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Microwave-assisted synthesis of photochromic fulgides

SIVASANKARAN NITHYANANDAN, CHINNUSAMY SARAVANAN, SENGODAN SENTHIL and PALANINATHAN KANNAN*
Department of Chemistry, Anna University, Chennai 600 025
e-mail: pakannan@annauniv.edu

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Abstract. The oxazole and indole based heterocyclic photochromic fulgides were synthesized from their corresponding fulgenic acid derivatives by clay catalysed microwave irradiation methodology. Improved yields of fulgides were observed by the microwave irradiation method as compared other chemical methods employed so far. The proportions of clay (montmorillonite KSF) and isopropenyl acetate play a key role in increasing the yields of fulgides.

Keywords. Photochromism; fulgenic acid; fulgides; microwave-assisted synthesis; anhydride; cyclization.

1. Introduction

Microwave heating has taken as incontestable place in analytical and organic laboratories practice as a very effective and non-polluting method of activation. The organic reactions were carried out under solvent-free reaction conditions and microwave irradiation lead to large reductions in reaction times, enhancement in conversions, and sometime in selectivity with several advantages of environmental approach termed green chemistry.[1,2] The design and development of highly sensitive and reliable methods for growth of molecular level device is of scientific interest, wherein the yield restrict and suppress the development of new concepts and a challenging task in confronting chemistry. Fulgide is one of the most promising organic photochromic candidates for optical device application. Fulgides undergo reversible photo-cyclization reaction between their two isomers at well-separated absorption maximum upon irradiation with appropriate wavelength of light.[3] This unique property made these materials considered to utilize in optical switches and optical data storage devices.[4] These devices should be capable of ultrafast parallel access of stored information, erasable, good thermal stability and good fatigue resistance with proficient in non-destructible read-out.[5] The aromatic heterocyclic ring structures containing photochromic fulgides are excellent candidates; especially indolyl and oxazolyl fulgides have distinguished photochromic properties attributed to their high thermal stability, strong fluorescence and enhanced fatigue resistance compared to other fulgides.[6–9] The research articles regarding fulgides mainly focused on their thermal irreversibility, photofatigue resistance and high efficiency in a rapid photoconversion processes. The fulgide synthesis involves Stobbe condensation of carbonyl compounds with isopropylidene diethyl succinate followed by cyclization of fulgenic acid using DCC and acetyl chloride does not provide high yield of desired product, particularly when the reactants are highly substituted.[10] To increase the yield of fulgide, Thomas *et al* attempted to synthesize indole substituted fulgide through base catalysed ring-opening reaction of lactones followed by dehydration using acetyl chloride provide below 30% of yield.[11] Lee *et al* recently prepared fulgimide from fulgides through microwave-assisted reaction with good yield at low reaction time.[12] This work deals with hitherto unreported synthesis and characterization of oxazole and indole based heterocyclic photochromic fulgides through clay catalysed microwave irradiation method from their corresponding fulgenic acid. In addition, preparation of new vanillin containing oxazolyl fulgenic acid is discussed.

2. Experimental

2.1 *Reagents*

Diethylsuccinate, acetone, *t*-butyl alcohol, potassium tertiarybutoxide, sodium hydride, 4-methoxyaniline,

*For correspondence

sodium hydroxide, hydroquinone, and 1-bromobutane (Merck, Germany) were used as received. Methanol, ethanol, phenol, THF, diethyl ether, chloroform, triethylamine, dimethylformamide (DMF) (SRL, India) and other solvents were purified by the reported procedures.[13]

2.2 *Instrumentation*

The infrared spectra were obtained on a Bruker IFS 66 V Fourier transform spectrometer using KBr pellets. High-resolution ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker 300 MHz spectrometer in $CDCl_3$ with TMS as an internal standard. The absorption spectra of fulgides in spectroscopic grade chloroform solution were measured on a Shimadzu UV-260 spectrophotometer. The *photocoloration–decolaration* reaction of fulgides was carried out using a 500-W high-pressure Hg lamp (Ushio SX-UI 5000) equipped with a cut filter (Sigma, UTVAF-35U) for UV irradiation (360 nm) and with a cut filter (Sigma, DIF-GRE) for visible light (560 nm).

