

Synthesis of some new compounds of 3-(2,4-dichlorophenyl)-1-(4'-X-phenyl)-3-nitromethylpropan-1-one

Hanoy K. Al-Amood

Department of Chemistry, College of Sciences, University of Basrah

E-mail:- hanoy9999@yahoo.co.uk

Abstract:- Four new compounds namely **3-(2,4-dichlorophenyl)-1-(4'-X-phenyl)-3-nitromethylpropan-1-one** where X= H, CH₃, Cl and F have been prepared from alkylating of **3-(2,4-dichlorophenyl)-1-(4'-X-phenyl)-2-propen-1-one (chalcones)**. The structures of the prepared compounds were determined by spectroscopic technique and elemental analysis. Elemental analysis showed good agreement between measured and calculated percentage. FT-IR and ¹H and ¹³C NMR Spectroscopy techniques were used to identify structures of prepared compounds.

Keyword: chalcone, alkylation of chalcone

1-Introduction

Chalcones are well known intermediates for synthesizing various heterocyclic compounds. The compounds with the backbone of chalcones have been reported to possess various biological activities such as antimicrobial (Mokle *et al.*, 2004), anti-inflammatory (Hsieh *et al.*, 2000), analgesic (Viana *et al.*, 2003), antiplatelet (Zhao *et al.*, 2005), antiulcerative (Mukarami *et al.*, 1991), antimalarial (Liu *et al.*, 2001), anticancer (Francesco *et al.*, 2007), antiviral (Onyilagna *et al.*, 1997), antileishmanial (Nielsen *et al.*, 1995), antioxidant (Miranda *et al.*, 2000),

antitubercular (Sivakumar *et al.*, 2007), antihyperglycemic (Satyanarayana *et al.*, 2004), immunomodulatory (Barford *et al.*, 2002), inhibition of chemical mediators release (Koh *et al.* 2003), inhibition of leukotriene B₄ (Deshpande *et al.*, 1999), inhibition of tyrosinase (Khatib *et al.*, 2005), inhibition of aldose reductase (Severi *et al.*, 1998) activities. The presence of a reactive α,β -unsaturated keto function in chalcones is found to be subject to many addition reactions (Robert *et al.*, 1978). The addition occurs at the alkene bond, the orientation always is such

that the nucleophile adds at the β carbon (Luis *et al.*, 2004). An example is the

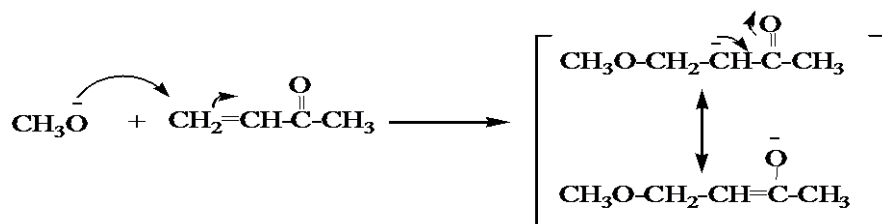
addition of methanol catalyzed by sodium methoxide; Scheme 1:



Scheme 1

Nucleophilic reagents normally do not attack carbon-carbon double bonds. The adjacent carbonyl function therefore must greatly enhance the reactivity of the double bond toward such reagents. This :

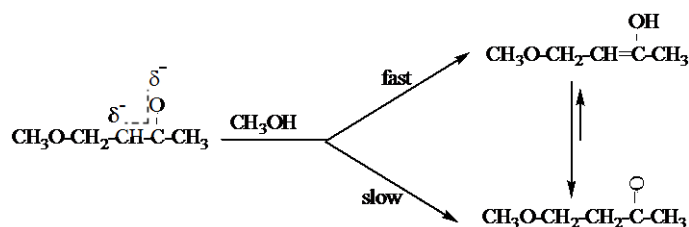
enhancement is not surprising when it is realized that the attack of a nucleophile produces a stabilized enolate anion; Scheme 2



Scheme 2

The products are formed from the enolate intermediate by proton transfer to either carbon or oxygen. If the proton is added

to oxygen the enol is formed, which is unstable with respect to the ketone and ultimately will rearrange; Scheme 3:



Scheme 3

Reaction of this type is referred to in a variety of terms, many of which are rather

confusing and non-descriptive. They sometimes are classified as 1,4-additions,

implying that addition occurs across the terminal position of the conjugated system. When the nucleophile is a carbanion, the reaction is called a Michael addition (Jerry March, 1985). Michael-type additions, like aldol additions, are

useful for the formation of carbon-carbon bonds (Geoege H. 1996).

The aim of project is to prepare new compounds from chalcone that could be used as intermediate compounds to prepare heterocyclic compounds (Mohamed *et. al.* 2012).

2-Experimental

General procedures

2.1-Preparation of 3-(2,4-dichlorophenyl)-1-(4'-X-phenyl)-2-propen-1-one (chalcones) :-

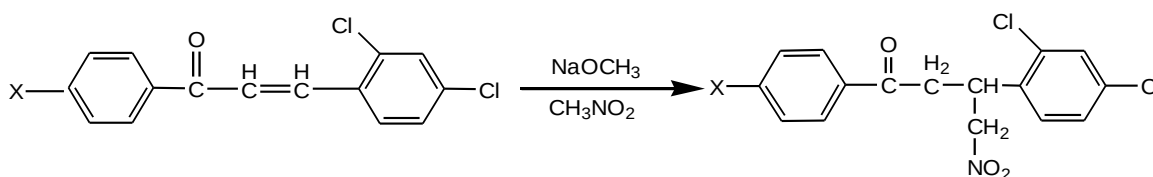
The preparation of chalcones was performed according to the methodology

2.2-Preparation of 3-(2,4-dichlorophenyl)-1-(4'-X-phenyl)-3-nitromethylpropan-1-one:-

Equimolar mixture of chalcone and sodiummethoxid salt were reacted(Table 1,scheme 4). The chalcone was dissolved in (10 ml) nitromethane and (50 ml) abs. methanol. The salt was dissolved in (50 ml) abs. methanol and left in cool water bath for 10 minutes. The chalcone solution was gradually added to the cold salt solution with the stirring. The reaction mixture was left with stirring overnight. Later, distilled water (150 ml) was added to the reaction mixture (heat of solution was risen and white loblolly suspension

previously described (Perjessy et al., 2011).

was formed). A white solid product was obtained by using rotary vacuum (except para substituted chloro compound was obtained by leaving it in refrigerator overnight). The product was filtered, dried and purified by recrystallization from suitable solvent. Table1 gives the melting points. The follow-up of reactions and sample purity were checked by TLC using Merck silica gel 60 F₂₅₄ aluminum sheets and were developed with the solvent mixture indicated in Table 1.



