Structural Tuning of β-Enamino Diketones: Exploration of Solution and Crystalline State Photochromism

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Abstract

A library of β-enamino diketones was prepared via base-mediated, three-component reaction of 4-hydroxycoumarins with various aromatic/aliphatic amines and β-nitrostyrenes under microwave irradiation conditions to investigate their photochemical properties. Among the prepared compounds, a thiophene derived β-enamino diketone was found to be light-sensitive and to exhibit unique photochromic behavior, that is, positive photochromism in solution and negative photochromism in crystalline phase. In addition, this prepared photochromic compound was further covalently linked to a structure-related, piezochromic β-enamino diketone moiety to explore its potential multi-stimuli responsive properties.

1 Introduction

The β-enamino diketones represent important and versatile synthons for the synthesis of natural products and other heterocycles (Michael et al., 2001; Valduga et al., 1998; Ferraz et al., 1995; White et al., 2006; Li et al., 2007). Compounds bearing β-enamino diketone moiety, especially six-membered cyclic ones, were found to possess many biological properties. For instance, as shown in Figure 1, β-enamino diketone **1** is an antioxidant agent (Mladenovic et al., 2009). Compound **2** possesses strong inhibitory activity against fungus *C. albicans* (Vukovic et al., 2010). Compound **3** exhibits potent cytotoxicity against A546, HeLa, and K562 cells (Budzisz et al., 2004). Owing to their diverse biological activities, a plethora of multi-component reaction (MCR) methodologies for the synthesis of β-enamino diketones have been reported in the literature (Kuo et al., 2009; Ghabraie et al., 2011; Ye et al., 2015). While most efforts were focused on the biological activities of the prepared compounds, their potential photochemical and functional properties were much less explored. Recently, we have reported that coumarin-based *N*-aryl-β-enamino diketone **4** (Figure 1) exhibits piezochromic properties (Hsieh et al., 2019); that is, upon grinding, compound **4** changes from yellow to red and can be swiftly reverted to the original color when exposed to methylene chloride vapor. Further, the furan-derived enaminones **5** serve as amine-protected compounds for primary alkyl amines protection. These acid/base stable amine-protected **5** can be readily deprotected by treating with ethylene diamine under reflux conditions (Chithanna et al., 2019). Similarly, the phenyl-derived enaminones **6** function as amine-protected products for aryl amines and amino acids in both solution and solid phase peptide synthesis. The free aryl amines and amino acids can be regenerated by treating with hydrazine hydrate in ethanol under mild conditions (Chithanna et al., 2020). These successful examples prompted us to speculate that new or unique functional properties of β-enamino diketones might be discovered via structural tuning of their three major molecular scaffolds, namely, cyclic diketone, aryl/alkyl amine, and aryl group. In our continuous efforts to unearth novel functional properties from the heterocycles synthesized via MCR, herein we reported the preparation of a library of β-enamino diketones from a microwave-assisted, three-component reaction of 4-hydroxycoumarins with various aromatic/aliphatic amines and β-nitrostyrenes in toluene under basic conditions. Their stimuli responses towards UV and visible light in solution, thin film, and crystalline state were examined. Further, the photochromic compound prepared from 7-*N*,*N*-dimethylamino-4-hydroxycoumarin, benzylamine, and 5-chlorothiophene-2-carbaldehyde was further linked to a structure-related, pressure-sensitive β-enamino diketone scaffold to investigate its potential multi-stimuli responsive properties.

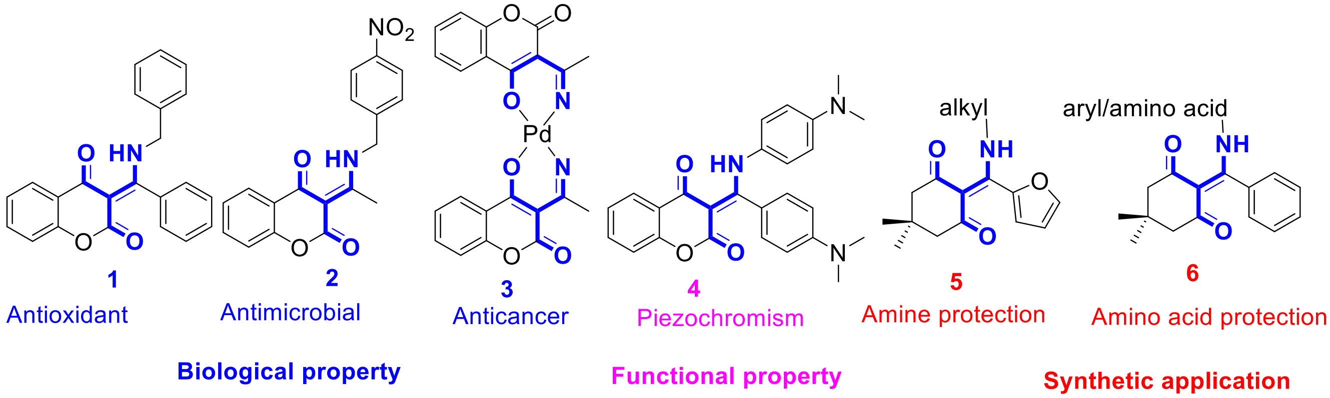
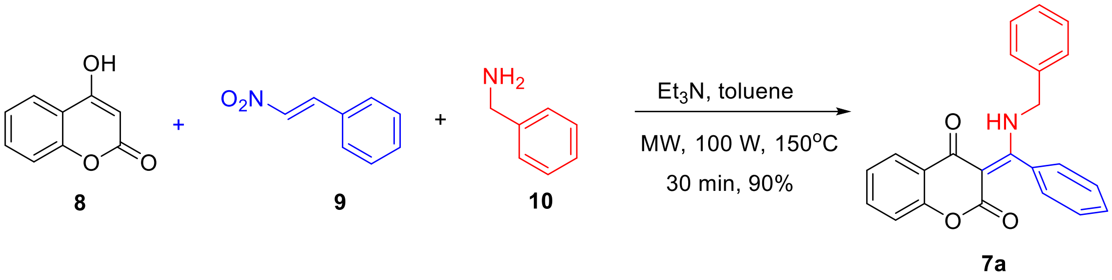


Figure 1. Structures of representative β-enamino diketones with biological/functional properties and synthetic applications.

2 Results and Discussion

Scheme 1 outlines the microwave-assisted, three-component preparation of β-enamino diketone **7a**. With slight modifications from the literature reported procedure (Hsieh et al., 2019; Manjappa et al., 2018), it could be easily obtained via Et_3N-mediated coupling of 4-hydroxycoumarin (**8**), β-nitrostyrene (**9**), and benzylamine (**10**) in toluene under microwave conditions for 30 min in 90% yield.