2.3 *Synthesis of 2-[1,3-dimethyl-2-indolyl-methylene]-3-isopropylidenesuccinic acid* **(IFA)**

The **IFA** was synthesized according to the reported procedure.[10] A flask charged with 60% sodium hydride in paraffin oil (0·06 mol, 3·45 g) and washed with hexane to remove the oil completely, to this, benzene (120 mL) was added at room temperature and stirred. A solution of 1,3-dimethylindole-2-carboxyaldehyde (0·04 mol, 7 g) (**1**) and isopropylidenediethyl succinate (**2**) (0·04 mol, 8·6 g) in benzene (50 mL) were added drop-wise to the reaction mixture at ambient temperature. After 1 mL of above solution was added, ethanol (2 drops) was added to initiate the reaction, followed by addition of remaining solution in a period of 3 h. After completion of addition, the reaction mixture was allowed to stir for another 16 h. The reaction mixture was subsequently quenched with ethanol and poured into crushed ice. The organic layer was separated and extracted with 10% sodium hydroxide solution (3 × 150 mL). All the aqueous layers were combined and acidified with dilute hydrochloric acid. Liberated product was extracted with ethyl acetate and dried over anhydrous sodium sulphate. Solvent was removed under vacuum to afford diacid, which was hydrolysed in potassium hydroxide ethanol solution under reflux condition for 6 h. After completion of reaction, flask was cooled to room temperature; dipotassium salt was filtered and washed with excess of ethanol. Then salt was dissolved in water and acidified with dilute hydrochloric acid to afford crude diacid. The obtained diacid was filtered, washed with excess of water and dried. The crude product was further purified by column chromatography (silica gel, ethyl acetate and chloroform) to afford bright yellow coloured powder, which was used as such for subsequent reaction.

2.4 *Synthesis of 2-[1,3-dimethyl-2-indolyl-methylene]-3-isopropylidenesuccinic anhydride* **(IFO)**

The isopropenyl acetate (6·6 mL, 60 mmol) was added into blended mixture of **IFA** (1·57 g, 7.0 mmol) and montmorillonite KSF (1 g) in a flat-bottomed flask and stirred. It was irradiated under focused microwave (2450 MHz) for 10 min. After completion of reaction, mixture was cooled to room temperature and poured with excess of chloroform and stirred. After 30 min of stirring, the clay was filtered off and removed the chloroform under vacuum. The crude product was further purified by column chromatography to afford **IFO** as dark brown coloured powder (1·23 g, 84%). M.p.: 123–125°C. FT–IR (KBr, cm^{-1}): 1852, 1768 (–C=O), 1635 (–CH=C–), 1606 (–C=C$(CH_3)_2$), 1371 (N–CH_3), 856 (substituted aromatic). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7·70 (*s*, 1H, (Ar-CH=C), 7·55 (*d*, 1H, Ar), 7·05–7·29 (*m*, 3H, Ar), 3·67 (*s*, 3H, N-CH_3), 2·45 (*s*, 3H, Ar-CH_3), 1·83 (*s*, 3H, –C=C$(CH_3)_2$), 1·24 (*s*, 3H, –C=C$(CH_3)_2$. ^{13}C-NMR (400 MHz, $CDCl_3$) δ: 165·5, 163·0 (carbonyl), 159·3 (Ar-CH=C), 139·0, 132·2, 128·9, 127·4, 125·4, 124·7, 120·5, 119·9, 117·5, 109·4 (aromatic), 30·85, 27·46, 25·9, 23·41, 11·02. Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73·26%, H, 5·88%, N, 4·75%. Found C, 73·24%, H, 5·88%, N, 4·70%.

2.5 *Synthesis of 4-butyloxy-3-methoxybenzaldehyde* **(3)**

A suspension of anhydrous K_2CO_3 (36·29 g, 0·268 mol), pinch of KI and vanillin (10 g, 0·066 mol) in dry DMF (260 mL) were stirred at 90°C for 1 h. 4-Bromobutane (11·19 mL, 0·06 mol) was added drop-wise to the reaction mixture and stirred additionally for 48 h at the same temperature. After completion of reaction, mixture was cooled to room temperature, poured into ice/water mixture and neu-

tralized with 10% hydrochloric acid. The aqueous solution was extracted with diethyl ether (3 × 200 mL) and combined organic layer washed with 10% KOH solution (3 × 250 mL), saturated brine solution (3 × 250 mL) and dried over anhydrous sodium sulphate. Solvent was removed under vacuum to afford compound **3** as brown coloured oil (7·5 g, 60%). FT–IR (KBr, cm^{-1}): 2942 and 2865 (–CH_2–), 1603 and 1514 (aromatic C–H), 1681 (Ar-C=O), 1164 and 1084 (C–O–C). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9·67 (*s*, 1H, –CHO), 7·21 (*s*, 1H, Ar), 6·82–7·04 (*m*, 2H, Ar), 3·72 (*s*, 3H, Ar–O–CH_3), 3·56 (*t*, 2H, Ar–O–CH_2–), 0·82–1·52 (*m*, 7H, –CH_2–CH_2–CH_3). ^{13}C-NMR (400 MHz, $CDCl_3$) δ: 190·4 (carbonyl), 153·9, 149·5, 129·5, 126·4, 111·1, 108·9 (aromatic), 68·4, 55·6 (methoxy), 30·6, 18·8, 13·4 (aliphatic).

