Synthesis and Photochromism of 3-(2,6-dichlorophenyl)-1-(Naphthalen-1-yl)Prop-2-en-1-one (Part II)

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Abstract

A practical and environmentally friendly method for the design of unique chalcone 5N and chromene 5NR in high yields is provided by reacting 2,6-dichlorobenzaldehyde with 1-acetonaphthone. The matching chromene 5NR was also made possible by the photochromism of 5N using a UV-Visible spectrophotometer. The structure of the obtained chalcones 5N was established by using IR, 1H NMR, 13C NMR and LC-MS. The advantages of photochromism method are very cheap, available, non-toxic, easy work-up, improved yields and the product of the reaction is very pure. Moreover, photochromism and kinetic of the target product were studied using irradiation with xenon (XL) lights using different solvents such as chloroform (CHF), acetone (ACT), and ethyl acetate (ETAC). It has been found that CHF was the best solvent of photochromism for 5N unlike ETAC which has poor reaction, while in ACT chromene did not produce. The synthesis compound 5N was the faster one to get photostationary state 91 min at (λmax 503nm) in CHF, in other hand ETAC was the slowest (1730 min) solvent used for 4NR chromene formation. The chromene 5N was the faster returning back to chalcone in dark reaction (DR) 3.5 days when decreases the concentration in CHF. The rate constant (k) at the DR when using XL light was 0.0155, furthermore XL light produce a maximum yield (20%).

Key words: *Chalcone, chromene, NIR, Orbitrap, photochromism, Raman.*

1. INTRODUCTION

Chalcones (1,3-diaryl-2-propen-1-ones) containing α, β-unsaturated ketones consisting of two

aromatic rings (ring A and B) Scheme 1, are abundant in edible plants, member of flavonoids family, are important class of synthetic or natural products. They are protector of plants against insects and pathogens and give colour to the flowers of plants. Chalcones have a lot of pharmacologic effects and can be used as intermediates for synthesis of drugs[1].

Scheme 1 Chalcone structurec
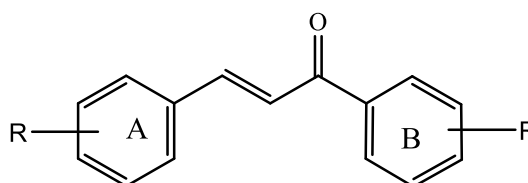
Synthetic chalcones are commonly synthesized with the reaction of acetophenone and benzaldehyde via the Claisen-Schmidt

condensation. This reaction is catalyzed by bases and acids under homogeneous conditions [1][2]. Chalcones may exist in two isomeric forms, could be stereochemically cis (Z) and trans (E), of which the trans form is thermodynamically favorable and stable. Unsaturated carbonyl group in the chalcone allows it to be active biologically active [3], such as antifungal[4], antiviral [5][6], antioxidant [7], analgesic [8], antihelmintic[9], anti-inflammatory [10], antiulcer [11], anticancer[12] [13], antibacterial[14] , and antimalarial [15][16], thus comprise a class with important therapeutic potential. For this reason, growing interest amongst the scientists continues to the chalcones [16][1]. Furthermore chalcones are widely used in industry, because of their properties of isomerization by light which called photo-isomerize, this properties appears when chalcones irradiate with light hence to change the geometry of the original structure accompanied by color change. The new isomer can return back to the original form by dark, heat or using different wavelength irradiation. This reaction is important in industrial applications such as smart membranes, solar thermal batteries, microfluidics, reversible optical data biosensors, storage, molecular shuttles, light-powered molecular machines and many other applications[17].

Spectral properties of chalcones are important to understand formation of chalcones and continue other synthesis steps if they are used as intermediates. It is known that the chalcones absorb light in the UV region and transmit in the remaining region [18][19]. The UV spectrum of chalcones consists of two essential absorption band I, band II the relatively a minor band, band II. In chalcones, band I usually appears in 340-390 nm, although a minor inflection or peak often occurs at 300-320 nm.

Band II appears in 220-270 nm. Increasing oxygenation generally causes bathocromic shifts, particularly in band I. The addition of an unsubstituted 2'-hydroxyl group to the chalcone causes a marked effect on the spectrum e.g. 2',4',4-trihydroxychalcone (λ max 370 nm), 4',4-dihydroxychalcone (λmax 348 nm). Glycosylation or methylation of 2'-position leads to 15-20 nm hypsochromic shift [20][21].

IT is obvious that the transformation of chalcone to chromene is established by light. While the reverse reaction (chromene to chalcone) occurs in three ways: One of them is to heat the sample, The second way by irradiate with different WL of light, finally is to transfer the sample of chromene to dark place at room temperature [17].