Scheme 4

X= H, CH₃, Cl and F

Table 1. Physical properties of compounds

X	Wt in gm (mole) of chalcone	Wt in gm (mole) of salt	m.p C° of product	Solvent of crystallization	Colour of crystal	R _f	Eluent (1:3)	Yield %
p-H	0.5 (0.0018)	0.097 (0.0018)	96-97	n-Hexane	White needle	0.5	n-Hexane: Ethyl acetate	47.6
p-CH₃	0.5 (0.0017)	0.096 (0.0017)	83-84	n-Hexane	Bright white	0.7	n-Hexane: Ethyl acetate	35
p-F	0.5 (0.0017)	0.09 (0.0017)	101-102	n-Hexane	Bright white	0.61	n-Hexane: Ethyl acetate	85.3
p-Cl	0.5 (0.0016)	0.086 (0.0016)	82-84	Ethanol	White	0.5	Ethyl acetate: Cyclohexane	79

3-Physical measurements

IR spectra for prepared compounds were measured as KBr disks using shimadzu model FT IR-8400S spectrometer, at the laboratory of Basrah Petrochemical complex. The ¹H- NMR spectra were recorded on a Varian VXR 300 NMR spectrometer at 299.943 MHz in CDCl₃ as solvent at 25 °C with a concentration of 0.02 ml⁻¹. ¹³C-NMR spectra were recorded

on the same spectrometer at 75.429 MHz in CDCl₃ as solvent with TMS as an internal reference with CHN elemental analysis at Institute of chemistry, Comenius University, Bratislava, Slovak Republic.

4-Results and Discussion

4.1-Elemental analysis

The percentage of C, H and N of prepared compounds are shown in table 2. The measured percentage was showed

good agreement with the calculated results

Table 2. Elemental analysis

X	Calculated			Found		
	C %	H %	N %	C %	H %	N %
H	55.99	3.50	3.91	57.4	3.75	4.27
Me	57.80	3.92	3.98	58.09	4.25	4.03
Cl	50.66	2.94	3.72	50.51	3.02	3.58

Note: X=F derivative was not possible to make the analysis, since the instrument was using quartz-oxidation tubes, which could damage by fluoro-derivatives.

4.2- FT-IR Spectra:

The spectra of these compounds show that all compounds have common peaks with variable intensity of aromatic C-H stretching ($3010\text{--}3020\text{ cm}^{-1}$), strong peak of aromatic double bond C=C stretching ($1585\text{--}1600\text{ cm}^{-1}$), the peak of C-Cl stretching ($1090\text{--}1100\text{ cm}^{-1}$) (Cross and Alan, 1965). The strong peak at ($1665\text{--}1680\text{ cm}^{-1}$) is attributed to aromatic C=O stretching (Silver and Boykin, 1970 and Perjessy *et al.*, 1979). FT-IR of these compounds show additional peak at (1380 cm^{-1}) attributed to $-\text{CH}_2\text{NO}_2$ deformation (Cross and Alan). Strong peaks of $-\text{NO}_2$ (asym.) group at ($1520\text{--}1595\text{ cm}^{-1}$) and $-\text{NO}_2$ (sym.) at ($1340\text{--}1365\text{ cm}^{-1}$) and $-\text{NO}_2$ (sym.) at ($1340\text{--}1365\text{ cm}^{-1}$). IR spectrum was one of the important evidences, which proof that these compounds were prepared. The first evidence was the disappearance of the strong bands in region $1605\text{--}1619\text{ cm}^{-1}$, which is attributed to olefinic C=C vibration stretching in chalcones (starting material) (Hanoy, 1999) and the appearance of aliphatic C-H stretching bands at region $3010\text{--}3020\text{ cm}^{-1}$. The appearance of strong peaks of $-\text{NO}_2$ (asym.) group at ($1520\text{--}1595\text{ cm}^{-1}$) and NO_2 (sym.) at ($1340\text{--}1365\text{ cm}^{-1}$) was a second evidence.

4.3- NMR Spectra

4.3.1- ^{13}C -NMR of prepared compounds

The spectra of ^{13}C -NMR of these compounds are assigning depending on additivity method using CS-ChemDraw program (Chemical Structure Drawing Standard, 1997). All the values of the peaks positions are shown in Table 3 and Figures 1a-4a. Figure 5 shows proton and carbon atom numbering. ^{13}C -NMR spectra of these compounds support the results of

IR spectra. The appearance of three new peaks in aliphatic region at 39, 35 and 76 ppm, which were attributed to $-\text{C}(\text{O})\text{CH}_2-$, $-\text{CH}-$ and $-\text{CH}_2\text{NO}_2$ respectively (Chemical Structure Drawing Standard, 1997) (Table 3 and Figures 1a-4a), and disappearance of ^{13}C -NMR peaks of $\square$ and $\square$ carbon atoms of olefinic system in chalcones