2.6 *Synthesis of N-hydroxyiminoacetyl acetone* (**4**)

A solution of acetyl acetone (32·5 mL, 0·317 mol) in 50 mL of glacial acetic acid was stirred at 5–10°C and then the cooled solution of sodium nitrite (25 g, 0·362 mol) in water (500 mL) was added in portion wise over 30 min maintaining at the same temperature. After completion of addition, solution was slowly allowed to come up room temperature and additionally stirred for 5 h. The reaction mixture extracted with diethyl ether, washed with 10% sodium bicarbonate solution (3 × 150 mL) to remove unreacted acetic acid and dried over anhydrous sodium sulphate. The solvent was removed under vacuum to afford white powder of compound **4** (19·8 g, 48%) FT–IR (KBr, cm^{-1}): 3282 (C=N), 3065 (–N–OH), 1698 (–C=O). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2·38 (*s*, 3H, CH_3), ^{13}C-NMR (400 MHz, $CDCl_3$) δ: 195·8, 156·1, 28.

2.7 *Synthesis of 4-acetyl-5-methyl-2-phenyl (3-methoxy-4-butyloxy)oxazole* (**5**)

To a solution of 4-butyloxy-3-methoxybenzaldehyde (33 × 48 g 0·161 mol) in glacial acetic acid (16 mL) was added N-hydroxyiminoacetyl acetone (27·3 g, 0·21 mol) by one portion at room temperature. The reaction mixture was cooled to 0–5°C and subjected to flow of hydrogen chloride gas for 4 h with maintaining the same temperature. After the completion of flow of hydrogen chloride, the reaction mixture was poured into a beaker containing diethyl ether (500 mL) and stirred for 1 h to remove unreacted starting materials. The settled product at the bottom of beaker was filtered, dried and recrystallized by acetone to afford N-oxide hydrochloride of compound **5**. It was dissolved in glacial acetic acid (50 mL) and activated zinc dust (20 g) was added and stirred well. After stirring, the reaction mixture was poured into water (500 mL) to separate out the desired product and dried. The obtained product was recrystallized from methanol to afford compound **5** as light yellow coloured powder (42 g, 69·10%). FT–IR (KBr, cm^{-1}): FT-IR (KBr, cm^{-1}): 2942 and 2865 (–CH_2–), 1611 and 1518 (aromatic –C–H), 1678 (Ar–C=O), 1294 and 1264 (C–O–C). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7·47 (*s*, 1H, Ar), 6·85–7·08 (*m*, 2H, Ar), 3·78 (*s*, 3H, Ar–O–CH_3), 3·86 (*t*, 2H, Ar–O–CH_2–), 2·70 (*s*, 3H, –CO–CH_3), 2·48 (*s*, 3H, –CH_3), 0·82–1·53 (*m*, 7H, –CH_2–CH_2–CH_3). ^{13}C-NMR (400 MHz, $CDCl_3$) δ: 201·09 (carbonyl), 156·3, 153·5, 150·5, 148·8, 135·7, 124·3, 119·4, 118·8 (aromatic), 68·8, 56·1 (methoxy), 28·1, 23·4, 12·3, 10·4, 9·8 (aliphatic).

2.8 *Synthesis of 5-methyl-2-phenyl(3-methoxy-4-butyloxy)oxazolylethylidene(isopropylidene) succinic acid* (**OFA**)