The aim of this study is to synthesize new chalcone derivatives with structural variations by reacting some aldehydes, ketones and other reagents. The synthesized chalcones will be used to prepare new chromenes using irradiation by xenon lamp, and study the photochromism. These two products were characterized by different techniques such as, thin layer chromatography (TLC), infra-red (IR), 1H and 13C nuclear magnetic resonance (NMR), liquid chromatography mass spectroscopy (LC-MS)/ UHMR Hybrid Quadrupole Orbitrap™ Mass Spectrometer.

2.   Materials and Methods

2.1   Chemicals

2,6-Dichlorobenzaldehyde was obtained from Sigma Aldrich. 1-acetonaphthone was from Acros organics. Absolute ethanol, acetone, acetonitrile, chloroform, sodium hydroxide, toluene, ethyl acetate, hydrochloric acid were from Scharlau. The chemicals were used without further purification

2.2 Apparatus and Equipment

UV-vis double beam spectrophotometer Jenway 6800 (190-1100 nm) was used for spectral absorption measurements with (0.1nm) WL (wave length) resolution, abs. resolution (0.0001Abs) and quartz cells of 1cm path length. Thermo Scientific Nicolet iS 20 FT-IR Spectrometer station (400-4000cm-1) was used for vibrational measurements with (4cm-1) resolution. The software Omnic 9.2.86, Firmware version 1.02 by Thermo Fisher Scientific was used for data collection and for drawing FT-IR spectra. Thermo Scientific Nicolet iS50 NIR. FTIR and Raman, Gemini TFC MNM 100, Thermo Fisher Scientific Inc. Thin Layer Chromatography (TLC) sheets silica gel 60, F254 Aluminum, Supertek, M19-CDb-001. Preparative TLC silica gel 60, F254 Glass used for clean-up compounds. 55WAuto Car HID Xenon Headlight Lamp 7 was used as a source of light. 15W UV type B florescent 2 lamp was used. Electro-thermal Mel-temp M206780/02 was used for measuring the melting point. Thermo Scientific LC MS/MS, Q Exactive Focus. split Sampler FT, Vanquish Autosampler, Vanquish Binary Pump F, Vanquish Column Compartment H, Sample Loop 25uL (V=50uL), Column Accucore aQ 100*2.1*2.6U. Mass Spectrometer Q Exactive Focus, used for mass analysis. HRAM GC-MS, GC trace 1310, MASS TSQ 9000-VPI Triple quad, TriPlus 100LS, AutoSampler, Trace 1300 PTV INJ. and Trace 1300 SSL INJ. Module Injector, column SC-5MS, 50m* 0.53mm* 1.5Um All NMR spectrum measurement were made on a Bruker (400MHz) using MestReNova 14.2.1-27684 software for processing data.

## 3. Results and Discussion

3.1 Methods of Synthesis

There are different ways to prepare chalcones depending on the nature of the compensators and on the acetophenone and benzaldehyde used in the preparation Scheme 2. generally chalcone compounds were synthesized by an adaptation of the general method of the Claisen-Schmidt condensation [21][17][22].

Scheme 2 Reaction pathway for the synthesis of chalcones 5N.   B: NaOH+ ethanol
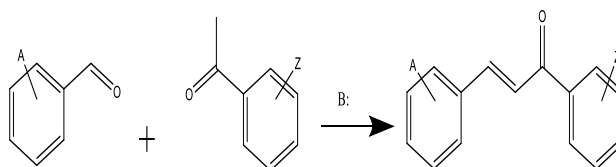
The method foresees equimolar quantity 1.7g (0.01 mol) of 2,6-Dichlorobenzaldehyde and 1.75g (0.01 mol) of 1-acetonaphthone were mixed in conical flask in ice bath with stirring, adding 8 mL of absolute ethanol, with 10 mL of 10% NaOH into the mixture. Stirring was carried on ice bath, a thick yellow precipitate formed after 5 hours. After 24 h of stirring in the ice bath the mixture the precipitate was filtered off using Buchner funnel and washed well with distilled water to get rid of the excess base. Several recrystallizations of the residue from an appropriate solvent of hot water and ethanol gave pure crystals compounds. The progress of the reaction and purity test of the products was performed by the TLC methods on silica gel plates (Merck) using toluene: ethyl acetate (3:1) as the mobile solvent; spot detection was performed with UV 254 and 365nm. Melting points were measured with an Electro-thermal melting point apparatus without correction. The purity after cleanup was performed by LC-MS. The structure of the compounds synthesized was proved by NMR spectroscopy, IR and LC-MS.

