

NOVEL PHOTOSYNTHESIS AND CHARACTERIZATION OF 4-(5,7-DICHLORO-8aH-CHROMENE-2-YL)-N, N-DIMETHYLANILINE FROM ITS CHALCONE ISOMER

NIROZH A. CHALABI* and GHAZWAN F. FADHIL**

* Dept. of Medicinal Chemistry, College of Pharmacy, University of Duhok, Kurdistan Region – Iraq

** Dept. of Chemistry, College of Science, University of Duhok, Kurdistan Region- Iraq

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ABSTRACT

In the present study, *trans*-3-(2,4-dichlorophenyl)-1-(4-(dimethylamino)phenyl)prop-2-en-1-one (*trans* 2,4-dimethyl amino chalcone) was synthesized by Claisen-Schmidt reaction in the presence of aqueous alcoholic alkali solution by condensation of a substituted acetophenone with substituted benzaldehydes. Then, The photosynthesis of 4-(5,7-dichloro-8aH-chromen-2-yl)-N,N-dimethylaniline (2,4-dimethylamino chromene) was accomplished from the irradiation of the (*trans* 2,4-dimethyl amino chalcone) with xenon light. The products were characterized by UV-Visible, FT-IR, ¹HNMR, thin layer chromatography Elemental analysis(CHNO) and liquid chromatography-quadrupole-time-of-flight mass spectrometry (LC-Q-ToF-MS).

KEYWORDS: Chalcone, Chromene, FT-IR, NMR, LC/Q-TOF/MS, CHNO.

1.INTRODUCTION

Chalcones (1,3-diaryl-2-propen-1-ones) belong to the flavonoid class as natural or synthetic compounds. Chemically, they consist of open-chain flavonoids in which a 3 Cs α , β -unsaturated carbonyl system joins the 2 aromatic rings. They include the keto-ethylene group(-CO-

CH=CH). Chalcones have conjugated double bond and a fully delocalized π -electrons framework on both benzene rings(Yadav et al., 2012). Chalcone could be stereochemically *trans* (*E*) and *cis* (*Z*) isomers, but the *Z* conformer is most unstable due to the steric effects of ring A with carbonyl group(Rammohan, 2020).

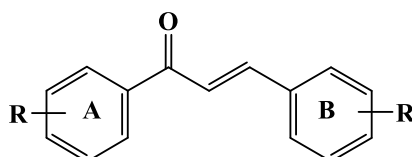


Fig. (1): Chalcone structure

Unsaturated carbonyl group in the chalcone allows it to be active biologically active(Archit, Mythili, and Sathiavelu, 2014). It has been reported that compounds with the backbone of chalcones have different biological activities. For example antimicrobial(Dekić et al., 2017), ant-inflammatory(Zhuang et al., 2017), analgesic(Asiri et al., 2015), anticancer(Tran et al., 2016), antiviral and antioxidant(Orlikova, Tasdemir, Golais, Dicato, and Diederich, 2011). Due to their interesting uses such as chemical probes, electrochromic products, Fluorescent dyes, sensors, as additives in dye-sensitized solar cells, and more specifically in the evaluation of

new drug production. Fluorescent products have a lot of interest(Watanabe, Saji, and Ono, 2018)(Zhou, Jiang, Lu, and Xing, 2016)(Tomasch, Schwed, Weizel, and Stark, 2012)(RJ, 2011) . Chromenes, probably, represent an important structural class of oxygen heterocycles. The chromene ring (benzopyran) system consisting of a benzene ring fused to a pyran ring(Costa, Dias, Brito, and Proença, 2016). Classification of heterocyclic pyran compounds depends on the existence of the pyran scaffold 2H or 4H. So, the 2H-pyran benzo analogue is called 2H-1-benzopyran (usually 2H-chromene) and the 4H-pyran benzo

analog is called 4*H*-1-benzopyran (usually 4*H*-chromene)(Kumar et al., 2017). Of the nine ring structure carbons, eight are sp^2 and one is sp^3 hybridized. These are often referred to as 2*H*- and 4*H*-chromenes based on the position of sp^3 C in relation to ring oxygen. Chromene reactions with weaker nucleophiles give a replacement

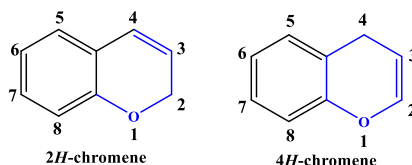


Fig. (2): General structure of 2*H*-chromenes and 4*H*-chromene

The aim of this study is to synthesize *trans*-3-(2,4-dichlorophenyl)-1-(4-(dimethylamino)phenyl)prop-2-en-1-one (*trans* 2,4-dimethylamino chalcone) by Claisen Schmidt reaction, then using simple photochemical conversion by the xenon light to synthesize the 4-(5,7-dichloro-8*H*-chromen-2-yl)-*N,N*-dimethylaniline(2,4-dimethylaminochromene). These two products will be characterized by different techniques such as, thin layer chromatography, FT-IR, ^1H and ^{13}C nuclear magnetic resonance, liquid chromatography/quadrupole time-of-flight mass spectrometry and elemental analysis (CHNO).

2. EXPERIMENTAL

Materials and Methods

All the needed chemicals and solvents were of reagent grade bought from Sigma Aldrich and Merck. The melting points have been identified and recorded using an open capillary method and are uncorrected by using the Mel-temp M206780/02 electro thermal melting point apparatus. ^1H and ^{13}C NMR data were recorded on BRUKER AV400-MHz NMR (Bruker Corporation, USA) spectrometer in CDCl_3 and DMSO solvents. For 2,4-dimethylamino chromene, one drop of 1M HCl was added with solvent to prevent the conversion of chromenes to chalcones during NMR measurement like the flavylum salt compounds(Gavara, Gago, Jordão, and Pina, 2014). The NMR spectra obtained were carried out in laboratories of Chemistry Department at the University of Dicle, Turkey. Chemical shift is expressed in part per million (δ) using tetra methyl silane (TMS) as internal standard. Deuterated solvents were supplied from Merck (Darmstadt, Germany). ATR-FT-IR was employed to receive infrared spectra

product at C-4, whereas strong nucleophile attacks at C-2 carbon produce dianion of phenolic acid by cleavage of pyran ring. In case of 4*H*-chromene, the C=C bond is not in conjugation with a benzene ring like 2*H*-chromene(Pratap and Ram, 2014)