Scheme 1. Three-component synthesis of β-enaminone diketone **7a**.

Figure 2 lists the structures and yields of the prepared **7a**–**o**. Most of the reactions gave good to excellent yields, except for compound **7k** in which 4-bromofuran-2-carbaldehyde was used as the aldehyde source. This observation could be attributed to the furan’s high propensity to be attacked by a nucleophilic amine(Chithanna et al., 2019; Helmy et al., 2014). In the present investigation, we focused mainly on 7-*N*,*N*-dimethylamino-4-hydroxycoumarin, benzylamine, and thiophene aldehydes derived β-enaminone diketones. The molecular structures of diketones **7a**–**o** were elucidated by spectroscopic data along with X-ray crystal analysis (**7b**, **7g**, **7i**, and **7m**) (CCDC No). A broad signal appearing around 13–14 ppm in the proton NMR spectrum was detected for all prepared compounds, indicating the presence of an intramolecular hydrogen bond in the molecular scaffold. Indeed, an intramolecular hydrogen bonding between the amine hydrogen (*N*-H) and carbonyl oxygen (C=O) of coumarin was distinctly observed in the ORTEP diagrams shown in Figure 2. Generally, changes of amines (aryl or aliphatic) or aromatic/heterocyclic aldehydes had little effect on product yields.

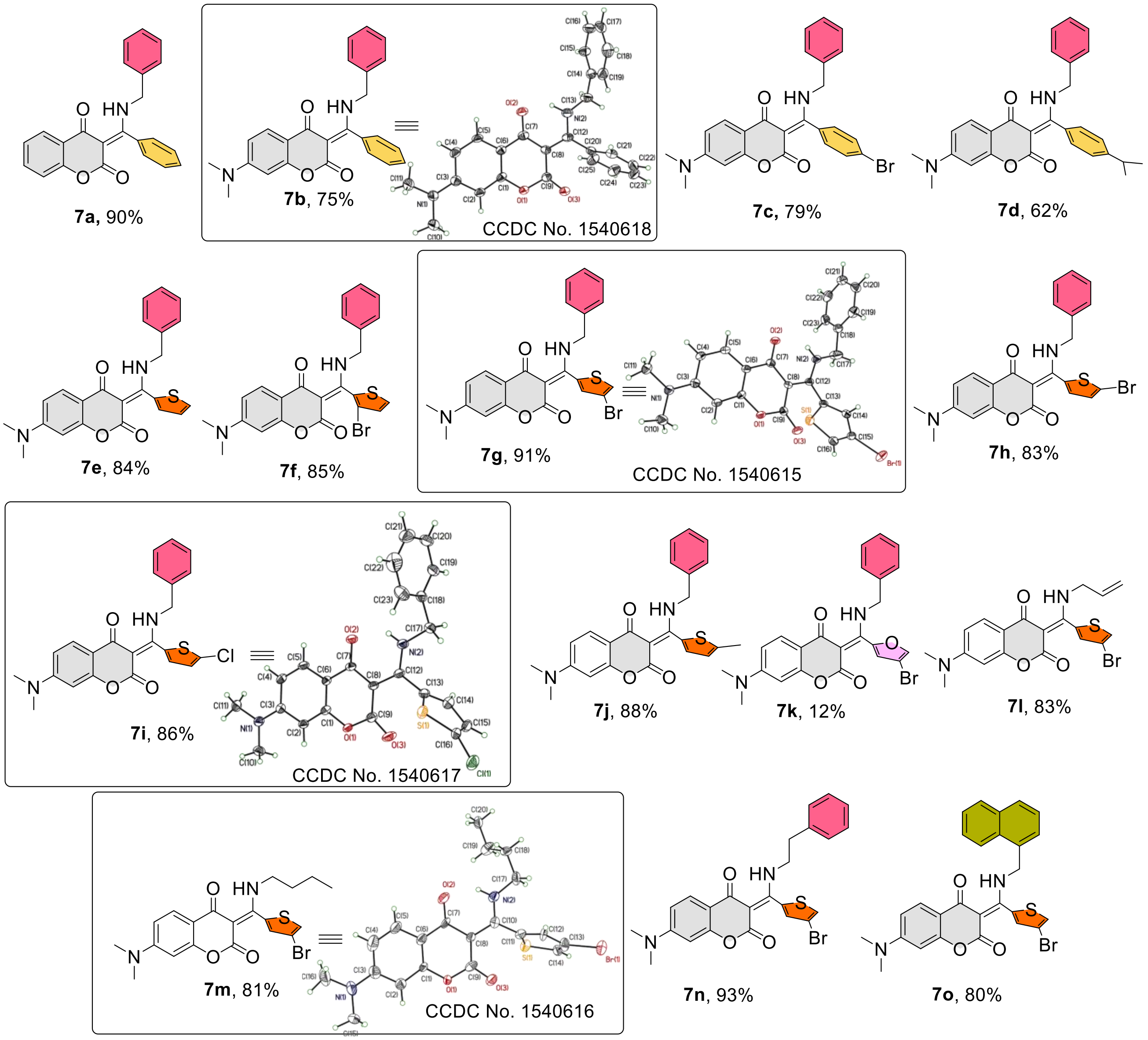


Figure 2. Structures and yields of the prepared β-enamino diketones **7a**–**o** and ORTEP crystal structures of **7b**, **7g**, **7i**, and **7m** with atomic displacement shown at 50% probability.

With β-enaminone diketones **7a**–**o** in hand, their photochemical properties were then explored. Compound **7a**, in which benzaldehyde was used as the aldehyde substrate, was found to be sensitive to UV light. Figure 3 shows the absorption spectra of **7a** in acetonitrile when exposed to UV irradiation

(352 nm) for 60 sec. With the increase of exposure time, the absorbance at wavelength of 330 and 342 nm gradually decreased, along with the emergence of broad shoulder around 380 nm. Also, two isosbestic points located at 305 and 355 nm were clearly observed. Presumably, upon UV irradiation, compound **7a** undergoes *E*-*Z* isomerization of the central carbon-carbon double bond to generate the isomer **11**, as shown in Scheme 2. To our surprise, when an *N*,*N*-dimethylamino group was introduced onto the 7-position of the coumarin moiety, the resulting compound **7b** became light-insensitive. Prolonged irradiation of **7b** did not exhibit considerable changes in the UV-vis absorption profiles (Figure 3, b). This observation suggests that the photochemical property of the β-enaminone diketones can be influenced by the substituents on the coumarin moiety.