Scheme 3 Synthesis of 5N chalcone, B: =Ethanol +NaOH
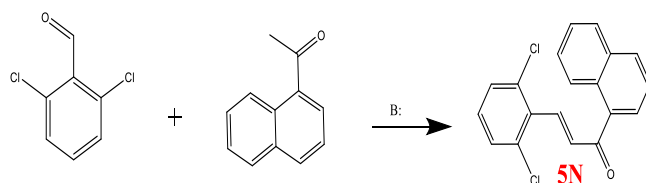
(E)-3-(2,6-dichlorophenyl)-1-(naphthalen-1-yl)prop-2-en-1-one (5N)

White crystals, very soluble in Chloroform, acetone, poorly soluble in methanol and ethanol non soluble in water; Yield 93.5%; mp: 92.1-93.3oC; FT-IR (cm−1): 1671, 1609, 1576, 1348, 1180, 1068-3053-3089; HRMS-ESI (m/z) calculated for C19H12Cl2O [M+H]+ 327.03380 found 327.03323; (MW: 327.204); UV (λmax nm, CHF): 284; 1NMR (400 MHz, CDCl3) δ 8.50 (d, J = 8.4 Hz, 1H), 8.00 (s, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.89 (s, 1H), 7.73 (d, J = 16.4 Hz, 1H), 7.61 (dd, J = 6.8, 1.3 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.55 – 7.52 (m, 1H), 7.44 (d, J = 16.4 Hz, 1H), 7.36 (d, J = 8.1 Hz, 2H), 7.19 (t, J = 8.0 Hz, 1H); Rf 0.77.
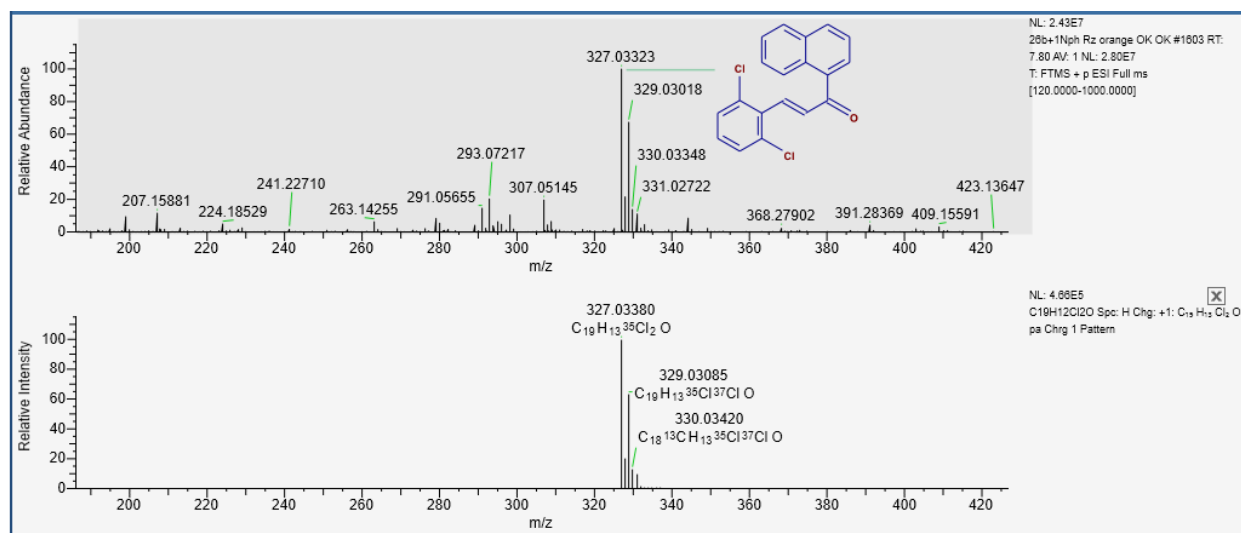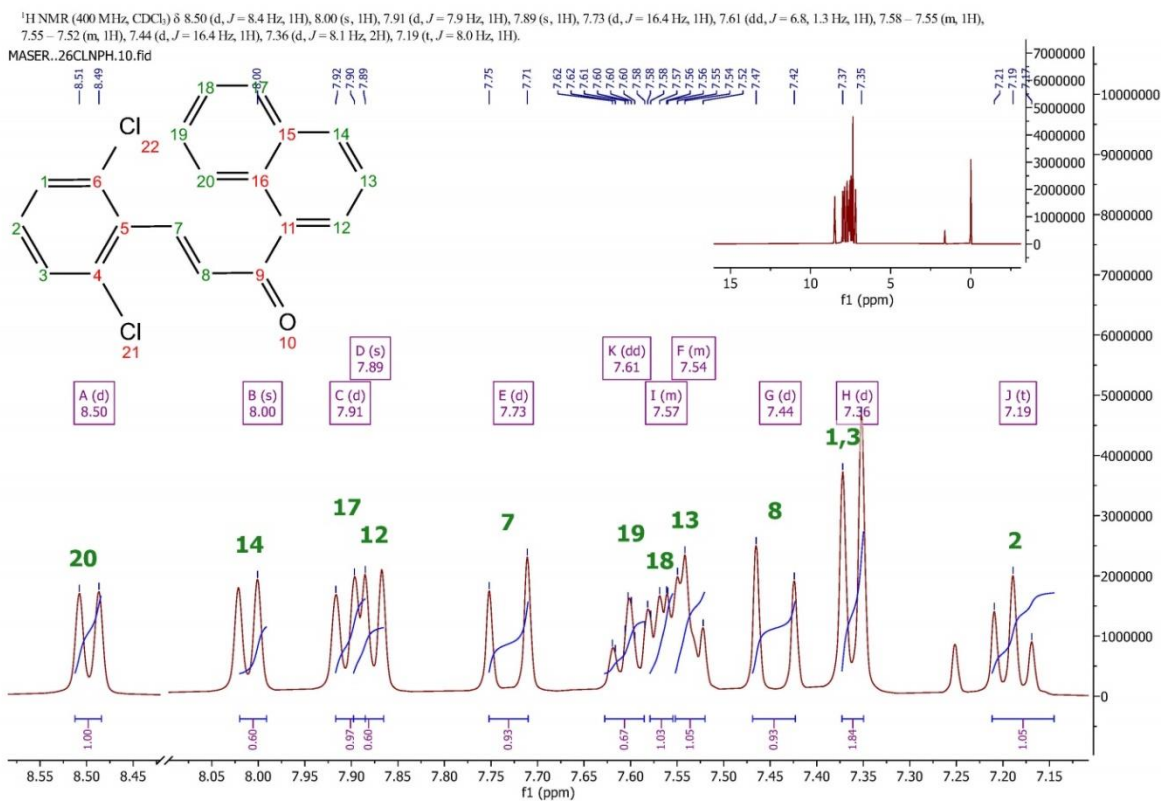
5,8a-dichloro-2-(naphthalen-1-yl)-8aH-chromene (5NR)