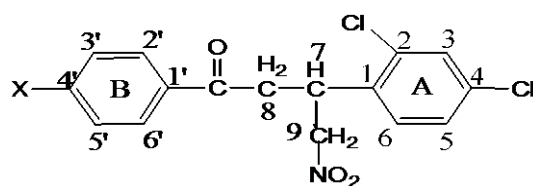


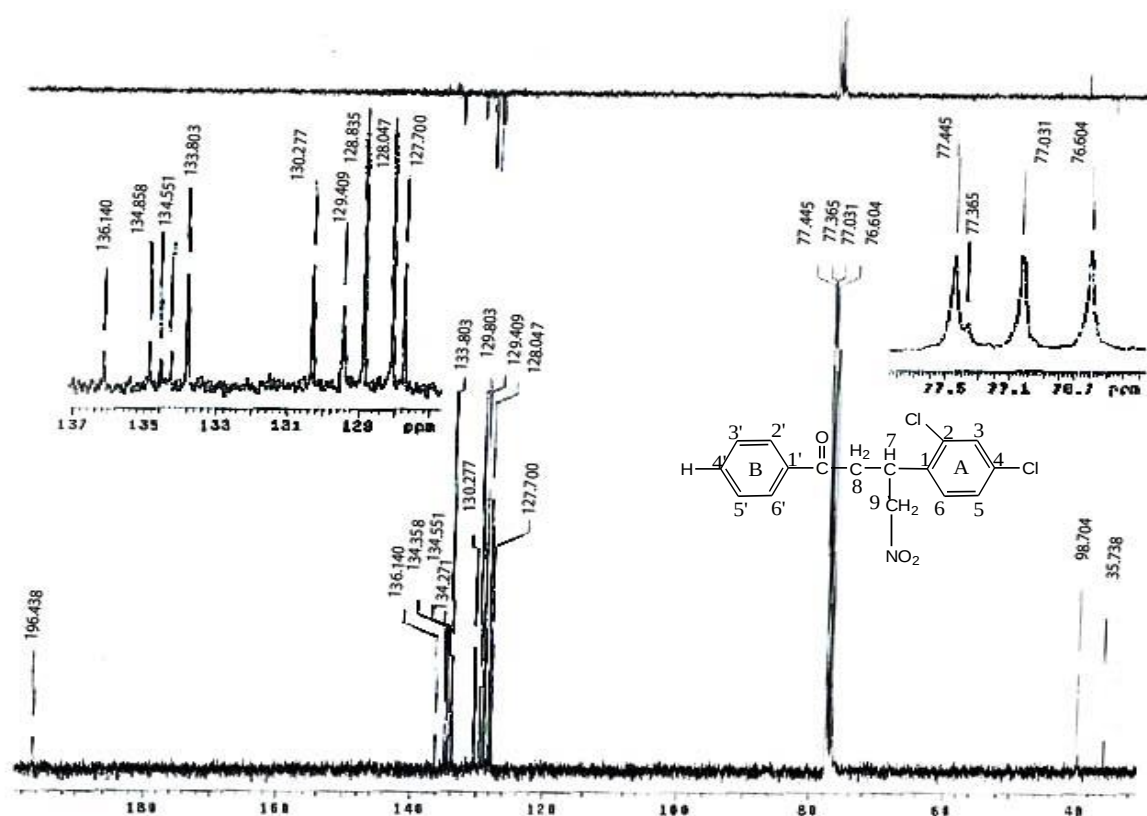
Figure 5

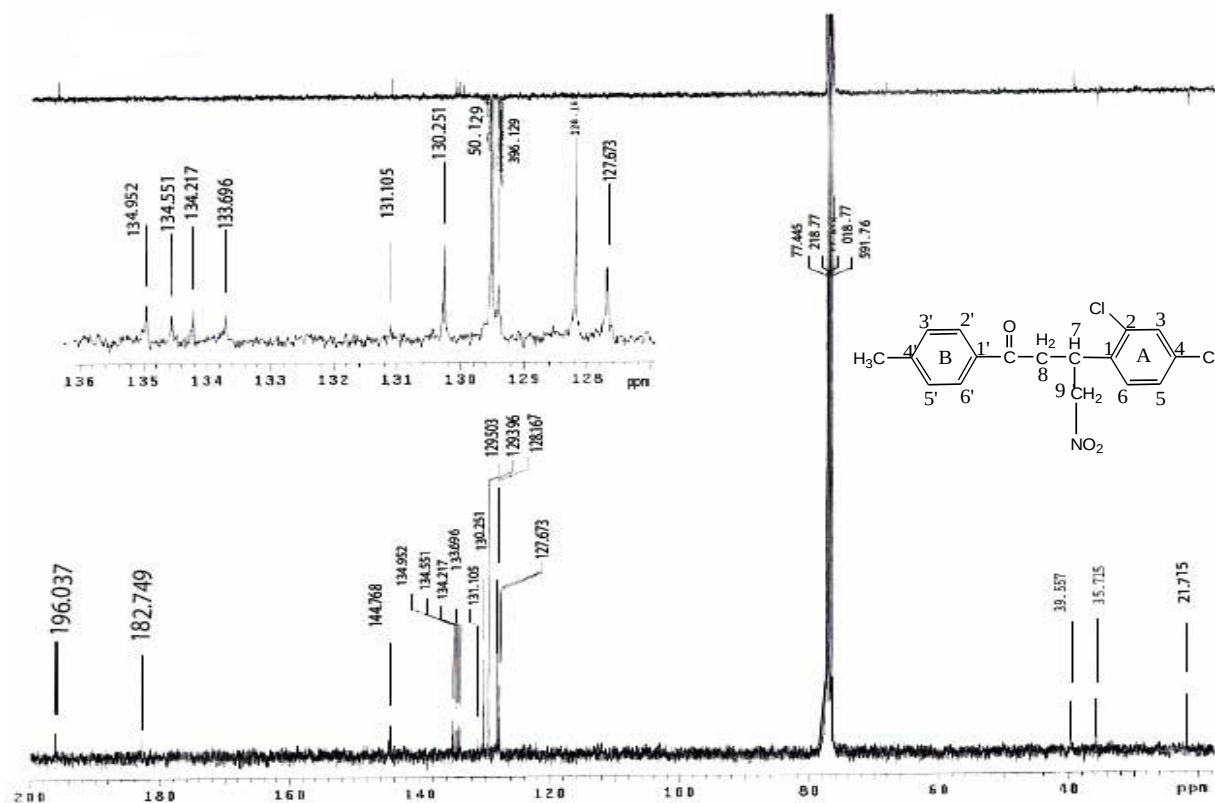
