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Synthesis and spectrometric study of some nucleophilic reactions of the antiepileptic molecule; 5,5-diphenyl imidazolidine-2,4-dione.

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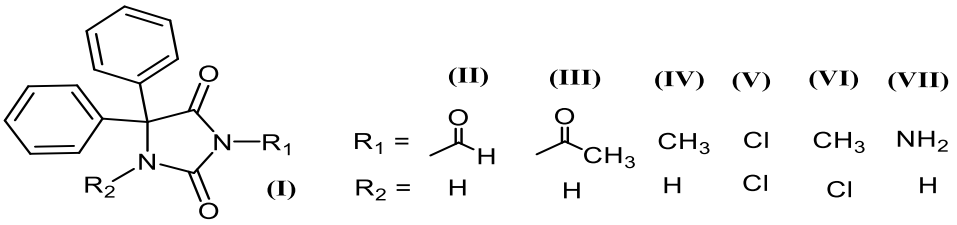
ABSTRACT

New reaction routs were performed for the compound 5,5-diphenyl 2,4-imidazolidinedione (**I**) to give derivatives (**II** – **VII**). These reactions include acylation, halogenation, reduction, and nucleophilic substitutions.



Most of the derivatives showed variable chemical reactivities and thermal stability, and the N_1 and N_3 disubstituted analogue were found much less stable, and hydrolyzes easily in the reaction medium. According to ^1H and ^{13}C NMR measurement's, 1,3-Dichloro-5,5-diphenyl imidazolidine-2,4-dione **(V)** was found to chlorinate the methyl group of the solvent DMSO-d6. Sodium hydroxide consumption analysis was established to reveal the molecularity against NaOH, by following acid-base volumetric method.

1. Introduction:

Almost eighty six decades has been passed, since Putnam discovery, that, commonly named as phenytoin or dilantin (IUPAC, 5,5-diphenyl imidazolidine-2,4-dione **(I)**, is the drug

of choice for the treatment of generalized tonic-clonic seizures (so-called grand mal epilepsy) and focal motor seizures [1-3]. Phenytoin **(I)** was first synthesized in 1908 by Biltz [1], but its anti-epileptic activity (AEA) was not discovered until 1938 by Putnam [2]. Phenytoin was not synthesized again until the 1920`s, and shelved as "inactive" compound [1–4], their analogues are key compounds with variable biologically and medicinally active compounds.

Among the best-used syntheses include; Biltz synthesis, the Read synthesis and the Bucherer-Bergs synthesis [1, 5-10]. N_3-alkylation of 5,5-diphenyl-imidazolidine-2,4-dione is an overall applied reaction to modify the core scaffold and so the properties of the resulting materials[11].

Many phenytoin **(I)** derivatives were synthesized and reported to possess a wide range of pharmacological activities such as anticonvulsants [11-13]. The anticonvulsant activity of hydantoin derivatives is mediated by their interaction with and inhibition of the brain Na^+ channels [14]. Phenytoin medicinal activities are so wide to include antitumor [13, 15-16], antimicrobial activity [17-18], structure-activity relationships were evaluated as antiproliferative activities against HCT-116 human

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colon carcinoma cells were evaluated, as well as their in vitro antibacterial activities against several bacteria [18]. Antioxidant effects of varying concentration of twelve 3-substituted-5,5-diphenylhydantoins on human colon cancer [19], antiarrhythmic [20], HIV protease inhibitors [21], and as antiviral agents [22].

5,5-Diphenyl-imidazolidine-2,4-dione **(I)** and its derivatives is highly suited for use as pharmaceuticals for having long shelf life but easy decomposition in the body is desirable [10, 23]. In spite of stability to much drastic chemical and thermal condition, it can be hydrolyzed more easily in biological systems in the presence of hydantoinase enzymes. This means that this compound this molecule can be easily undergoes nucleophilic substitution reaction, and hence mono-alkylated at the imide position N_3-H is an overall applied reaction to modify the core scaffold and so the properties of the resulting materials [24]. Water soluble prodrugs of 5,5-diphenyl-imidazolidine-2,4-dione were also determined by attaching appropriate side chains at the imidic group N_3-H [25-26].

The present work reports several improvements and investigation of new reliable route to prepare derivatives of 5,5-diphenyl imidazolidine-2,4-dione **(I)** as a building block by using acylation, halogenation, reduction, and nucleophilic substitution reactions.

2. Experimental:

2.1 Materials: All the solvents and reagents were used along this study without further purification, ethanol, hydrochloric acid, ammonia solution from BDH, UK; Formic acid from THOMAS BAKER, India; Sodium hydroxide from Fluka-France; Dimethyl sulphate from MERCK-Schuchardt, Germany; Dimethyl sulfoxide (DMSO-d_6), Chloroform ($CDCl_3$) from Aldrich, Germany.

2.2 Instruments: Melting points of synthesized compounds were recorded in open capillary tubes using model SMP1 from UK melting point apparatus in the University of Technology. UV-visible spectra were recorded by using model 1800, Shimadzu spectrophotometer, Japan. All the spectra were recorded by using 10.0 mm quartz cuvette, within the range 190 - 1100 nm at the University of Technology. The infrared absorption spectra were recorded by using an Attenuated Total Reflectance (ATR) spectrometer, Bruker model VERTEX 70, Germany, in the range 400-4000 cm^{-1} after the atmospheric compensation, averaging, and baseline correction applications, in the Ministry of Science and Technology. The elemental analysis were measured by EuroEA model 3000/Italy elemental Analyzer for C, H, S, and N in Abn alhaitham collage Baghdad University. ^{1}H NMR ,^{13}C NMR spectra were recorded by using Bruker spectrometer model Ultra-Shield at 300.15 MHz using deuterated dimethyl sulphoxide (DMSO-d_6) and chloroform ($CDCl_3$) as a solvent for samples with TMS as internal reference at 298 K, in Al al-Bayt university. Data for ^{1}H NMR spectra were reported as follows: chemical shift, multiplicity (s = singlet, b = broad). Mass spectra were recorded by using GC-MS model GCMS-QP2010 SE from Shimadzu, Japan, in the Ministry of Science and Technology.