Dark red solid, very soluble in Chloroform, acetone, poorly soluble in methanol and ethanol non soluble in water; Yield 20.15%; mp: 138-147oC; FT-IR (cm−1): 1594, 1344, 1184, 1071-3050, 1143-1184; HRMS-ESI (m/z) calculated for C19H12Cl2O [M+H]+ 327.03380 found 327.03345. (MW: 327.204); UV (λmax nm, CHF 503; 1H NMR; δ 7.55 - 6.98 (8H, Ar); Rf 0.

3.2 Assignment of FTIR, NIR and Raman Spectra

Appendix Table 2 is for the most important absorbance wavenumbers of these chalcones and chromene with their assignment. The ethenyl carbon-carbon double bond and the carbonyl group are the most observed characteristic bands which confirm the synthesis of the chalcones. Appendix Fig. 10 shows 5N chalcone, Fig. 11 for 5NR chromene FTIR spectrum and Fig. 12 is the overly for both that confirming products occurrences. Appendix Fig. 13 illustrate the NIR overlay spectrum of syntheses compound 5N and 5NR, also confirming the products occurrences. The Appendix Fig. 14 shows the Raman overly spectrum for the synthesis compounds the 5N have 1610 cm-1 base peak, while the 5NR chromene start broad peak increase from 2400 cm-1 due to high florescence of heterocyclic compound 5NR. Analysis of 5N and 5NR via LCMS/MS using HRMS the spectrum shown in Fig. 1 for 4N and Appendix Fig. 15 for 5NR where eluted at RT: 7.8 and 11.82 respectively.

Fig. 1 Mass spectrum for 5N chalcone

Fig. 2 1H -NMR spectrum of 5N chalcone

¹H NMR (400 MHz, CDCl₃) δ 8.50 (d, J = 8.4 Hz, 1H), 8.00 (s, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.89 (s, 1H), 7.73 (d, J = 16.4 Hz, 1H), 7.61 (dd, J = 6.8, 1.3 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.55 – 7.52 (m, 1H), 7.44 (d, J = 16.4 Hz, 1H), 7.36 (d, J = 8.1 Hz, 2H), 7.19 (t, J = 8.0 Hz, 1H).

4. Photochromism 5

The photochromism of chalcone was studied by using UV-Visible spectrophotometer, different concentrations of chalcones were prepared in CHF, ACT and ETAC solution for all chalcones. Then, the solutions were irradiated by using xenon lamp (7*55W) at room temperature the colour changed to red until

arrive to photo stationary state photostationary state that means there is no further increase in the Abs of chromene in the visible region, then transfer the sample to dark place and follow up the DR for long time until all chrome returning back to chalcone, and the Abs return back to initial value.