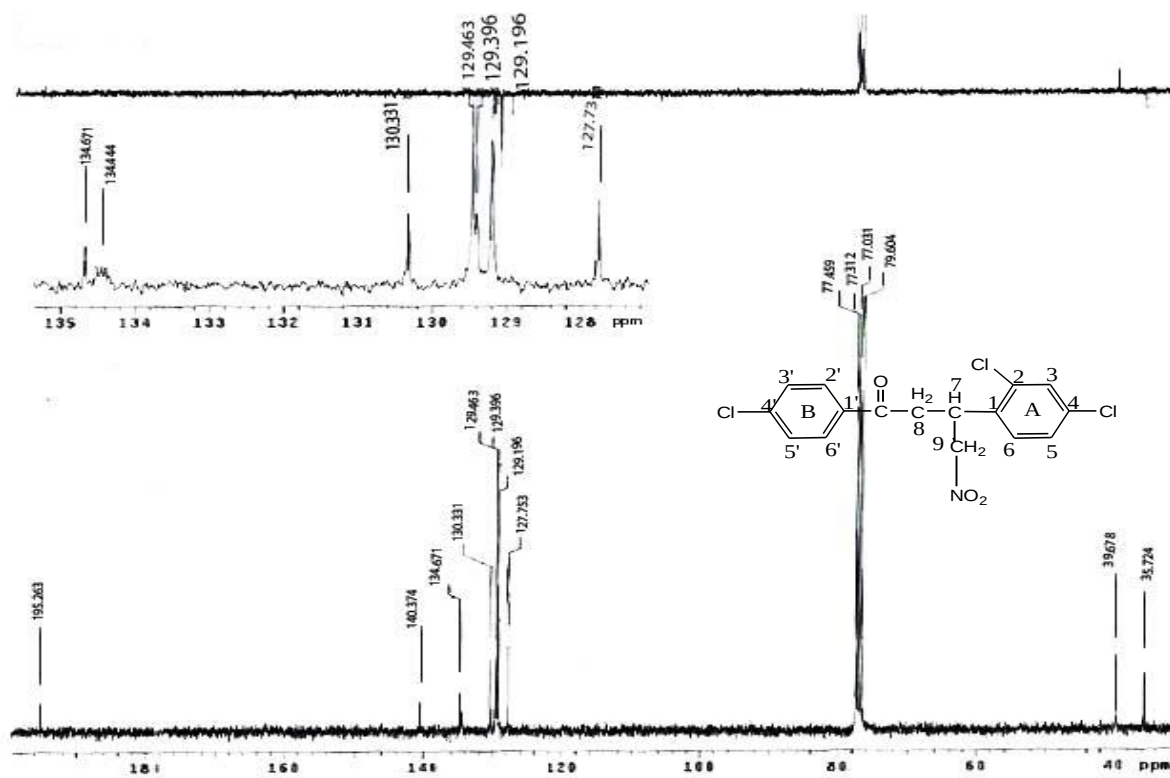
X=H, CH_3 , Cl and F

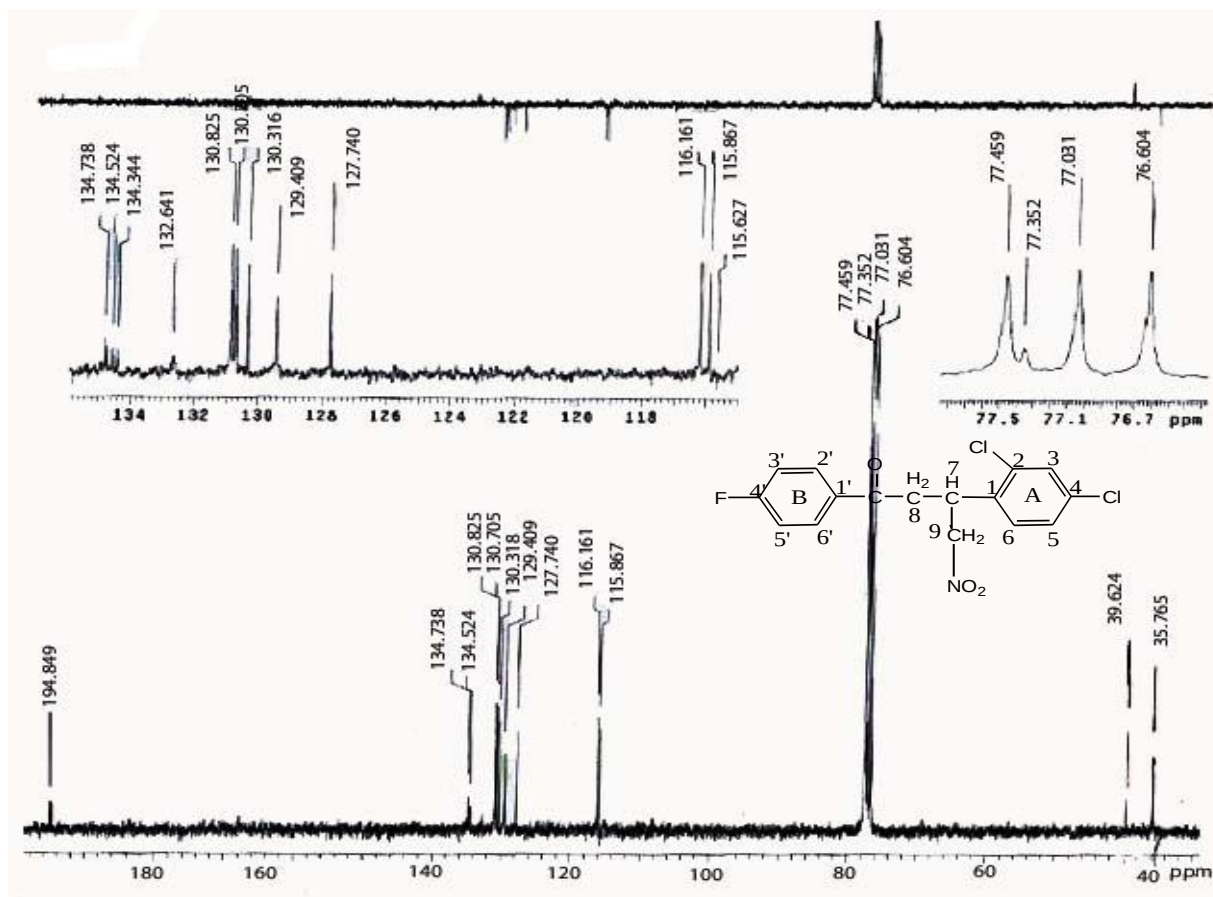
Table 3. Bands of ^{13}C -NMR spectra of new compounds