2.3 Methods:

2.3.1 ***5,5-Diphenyl imidazolidine-2,4-dione (I):*** 5,5-Diphenyl imidazolidine-2,4-dione was prepared according to the modified procedure

of the literature. m.p. was found to be 294-296°C (literature 293°C [20]).

2.3.2 ***3-Acetyl 5,5-diphenyl imidazolidine-2,4-dione (II):*** 5,5-diphenyl 2,4-imidazolidinedione **(I)** (2.52 g, 10.0 mmol) was treated with amixture acetyl chloride (0.9 g, 0.82 mL, 11 mmol), and pyridine (0.87 g, 0.85 mL, 11 mmol) in 50 mL acetone, and the mixture was refluxed for 5.0 hours. The solvent was evaporated to the third of its volume, cooled to room temperature and then treated with 25 mL of distilled water. The precipitated solid was filtered off through filter paper, and washed with ethanol (2 mL × 3). The filter paper was dried with its content in well ventilated cabinet for 24 hour, then in an oven at 70ºC for 1 hour. Product of the title compound was recrystallized from minimum amount of 95 % ethanol (yield 1.41 g, 56.0 %, m.p. 221-223 ºC (215-217 ºC lit. [1]).

2.3.3 ***2,5-Dioxo-4,4-diphenylimidazolidine-1-carbaldehyde (III):*** 5,5-Diphenyl 2,4-imidazolidine -dione (2.52 g, 10.0 mmol) was mixed with formic acid (25 mL), and refluxed for 7.0 hours. The solvent was evaporated to dryness, and the product of the title compound was recrystallized from minimum amount of 95% ethanol (yield 1.57 g, 56.0 %, m.p. 285-286ºC).

2.3.4 ***3-Methyl-5,5-diphenyl imidazolidine-2,4-dione (IV):*** 5,5-diphenyl 2,4-imidazolidinedione (2.52 g, 10.0 mmol) was dissolved in a solution of sodium hydroxide (0.44 g, 11.0 mmol) in 40 mL distilled water. The clear solution of the mixture was slowly treated with dimethyl sulfate ($(CH_3O)_2SO_2$) (4.66 g, 3.5 mL, 11.0 mmol), and stirred for 5 hours. The precipitated solid was filtered through filter paper, and washed with distilled water (5 mL × 3). The filter paper was dried with its content in well ventilated cabinet for 24 hour, then in an oven at 70ºC for 3 hour. Product of the title compound was recrystallized from minimum amount of ethanol (2.38 g, 92 % yield, 155-157 ºC, lit. 154ºC [1]).

2.3.5 ***1,3-Dichloro-5,5-diphenyl imidazolidine-2,4-dione (V):*** 5,5-diphenyl 2,4-imidazolidine-dione **(I)** (2.52 g, 10.0 mmol) was treated with a solution of 10 % sodium hypochlorite (25 mL), and the mixture was stirred for 1 hour [27]. The mixture was treated with a solution of 1N hydrochloric acid until the pH of the solution becomes within the range of 7.0 - 7.5. The precipitated solid was filtered through filter paper, and washed with ethanol (2 mL × 3). The filter paper was dried with its content in well ventilated cabinet for 24 hour, then in oven at 70ºC for 1 hour. Product of the title compound was recrystallized from minimum amount of boiling water (2.89 g, 90 % yield, m.p. 129-131ºC).

2.3.6 ***1-Chloro-3-methyl-5,5-diphenylimidazolidine-2,4-dione (VI):*** 3-Methyl-5,5-diphenyl imidazol idine-2,4-dione (2.663 g, 10.0 mmol) was treated with a solution of 10 % sodium hypochlorite (10 mL), and the mixture was stirred for 5 hour [27]. The mixture was treated with a solution of 1N hydrochloric acid until the pH of the solution become within the range of 7.0 – 7.5. The precipitated solid was filtered through filter paper, and the precipitate was washed with ethanol (2 mL × 3). Product of the title compound was recrystallized from minimum amount of ethanol and water, filtered and the filter paper with its content was dried in well

ventilated cabinet for 24 hour, then in an oven at 70ºC for 3 hour. (2.71 g, 90 % yield, 165-167ºC).

2.3.7 ***3-Amino-5,5-diphenylimidazolidine-2,4-dione (VII):*** 1,3-Dichloro-5,5-diphenyl imidazolidine-2,4-dione (3.23 g, 10.0 mmol) was treated with concentrated ammonia solution (20 mL), and the mixture was refluxed for 3 hour. The mixture was treated with a solution of 1N hydrochloric acid until the pH of the solution become within the range of 7.0 - 7.5. The precipitated solid was filtered through filter paper, and washed with distilled water (2 mL × 3). The filter paper was dried with its content in well.

2.3.8 ventilated cabinet for 24 hour, then in oven at 70ºC for 1 hour. Product of the title compound was recrystallized from minimum amount of ethanol (2.27 g, 85 % yield, 252-254ºC (d), lit. 190°C [28, 29]). It was observed that the melting point of this product was much higher than that reported in the literature [28-29]. As a matter of fact the introduction of -NH_2 group should increase the melting point and not to reduce it by 100°C. The measured value in this work is more acceptable. Although the literature did the X-ray for this compound, but no spectrometric datum were provided, probably due the poor yield [27-28].