A solution of potassium-t-butoxide (3·6 g, 0·032 mol) in 40 mL of *t*-butanol under nitrogen was stirred at room temperature. To this, solution of compound **5** (7·7 g, 0·0359 mol) and compound **6** (5·8 g, 0·019 mol) in *t*-butanol (40 mL) were drop-wise added. After completion of addition, the reaction mixture was heated under reflux condition for 6 h. Then, the mixture was cooled to room temperature; solvent concentrated under vacuum, poured into water (200 mL) and neutralized with 10% HCl solution. The product was extracted with diethyl ether (3 × 150 mL) and washed with 10% sodium bicarbonate solution (3 × 100 mL) to remove pure half ester from organic layer. The combined bicarbonate solution was neutralized by 10% HCl solution, extracted with diethyl ether again and dried over anhydrous sodium sulphate. The solvent was removed under vacuum to afford half acid, which was dissolved in ethanol (100 mL) and refluxed overnight with KOH (3 g). After completion of reaction, solvent was concentrated under vacuum and poured into water (200 mL) and neutralized with 10% HCl solution. The separated product was extracted with diethyl ether and dried over anhydrous sodium sulphate. The solvent was removed under vacuum to afford **OFA** as color-

less powder, which was used *in situ* for succeeding step.

2.9 *Synthesis of 5-methyl-2-phenyl(3-methoxy-4-butyloxy)oxazolylethylidene(isopropylidene) succinic acid* (**OFO**)

The isopropenyl acetate (6·6 mL, 60 mmol) was added into blended mixture of **OFA** (2·2 g, 4·97 mmol) and montmorillonite KSF (1 g) in a flat-bottomed flask and stirred. It was irradiated under focused microwave (2450 MHz) for 10 min. After completion of reaction, mixture was cooled to room temperature and poured excess of chloroform and stirred. After 30 min of stirring, the clay was filtered off and chloroform removed under vacuum. The crude product was further purified by column chromatography to afford **OFO** as dark brown coloured powder (1·52 g, 72·2%,). M.p.: 145–149°C. FT–IR (KBr, cm^{-1}): 2942 and 2865 (–CH_2–), 1834, 1756 (–C=O), 1610 (oxazole C=N), 1294 and 1264 (C–O–C), 1041 (Ar–C=C). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7·83 (*s*, 1H, Ar), 7·42–7·53 (*m*, 1H, Ar), 6·96–7·03 (*m*, 1H, Ar), 4·01 (*t*, 2H, –O–CH_2–), 3·78 (*s*, 3H, Ar-OCH_3), 2·49 (*s*, 3H, CH_3), 2.03 (*s*, 3H, –C=C(CH_3)), 0·99–1·79 (*m*, 13H, –CH_2–CH_2–CH_3, CH_3–C–CH_3). ^{13}C-NMR (400 MHz, CDCl3) δ: 172·8, 168·9 (carbonyl), 163·5, 159·8, 152·1, 148·4, 146·9, 142·3, 123·1, 122·7, 121·6, 113·3, 112·0, 111·8, 67·9, 55·5, 48·2, 35·2, 35·0, 30·6, 22·8, 22·7, 20·7, 18·7, 13·6. Anal. Calcd. for $C_{24}H_{27}NO_6$: C, 67·76%, H, 6·35%, N, 3·29% found C, 66·48%, H, 5·82%, N, 2·79.