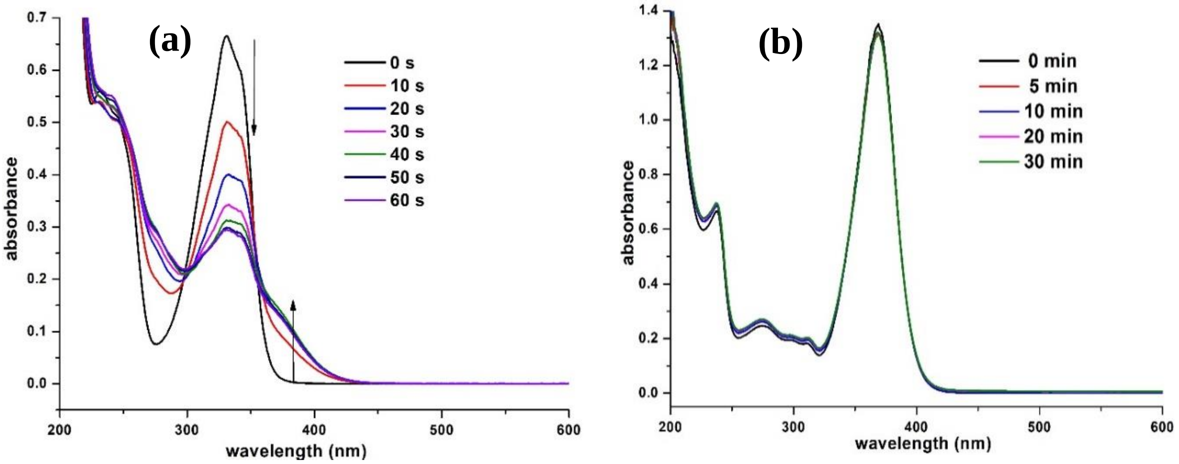
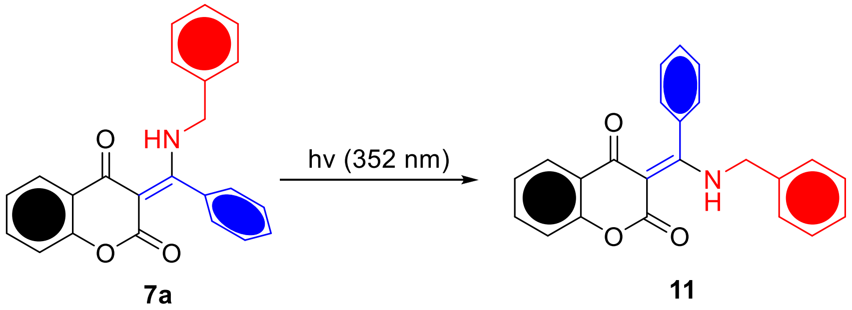


Figure 3. Absorption spectra of (a) **7a** (3.0×10^{-5} M in CH_3CN) and (b) **7b** (3.0×10^{-5} M in CH_3CN) obtained with different exposure times (352 nm).



Scheme 2. Proposed *E*-*Z* isomerization between **7a** and **11**.

Interestingly, compound **7i** bearing a 5-chlorothiophene moiety was found to be highly sensitive to UV light and exhibit unique photochemical properties. As shown in Figure 4, it turned from light yellow to red within seconds when exposed to UV irradiation in solution. Figure 5 (a) displays the time course of the UV–vis absorption spectra of **7i** in acetonitrile under continuous irradiation (352 nm) for 5 min. With the increase of exposure time, two broad absorbance peaks which centered at 527 and 551 nm exhibited smooth continuous growth. This process could be reverted by visible light irradiation (580 nm), indicating that compound **7i** possesses photochromic property (Figure 5, b).

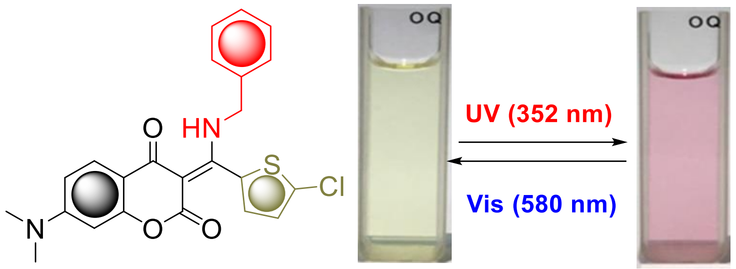


Figure 4. Photochromic behavior of **7i** in acetonitrile.

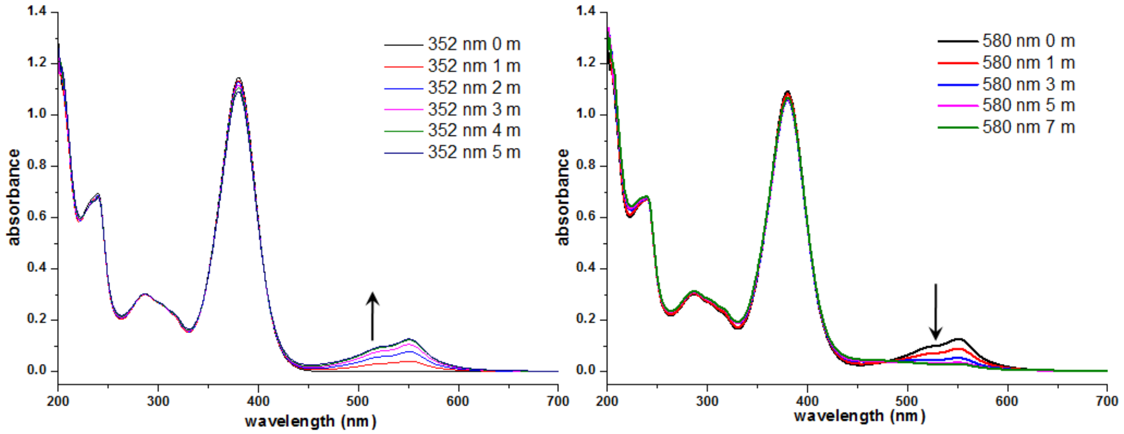


Figure 5. Absorption spectra of (a) **7i** (3.0×10^{-5} M in CH_3CN) obtained with different exposure times (352 nm), 0 to 5 m, in increments of 1 m. (b) the photogenerated product obtained with different exposure times (580 nm), 0 to 7 m, in increments of 2 m.

Isolation of the photogenerated product and subsequent characterization of its molecular structure proved to be difficult since prolonged UV irradiation of **7i** resulted in the *E-Z* isomerization to be the dominant process. Figure 6 depicts the evolution of absorbance profile of **7i** during the prolonged UV irradiation. Starting from the initial 5 min of UV irradiation, there was a surge in a broad absorption band around 520 to 560 nm, indicating the formation of photogenerated products. However, as the irradiation time was further extended (up to 120 min), the decrease in absorption at 372 nm and the appearance of a broad shoulder near 455 nm were also recorded. This observation suggests that prolonged irradiation of compound **7i** renders the *E-Z* isomerization to be a dominant process over the formation of photogenerated product. Therefore, current efforts to characterize the photogenerated product resulting from this photochromic behavior were futile.