2.4 NaOH consumption method:

Some of the prepared derivatives of 5,5-diphenyl imidazolidine-2,4-dione react with hot sodium hydroxide solution, through hydrolysis, nucleophilic substitutions , and other reactions, in which it consume NaOH in 1:1 and 1:2 molecularity ratio. This reaction can be used to get some useful information about their molecular structure. The procedure consists of boiling ~ 100 mg of the derivative in 0.1 N NaOH (10.00 mL) for 30 minutes. The excess NaOH was back titrated with 0.05 N HCl. The difference between the volume of HCl solution used for the blank and the derivatives were equivalent to the consumption of NaOH in the reaction. The following relation will reveal the molecularity of the reaction:

Total NaOH mEq = 10.00 mL × 0.1 N = 1.00 mEq …… (1)

The consumed NaOH = Total mEq of NaOH – HCl mEq

= 1.00 mEq of NaOH – [0.05 N HCl × Volume(mL)] … (2)

Molecularity = (mEq by titration)/(mEq by weight) … (3)

3. Results and discussion:

Many derivatives were prepared for 5,5-diphenyl 2,4-imidazolidinedione **(I)**, some of them were prepared earlier by other workers, but by following new synthetic route, reactions or reagents. The physical, spectroscopic and chemical properties of these products were presented in **Tables 1- 4**. 5,5-Diphenyl imidazolidine-2,4-dione **(I)** was prepared according to literature improved procedure [1, 20]. The downstream preparations of these derivatives **(I – VII)** were presented in **Fig.1**, and the detailed preparation procedures were found in the experimental part. 5,5-Diphenyl imidazolidine-2,4-dione **(I)** react with acetyl chloride in acetone to give compound (**II**). It is worth mentioning that this compound was prepared by using another reagent viz., chloroformate esters to introduce carbalkoxy groups into a variety of chemical compounds [1].

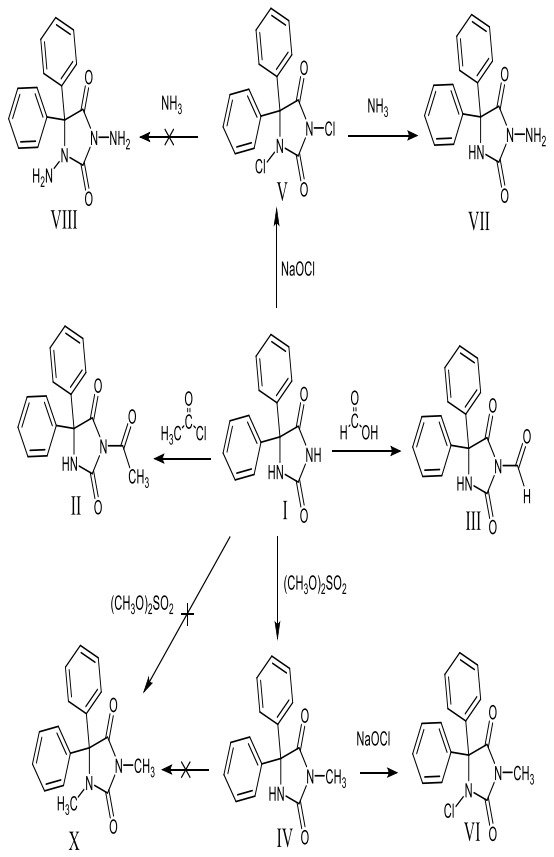

Figure 1: The downstream reaction and products mentioned in this work 5,5-diphenyl- 5,5-diphenylimidazolidine-2,4-dione derivatives **(II – VII).**

Table 1: The physical and chemical properties of 5,5-diphenyl- 5,5-diphenylimidazolidine-2,4-dione derivatives **(II – VII)**.

No	Compounds	Formula	Mol. Wt.	UV-visible		M. p °C)	Color	Solvent	Yield %
				λ (nm)	Є ($Mol^{-1}L.cm^{-1}$)				
I	5,5-diphenyl imidazolidine-2,4-dione	$C_{15}H_{12}N_2O_2$	252.27	214.46	11200	294-296	Colorless	THF, Ac*	60
II	3-Acetyl-5,5-diphenyl imidazolidine-2,4-dione	$C_{17}H_{14}N_2O_3$	294.31	217.12	14047.62	221-223	White	THF, Ac	56
III	2,5-Dioxo-4,4-diphenylimidazolidine-1-carbaldehyde	$C_{16}H_{12}N_2O_3$	280.28	214.45	8448.28	285-286	Colorless	THF, Ac	56
IV	3-Methyl-5,5-diphenyl imidazolidine-2,4-dione	$C_{16}H_{14}N_2O_2$	266.30	214.46	9860.87	155-157	White	THF, Ac	92
V	1,3-Dichloro-5,5-diphenyl imidazolidine-2,4-dione	$C_{15}H_{10}Cl_2N_2O_2$	321.16	215.74	10665	129-131	White	THF, $CHCl_3$	90
VI	1-Chloro-3-methyl-5,5-diphenyl-imidazolidine-2,4-dione	$C_{16}H_{13}ClN_2O_2$	300.74	213.17	8309.52	165-167	White	THF, $CHCl_3$	90
VII	3-Amino-5,5-diphenyl imidazolidine-2,4-dione	$C_{15}H_{13}N_3O_2$	267.29	217.03	10528.57	252-254	Cream	THF, Ac	85

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Table 2: Elemental analysis of the record derivatives of 3-substituted 5,5-diphenyl imidazolidine-2,4-dione.

#	Formula	Mol. Wt.	C %		H %		N %	
			Found	Calc.	Found	Calc.	Found	Calc.
I	$C_{15}H_{12}N_2O_2$	252.27	71.38	71.42	4.82	4.79	11.21	11.10
II	$C_{17}H_{14}N_2O_3$	294.31	69.35	69.38	4.81	4.79	9.49	9.52
III	$C_{16}H_{12}N_2O_3$	280.28	-	68.56	-	4.32	-	9.99
IV	$C_{16}H_{14}N_2O_2$	266.30	72.19	72.17	5.36	5.30	10.49	10.52
V	$C_{15}H_{10}Cl_2N_2O_2$	321.16	56.08	56.10	3.11	3.14	8.74	8.72
VI	$C_{16}H_{13}ClN_2O_2$	300.74	63.93	63.90	4.40	4.36	9.28	9.31
VII	$C_{15}H_{13}N_3O_3$	267.29	63.57	63.60	4.61	4.63	14.89	14.83

Table 3: The ATR-IR absorption bands of the major functional groups for 3-substituted 5,5-diphenyl imidazolidine-2,4-dione.