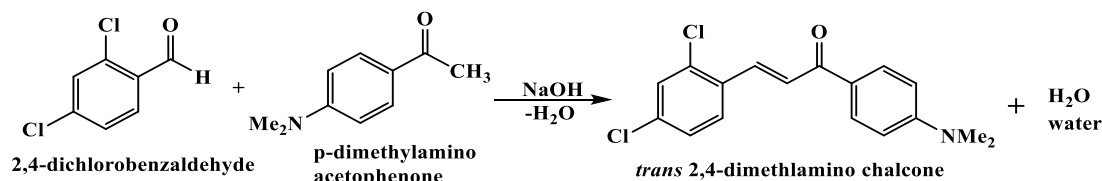
(Schimadzu, Japan). Chalcones and chromenes FTIR spectra were obtained in solid state. The obtained IR spectra were performed in the laboratories of Chemistry Department at Dicle University in the Diyarbakir Turkey. Elemental analysis (CHNO) was measured by Perkin Elmer EA 2400 series II (Perkin Elmer, USA). MS analysis was performed using an Agilent 6550 iFunnel high resolution Accurate-Mass Q-T-OF-MS (Agilent Technologies, Santa Clara, CA, USA). Thin Layer Chromatography was made on Macherey-Nagel, 805022, pre-coated TLC-sheets Polygram Sil/UV₂₅₄, the detection of spots on TLC sheet visualized with a UV lamp with λ_{max} 254 nm. The irradiation light source for performing the chalcone to chromene reaction is 100W Auto Car HID Xenon Headlight Lamp was used as a source of irradiation. ChemDraw professional 15.0 software was used for drawing structures. MestReNova software version:6.0.2-5475 was used for plotting FT- NMR spectra and for chemical shifts prediction.

Preparation of *trans*-3-(2,4-dichlorophenyl)-1-(4-(dimethylamino)phenyl)prop-2-en-1-one.[2,4-dimethylamino chalcone]

A quantity (24.9 mmol, 4g) of 4-dimethylamino acetophenone and (24.9 mmol, 4.3g) of (2,4-dichlorobenzaldehyd) were dissolved in 20 ml of absolute ethanol and then were mixed, to this solution 5 ml of (10%) sodium hydroxide NaOH was added slowly with stirring , after 1 h. A precipitate was formed then stirring was continued for 24 h. The reaction mixture then was placed in a refrigerator for an overnight. The formed precipitate was filtered and washed several times with cold distilled water to remove excess base and was recrystallized from hot absolute ethanol. The purity of product was checked by melting point

(112-115 °C) (uncorrected) and thin layer chromatographed (TLC) ($R_f = 0.64$) (toluene:

ethyl acetate) (6:2) were used as eluent. The yield of yellow precipitate was (80%).

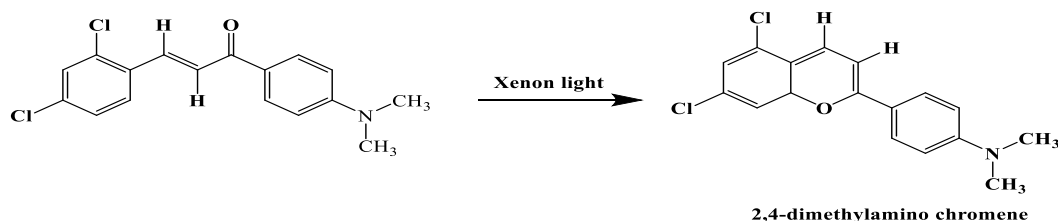


Scheme (1): Reaction equation for preparation of *trans*-3-(2,4-dichlorophenyl)-1-(4 (dimethylamino)phenyl) prop-2-en-1-one

Preparation of 4-(5,7-dichloro-8aH-chromen-2-yl)-N,N-dimethylaniline. [2,4-dimethylamino chromene]

A quantity (3.125mmol, 1g) of 2,4-dimethylamino chalcone was dissolved in a mixture of (80 ml of cyclohexane and 20 ml of chloroform) and was stirred in an ice bath. Then the solution was irradiated with the xenon light for 1 h, during time, color of the solution was changed from yellow to purplish-black solution.

The purplish-black solution starts to precipitate because of the low solubility of the product (2,4-dimethyl amino chromene) in cyclohexane. Under the xenon light the precipitate was filtered directly. The purity of the precipitate was identified by TLC ($R_f = 0$) using toluene and ethyl acetate as eluents (6:2) with one drop of 1M HCl. The yield of purplish-black precipitate was (80%) and the melting point was (115-117 °C).

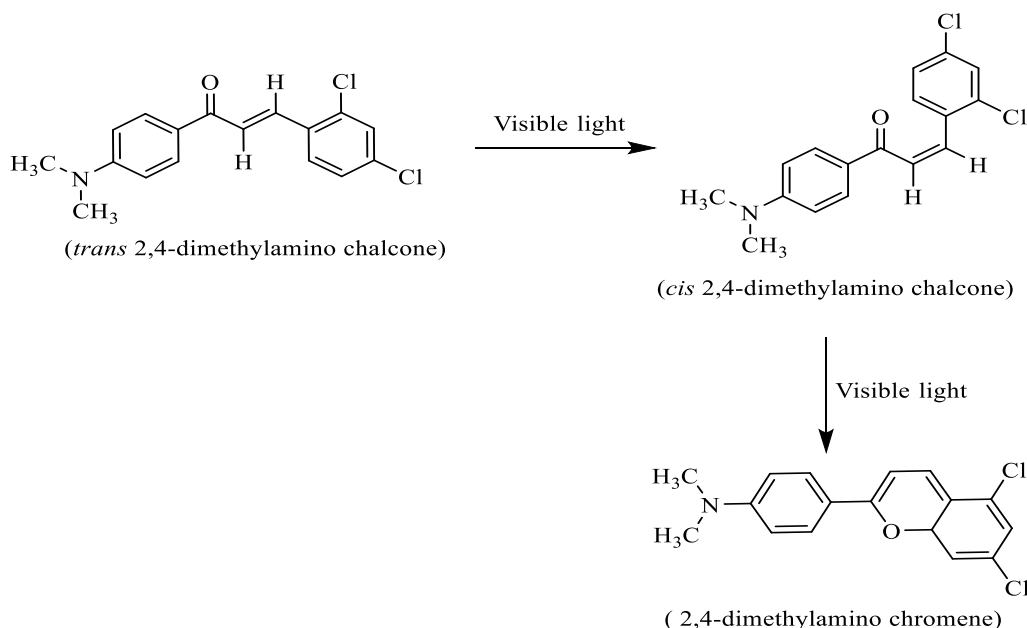


Scheme (2): Reaction equation for preparation of 4-(5,7-dichloro-8aH-chromen-2-yl)-N,N-dimethylaniline