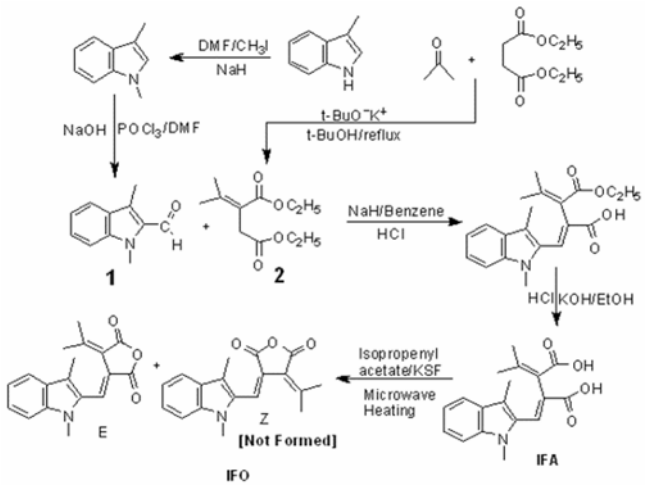
3. Results and discussion

The **IFO** and **OFO** were prepared from **IFA** and **OFA** in the presence of acetyl chloride and acetic anhydride in a relatively poor yield of 32% and 15% respectively.[14,15] The **IFA** and **OFA** were prepared via Stobbe condensation of one mole of isopropylidenediethyl succinate and one mole of corresponding carbonyl compounds using sodium hydride and potassium *tert*-butoxide as base at room temperature respectively. The resultant products were hydrolysed using alcoholic KOH at reflux temperature for overnight. The poor yield of fulgides limits the large-scale utilization of fulgides for commercial and scientific investigations. To improve the yield of fulgides, **IFO** and **OFO** were prepared from corresponding fulgenic acid with varying proportions of Montmorillonite KSF and isopropenyl acetate (table 1) according to reported procedure for synthesis of anhydrides from corresponding dicarboxylic acids[16] (schemes 1 and 2). To optimize the conditions for good yield, proportions of montmorillonite KSF and isopropenyl acetate were varied as shown in table 1. Both **IFO** and **OFO** show maximum yield when 60 mmol of isopropenyl acetate and 1g of montmorillonite KSF proportions (table 1) employed respectively. It revealed that the proportions of clay and isopropenyl acetate play a key role in the yield of fulgides. Specifically in the presence of excess isopropenyl acetate, non-ionizing radiation increases the molecular motion of ions, rotation of dipoles in the reaction site of clay and increase the penetration depth of microwave radiation.[16] Here, both **IFO** and **OFO** demonstrated good improvement in yield when compared with that of conventional chemical method used for synthesis of fulgides. The percentage yield of isomers of products was calculated from NMR spectral values of corresponding compounds. In the case of **IFO**, the *E-isomer* alone was formed (see supplementary informations) but in the case of **OFO**, *Z-isomer* was the major product. When compared to **IFO**, the **OFO** indicates less amount of yield with all concentration of isopropenyl acetate. The concentration of isopropenyl acetate is varied

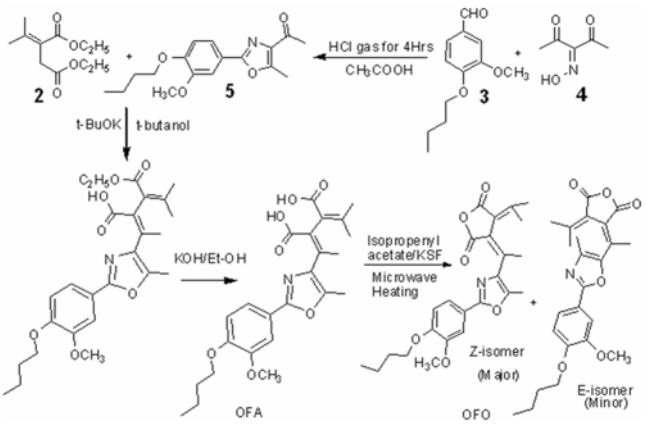
Table 1. Improved yields of Fulgides IFO and OFO with different proportions of KSF and isopropenyl acetate.

Fulgenic acid derivative **IFA** and **OFA** (mmol)	Isopropenyl acetate (mmol)	**IFO** (yield %)				**OFO** (yield %)			
		KSF (g)	Net yield	*E*	*Z*	Net yield	*E*	*Z*	Time (min)
5	20	5	51	51	0	39	1	38	10
5	30	4	60	60	0	44	2	42	10
5	40	3	68	68	0	52·7	2·4	52·3	10
5	50	2	76	76	0	65	1	64	10
5	60	1	84	84	0	72·2	1·2	71	10
5	60	0	20	20	0	10·6	0·7	9·8	10

from 20 to 60 mM. Accordingly, the yield of *Z-isomer* increases proportionately with minor product of *E-isomer* (table 1). In the presence of 40 mM of isopropenyl acetate and 3 g of KSF gives 54·7% yield with mixture of isomers. Methyl protons of *E-isomer* appeared at 2·46 ppm as singlet with integral value of 0·07 and methyl protons of *Z-isomer* appeared at 2·41 ppm as singlet with integral value of 1·64 in the ^{1}H-NMR spectrum. Percentage yield of isomers was calculated using the integral values from the total yield (table 1). The ^{1}H-NMR spectrum of **IFO** (see supplementary information, figure S1, see www.ias.ac.in) depicts four methyl groups resonated at four different positions between 1·24 and 3·67 ppm. The methylene proton resonated at 7·70 ppm as singlet. The ^{13}C-NMR spectrum (see supplementary information, figure S2) also shows four peaks in the aliphatic region corresponding to four methyl carbon atoms. It indicated no characteristic peak for isomers in **IFO**. The chloroform solution of **OFO** was irradiated with 360 nm UV light for long time (30 min); all the *Z-form* is isomerized to *E-form*. The methyleneoxy protons resonated as triplet at 4·00 ppm and methoxy protons resonated as singlet at 3·78 ppm in ^{1}H-NMR spectrum of irradiated solution of **OFO** (see Supplementary information, figure S3). The oxazolyl methyl protons appeared at 2·49 ppm as singlet. The ^{13}C-NMR spec-



Scheme 1. Synthesis of IFA and IFO.