#	Formula	υ_{N-H} (cm^{-1})	υ_{C-H} (cm^{-1}) Aromatic	υ_{C-H} (cm^{-1}) Aliphatic	$\upsilon_{C=O}$ (cm^{-1})	$\upsilon_{C=C-C}$ (cm^{-1}) Aromatic	Others ands (cm^{-1})
I	$C_{15}H_{12}N_2O_2$	3266.08 , 3199.24	3070.16	-	1770.64 , 1738.39 , 1715.02	1594.14 , 1494.14 , 1448.87	-
II	$C_{17}H_{14}N_2O_3$	3269.13 , 3203.16	3070.31	2925.31	1771.76 , 1739.32	1595.40 , 1493.90 , 1448.89	υ_{CH3}: 1286.61
III	$C_{16}H_{12}N_2O_3$	3268.77, 3203.68	3071.14	2798.46 , 2708.66	1771.36 , 1740.87 , 1715.87	1597.69, 1494.25, 1448.85	-
IV	$C_{16}H_{14}N_2O_2$	3283.49	3191.05	3058.17 , 2810.19	1771.55, 1698.12	1596.50 , 1492.96	υ_{CH3}: 1192.81
V	$C_{15}H_{10}Cl_2N_2O_2$	-	3064.48	-	1797.81 , 1745.99	1493.47 , 1445.23	υ_{Cl} : 868.98
VI	$C_{16}H_{13}ClN_2O_2$	-	3062.15	-	1783.37 , 1749.40 , 1720.29	1585.24, 1482.61	υ_{Cl} : 875.07 υ_{CH3}: 1283.42
VII	$C_{15}H_{13}N_3O_3$	3270.48, 3202.78	3071.01	-	1771.71 , 1740.27 , 1716.92	1597.44, 1493.94	-

* Ac = Acetone

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Table.4 : The Sodium hydroxide consumption analysis of the reactions products of 5,5-diphenylimidazolidine-2,4-dione **(I – VII)**.

No	Compounds	M. wt	mEq of Compounds	0.05 N of HCl (mL)	Consumed 0.1N NaOH (mL)	mEq of consumed 0.1 N NaOH	Compound mEq (Determined)
I	5,5-diphenyl imidazolidine-2,4-dione	252.27	0.3965	20.00	0.00	0.000	1: 0.0
II	3-Acetyl-5,5-diphenyl imidazolidine-2,4-dione	294.31	0.3398	12.95	3.52	0.352	1:1.03
III	2,5-Dioxo-4,4-diphenylimidazolidine-1-carbaldehyde	280.28	0.3568	13.60	3.21	0.321	1:0.90
IV	3-Methyl-5,5-diphenyl imidazolidine-2,4-dione	266.30	0.3755	13.75	3.12	0.312	1:0.84
V	1,3-Dichloro-5,5-diphenyl imidazolidine-2,4-dione	321.16	0.3114	7.40	6.30	0.630	1:2.02
VI	1-Chloro-3-methyl-5,5-diphenyl-imidazolidine-2,4-dione	300.74	0.3325	7.95	6.03	0.603	1:1.81
VII	3-Amino-5,5-diphenyl imidazolidine-2,4-dione	267.29	0.3741	20.00	0.00	0.000	1:0.0

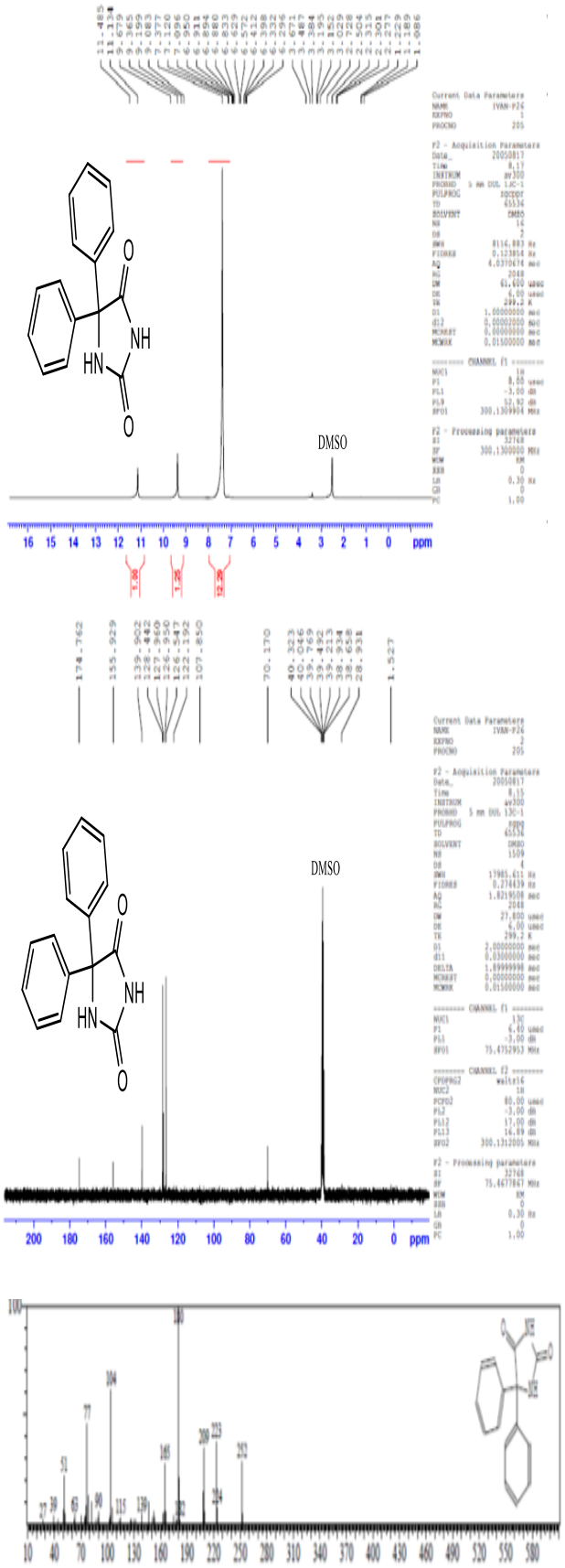

Figure.2 : ^{1}H, ^{13}C NMR, and mass spectrum of 5,5-diphenyl imidazolidine-2,4-dione **(I)**.