3. RESULTS AND DISCUSSION

In the reaction of 2,4-dimethylamino chromene synthesis, the newly synthesized *trans* 2,4-dimethylamino chalcone was irradiated in chloroform for a limited period of time. The irradiated *trans* 2,4-dimethylamino chalcone

expected to undergo *trans-cis* isomerization to give the *cis* 2,4-dimethylamino chalcone isomer. Further isomerizes of *cis* 2,4-dimethylamino chalcone isomer gives the corresponding 2,4-dimethylamino chromene. The suggested reaction route is given below.



Scheme (3): The synthetic route of 2,4-dimethylamino chromene form *trans* 2,4-dimethylamino chalcone

FT-IR Spectra Elucidation

The experimental FT-IR spectra of *trans* 2,4-dimethylamino chalcone and 2,4-dimethylamino chromene are illustrated in Figure (3) and (4).

The (C=C) stretching vibration for alkene usually occurs in the region 1600-1660 cm^{-1} and for aromatic ring is 1475 -1620 cm^{-1} (Pavia, D.L., Lampman, G.M., Kriz, G.S. and Vyvyan, 2014). The (C=O) carbonyl stretching frequency is the most widely studied by infrared spectroscopy (Sudha, Sundaraganesan, Vanchinathan, Muthu, and Meenakshisundaram, 2012). The carbonyl group of ketones (Ar-CO-Ar) conjugated with two aromatic rings appear in region 1600-1670 cm^{-1} . The stretching bands of (C=C) of vinyl and (C=O) of *trans* 2,4-dimethylamino chalcone observed at 1606 cm^{-1} and 1648 cm^{-1} respectively. But in 2,4-dimethylamino chromene no C=O vibrating bands were observed, this is an important indication that *trans* 2,4-dimethylamino chalcone is entirely transformed into 2,4-dimethylamino chromene. Also, for aromatic ring the (C=C) stretching is appeared at 1580 cm^{-1} for *trans* 2,4-dimethylamino chalcone and 1511 cm^{-1} for 2,4-dimethylamino chromene respectively.

Absorption frequency in aromatic amines is higher than aliphatic amines because resonance elevates double bond character between the ring and the linked nitrogen (-N(CH₃)₂) atom (Sudha et al., 2012).

In this study, the C-N stretching band observed in overlap with other groups at

1231 cm^{-1} for *trans* 2,4-dimethylamino chalcone and 1227 cm^{-1} belongs to 2,4-dimethylamino chromene.

The stretching vibration of sp² (C-H) of aromatic compounds commonly shows multiple weak bands in the region 3000 and 3150 cm^{-1} . The experimental vibrational wavenumbers of sp² (C-H) of *trans* 2,4-dimethylamino chalcone and 2,4-dimethylamino chromene were observed at 3065 cm^{-1} and 3064 cm^{-1} respectively. Whereas sp² (C-H) out of plane (oop) bending and in plane (ip) ring (Ar) bending vibration occurs in the range 1000-650 cm^{-1} and 1000-1300 cm^{-1} respectively (Mahadevan, Periandy, and Ramalingam, 2011). For *trans* 2,4-dimethylamino chalcone (C-H) out of plane (oop) bending and in plane (ip) vibration appears in the 813 cm^{-1} and 1337 cm^{-1} respectively and 828 cm^{-1} , 1185 cm^{-1} for 2,4-dimethylamino chromene. Stretching vibration of sp³ (C-H) occur in the region of 2850-3000 cm^{-1} (Robert, 2005). The symmetric bending vibration (CH₃) appears around 1375 cm^{-1} , and the asymmetric bending vibration (CH₃) is about 1450 cm^{-1} . for the synthesized chalcone The stretching sp³ (C-H), C-H bending symmetrical (CH₃) and asymmetric bending vibration (CH₃) observed in the 2990 cm^{-1} , 1369 cm^{-1} and 1444 cm^{-1} , respectively. However, for 2,4-dimethylamino chromene stretching sp³ (C-H) appeared in 2918 cm^{-1} , whereas C-H bending symmetrical (CH₃) and asymmetric bending vibration (CH₃) were

appeared in 1372 cm^{-1} and 1468 cm^{-1} respectively.

The experimental vibrational wavenumbers of ($=\text{C-H}$) of the *trans* 2,4-dimethylamino chalcone and 2,4-dimethylamino chromene were observed at 3065 cm^{-1} and 3064 cm^{-1} respectively. Whereas ($=\text{C-H}$) out of plane (oop) bending and in plane(ip) (C-H ring(Ar) bending vibration) occurs in the range $1000\text{-}650\text{ cm}^{-1}$ and $1000\text{-}1300\text{ cm}^{-1}$ respectively (Mahadevan et al., 2011). For the *trans* 2,4-dimethylamino chalcone, ($=\text{C-H}$) out of plane (oop) bending and in plane(ip) bending vibrations were appeared in the 813 cm^{-1} and 1337 cm^{-1} respectively, and at 828 cm^{-1} , 1185 cm^{-1} which belongs to 2,4-dimethylamino chromene. The stretching vibration of (C-H) occurs in the region of $2850\text{-}3000\text{ cm}^{-1}$ (Robert, 2005). The symmetric bending vibration (CH_3) appears around 1375

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Aryl (C-Cl) stretching vibration absorbed in the region $1035\text{-}1100\text{ cm}^{-1}$, while for aliphatic C-Cl is absorbed at $550\text{-}850\text{ cm}^{-1}$ (Pavia, D.L., Lampman, G.M., Kriz, G.S. and Vyvyan, 2014). For the studied compounds, the bands of C-Cl stretching were observed experimentally at 1099 cm^{-1} for *trans* 2, 4-dimethylamino chalcone and at 591 cm^{-1} for 2, 4-dimethylamino chromene.