4.1   Photochromism of 5N chalcone

The full reaction of photochromism of compound 5N shown in Scheme 4

Scheme 4 Photochromism of 5N trans-chalcone to 5NR chromene and vice versa.
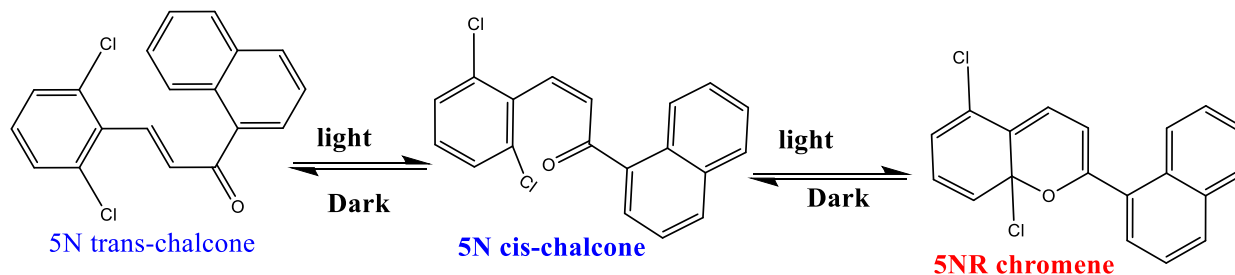
The time required to form 5NR chromene in CHF is long when compared to other studied [17], it takes about 150 min. to reach the PSS at WL (λmax 503nm).

An inverse relationship was found between the time required to form 5NR chromene from trans 5N chalcone (λmax 503nm)in a given solvent and the energy of the trans and cis-chalcone in the same solvent[17] .
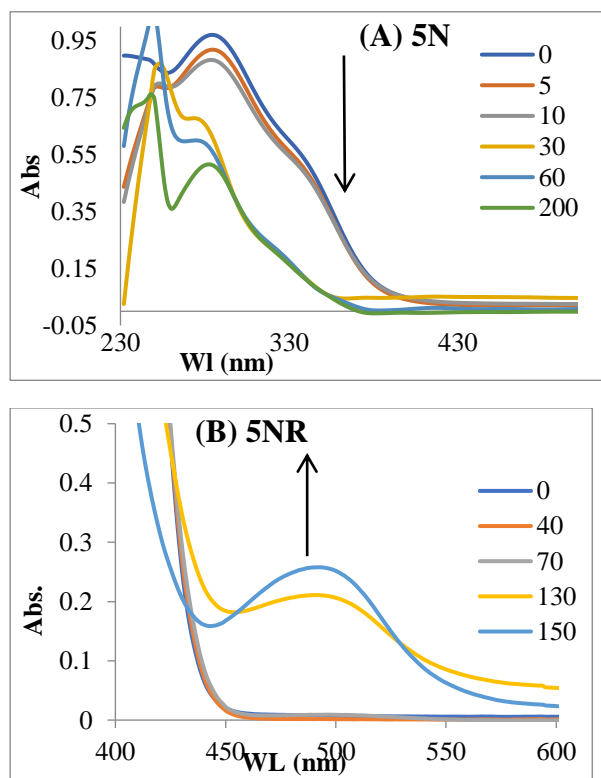
4.2   Photochromism of 5N chalcone

The follow up of the photochromism process shows in Fig. 3. In the lower concentration 0.0001M of chalcone the chromene did not appear, because of low absorptivity of 5NR chromene, therefore, using more concentration 0.0153 M to follow up the 5NR chromene formation. It is obvious at zero time there is no any absorption of the 5NR chromene and as the time proceeds the appearance of new spectra starts to develop and the Abs of this new spectra increases as time evolves.

Fig. 3 Photochromism process during irradiation by X light at each time (min) (A) 5N chalcone (0.0001M) reaction (B) 5NR chromene formation using (0.0153M) chalcone.

The concentration of 0.0061 M was used Appendix Fig. 16 gives good results but using the 0.0153 M of chalcone was the best to follow up photochromism reaction Fig. 3(B). The irradiation of chalcone with xenon lamp cased decrease of Abs due to chalcone reaction and convert to cis form then finally chromene formation, obviously the decrease of chalcone concentration led to increase of chromene concentration. The limit of quantification (LOQ) for the spectrophotometer is 0.0002 therefor it can be depend on the chromene formation with range 0.005-0.02 Abs.

After irradiation of chalcone, the chromene produce until the reaction complete, it arrive to photostationary state then the solution transfer to dark place and start the follow up DR Fig. 4