From ^{1}H, ^{13}C NMR and MS, there is many distinctive features concerning the formation of compound (**I**) which can be summarized as follows; ^{1}H NMR (DMSO-d_6) showed signals at δ: 11.13 (s, 1H, N_3-H) ppm, 9.36 ppm (s, 1H, N_1-H) , and 7.09-7.37 ppm (b, 10H, Ar-H); ^{13}C NMR (DMSO-d_6) showed signals at δ: 174.762 ppm (C_4=O) ppm, 155.929 ppm (C_2=O), 139.902 ppm (i-Ar), 128.442 ppm (m-Ar), 127.960 ppm (o-Ar), 126.547 (p-Ar), 70.170 ppm and the Mass spectrum (MS) showed signals at m/z (% relative intensity) 252 for M^+ (30 %), 223 (35 %), 209 (333) 180 (100), 165 (25 %), 139 (5 %) 104 (60 %), and 77 (50 %).

In ^{1}H and ^{13}C NMR there are many distinctive features concerning the formation of compound (**II**) which can be summarized by the following; The disappearance of N_3-H signal in ^{1}H NMR (DMSO-d_6) signal at 11.13 ppm, as well as the appearance of new signal for the methyl group of the acetyl group at δ: 2.014 (s, 3H, C-H) ppm at N_3 position; and The appearance of new signals ^{13}C NMR (DMSO-d_6) at δ: 22.648 (CH_3), and 197.57 (N_3-C=O) ppm are related to the new acetyl group.

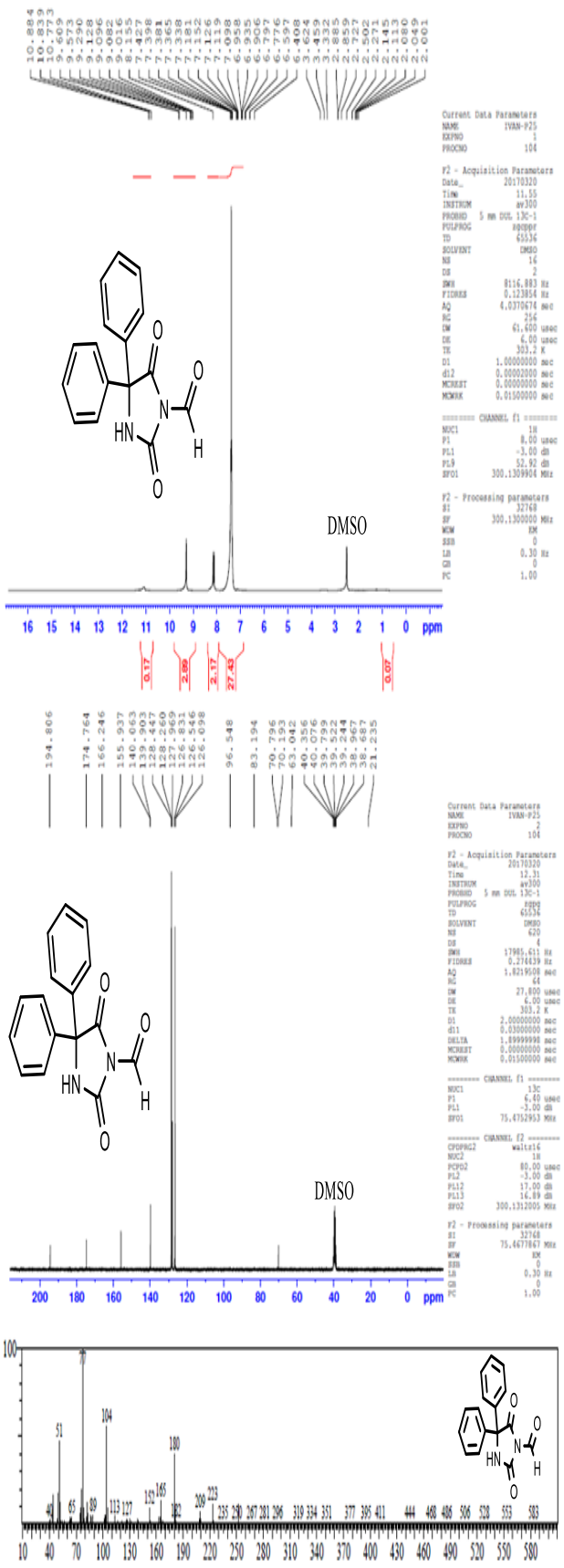

Figure.4 : ^{1}H, ^{13}C NMR, and MS spectra of 2,5-Dioxo-4,4-diphenylimidazolidine-1-carbaldehyde **(III)**.