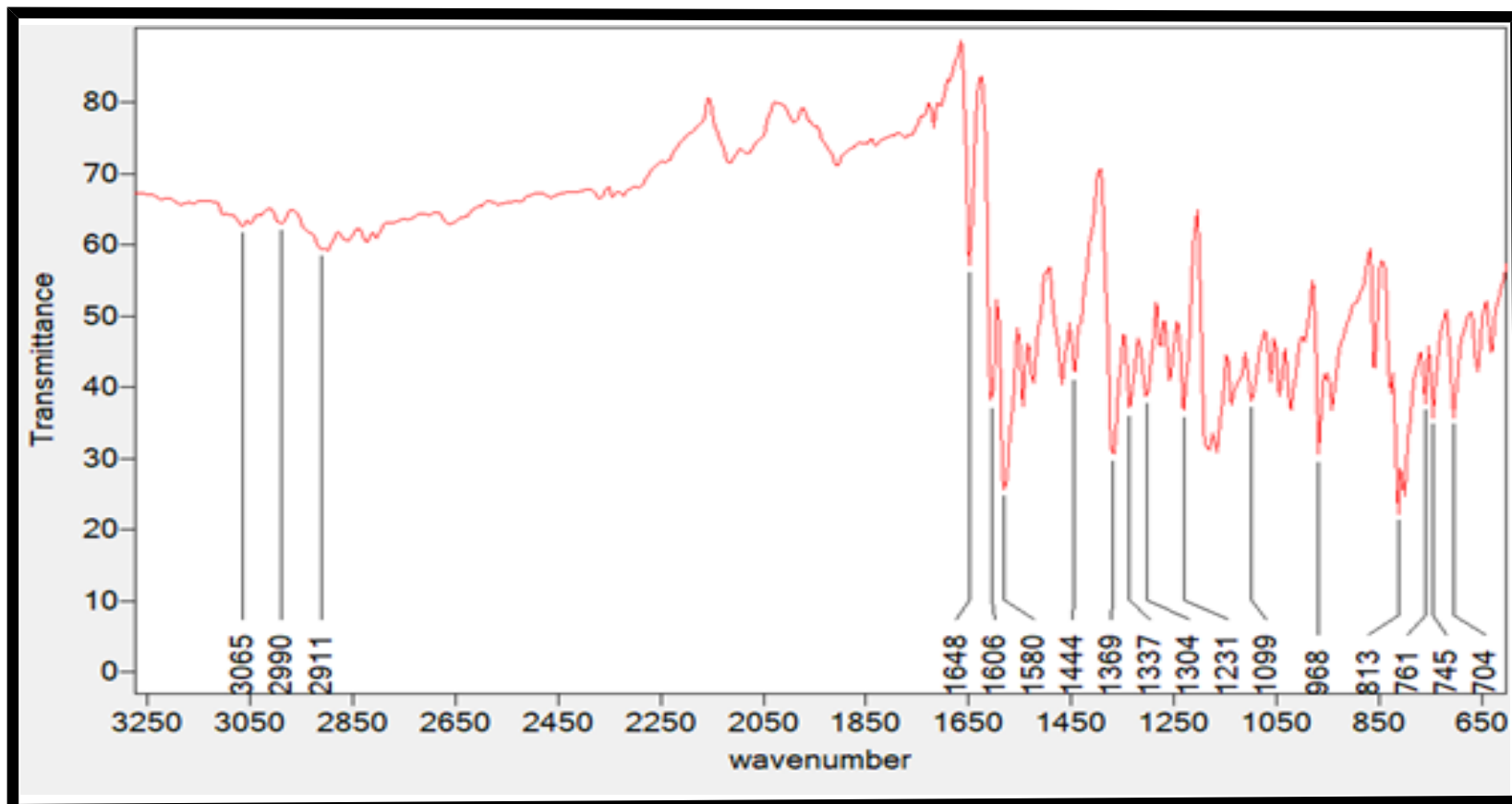


Fig. (3):.ATR- FT-IR spectrum of *trans* 2,4-dimethylamino chalcone

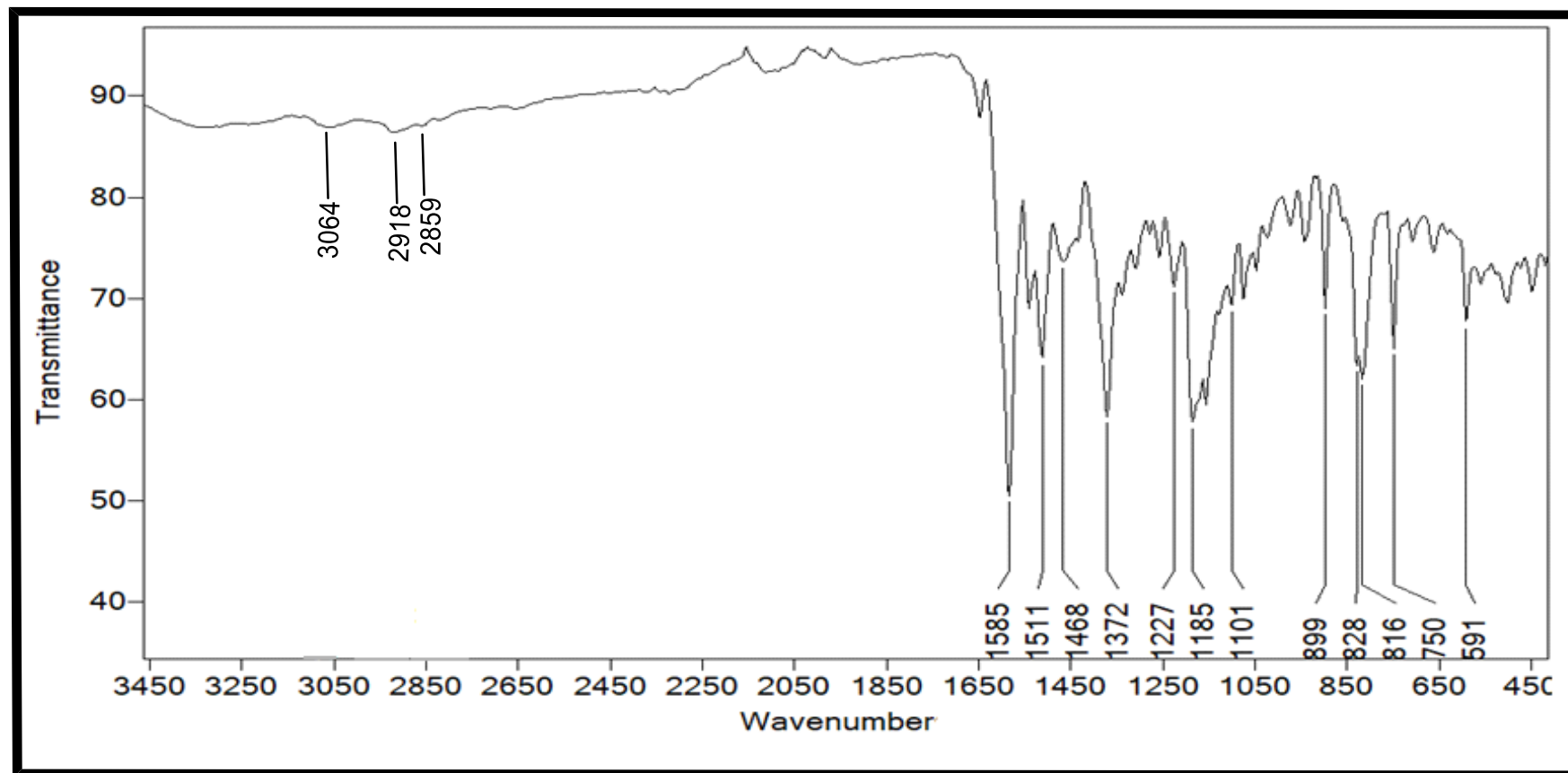


Fig. (4): ATR-FT-IR spectrum of 2,4-dimethylamino chromene

NMR Analysis

The ^1H -NMR and ^{13}C -NMR spectra of *trans* 2,4-dimethylamino chalcone and 2,4-dimethylamino chromene are illustrated in Figures (6), (7) and (8) respectively. Table 1 and 2 show the ^1H -NMR chemical shifts, J coupling constants and integrations of *trans* 2,4-dimethylamino chalcone and 2,4-dimethylamino chromene, respectively.

The H5 (α) and H6(β) vinyl group protons belong to the AB (Zhou et al., 2016) system in which the four signals are classified as doublet of doublet. The signals of each splitted doublet with not equal intensity i.e. not like the first order splitting. The *trans*-vinyl protons have coupling constant that is noticeably greater than the coupling constant of the *cis*-vinylic protons. In *trans* 2,4-dimethylamino chalcone the chemical shift of α hydrogen (H5) is lower than for β hydrogen (H6) (Table, 1) due to high electron density around H5 as a result of the resonance interaction of the vinyl double bond with the carbonyl group. The coupling constant (J) for these protons is 16.084 Hz agrees with the *trans* coupling constant of protons. Chemical shifts and coupling constants of H5 and H6 of 2,4-dimethylamino chromene are given in Table (2). The splitting pattern of these protons gives two doublets, however, the peak ratio of each doublet is not like that in H5 and H6 of *trans* chalcone, and the coupling constants for 2,4-dimethylamino chromene is 8.5 Hz. This is due to non-*trans* geometry and confirms the *cis* relationship between the H5 and H6 protons in the synthesized chromene. This is one of the significant evidence of the chromene synthesis from *trans* chalcone. The chemical shifts of C8 and C9 ^{13}C -NMR of *trans* 2,4-dimethylamino chalcone behave in a similar manner as H5 and H6 due to the same resonance effect discussed above.

The protons of dimethyl amino group ring belong to AA'BB' (Bruice, 2004) splitting pattern which is a typical pattern of splitting of para di-substituted benzene ring. The observed ^1H -NMR spectrum for H1, H2, H3 and H4 of the aniline ring of *trans* 2,4-