Inspired by the photochromic behavior in solution, we chose to investigate the photosensitivity of **7i** in solid phase. The thin film of **7i** was prepared by spin coating on a quartz plate and then irradiated with light. When exposed to blue LED for 1 hour, no apparent color change of **7i** was observed. Conversely, compound **7i** (thin film) changed from colorless to red in 5 min upon UV (352 nm) irradiation. Figure 7 shows the color change and absorption profile of **7i** (thin film) prior to and after irradiation. As UV exposure increased, the absorbance centered at 388 nm decreased along with a smooth enhancement of the shoulders near 450 nm and 530 nm. This evolution of the absorbance resulted in the formation of two isosbestic points at 366 and 412 nm, which indicates the presence of two distinguishable species in the film. The fact that UV-vis spectra of **7i** in thin film (solid state) exhibited strong resemblance to that of **7i** in solution phase (Figure 6) implies that similar photochromic mechanisms may be involved for **7i** in solution and solid state.

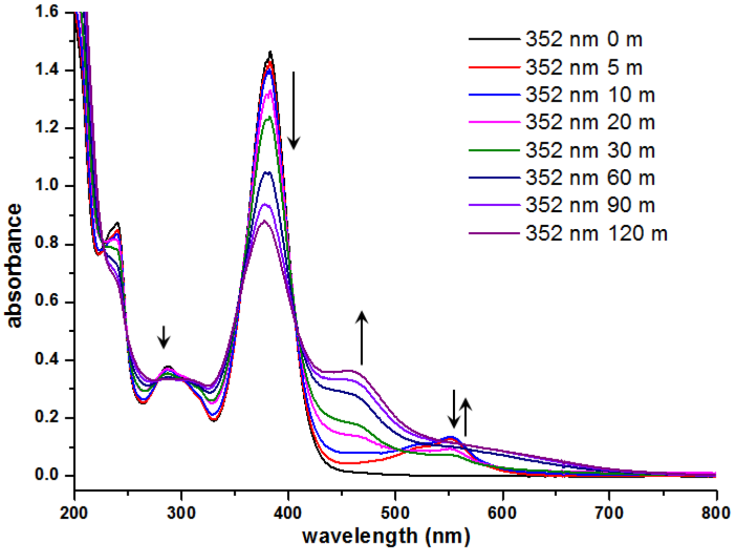


Figure 6. UV-vis spectra of **7i** (3.0×10^{-5} M in CH_3CN) after continuous irradiation at 352 nm for 2 h.

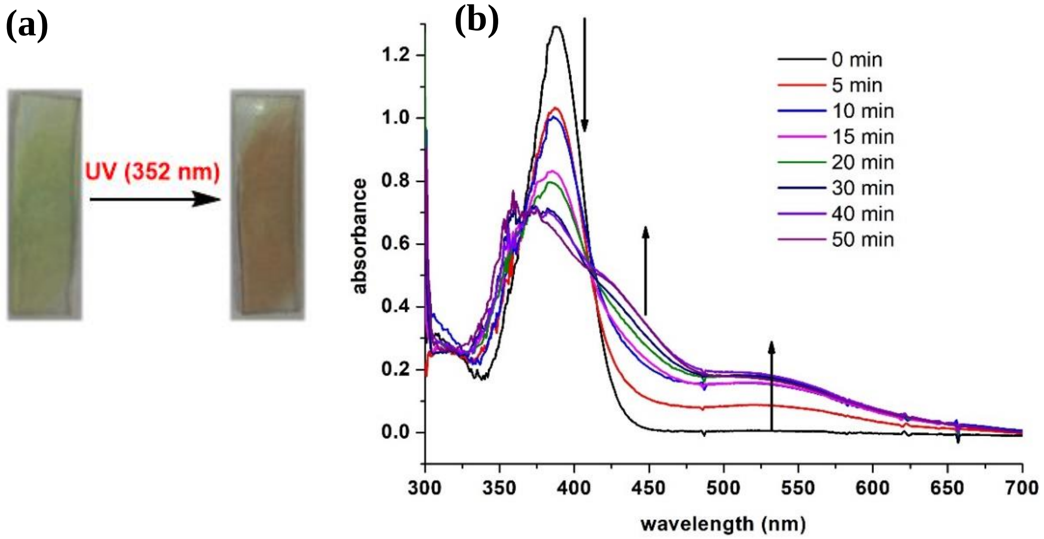


Figure 7. (a) Color change prior to and after UV irradiation of **7i** (thin film). (b) UV-vis spectra of **7i** (spin-coated on quartz plate) after continuous irradiation at 352 nm for 50 min.

After discovering the photochromism of **7i** in both solution and solid state, we embarked upon our investigations on its photochromic behavior in crystalline state (Irie et al., 2014; Sun et al., 2022; Zhang et al., 2021; Funasako et al., 2019; Avadanei et al., 2014; Loan et al., 2023). A fine, moderate-sized crystal of **7i** was grown and subjected to photoirradiation. To our surprise, **7i** was found to be highly sensitive to visible light in crystalline state. When exposed to blue LED (455 nm), the crystal of **7i** changed from yellow to violet within 15 sec. Gratifyingly, this process was reversible upon exposure to the compact fluorescent lamp (CFL) for 2 h. Figure 8 shows the color transition of **7i** at crystalline state as well as UV-vis absorption profiles of **7i** prior to and after the blue LED irradiation. Before the exposure, **7i** displayed a maximum absorbance (λ_{max}) around 416 nm. After blue LED exposure (40 min), the λ_{max} was red-shifted to 425 nm along with the broad absorbance increase from 425 to 550 nm. This change in the absorbance was visible to the naked eye as blue LED imparted dark pink-red color to the **7i** crystal. The pink crystal of **7i** gradually returned to yellow upon exposure to CFL light, suggesting possible reversibility. In the case of color change of **7i** in solution photochromism, the number of cycles is limited to 3-4 times only. We believe that poor performance in solution state can be attributed to the gradual enhancement of *E*-*Z* isomerization over photochromic behavior (Figure 6). On the other hand, the number of photochromic cycles for **7i** in crystalline state is up to 25 times (see the SI for details), which is comparatively higher than that of in solution state. Although the mechanistic details for the photochromic switch of **7i** in solution, thin film, and crystalline state remain to be investigated, compound **7i** represents one of the rare examples that exhibit opposite photochromic property under different states (Funasako et al., 2020), that is, positive photochromism in solution and thin film as well as negative photochromism in crystalline state.