Fig. 4 Photochromism for DR of 5NR chromene starting from photostationary state at each time (days) in CHF (A) using 0.0153 M of 5N chalcone. (B) 0.00611 M 5N chalcone used
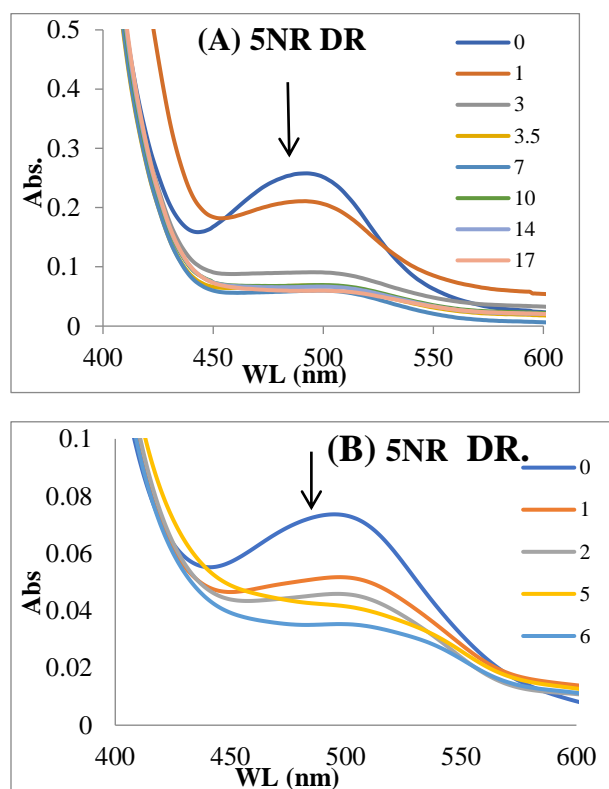
Using different (low) concentration of chalcone 0.00611M, the photochromism follow up reaction shows in Fig. 6 (a) that increase of 5N conc. led to increase in Abs of 5NR, therefore higher concentration than 0.0061 M is biter for photochromism analysis than low concentration. If using more concentration than 0.015 M, chalcone and chromene peaks will interfaces and will be difficult to analysis.

Fig. 5 Variation of Abs with time (min) of 5N chalcone reaction in CHF, ACT and ETAC solvents (A) first peak Abs at each WL (B) second peak Abs at each WL.
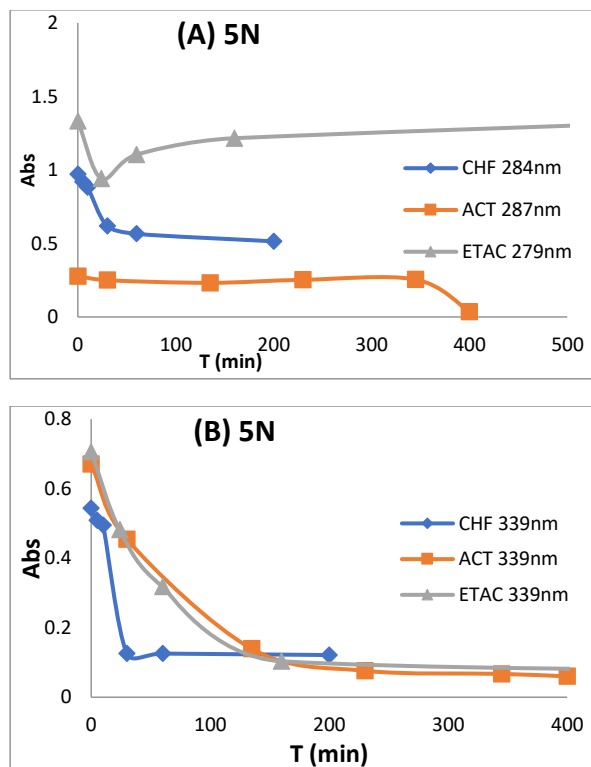
The follow up photochromism process of 5N chalcone reaction under XL light shows in Fig. 5 (A,B), the decrease of Abs with time refer to consuming of chalcone at different solvent. CHF was the best solvent which gives sharp curve or faster reaction of 5N than ACT and ETAC at λmax 339nm, while at λmax 279-287nm the CHF also was the best while ACT has long time and ETAC independent,

furthermore in the different three solvent the second peak of 5N chalcone has same λmax 339nm while the first peak was different. On other hand the concentration of 5N effect on photochromism process, as the concentration decrease Fig. 6 the photostationary state decrease, while the decay increases with decrease of conc.

The follow up of the photochromism process of 5NR chromene formation using ACT solvent show in Fig. 7(A). Using lower conc. 0.000139 M of chalcone the chromene did not appear. It was found that chromene did not produce even if use high concentration. Although the Abs of chalcone decrease with irradiation of light and decrease in the dark that refer to changing in isomerization from trans to cis and return back without chromene formation.

The increasing of concentration of 5N from 0.001 to 0.006 M caused decreasing the time (91 min) for 5NR formation or to get photostationary state in CHF Table 1, while in ETAC the time was about 10 fold than the CHF.

Fig. 6 Variation of Abs with time at 503 nm(A) 5NR chromene formation in CHF and ETAC solvents at time (min) (B) 5NR chromene DR follow up. (M) Refers to the conc. of chalcone used (starting material).