dimethylamino chalcone and 2,4-dimethylamino chromene are shown in Figures (6) and (7), respectively. The pattern of splitting gave two pairs of signals one pair for H1 and H2 which is similar image with the pair of signals of H3 and H4. The electron-donating by resonance effect of the dimethyl amino group increases the electron density on ortho and para position while has no effect on meta position. According to that, the chemical shifts of H1-H2 and C2-C3 are lower (up field shifted) than that of H3-H4 and C4-C5. The chemical shift of ^{13}C -NMR of carbonyl group (C7) appears at 187.16 ppm in the *trans* 2,4-dimethylamino chalcone is higher chemical shift value (downfield) in the ^{13}C spectrum is due to the anisotropic effect of the carbonyl group.

The tree diagram for the splitting pattern of the H7, H8 and H9 of dichlorobenzene ring for *trans* 2,4-dimethylamino chalcone shown in Figure (5). Also, the corresponding chemical shifts and coupling constants are given in Table (1). The trend of these protons chemical shift is H9 most downfield then H7 which lies between the two chlorines, after that the least deshielded is H8 which gives doublet of doublet signal at 7.28 ppm embraces the residual proton signal of CDCl_3 . The largest coupling constant is between H8 and H9, and it is 8.51 Hz; however, this signal was splitted further by the H7 with J_{87} equal to 2.2 Hz. The chemical shift of H7 is 7.45 ppm which appears as doublet signal due to coupling with H8 only and the J_{78} equal to 2.13. The H9 chemical shift at 7.68 is also doublet due to coupling to H8 only with J_{98} equal to 8.5 Hz. The ^1H NMR of 2,4-dimethylamino chromene is shown in Figure (7). Most of the signals of the chalcone and chromene in this spectrum are overlapped. Two doublets could be recognized belong to H3 and H4 at 7.22 and 7.34 ppm with J_{34} equal to 8.1 Hz. The doublet signal at 7.81 ppm assigned to H2' and H6' of the di-substituted benzene ring of the chromene. In 2,4-dimethylamino chromene, H9 is the most up-field due to cyclization reaction and formation of pyrane ring.