Comp.	CO	CH ₂ -CO (C8)	-CH- (C7)	CH ₂ -NO ₂ (C9)	C-1 C-1'	C-2 C-2'	C-3 C-3'	C-4 C-4'	C-5 C-5'	C-6 C-6'	others
p-H	196.4	39.7	35.7	76.6	136.1 134.8	134.5 129.4	129.4 128.8	133.8 134.2	127.7 128.8	130.2 129.4	
p-CH ₃	196.0	39.5	35.7	76.5	134.9 134.5	134.2 128.1	130.2 129.5	133.6 144.7	127.6 129.5	131.1 128.1	21.7
p-Cl	195.2	39.6	35.7	76.6	134.6 130.3	134.4 129.4	129.3 129.1	134.4 140.3	127.7 129.1	129.3 129.4	
p-F*	194.8	39.6	35.7	76.6	134.7 132.6	134.5 130.7	129.4 115.9	134.3 166.1	127.7 115.9	130.3 130.7	

* J (CF)1=286.5, J(CF)2=22.16, J(CF)3=9.0

**Figure (1a) ^{13}C -NMR Spectrum of New Unsubstituted Compound**

Figure (2a) ^{13}C -NMR Spectrum of New p-CH₃ Substituted CompoundFigure (3a) ^{13}C -NMR Spectrum of New p-Cl Substituted Compound