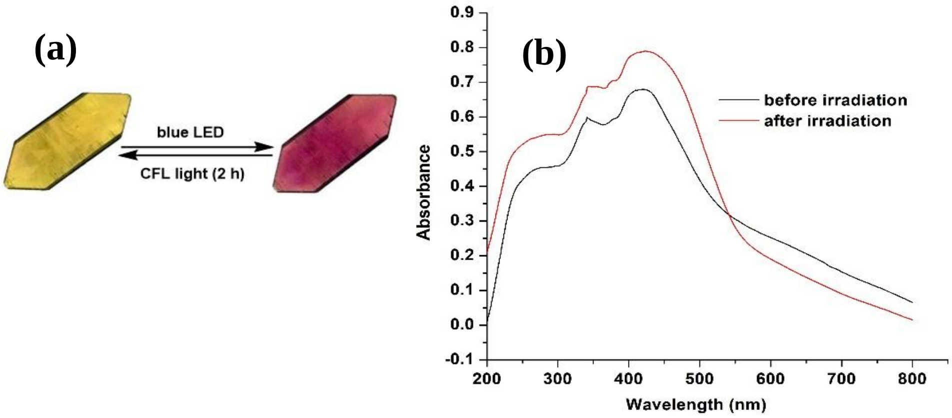
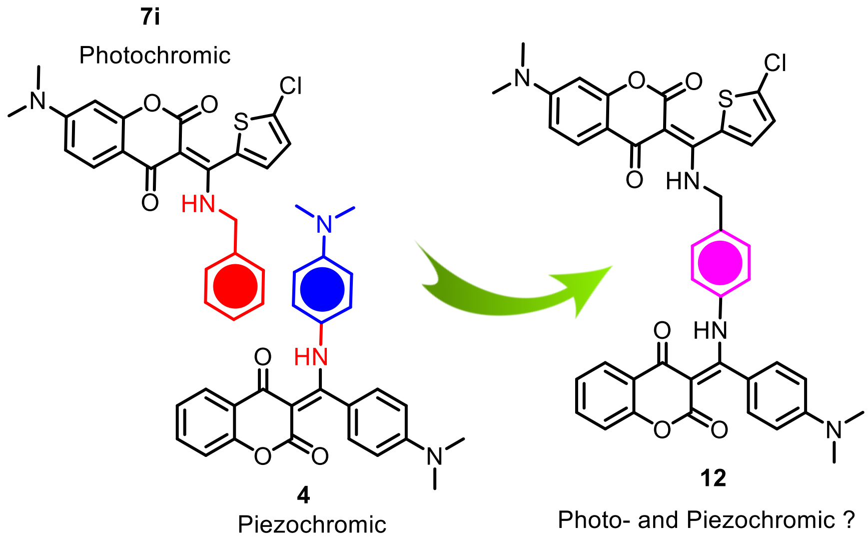


Figure 8. (a) Crystalline state reversible color change observed for **7i**. (b) UV-vis absorption profiles of **7i** prior to and after blue LED irradiation (40 min).

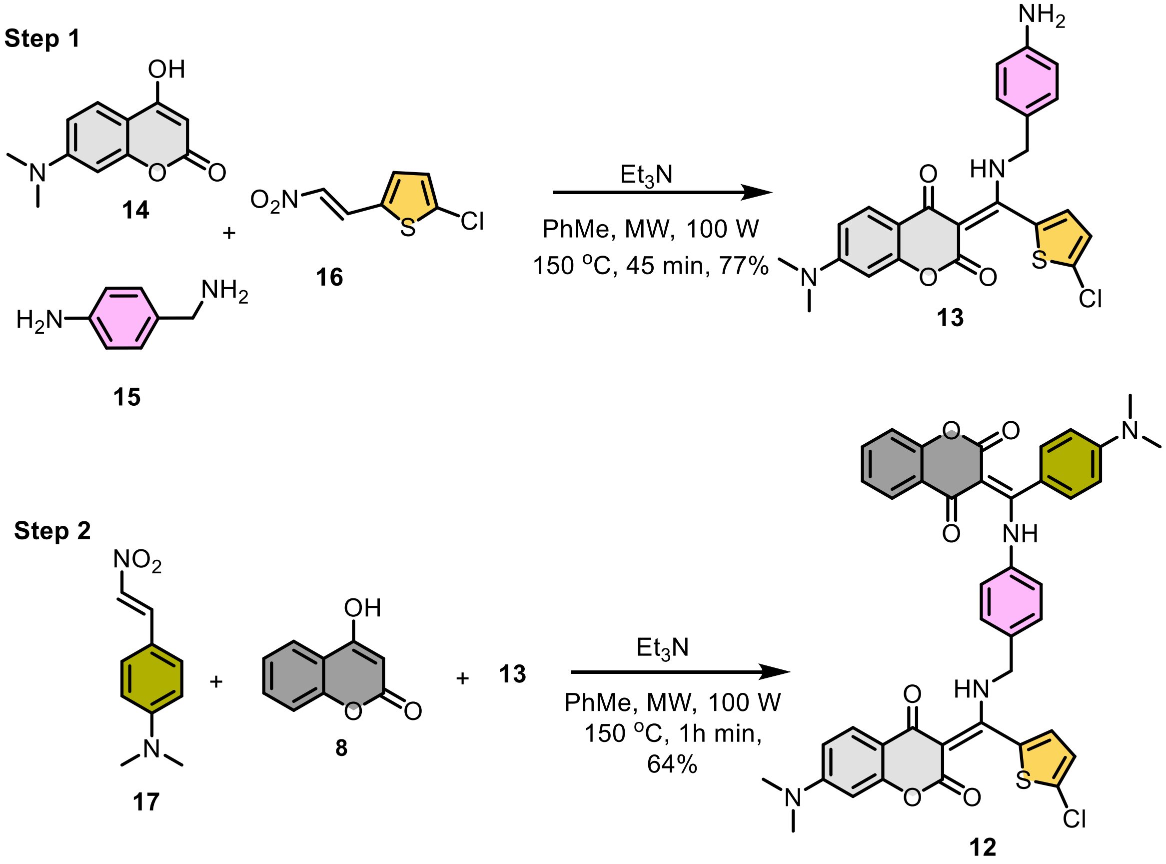
As illustrated in Figure 1, our previous study has demonstrated that coumarin-based *N*-aryl-β-enamino diketone **4** exhibits piezochromic behavior (Figure 1) (Hsieh et al., 2019). We speculate that by linking this pressure-sensitive molecular scaffold (Wang et al., 2015; Sagara et al., 2007; Zhang et al., 2015; Li et al., 2021; Yude et al., 2023; Sagara et al., 2009; Ma et al., 2015) of **4** with the present light-sensitive moiety of **7i** into one molecule, the resulting hybrid compound may exhibit multi-stimuli responsive properties in solid state (Wang et al., 2022; Zhang et al., 2011; Vaidya et al., 2021; Martinez-Junquera et al., 2022; Chiu et al., 2020). Scheme 3 depicts the conceptual design of the potential dual responsive *N*-aryl-β-enamino diketone **12**. Since both piezochromic **4** and photochromic **7i** share a phenyl group on the *N*-substituent, this common phenyl group was then used to connect the two molecular scaffolds to form the hybrid **12**.