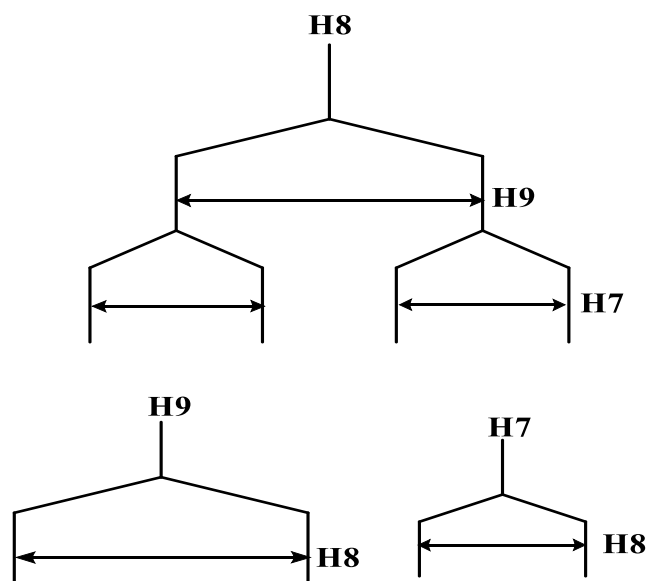
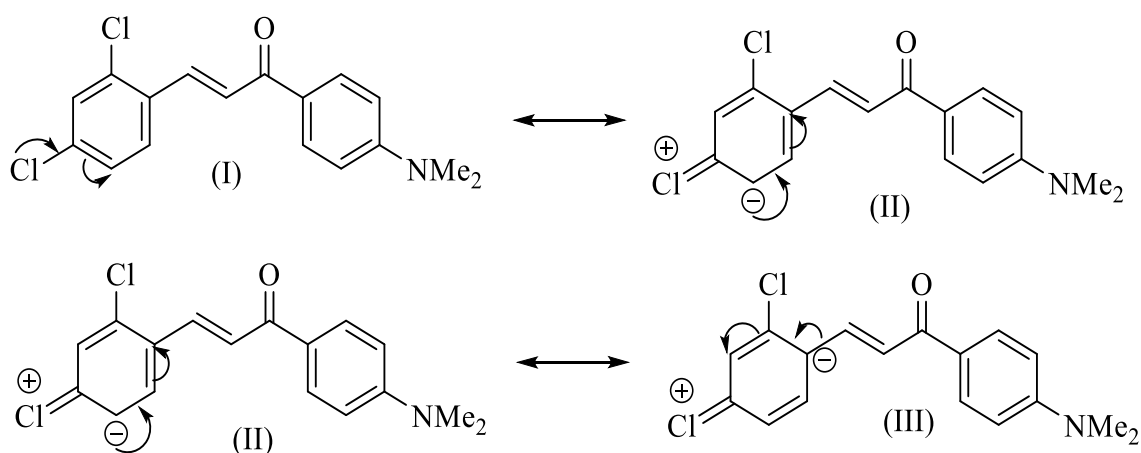


Fig. (5): Tree diagram of the splitting pattern of H7, H8 and H9 protons in *trans* 2,4-dimethylamino chalcone

The chemical shift of C4 and C5 is (128.44 ppm) for *trans* 2,4-dimethylamino chalcone are down field compared to the chemical shift of the C2 and C3 at (110.84) as shown in Table (3). The C4 and C5 are at *ortho* positions with respect to the carbonyl group, and hence they are under the influence of the electron withdrawing effect of the carbonyl group.

The resonance interactions of the chlorine and the π -system of the dichlorophenyl ring in *trans* 2,4-dimethylamino chalcone generates three negative charges at carbons C12, C14 and C10 scheme (4) structures (II and III). The chemical shift of the C14

is the most up field of the three chemical shifts and the chemical shift of C12 is also up field compared to chemical shift of C10 as shown in Table (3). Both positions C12 and C14 accommodate negative charges due to the resonance interactions, hence the up field may be justified. The C12 is between two chlorines, so it may suffer from some electron withdrawing and consequently its chemical shift is slightly down field to the chemical shift of C14. However, the chemical shift of C10 is the most down field compared to the chemical shifts of C12, C14.



Scheme (4): Resonance structures of *trans* 2,4-dimethylamino chalcone are generated by chlorine at C13. Similar resonance structure could be generated from chlorine at C11.

Table (1): The chemical shift, J coupling constant and integration of *trans* 2,4-dimethylamino chalcone by $^1\text{H-NMR}$

Proton type	Chemical shift (ppm)	Coupling constant (J) (Hz)	Integration
H1 and H2	6.70	9.11	2
H3 and H4	7.99	9.12	2
H5	7.53	15.64	1
H6	8.07	15.64	1
H7	7.45	2.1	1
H8	7.28	7.61	1
H9	7.68	8.48	1
-N(CH ₃) ₂	3.09	-	6

Table (2): The chemical shift, J coupling constant and integration of 2,4-dimethylamino chromene by $^1\text{H-NMR}$

Proton type	Chemical shift (ppm)	Coupling constant (J) (Hz)	Integration
H1 and H2	7.28	8.60	2
H3 and H4	7.81	8.61	2
H5	7.22	8.5	1
H6	7.34	8.5	1
H7	7.16	-	1
H8	7.30	3.58	1
H9	6.09	29.74	1
-N(CH ₃) ₂	2.84	-	6

Table (3): The chemical shift of *trans* 2,4-dimethylamino chalcone by $^{13}\text{C-NMR}$

Carbon type	Chemical shift (ppm)
C1	153.55
C2 and C3	110.84
C4 and C5	128.44
C6	125.33
C7	187.16
C8	125.52
C9	137.01
C10	132.51
C11	135.72
C12	130.98
C13	135.75
C14	127.42
C15	129.97
-N(CH ₃) ₂	39.61

