

## تحضير مشتقات من الباريتيورات لحمض D-ارثرواسكوريك

استلم البحث في : 15 أيلول 2010

قبل البحث في : 9 تشرين الثاني 2010

عبد الجبار عبد القادر مخاض ، باسمة محسن سرحان ، رسمية محمود رميز  
قسم الكيمياء ، كلية التربية-ابن الهيثم ، جامعة بغداد

## الخلاصة

يتضمن هذا البحث تحضير مشتقات جديدة من الباريتيورات لحمض D-ارثرواسكوريك للحصول على هذه المشتقات تم اختيار 6,5-O-ايزوبروبيليدين-L-حامض الاسكوريك (4) التي حضرت من تفاعل L-حامض الاسكوريك (3) مادة اولية مع الاسيتون الجاف بوجود غاز كلوريد الهيدروجين. تمت استرة مجاميع الهيدروكسيل في المواقع C-2 و C-3 باستعمال زيادة من كلوريد البنزويل بوجود البيريدين الجاف ،اذ تم الحصول على المركب (5). التحلل المائي للمركب (5) باستعمال حامض الخليك (65%) ،اذ اعطى المركب (6). بعدها تمت اكسدة المركب (6) ببرايونات الصوديوم لينتج الالديهيد (7) الذي يتفاعل مع ثنائي مثيل المالونات بوجود هيدروكسيد البوتاسيوم ليعطي المالونات (8). ان تفاعل التكايف الحلقي للمركب (8) مع اليوريا والثايويوريا والكواندين هايدروكلورايد اعطى المركبات (9) و (10) و (11) على التوالي.

شخصت المركبات المحضرة بوساطة كروماتوغرافيا الطبقة الرقيقة (TLC) واطياف الاشعة تحت الحمراء (FTIR) وبعض من هذه المركبات تم تشخيصه بوساطة اطياف الاشعة فوق البنفسجية والمرئية (U.V-Vis) واطياف الرنين النووي المغناطيسي ( $^1\text{H-NMR}$ ) واطياف كاربون الرنين النووي المغناطيسي ( $^{13}\text{C-NMR}$ ).

الكلمات المفتاحية: الباريتيورات، حامض الارثرواسكوريك، حامض الاسكوريك، المالونات.

# Synthesis of Barbiturate Derivatives of D-Erythroascorbic Acid

Received in : 15 September 2010

Accepted in : 9 November 2010

A-J.A. Mukhlis, B. M. Sarhan, R. M. Rumez

Department of Chemistry , College of Education- Ibn-Al-Haitham ,  
University of Baghdad

## Abstract

The aim of this work is the synthesis of new derivatives of barbiturate of D-erythroascorbic acid. To obtain these derivatives, the 5,6-O-isopropylidene-L-ascorbic acid (4) was chosen, which was prepared from the reaction of L-ascorbic acid (3) as a starting material with dry acetone in the presence of hydrogen chloride. The esterification of hydroxyl groups at C-2 and C-3 positions with excess of benzoyl chloride in dry pyridine was obtained compound (5). Hydrolysis for compound (5) in acetic acid (65%) gave the compound (6). Oxidation of the product (6) with sodium periodate results an Aldehyde (7), which was reacted with dimethyl malonate in the presence of potassium hydroxide to give the malonate (8). The cyclocondensation reaction for compound (8) with urea, thiourea and guanidine hydrochloride gave the following compounds (9), (10) and (11) respectively.

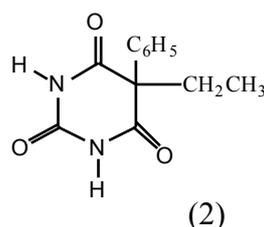
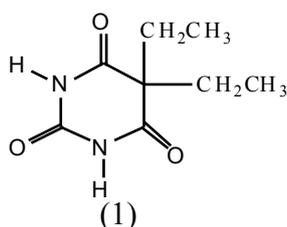
All these compounds were characterised by Thin Layer Chromatography (TLC) and FTIR spectra and some were characterised by (U.V-Vis) spectra,  $^1\text{H}$ NMR spectra and  $^{13}\text{C}$ NMR spectra.

**Key words:** barbiturate, erythroascorbic acid, ascorbic acid, malonate.

## Introduction

Barbituric acid was discovered in the mid-19th century, with the first medical barbiturate, barbitone (1), being synthesized in 1903. Phenobarbitone (2) was introduced as a pharmaceutical in 1912. Therapeutically, these drugs are used as sedatives, anaesthetics and anticonvulsants. Phenobarbitone is also used in the treatment of epilepsy[1]. Most of the known barbiturate compounds possess low solubility in water, therefore, researches claimed synthesis of new carbohydrate derivatives containing barbiturate,[2],[3] these derivatives have high solubility in water in addition of possessing possible biological activity.

Khalafi-Nezhad et al.[4] prepared barbituric acid derivative from reaction barbituric acid with different aromatic aldehyde on basic alumina was performed in a conventional microwave oven in the absence of solvent. Recently, Kidwai et al.[5] reported the preparation of barbituric acid derivatives by heating reactants with microwave irradiation and confirm all the compounds synthesized were found to possess good antifungal activity.