Figure (4a) ^{13}C -NMR Spectrum of New P- F Substituted Compound

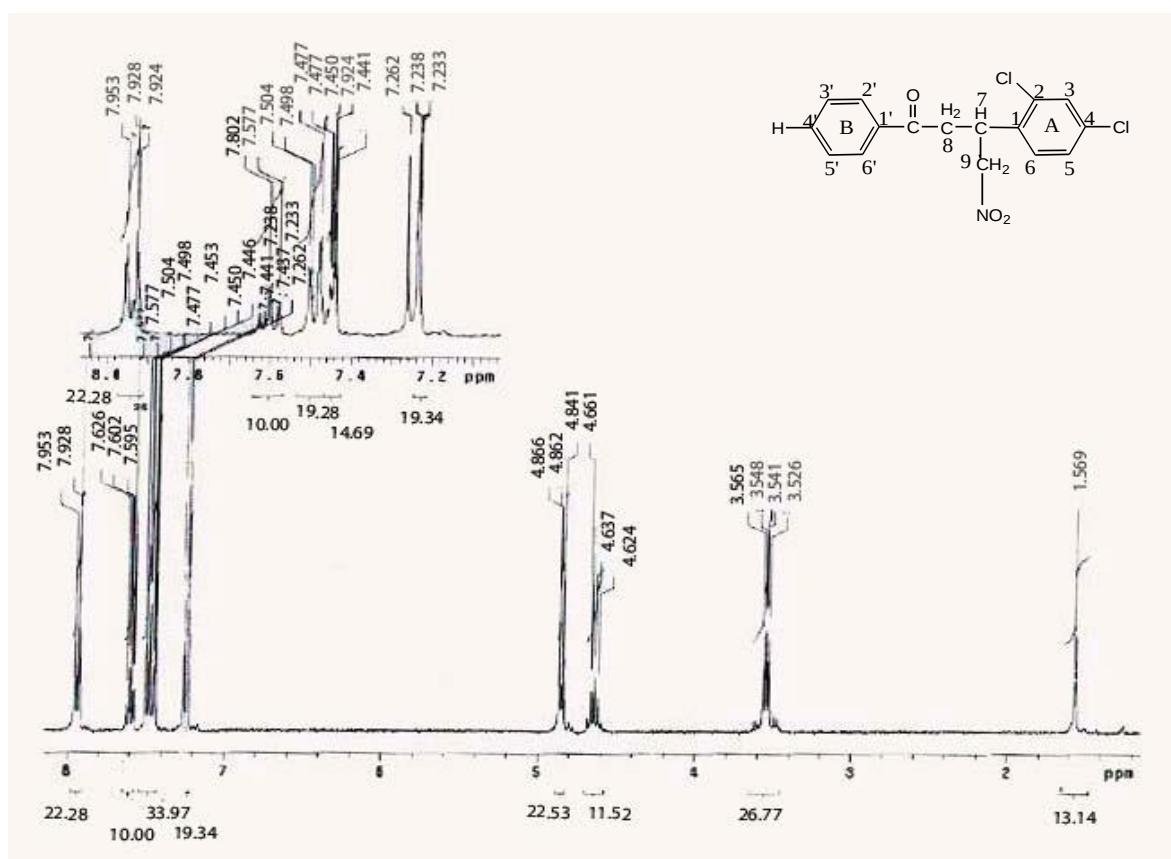
4.3.2- ^1H -NMR of prepared compounds

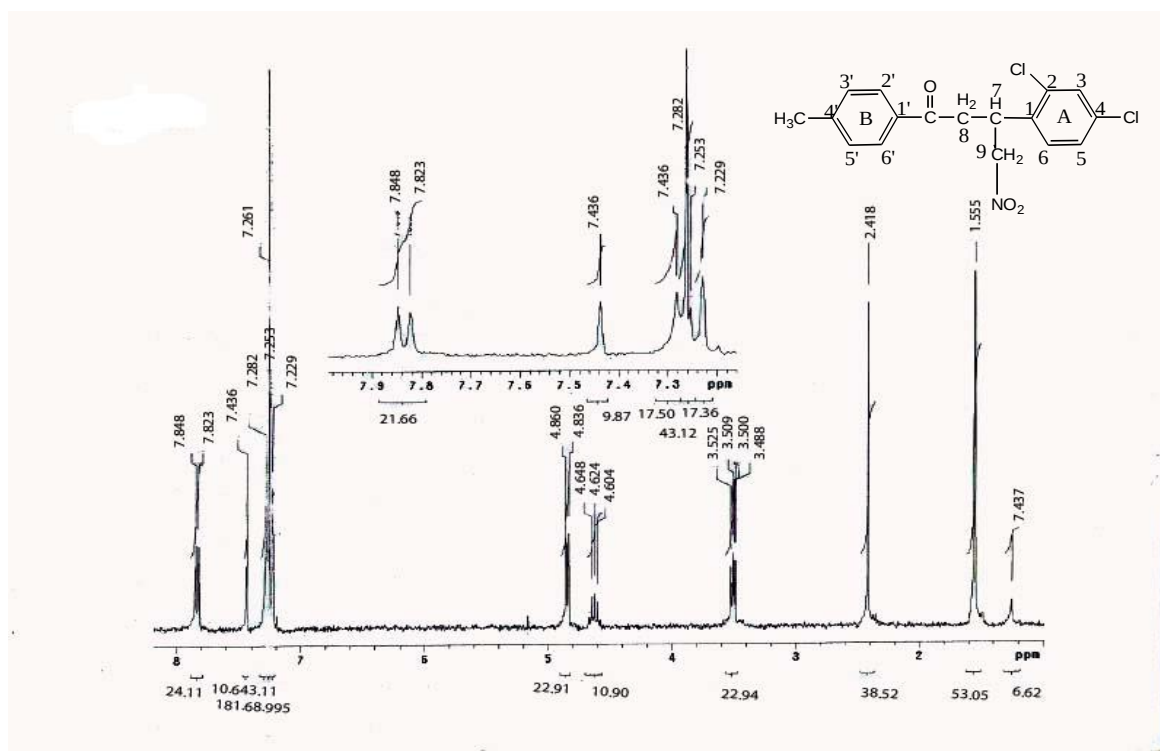
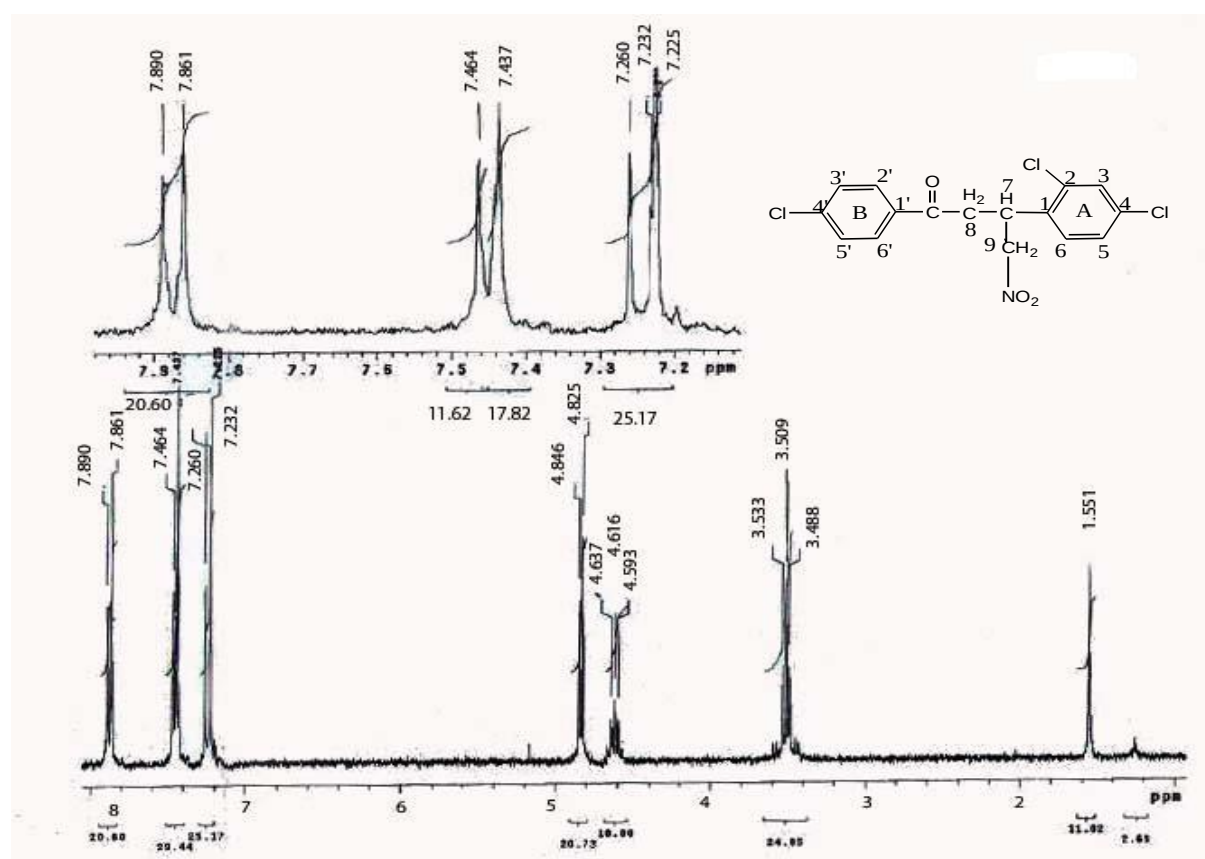
The ^1H -NMR spectra of these compounds showed different spin systems. All the values of the peaks positions are shown in Table 4 and Figures 1b-4b. ^1H -NMR spectra showed different spin systems. The aliphatic region of spectra appeared as multiplet peak at (3.5) ppm and it is attributed to (2H, $-\text{C}(\text{O})-\text{CH}_2-$). Multiplet peaks at (4.6) ppm were attributed to (1H, $-\text{CH}-$). Doublet peaks at (4.8) ppm were attributed to (2H, CH_2NO_2). Protons on ring A in chalcones (starting material) showed an AMX system of splitting (Perjessy, 2011), however in the product

