zhang, Z. Huang, A. Lei, Chem. Sci. 13 (2022) 6316–6321.

[6] An intramolecular cyclization method see: Rivero AR, Fodran P, Ondrejková A, Wallentin C-J. Org Lett. 2020; 22: 8436–8440.

[7] (a) S. Nohara, S. Iwai, N. Yamaguchi, Y. Asada, Y. Kamiyama, Y. Tanaka, K. Tanaka, Y. Hoshino, Synlett 34 (2023) 2525–2529;
(b) K. Tanaka, Y. Asada, Y. Hoshino, K. Honda, Org. Biomol. Chem. 18 (2020) 8074–8078;
(c) K. Tanaka, D. Omata, Y. Asada, Y. Hoshino, K. Honda, J. Org. Chem. 84 (2019) 10669–10678;
(d) K. Tanaka, M. Kishimoto, Y. Asada, Y. Tanaka, Y. Hoshino, K. Honda, J. Org. Chem. 84 (2019) 13858–13870;
(e) K. Tanaka, M. Kishimoto, Y. Hoshino, K. Honda, Tetrahedron Lett. 59 (2018) 1841–1845;
(f) K. Honda, K. Tanaka, Y. Hoshino, Heterocycles 95 (2017) 474;
(g) K. Tanaka, M. Sukekawa, Y. Shigematsu, Y. Hoshino, K. Honda, Tetrahedron 73 (2017) 6456–6464;
(h) K. Tanaka, Y. Shigematsu, M. Sukekawa, Y. Hoshino, K. Honda, Tetrahedron Lett. 57 (2016) 5914–5918;
(i) K. Tanaka, Y. Hoshino, K. Honda, Tetrahedron Lett. 57 (2016) 2448–2450.

[8] (a) A.L. Berger, K. Donabauer, B. König, Chem. Sci. 9 (2018) 7230–7235;
(b) V.Q. Dang, T.S. Teets, Chem. Sci. 14 (2023) 9526–9532;
(c) J. Jo, S. Kim, S. Park, S. Kim, S. Lee, J.-H. Choi, W. Chung, J. Org. Chem. 89 (2024) 8985–9000;
(d) S. Kundu, L. Roy, M.S. Maji, Org. Lett. 24 (2022) 9001–9006;
(e) S. Okamoto, K. Kojiyama, H. Tsujioka, A. Sudo, Chem. Commun. 52 (2016) 11339–11342;
(f) E. Fava, M. Nakajima, A.L.P. Nguyen, M. Rueping, J. Org. Chem. 81 (2016) 6959–6964.

[9] Q. Zhou, Y. Zou, L. Lu, W. Xiao, Angew. Chem. Int. Ed. 58 (2019) 1586–1604.

[10] Á. Péter, S. Agasti, O. Knowles, E. Pye, D.J. Procter, Chem. Soc. Rev. 50 (2021) 5349–5365.

[11] (a) Böttcher C, Zeyat G, Ahmed SA, Irran E, Cordes T, Elsner C, Zinth W, Rueck-Braun K. Beilstein J. Org. Chem. 2009; 5; 25.
(b) Deodhar M, Black DS, Kumar N. Tetrahedron 2007; 63: 5227–5235.

[12] (a) D.S. Tabirja, V.V. Kostjukov, Phys. Chem. Chem. Phys. 26 (2024) 4412–4421;
(b) P.J. Coelho, C.J.R. Silva, C. Sousa, S.D.F.C. Moreira, J. Mater. Chem. C 1 (2013) 5387;
(c) Q. Meng, G. Wang, H. Jiang, Y. Wang, S. Xie, J. Mater. Sci. 48 (2013) 5862–5870;
(d) P. Brun, R. Guglielmetti, S. Anguille, Appl. Org. Chem. 16 (2002) 271–276;
(e) S. Jockusch, N.J. Turro, F.R. Blackburn, J. Phys. Chem. A 106 (2002) 9236–9241.

[13] (a) J.N. Moorthy, A.L. Koner, S. Samanta, A. Roy, W.M. Nau, Chem. Eur. J. 15 (2009) 4289–4300;
(b) T.-F. Tan, J. Han, M.-L. Pang, Y.-F. Fu, H. Ma, Y.-X. Ma, J.-B. Meng, Tetrahedron 62 (2006) 4900–4906.

[14] See supporting information.