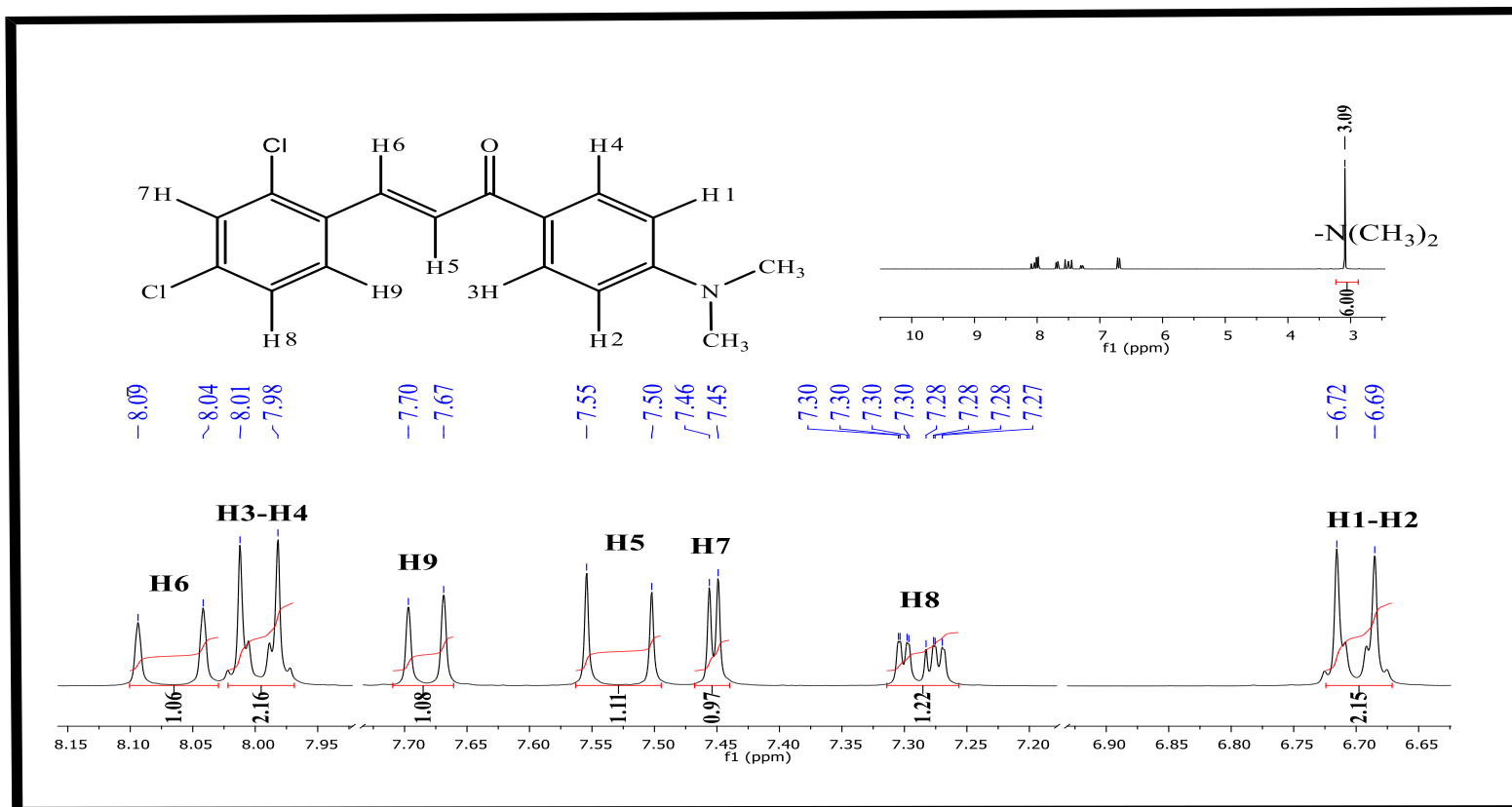


Fig. (6): ¹H-NMR spectrum of *trans* 2,4-dimethylamino chalcone in CDCl₃

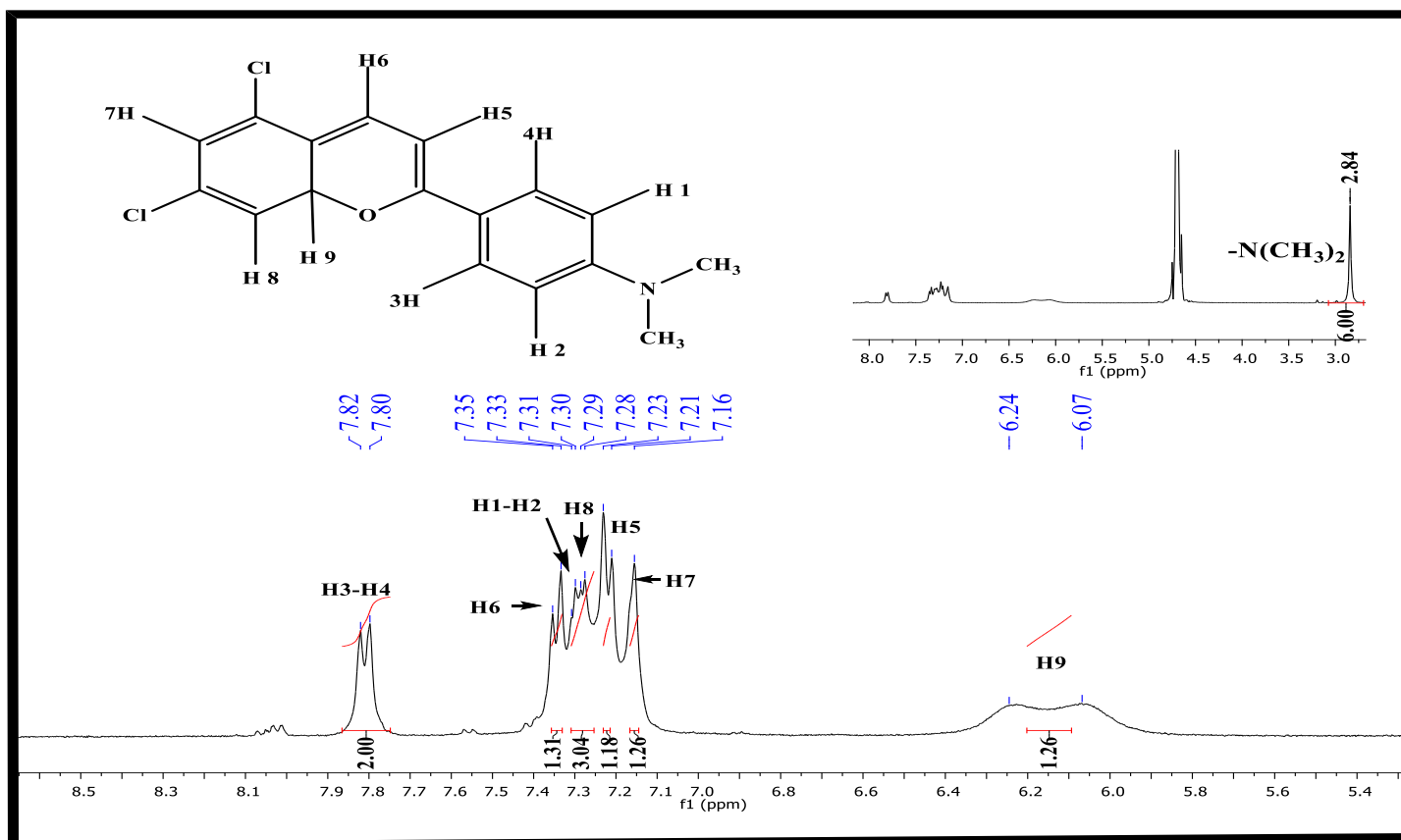


Fig. (7): ¹H-NMR spectrum of 2,4-dimethylamino chalcone in DMSO

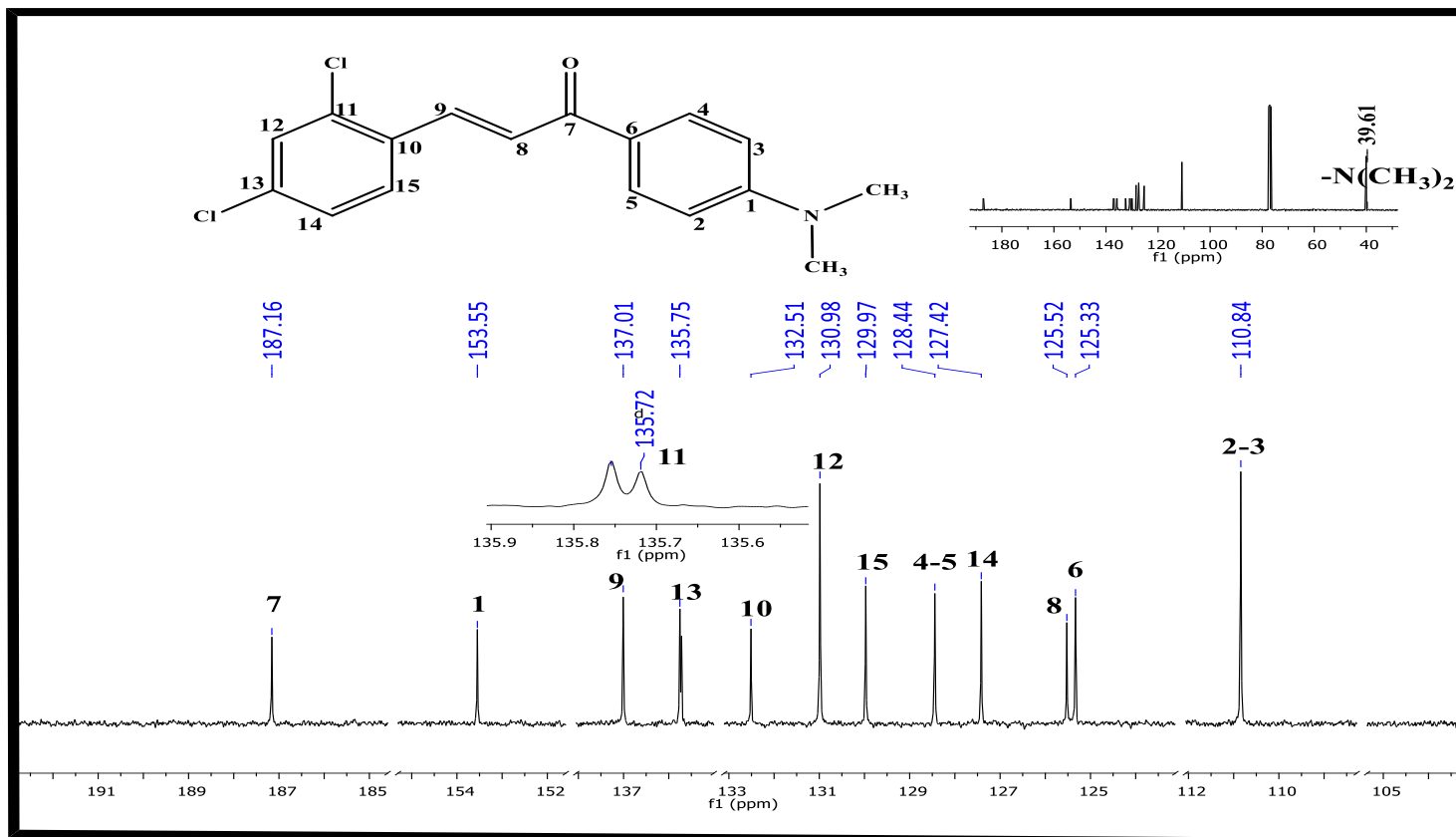


Fig. (8): ^{13}C -NMR spectrum of *trans* 2,4-dimethylamino chalcone in CDCl_3

Liquid Chromatography/Quadrupole Time-Of-Flight/ Mass Spectrometry (LC/Q-TOF/MS)

The molecular ion of 2,4-dimethylamino chalcone was determined by LC/Q-TOF-MS which is equal to $[M + 1H]^+$ (320.0522) at the retention time 7.396 min, the calculated exact mass of 2,4-dimethylamino chromene is 320.0531.

Elemental Analysis (CHNO)

The experimental and calculated elemental analysis (CHNO) results of *trans* 2,4-dimethylamino chalcone and 2,4-dimethylamino chromene are shown in Table 4.

Table (4): Calculated and found CHNO analysis of *trans* 2,4-dimethylamino chalcone and 2,4-dimethylamino chromene

	Calculated				Found			
	C	H	N	O	C	H	N	O
2,4-dimethylamino chalcone	63.77	4.72	4.37	5.00	63.76	4.71	4.35	4.98
2,4-dimethylamino chromene	63.77	4.72	4.37	5.00	63.70	4.79	4.33	5.04

4. CONCLUSION

The irradiation of *trans* 2,4-dimethylamino chalcone with xenon light provided a simple and easy method to synthesize 2,4-dimethylamino chromene from simply synthesized *trans* 2,4-dimethylamino chalcone via the well-known method of Claisen-Schmidt. 1H NMR of chalcone and chromene shows all the prominent peaks as in the chemical structure. Chalcone molecules can be considered as photo switches since the synthesized chromene can go back to chalcone in dark or heat and by light to chromene again.

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