of reacted chalcone appeared as single peak in all compounds at (7.4) ppm this represents (1H, H_3'). Protons H_5' and H_6' appear as separated doublet of doublet peaks, each doublet represent one proton at (7.2-7.4) ppm, almost near protons peaks of ring (B). Protons on ring B showed an AA'BB' and AA'XX' depending on type of substituent at para position. Protons H_2 and H_6 appear at (7.8-7.9) ppm, (Table 4 and Figures 1b-4b). Protons H_3 and H_5 appeared at (7.1-7.2) ppm.

Table 4. Bands of ^1H - NMR spectra of new compounds

Comp.	H3	H5,6	H2',6'	H3',5'	-CH ₂ CO- (multiplet)	-CH- (multiplet)	-CH ₂ NO ₂ (doublet)	J Hz	others
p-H	7.504	7.262- 7.233	7.953- 7.924	7.477- 7.437	3.565- 3.526	4.661-4.614	4.866-4.841	7.5	7.602-7.577
p-CH ₃	7.436	7.233- 7.229	7.848- 7.823	7.282- 7.261	3.525- 3.488	4.648-4.604	4.860-4.836	7.2	2.418
p-Cl	7.464	7.260- 7.225	7.890- 7.861	7.437	3.533- 3.488	4.637-4.583	4.846-4.825	6.3	
p-F	7.443	7.178- 7.119	7.997- 7.948	7.263- 7.231	3.538- 3.484	4.646-4.588	4.856-4.832	7.2	7.149



Figure (2b) ¹H-NMR Spectrum of New p-CH₃ Substituted CompoundFigure (3b) ¹H-NMR Spectrum of New p-Cl Substituted Compound

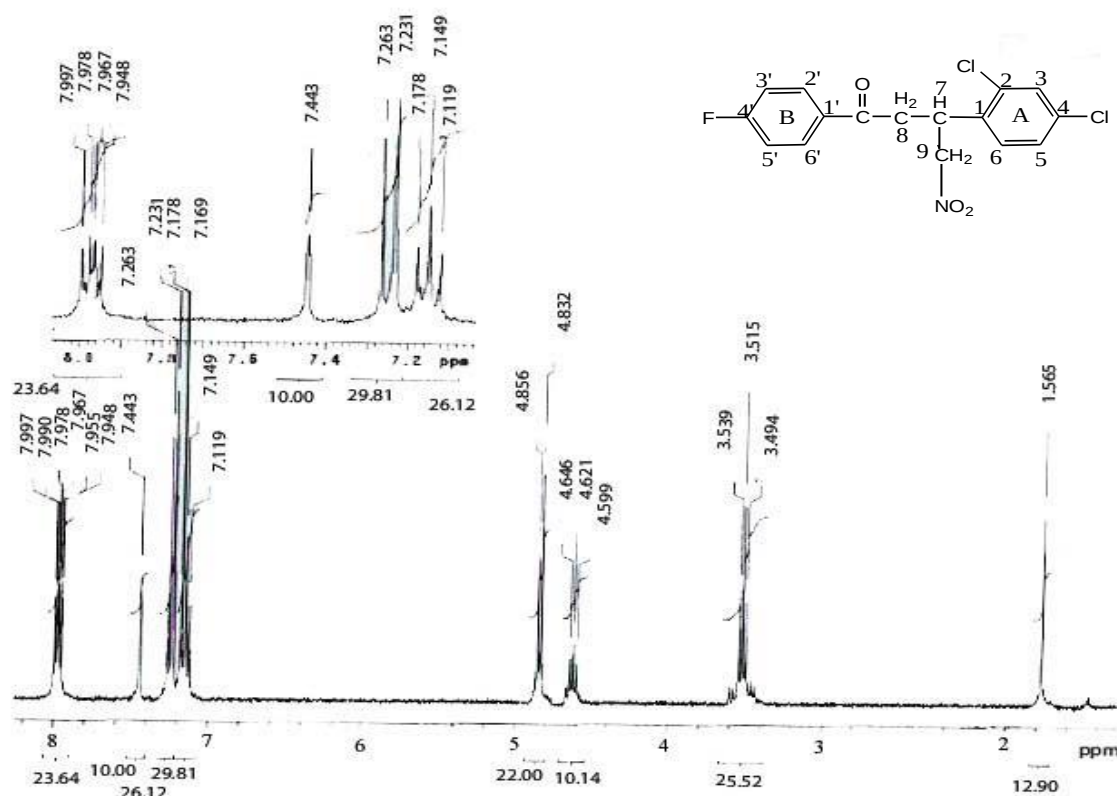


Figure (4b) ¹H-NMR Spectrum of New p-F Substituted Compound

References

Barford L, Kemp K, Hansen M and Kharazmi A, Chalcones from Chinese liquorice inhibit proliferation of T cells and production of cytokines. *Int. Immunopharmacol*, 2002, 2, 545.

Cross A.D. and Jones R. A, *An Introduction to Practical Infrared Spectroscopy*, 3rd. ed. London, 1965.
Chemical Structure Drawing Standard, copyright by Cambridge soft Corporation, publication 1997.