Scheme 4 outlines the two-step synthesis of the target compound **12**. The photochromic unit **13** was synthesized via base-promoted, three-component reaction of 7-*N*,*N*-dimethylamino-4-hydroxycoumarin (**14**), 4-aminobenzylamine (**15**), and β-nitrostyrene **16** under microwave conditions. As expected, the less nucleophilic aniline nitrogen on 4-aminobenzylamine (**15**) did not participate in the reaction, and the desired β-enamino diketone **13** was isolated as an exclusive product in 77% yield. The subsequent three-component reaction of **13** with 4-hydroxycoumarin (**8**) and *p*-*N*,*N*-

dimethylamino-β-nitrostyrene (**17**) under basic conditions yielded the hybrid β-enaminone **12** in 64% yield.



Scheme 3. Conceptual design of the hybrid **12**.



Scheme 4. Two-step preparation of β-enamino diketone **12**.

After realizing compound **12**, we then explored its functional properties by applying external stimuli such as mechanical force and UV irradiation to examine its potential piezochromic and photochromic responses. Upon grinding, compound **12** turned slowly from yellow to dark brown (Figure 9), indicating that the hybrid **12** remained pressure-sensitive. Nevertheless, the ground **12** failed to return to its original color when exposed to various solvent vapors such as methylene chloride, dichloroethane, acetone, chloroform, and THF, etc. This irreversible response of the hybrid **12** towards mechanical force suggests that it is not piezochromic anymore.

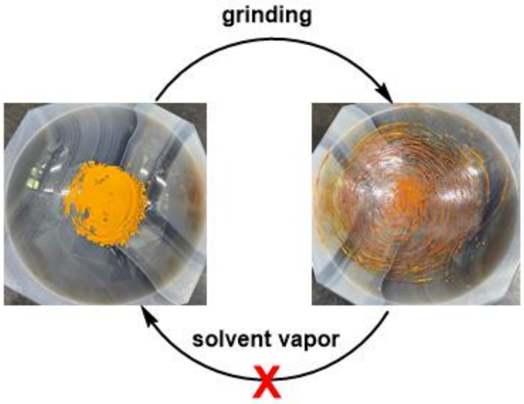


Figure 9. Irreversible response of compound **12** towards mechanical force.

Compound **12** was also subjected to UV (352 nm) irradiation in solid state as it consisted of a light-sensitive β-enamino diketone moiety. Regrettably, the hybrid **12** failed to respond to UV light in solid state. As shown in Figure 10 (a), compound **12** did not show noticeable color change even after exposed to UV light (352 nm) for 30 min. Further, no major change was observed in the solid state absorbance spectra of **12** prior to and after UV irradiation (Figure 10, b). Our studies suggest that a multi-stimuli responsive molecule cannot be constructed simply through combination of two different chromic moieties into one, even though structures of the two chromic molecular scaffolds are closely related.

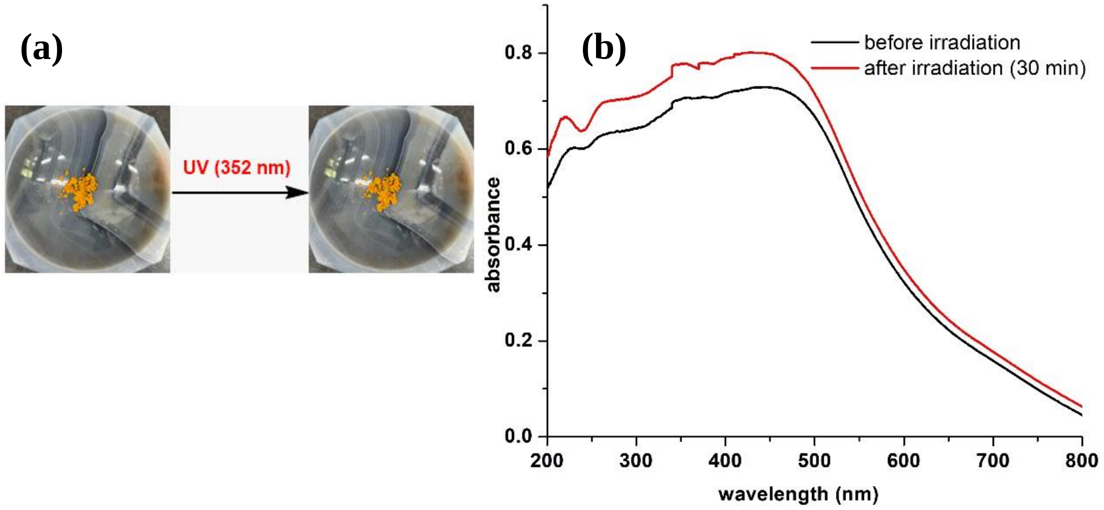


Figure 10. (a) No color change of **12** prior to and after UV (352 nm) irradiation. (b) Solid state absorption profiles of **12** prior to and after UV (352 nm) irradiation.

3 Methods and materials

3.1 General information

Microwave reactions were performed using a CEM Discover unit (operating at 110 V, microwave irradiation of 2.45 GHz, maximum microwave output of 300 W) in 50 mL capacity open round-bottom flasks. Visualization was accomplished by using portable UV light and an iodine chamber. Flash chromatography was performed in columns of various diameters with Merck silica gel (230–400 mesh ASTM 9385 kieselgel 60H) by elution with the solvent systems. Solvents, unless otherwise specified, were reagent grade and distilled once before use. All new compounds exhibited satisfactory spectroscopic and analytical data. ^{1}H NMR (400 MHz) and ^{13}C NMR (100) spectra were recorded on a Bruker 400 spectrometer. Chemical shifts were reported in parts per million on the scale relative to an internal standard (tetramethylsilane, or appropriate solvent peaks) with coupling constants given in hertz. ^{1}H NMR multiplicity data are denoted by s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel 60G-254 plates (25 mm) and developed with the solvents mentioned. Melting points were determined on a Mel-Temp melting point apparatus in open capillaries and are uncorrected. High-resolution mass spectra (HRMS) were obtained on a Thermo Fisher Scientific Finnigan MAT95XL spectrometer using a magnetic sector analyzer. Infrared (IR) spectra were recorded using 1725XFT-IR spectrophotometer. Single-crystal structures were determined with a Bruker AXS SMART-1000 X-ray single-crystal diffractometer. The absorption spectra were obtained using a UV/vis/NIR spectrophotometer (Jasco V-770) with a deuterium lamp (190– 350 nm) and halogen lamp (300–2700 nm) light sources and the detector was a photomultiplier tube.