(B) 9NR DR
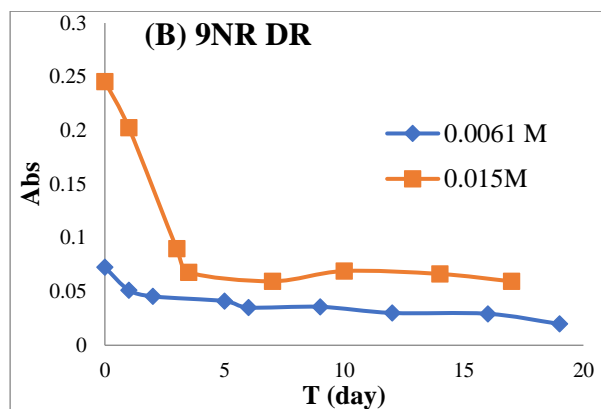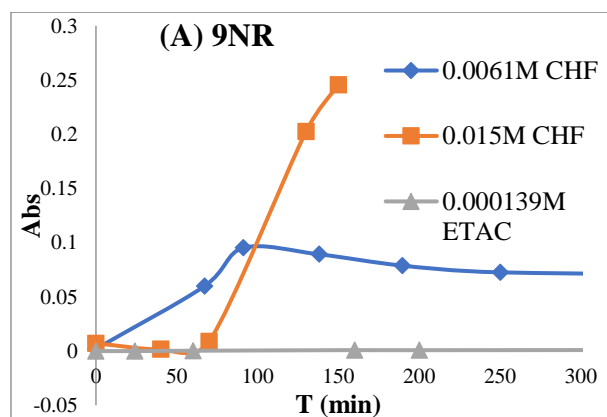
The follow up of the photochromism process for 5N chalcone reaction shows in Fig. 7(B) using ETAC. Chalcone have (λmax 279 and 339nm), in the lower conc. 0.000139M of chalcone, trace chromene appear. It is obvious at zero time there is lower absorption of the 5NR chromene in 503 nm and as the time proceeds the appearance of new spectra starts to develop and the Abs of this new spectra increases as time evolves but it is independent. Even if using high concentration of chalcone, the 5NR chromene with very low Abs that mean lower than LOQ, therefore it is difficult to determine yield for light reaction and rate constant for DR Appendix Fig. 17.

Fig. 7 Photochromism process of 5N chalcone during irradiation at each time (min). (A) 0.000139 M in ACT solvent (B) 0.0061 M ETAC solvent used.
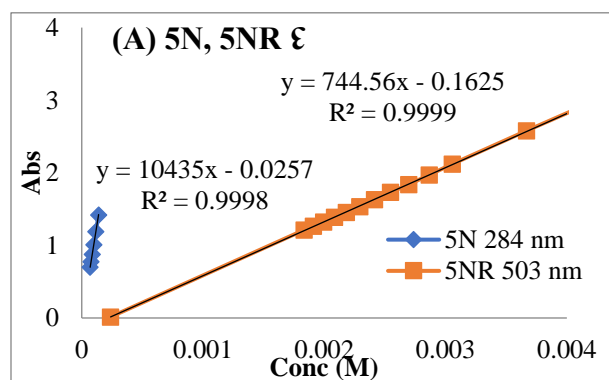

(A) 9NR

(A) 5N ACT
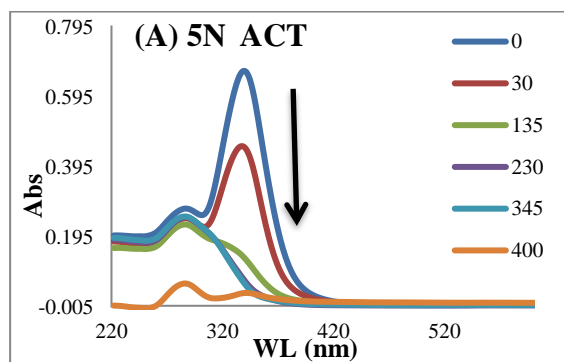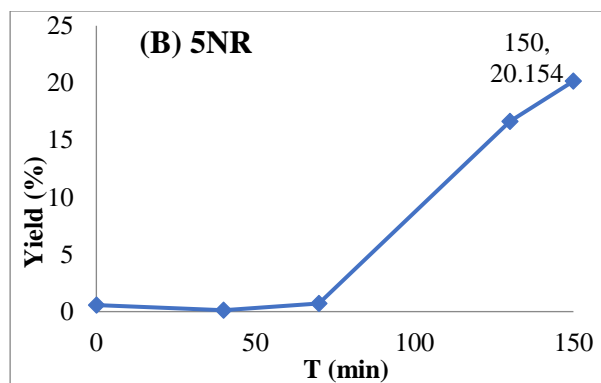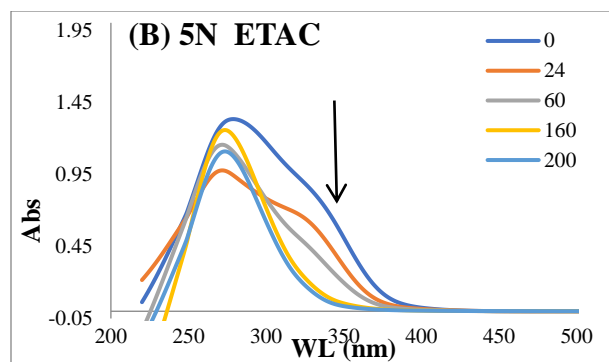
4.3 Yield calculation

The percentage yield of 5NR chromene is calculated in CHF with the variation of time, after irradiate 5N trans-chalcone with a xenon light Fig. 8. The yield of 5NR chromene in CHF after 150 min at photostationary state was 20.15%. Using the calibration curve Fig. 8 to determine the absorptivity and calculating the %yield.