Scheme 2. Synthesis of OFA and OFO.

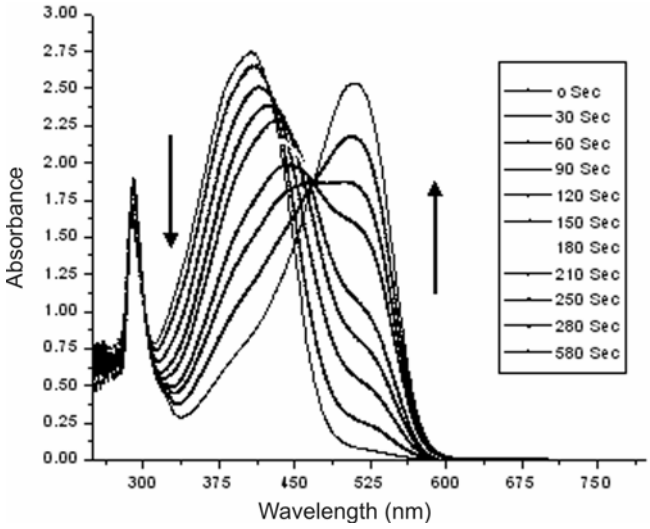


Figure 1. The absorption spectral pattern of IFO in chloroform solution upon irradiation 360 nm light.

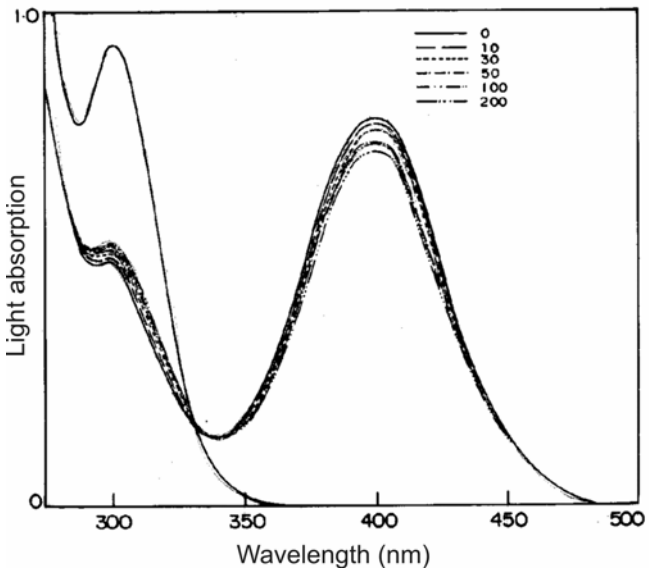


Figure 2. The absorption spectral pattern of OFO in chloroform solution upon irradiation with 360 nm light.

trum (see Supplementary information, figure S4) also shows two peaks at 67·9 and 57·4 ppm corresponding to methyleneoxy and methoxy protons respectively. After UV irradiation, the ^{1}H-NMR spectrum of **OFO** confirms with no characteristic peaks for isomers (see Supplementary information, figure S3). The deviation in yield and *E* and *Z* isomeric ratios were around 2–3%. The photochemical properties of fulgides were evaluated in chloroform solution. The absorption spectral changes of **IFO** and **OFO** in solution upon irradiation with 360 nm UV light are shown in figures 1 and 2 respectively. The solution of **IFO** shows an absorption band at 396 nm corresponding to *E-form* fulgide unit. Upon irradiation with 360 nm UV light, pale-orange colour solution of **IFO** turns blood red, with a new absorption band rising at 528 nm with a concomitant decrease in absorbance at 396 nm as shown in figure 1. In the case of **OFO**, *E-form* is converted to *C-form* and appeared at 452 nm upon irradiation with 360 nm UV light and the same solution was irradiated with 560 nm visible light, the intensity of absorption band at 362 nm increases with decrease at 452 nm. These observations confirm the switching properties of **IFO** and **OFO**.[14,15]

Supplementary material

For all supplementary information see the website (www.ias.ac.in/chemsci).

4. Conclusion

The clay catalysed microwave-assisted strategy managed to synthesize fulgide of **IFO** and **OFO** successfully by simple and efficient means with improved yield over conventional methods. This methodology also brought down the reaction time and usage of organic solvents. This method found suitable for small-scale preparation and can be transformed to wide range of other fulgides.

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