3.2 Synthesis of compound 7a-o, 12 and 13

Mixtures of appropriately substituted *4*–hydroxycoumarin (1 equiv.), β-nitrostyrene (1.2 equiv.), substituted amine (1.2 equiv.), and a few drops of TEA in toluene (~20 mL) were refluxed in Microwave at 100 W, 150 °C for about 25-30 min (unless otherwise specified). The cooled reaction mixture was concentrated, and re–dissolved in DCM. The solution was washed with plenty of water, brine, dried over $MgSO_4$ and was evaporated *in vacuo*. The silica gel slurry was made from these organic solvent and crude product was purified by column chromatography. These products further recrystallized from DCM–Hexanes.

4 Conclusions

In summary, a total of 15 structurally diverse β-enamino diketone derivatives were synthesized in good to excellent yields via microwave-assisted, base-mediated, three-component reaction between 4-hydroxycoumarins, substituted β-nitrostyrene, and primary amines. Among prepared compounds, compound **7i** was found to exhibit positive photochromism in solution/thin film and negative photochromism in crystalline state. Further, compound **12** bearing pressure- and light-sensitive molecular scaffolds was designed and synthesized in two steps as a potential dual-responsive material. Unfortunately, the prepared **12** failed to show any expected functional behavior. The in-depth investigation of the photochromic mechanism of this intriguing thiophene-derived β-enamino diketone **7i** at the molecular level is currently underway and will be reported in due course.

5 Conflict of Interest

The authors declare no competing financial interest.

6 Funding

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8 Supplementary Material

Supplementary Material templates can be found in the Frontiers Word Templates file.

Please see the Supplementary Material section of the Author guidelines for details on the different file types accepted.

9 Reference

(a) Michael, J. P., Koning, C. B., Hosken, G. D., Stanbury, T. V. (2001). Reformatsky reactions with *N*-arylpyrrolidine-2-thiones: synthesis of tricyclic analogues of quinolone antibacterial agents. *Tetrahedron* 57, 9635–9648. doi:10.1016/S0040-4020(01)00964-4 (b) Valduga, C. J., Braibante, H. S., Braibante, M. E. F. (1998). Reactivity of p-phenyl substituted β-enamino compounds using k-10/ultrasound. I. synthesis of pyrazoles and pyrazolinones. *J. Heterocycl. Chem.* 35, 189–192. doi: 10.1002/jhet.5570350136 (c) Ferraz, H. M. C., de Oliveira, E. O., Payret-Arrua, M. E., Brandt, C. A. (1995). A New and Efficient Approach to Cyclic b-Enamino Esters and b-Enamino Ketones by Iodine-Promoted Cyclization. *J. Org. Chem.* 60, 7357–7359. doi: 10.1021/jo00127a051 (d) White, J. D., Lhle, D. C. (2006). Tandem Photocycloaddition−Retro-Mannich Fragmentation of Enaminones. A Route to Spiropyrrolines and the Tetracyclic Core of Koumine. *Org. Lett.* 8, 1081–1084. doi: 10.1021/ol052955y (e) Li, G., Watson, K. Buckheit, R. W. Zhang, Y. (2007). Total Synthesis of Anibamine, a Novel Natural Product as a Chemokine Receptor CCR5 Antagonist. *Org. Lett.* 9, 2043–2046. doi: 10.1021/ol070748n

(a) Mladenovic, M., Vukovic, N., Niciforovic, N., Sukdolak, S., Solujic, S. (2009). Synthesis and Molecular Descriptor Characterization of Novel 4-Hydroxy-chromene-2-one Derivatives as Antimicrobial Agents *Molecules* 14, 1495–1512. doi: 10.3390/molecules14041495 (b) Vukovic, N., Sukdolak, S., Solujic, S., Niciforovic, N. (2010). Substituted imino and amino derivatives of 4-hydroxycoumarins as novel antioxidant, antibacterial and antifungal agents: Synthesis and in vitro assessments *Food Chem.* 120, 1011–1018. doi: 10.1016/j.foodchem.2009.11.040 (c) Budzisz, E., Keppler, B. K., Giester, G., Wozniczka, M., Kufelnicki, A., Nawrot, B. (2004). Synthesis, Crystal Structure and Biological Characterization of a Novel Palladium(II) Complex with a Coumarin-Derived Ligand. *Eur. J. Inorg. Chem.*, 22, 4412–4419. doi: 10.1002/ejic.200400483

(a) Kuo, P. Y., Chuang, R. R., Yang, D. Y. (2009), Reactions of 3-benzoyl-7-dimethylamino-4-hydroxycoumarin and their potential applications in solution- and solid-phase synthesis. *Mol. Divers. 13*, 253−260. doi: 10.1007/s11030-009-9107-2 (b) Ghabraie, E., Bararjanian, M., Balalaie, S., Rominger, F., Bijanzadeh, H. R. (2011). Efficient Synthesis of (3*E*)-3-[Amino(aryl)methylidene]chromane-2,4-diones (=(3*E*)-3-[Amino(aryl)methylene]-2*H*-1-benzopyran-2,4(3*H*)-diones) *via* a Three-Component Reaction. *Helv. Chim. Acta* 94, 1440–1446. doi:

10.1002/hlca.201100001 (c) Ye, W. J., Li, Y., Zhou, L. X., Liu, J. J., Wang, C. D. (2015). Three-component reaction between substituted β-nitrostyrenes, β-dicarbonyl compounds and amines: diversity-oriented synthesis of novel β-enaminones. *Green Chem.* 17, 188–192. doi: 10.1039/C4GC01234H

Hsieh, W. C., Manjappa, K. B., Yang, D. Y. (2019). Structural tuning enables piezochromic and photochemical properties in *N*-aryl-β-enaminones. *RSC Adv.* *9*, 34088−34094. doi: 10.1039/C9RA07598D

Chithanna, S., Yang, D. Y. (2019). Multicomponent Synthesis of 1,3-Diketone-Linked *N*-Substituted Pyrroles, Pyrrolo[1,2-*a*]pyrazines, Pyrrolo[1,4]diazepines, and Pyrrolo[1,4]diazocines. *J. Org. Chem.* 84, 1339−1347. doi: 10.1021/acs.joc.8b02819

6. Chithanna, S., Vyasamudri, S., Yang, D. Y. (2020). Application of Dimedone Enamines as Protecting Groups for Amines and Peptides. *Org. Lett.* 22, 2391−2395. doi: 10.1021/acs.orglett.0c00586