Fig. 8 (A) Calibration curve for 5N chalcone measured in 284 nm and 5NR chromene measured in 503 nm in CHF solvent. (B) Percentage yield formation of 5NR chromene after irradiation of 5N trans-chalcone at a given time

Since the Abs is directly proportional to the concentration according to Beer's law, the molar absorptivity (ε) of 5N chalcone was 1043 mol-1.cm-1, while for 5NR chromene was 744.56 mol-1.cm-1 that calculated from calibration curve of each one.

The percentage yield of 5NR chromene was calculated in CHF with the variation of time after irradiating 5N trans-chalcone with a XL light Fig. 8 (B). The yield of 5NR chromene in CHF after 150 min at photostationary state was 20 % using the calibration curve Fig. 8 (A) to determine the absorptivity and calculating the %yield.

4.4 Kinetic study

The transformation of 5N chalcone to 5NR chromene is established by light. While the reverse reaction (5NR chromene to 5N chalcone) occurs when the sample of 5NR chromene is transferred to a dark place at room temperature[17]. The 5NR chromene is thermodynamically less stable than the 5N trans-chalcone, which has less energy than the geometry of the (0.0091M) 5N cis-chalcone Scheme 4. The kinetics of DR from 5NR chromene to 5N chalcone has been monitored by measuring the decrease in Abs of 5NR chromene (λmax 503) with time Fig. 9 in CHF.

The rate constant was estimated by examining the order of degradation at peak 503 nm. For this reason, the log-log graphic approach as

well as integral and deferential rate laws, have been applied. The validity of the kinetic order can also be assessed using the correlation coefficient (R2) obtained from fitting curves [23][24][25][26], especially when R2 is close to unity, as shown in Fig. 9. It is worth to mention that the rate constant was obey first order kinetic with R2 0.9816 [27].

Fig. 9 Plot of ln Abs versus time h of the DR of 5NR chromene in CHF measured at 503nm at room temperature.
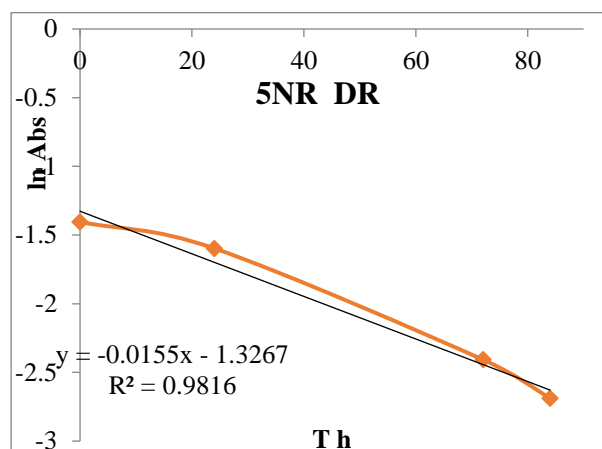
The ln Abs. against time is plotted for the DR of 5NR chromene in CHF [23][24], Fig. 9, to determine the rate constant (0.0155 h-1) from the slope [27], at room temperature for 1st order kinetic.

Table 1 Photochromism result data

Results	Variables	Conc. M	T	Abs	λ_{max}
photostationary state T (min)	CHF	0.00152	150	0.245	503
	CHF	0.0061	91	0.095	503
	ACT				
	ETAC	0.000139	1730	0.003	503
Final decay T (day)	CHF	0.00152	3.5	0.068	503
	CHF	0.0061	19	0.02	503
	ETAC				
k (1/h)	CHF	0.0155			
Yield (%)/ T min	CHF	20.15	150		
Ɛ (1/mol.cm)	Chalcone	10435			346
	Chromene	744.56			483

5. CONCLUSION

The synthesized compound 5N that belong to chalcone produced in 24 h. Their chromenes produce in CHF, faster than ETAC. The 5N undergo photochromism reaction in CHF solvent while in ETAC take very long time with very low chromene product, furthermore in ACT solvent no photochromism process. Increasing the conc. of 5N leads to decrease the time of reaction in CHF while highly increases in ETAC, Increasing the concentration of 5N increases the time require for backward reaction in CHF, while in ETAC unnoticeable. The rate of reaction was 0.0155 1/h for 5NR at room temperature in CHF. The 20% yield of 5NR was high comparing with other chalcones.

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