This compound (**III**) was identified by ^{1}H and ^{13}C NMR, ATR-IR, UV-visible and MS spectrometry, and many distinctive features concerning the formation of this compound were given in the following: the disappearance of N_1-H signal in ^{1}H NMR at 11.13 ppm, is an indication for the formylation at N_1 position. The appearance of new signal for the aldehyde proton at 8.155 (s, 1H, C-H) ppm is another indication for the formylation reaction at N_3 position.; The appearance of new signals at ^{13}C NMR at 194.8 ppm (-N_1-C=O) ppm which stand for the formyl carbon; MS analysis showed the difference in the defragmentation spectrum from that of the parent molecule viz. 5,5-diphenyl imidazolidine-2,4-dione. Very small signal of the parent ion with m/z appeared at 281 amu, as well as a different base peak at 77 amu

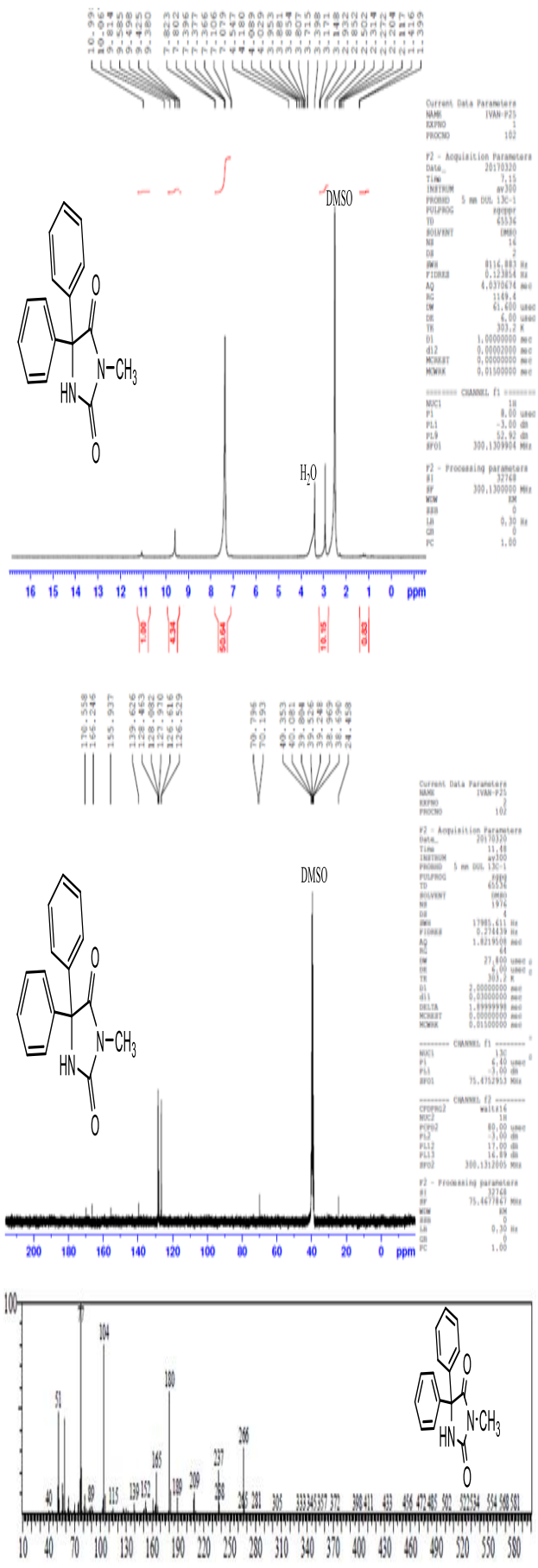

Figure.5 : ^{1}H, ^{13}C NMR, and MS spectra of 3-methyl-5,5-diphenyl imidazolidine-2,4-dione **(IV)**.

The compound (**IV**) was identified by the techniques ^{1}H and ^{13}C NMR, ATR-FT, UV-visible and MS spectrometry, and many distinctive features concerning the formation of this compound (**IV**) were obtained in the following; the disappearance of N_3-H signal in ^{1}H NMR signal at δ: 11.13 ppm, as well as the appearance of new signal at δ: 2.85 (s, 3H, CH_3) ppm are related to the methyl group proton at N_3 position. the appearance of new signals at ^{13}C NMR at δ: 24.46 ppm stand for the carbon of methyl group. MS analysis showed difference in the defragmentation spectrum from that of the parent molecule viz. 5,5-diphenyl imidazolidine-2,4- dione. Very small signal of the parent ion with m/z appeared at 266 m/z, as well as a different base peak at 77 m/z.

The compound (**V**) was identified by the available techniques; ^{1}H and ^{13}C NMR, ATR-FT, UV-visible and MS spectrometry, and many distinctive features concerning the formation of this compound were obtained; the disappearance of N_3-H and N_1-H signals in ^{1}H NMR, as well as the phenyl proton signals is appeared at δ: 7.459-7.258 ppm., The aromatic carbon atoms ^{13}C NMR signals appeared at signals similar to that of the parent molecule (**I**). The rest of the molecule showed similar shift by 2 ppm compared with the parent molecule (**I**). The ^{13}C NMR signals of $CDCl_3$ appeared in 76.585 ppm and that of $CHCl_3$ at 77.008 ppm.