Deshpande A. M, Argade N. P, Natu A. A and Eckman, Synthesis and screening of a combinatorial library of naphthalene substituted chalcones: inhibitors of leukotriene B₄. *Bioorg. Med. Chem*, 1999, 7, 1237 .

Francesco E, Salvatore G, Luigi M and Massimo C, Chemistry and pharmacology of oxyphenylated secondary plant metabolites. *Phytochem*, 2007, 68, 939

George H. Schmid; *Organic Chemistry*, 1996, 765.

Hanoy K. AL-Amood, MSc. Thesis, Synthesis and substituent effect study of new chalcone series, university of basrah, Iraq 1999.

Hsieh H.K, Tsao L.T. and Wang J.P, Synthesis and anti-inflammatory effect of chalcones. *J. Pharm. Pharmacol.*, 2000, 52, 163

Jerry March; *Advanced Organic Chemistry*, 1985, 117.

Khatib S, Nerya O, Musa R, Shmnel M, Tamir S. and Vaya J, Chalcones as potent tyrosinase inhibitors: the importance of a 2,4-substituted resorcinol moiety. *Bioorg. Med. Chem.* 2005,13,433.

Ko H.H, Tsao L.T, YuK L, Liu C.T, Wang J.P and Lin C.N, structure-activity relationship studies on chalcone derivatives: the potent inhibition of chemical mediator's release. *Bioorg. Med. Chem.* 2003,11,105

Liu M, Wilairat P. and Go L M, Antimalarial alkoxylated and hydroxylated chalcones: structure-activity relationship analysis. *J. Med. Chem.* 2001, 44, 4443

Luis R. Domingo, Patricia Pérez and Renato Contreras; *Tetrahedron.* 2004, 60, 6585.

Miranda C L, Stevens J F, Ivanov V, McCall M, Frei B, Deinzer ML, Buhler DR. Antioxidant and prooxidant actions of prenylated and nonprenylated chalcones and flavanones in vitro. *J Agric Food Chem.* 2000; 48: 3876.

Mohamed J, Elarfi and Hussniyia A. Synthesis of some heterocyclic compounds derived from chalcones. *Sci. Revs. Chem. Commun.* 2012; 2(2): 103.

Mokle S S, Sayyed M A, Kothawar, and Chopde. Studies on Synthesis and Antimicrobial Activity of some new Iodochalcones, Flavones and Flavonols. *Int. J. Chem. Sci.* 2004; 2(1): 96.

Murakami S, Muramatsu M, Aihara H and Otomo S Inhibition of gastric H⁺, K(+) -ATPase by the anti-ulcer agent, sofalcone. *Biochem. Pharmacol.* (1991); 42: 1447.

Silver N.L. and Boykin D.W.; *J. Org. Chem.* 1970, 35, 759.

Nielsen SF, Chen M, Theander T G, Kharazmi A and Christensen S B Synthesis of Antiparasitic Licorice Chalcones. *Bioorg. Med. Chem. Lett.* 1995; 5: 449

Onyilagna J. C, Malhotra B, Elder M. and Towers G. H. N, *Can. J. Plant Pathol.* 1997, 19, 133

Perjéssy A, Temkovitz P and. Boykin D. W, Jr. The C=O stretching vibration of aromatic α,β -unsaturated carbonyl and arylfurancarboxyl compounds *J. Org. Chem.* 1979, 44, Issue 9, 2832.

Perjessy, H. K. Al-Amood, G.F. Fadhil and N. Pronayova; Substituent effect investigation of 3-(2,4-dichlorophenyl)-1-(4'-X-phenyl)-2-propen-1-one. Part 1. Correlation analysis of ¹³C-NMR chemical shifts *J. phys. Org. Chem.* 2011, 24(2), 140.

Robert T. Morrison and Robert N. Boyd; *Organic Chemistry* 3rd, 1978, 865.

Satyanarayana M, Priti Tiwari, Tripathi K, Srivastava A K and Ram Pratap Synthesis and antihyperglycemic activity of chalcone based aryloxypropanolamines *Bioorg. Med. Chem.* 2004, 12, 883

Severi F, Benvenuti S, Costantino L, Vampa G, Melegari M and Antolini L Synthesis and activity of a new series of chalcones as aldose reductase inhibitors. *Eur. J. Med. Chem.* 1998; 33: 859.

Siva Kumar P M, Geetha Babu S K and Mukesh D, QSAR studies on chalcones and flavonoids as anti-tuberculosis agents using genetic function approximation (GFA) method. *Chem. Pharm. Bull.* 2007, 55(1), 44 .

Viana GS, Bandeira MA and Matos F Analgesic and antiinflammatory effects of chalcones isolated from *Myracrodruon*

urundeuva Allemao. J. Phytomedicine
2003; 10: 189.

antiplatelet activity of trihydroxychalcone
derivatives. Bioorg. Med. Chem. Lett.
2005; 15: 5027.

Zhao LM, Jin HS, Sun LP, Piao HR and
Quan ZS Synthesis and evaluation of

تحضير مركبات جديدة من 3-(4,2-ثنائي كلوروفينيل)-1-(4-X-فينيل)-3-نايترومثيل بروبان-1-اون

هانوي كمال العامود
قسم الكيمياء / كلية العلوم / جامعة البصرة

E-mail:- hanoy9999@yahoo.co.uk

الملخص

حضرت أربع مركبات جديدة وهي 3-(4,2-ثنائي كلوروفينيل)-1-(4-X-فينيل)-3-نايترومثيل بروبان-1-اون حيث ان $F, Cl, CH_3, H = X$ من خلال الكلة 3-(4,2-ثنائي كلوروفينيل)-1-(4-X-فينيل)-2-بروبين-1-اون. أظهرت نتائج التحليل العنصري الدقيق توافقاً جيداً بين النسب المئوية للعناصر (C,H,N) المقاسة عملياً والمحسوبة نظرياً. استخدمت كلاً من مطيافية الأشعة تحت الحمراء ومطيافية الرنين النووي المغناطيسي لغرض تشخيص المركبات المحضرة.