Manjappa, K. B., Yang, Y.-A., Santhosh, M. S., Yang, D. Y. (2018). Nitroalkane-Mediated Multicomponent Synthesis of β-Enaminones. *ChemistrySelect* 3, 10701–10705. doi: 10.1002/slct.201802742

Helmy, S., Oh, S., Leibfarth, F. A., Hawker, C. J., Read deAlaniz, J. (2014). Design and Synthesis of Donor–Acceptor Stenhouse Adducts: A Visible Light Photoswitch Derived from Furfural. *J. Org. Chem*. 79, 11316−11329. doi: 10.1021/jo502206g

Crystallographic data (excluding structure factors) for **7b**, **7g**, **7i**, and **7m** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-1540618, -1540615, -1540617 and -1540616, respectively. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/ cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

(a) Irie, M., Fukaminato, T., Matsuda, K., and Kobatake, S. (2014). Photochromism of diarylethene molecules and crystals: Memories, switches, and actuators. Chem. Rev. 114 (24), 12174–12277. doi:10.1021/cr500249p (b) Sun, F., Xiong, X., Gao, A.; Duan, Y., Mao, L., Gu, L., Wang, Z., He, C., Deng, X., Zheng, Y., Wang, D. (2022). Fast photochromism in solid: Microenvironment in metal-organic frameworks promotes the isomerization of donor-acceptor Stenhouse adducts. *J. Chem. Eng*. 427, 132037, doi: 10.1016/j.cej.2021.132037 (c) Zhang, L., Deng, Y., Tang, Y., Xie, C., Wu. Z. (2021). Solid-state spiropyrans exhibiting photochromic properties based on molecular flexibility. *Mater. Chem. Front*., *5,* 3119–3124. doi:10.1039/D0QM01086C (d) Funasako, Y., Ason, M., Takebayashi, J. Inokuchi, M. (2019). Solid-State Photochromism of Salts of Cationic Spiropyran with Various Anions: A Correlation between Reaction Cavity Volumes and Reactivity. *Cryst. Growth Des*. 2019, 19(12), 7308–7314. doi: 10.1021/acs.cgd.9b01185 (e) Avadanei, M., Cozan, V., Shova, S., Paixão, J. A. (2014). Solid state photochromism and thermochromism of two related N-salicylidene anilines. *Chem. Phy.* 444, 43-51. doi: 10.1016/j.chemphys.2014.10.007 (f) Loan T, Santra M and Bradley M (2023), Novel class of photochromic molecules exhibiting photo-switching in the solid state. *Front. Chem.* 11:1205452. doi: 10.3389/fchem.2023.1205452

Funasako, Y., Miyazaki, H., Sasaki, T., Goshima, K., Inokuchi, M. (2020). Synthesis, Photochromic Properties, and Crystal Structures of Salts Containing a Pyridinium-Fused Spiropyran: Positive and Negative Photochromism in the Solution and Solid State. *J. Phys. Chem. B ,124(33)*, 7251–7257, doi: 10.1021/acs.jpcb.0c04994

(a) Wang, Y., Tan, X., Zhang, Y.-M., Zhu, S., Zhang, I., Yu, B., Wang, K., Yang, B., Li, M., Zou, B. Zhang, S. X. (2015). Dynamic Behavior of Molecular Switches in Crystal under Pressure and Its Reflection on Tactile Sensing, *J. Am. Chem. Soc.* 137(2), 931–939. doi: 10.1021/ja511499p (b) Sagara, Y., Mutai, T., Yoshikawa, I., Araki, K. (2007). Material Design for Piezochromic Luminescence: Hydrogen-Bond-Directed Assemblies of a Pyrene Derivative. *J. Am. Chem. Soc. 6*, 1520–1521. doi: 10.1021/ja0677362 (c) Naumov, P., Chizhik, S., Panda, M. K., Nath, N. K., Boldyreva, E. (2015). Mechanically Responsive Molecular Crystals. *Chem. Rev.* 115(22), 12440–12490. doi: 10.1021/acs.chemrev.5b00398 (d) Li, A., Xu, S., Bi, C., Geng, Y., Cuib, H., Xu, w. (2021). Piezochromic mechanism of organic crystals under hydrostatic pressure. *Mater. Chem. Front.*, 5, 2588-2606. doi:10.1039/D0QM00975J (e) Yude, W., Runqing, Y., Guangzhen, G., Shuting, D., Guocui, P., Jing., W., Haoxuan, R., Wenyue, M., Zijian, G., Chenchen, Z., Guangming; X., Liu, Z., Bin, X., Wenjing, T. (2023). Piezochromism and Conductivity Modulations under High Pressure by Manipulating the Viologen Radical Concentration. *Chem. Eur. J.* 29, 48. doi: 10.1002/chem.202301575 (f) Sagara, Y., Kato, T. (2009). Mechanically induced luminescence changes in molecular assemblies. *Nature Chem*. 1, 605–610. doi: 10.1038/nchem.411 (g) Ma, Z., Wang, Z., Teng, M., Xu, Z., Jia Ma, (2015), Mechanically Induced Multicolor Change of Luminescent Materials. *ChemPhysChem*, 16, 1811-1828. doi: 10.1002/cphc.201500181

(a) Wang, J., Zhang, M., Han, S., Zhu, L., Jia, X. (2022). Multiple-stimuli-responsive multicolor luminescent self-healing hydrogel and application in information encryption and bioinspired camouflage. *J. Mater. Chem. C*, 10, 15565–15572. doi: 10.1039/D2TC03072A (b) Zhang, Z., Yao, D., Zhou, T., Zhang, H., Wang, Y. (2011) Reversible piezo- and photochromic behaviors accompanied by emission color switching of two anthracene-containing organic molecules. *Chem. Commun.*, 47, 7782–7784. doi: 10.1039/C1CC11882J (c) Vaidya, S., Sharma, M., Brückner, C., Kasi, R. M. (2021), Rhodamine-Installed Polynorbornenes: Molecular Design, Structure, and Stimuli-Responsive Properties. *ACS Omega* 6(23), 15017–15028. doi: 10.1021/acsomega.1c01160 (d) Martinez-Junquera, M., Lalinde, E., Moreno, M. T. (2022). Multistimuli-Responsive Properties of Aggregated Isocyanide Cycloplatinated(II) Complexes. *Inorg. Chem.* 61, 10898−10914. doi: 10.1021/acs.inorgchem.2c01400 (e) Chiu, C.-W., Yang, J.-S. (2020), Photoluminescent and Photoresponsive Iptycene-Incorporated π-Conjugated Systems: Fundamentals and Applications. *ChemPhotoChem* 4, 538-563. doi: 10.1002/cptc.201900300