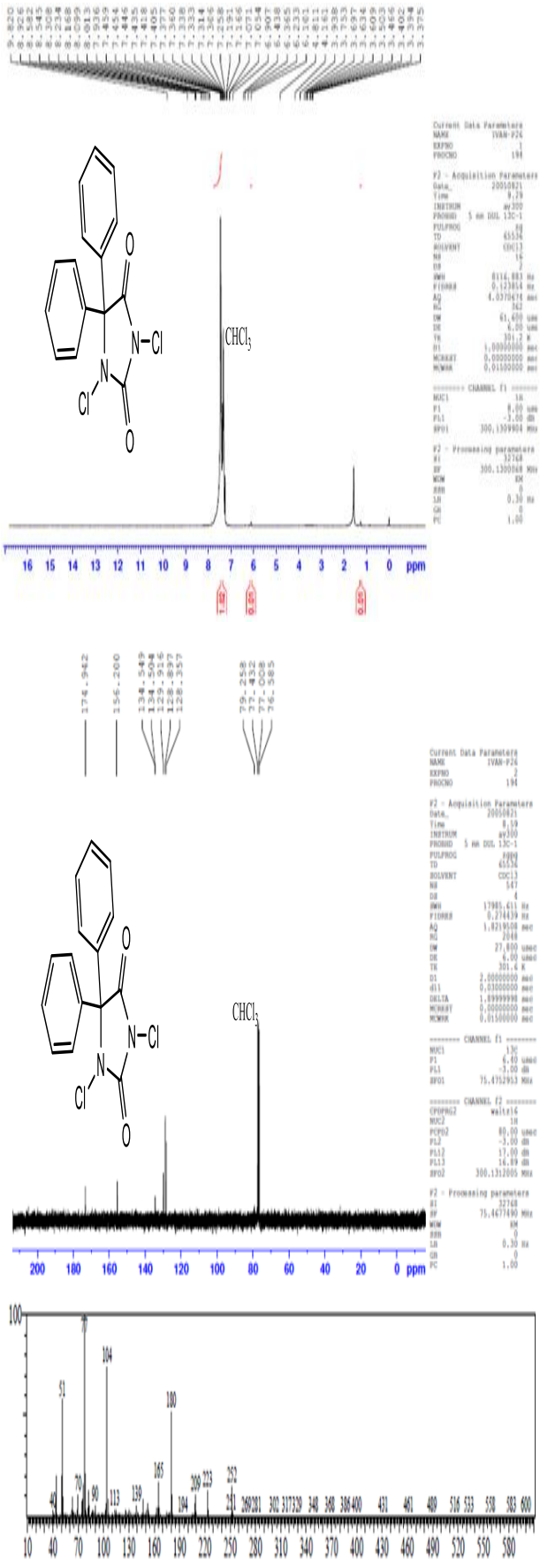

Figure.6 : ^{1}H, ^{13}C NMR of reaction of 1,3-dichloro-5,5-diphenyl imidazolidine-2,4-dione **(V)** with DMSO-d_6.

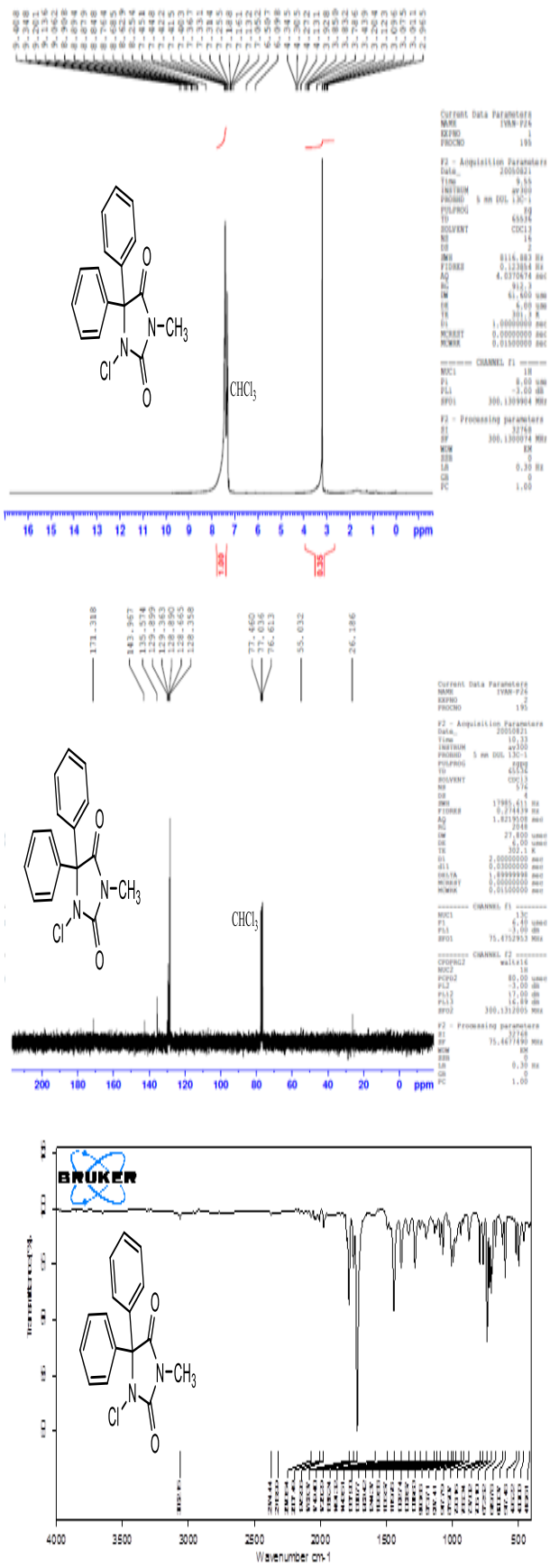

Figure.7 : ^{1}H, ^{13}C NMR and ATR-IR spectra of 1-Chloro-3-methyl-5,5-diphenyl imidazolidine-2,4-dione **(VI)**.

1-Chloro-3-methyl-5,5-diphenylimidazolidine-2,4-dione **(VI)** was obtained by treating 3-methyl-5,5-diphenyl imidazolidine-2,4-dione with a solution of 10 % sodium hypochlorite, recrystallized from mixture of ethanol: water. It was obtained as white crystals with m.p. 165-167ºC, freely soluble in THF, DMF, CCl_4, $CHCl_3$, CH_2Cl_2, acetone, and insoluble in H_2O. It was identified by the available techniques, and many distinctive features concerning its ^{1}H NMR showed the disappearance of N_1-H signal (as shown in **Fig.7**). An observed shift in the signal of the methyl group to higher field position from 2.85 to 3.2 is due to the effect of the attached electronegative chlorine atom, 7.2-7.45 (b, 10H, Ar-H) and 7.05-7.18 due to chlorine proton.The ^{13}C NMR showed a shift in the signal of the methyl group to a higher field position of 26.19 ppm [101, 103] due to the effect of the attached electronegative chlorine atom. The rest of the molecule showed similar shift by 2 ppm compared to the parent molecule 3-methyl-5,5-diphenyl imidazolidine-2,4-dione **(IV)**.

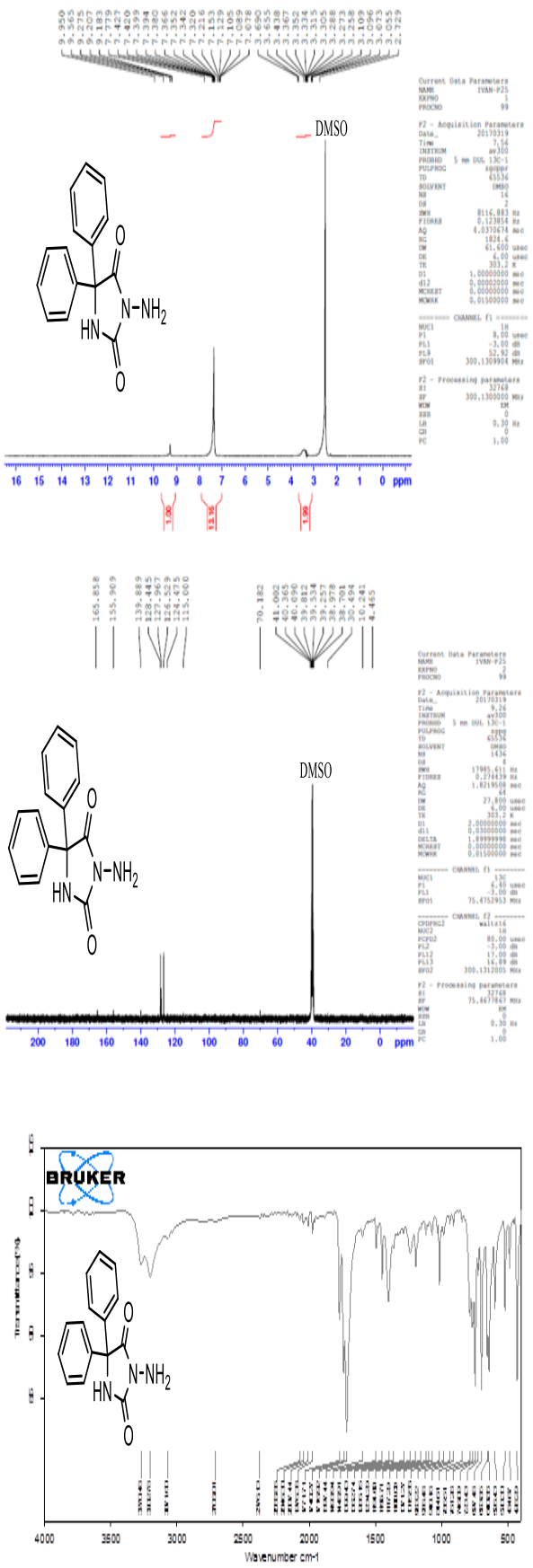

Figure.8 : ^{1}H, ^{13}C NMR and ATR-IR spectra of 3-amino-5,5-diphenylimidazolidine-2,4-dione **(VII)**.

3-Amino-5,5-diphenylimidazolidine-2,4-dione **(VII)** was prepared by refluxing 1,3-dichloro-5,5-diphenyl imidazolidine-2,4-dione with concentrated ammonia solution for few hours, and the product obtained as cream color crystal with m.p. 252-254ºC (d) (lit. 190°C [28,29]). It was identified by the following techniques; The disappearance of N_3-H signal in ^{1}H NMR signal at 11.0 ppm, as well as the appearance of new signal for the amine group at δ: 3.33 ppm (S, 2H, NH_2) at N_3 position. The aromatic carbon atoms ^{13}C NMR signals appeared at similar signals to that of the parent molecule **(I)**. The rest of the molecule showed slightly shift with the parent molecule **(I)**, the difference was evident, especially in the shift of C_4=O δ: 174.76 to 165.85 ppm [98], as shown in figure 3- 30. The ATR-IR spectrum showed similar bands for the carbonyl groups, with significant increase in the N-H band due to the additional NH_2 group [82], as shown in **Fig.8**

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تحضير ودراسة طيفية لبعض التفاعلات النيوكليوفيلية من جزيء مضاد للصرع 5,5-ثنائي فينل إيميدازوليدين-2،4-داي اون

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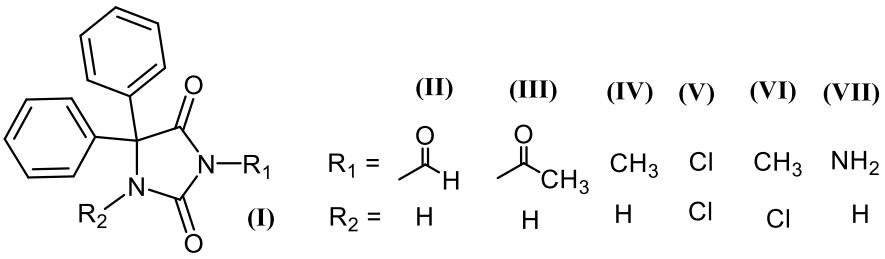
الخلاصة:

تم إجراء تفاعلات جديدة للمركب 5،5–ثنائي الفينل إميدازوليدين–2،4– ديون (I) لإعطاء المشتقات (II – VII). وتشمل هذه التفاعلات أستلة، هلجنة، اختزال، و الاستبدال نيوكليوفيلي.



وأظهرت معظم المشتقات استقرارا كيميائيا متغيرا وثباتا، وتم العثور على التناظرية N_1 و N_3 غير المستقرة أقل استقرارا بكثير، ويتحلل بسهولة في وسط التفاعل. وفقا H^1 و C^{13} NMR القياس، وعند اجراء دراسه على المركب 1،3–داي كلورو–5،5–ثنائي الفينيل إيميدازوليدين–2،4–داي اون (V) وجد انه يُكلور مجموعة الميثيل في المذيب d_6–DMSO. تم إنشاء تحليل استهلاك هيدروكسيد الصوديوم للكشف عن الجزيئية ضد هيدروكسيد الصوديوم، باتباع طريقة الحجمية حامض – قاعدة.