## Experimental

Melting points were determined by electrothermal Stuart melting point apparatus and are uncorrected. IR spectra (in KBr) were recorded on Shimadzu FT infrared spectrophotometer.  $^1\text{H}$  and  $^{13}\text{C}$ NMR spectra were recorded on Ultra Shield (300 MHz) spectrophotometer with tetramethyl silane as internal standard. Electronic spectra were obtained using a (U.V-Vis) spectrophotometer type Shimadzu, (160A). Thin layer chromatography (TLC) was performed on aluminum plates coated with layer of silica gel, supplied by Merck. The spots were detected by iodine vapor.

### Synthesis of 5,6-O-isopropylidene-L-ascorbic acid (4)

Dry hydrogen chloride was rapidly bubbled with stirring for 20 minutes into a (250ml) flask containing (10g, 57mmol) of powdered L-ascorbic acid (3) and (100ml) of dry acetone.

After addition of (80ml) n-hexane, stirring and cooling in an ice-water, the supernatant was decanted. The precipitate was washed four times with (154ml) of acetone-hexane mixture (4:7) (v/v), cooling in an ice-water and removal of supernatant after each addition. The last precipitate was dried under reduced pressure to give (4) (11.7g, 95.35%) as a white crystalline residue, m.p (206-208°C).  $R_f$  (0.68) (benzene: methanol, 5:5) (v/v). FTIR (KBr,  $\text{cm}^{-1}$ ): 3240, 3062 (O-H), 2993 (C-H<sub>ali.</sub>), 2908 (C-H<sub>ace.</sub>), 1751 (C=O<sub>lac.</sub>), 1662 (C=C), 1431 (-CH<sub>asym</sub>), 1388 (-CH<sub>sym</sub>), 1141-900 (C-O), 767  $\delta$ (O-H) (O.O.P.).

### Synthesis of 2,3-O-dibenzoyl-5,6-O-isopropylidene-L-ascorbic acid (5)

To a cold solution of (4) (10g, 46mmol) in pyridine (50ml), benzoyl chloride was added as drop wise (15ml, 129mmol) with stirring. The resulting mixture was stirred for 2 hours, then kept in dark place at room temperature for 22 hours.

The mixture was poured into ice-water and stirred for 20 minutes, the supernatant was decanted. Extraction with chloroform (150 ml). The chloroform layer was washed with water, dilute hydrochloric acid (5%) (2 × 100ml), water, saturated aqueous sodium hydrogen carbonate (100ml) and water. Dried over anhydrous magnesium sulfate. Chloroform was evaporated gave a brown syrup. The syrup was precipitated from chloroform: petroleum ether (60-80°C) (1:5) (v/v) to give (5) (15g, 76.5%) as a pale brown solid, m.p (83-85°C).  $R_f$  (0.73) (benzene: methanol, 5:5) (v/v). FTIR (KBr,  $\text{cm}^{-1}$ ): 3062 (C-H<sub>ar.</sub>), 2985 (C-H<sub>ali.</sub>), 2931 (C-H<sub>ace.</sub>), 1751 (C=O<sub>lac.</sub>), 1662 (C=O<sub>est.</sub>), 1627 (C=C<sub>ali.</sub>), 1600 (C=C<sub>ar.</sub>), 1261-1118 (C-O), 900-600  $\delta$ (C-H) (O.O.P.).

### Synthesis of 2,3-O-dibenzoyl-L-ascorbic acid (6)

Compound (5) (10g, 23.6mmol) was dissolved in (65%) acetic acid (30ml), absolute methanol (10ml) and stirred for 48 hours at room temperature. The TLC showed that the reaction was complete (benzene: methanol, 6:4).

Benzene (40ml) was added to the solution and evaporated the organic solvent (repeat this process four times). The residue was solid, recrystallized from chloroform and then diethyl ether to yield (6) (7g, 77.7%) as a white crystals, m.p (115-116°C),  $R_f$  (0.35). FTIR (KBr,  $\text{cm}^{-1}$ ): 3406 (O-H), 3074 (C-H<sub>ar.</sub>), 2939 (C-H<sub>ali.</sub>), 1716 (C=O<sub>est.</sub>), 1600 (C=C<sub>ar.</sub>), 1273-1118 (C-O), 900-600  $\delta$ (C-H<sub>ar.</sub>) (O.O.P.).

### Synthesis of pentuloso- $\gamma$ -lactone-2,3-enedibenzoate (7)

To the stirred solution of sodium periodate (5.6g) in distilled water (60ml) at (0°C), a solution of (6) (10g, 26mmol) in absolute ethanol (60ml) was added drop wise. After 15 minutes, ethylene glycol (0.5ml) was added as drop wise, stirring was continued at room temperature for 1 hour.

The mixture was filtered and water (40ml) was added to the filtrate. Extraction with ethyl acetate (3×50ml), the extracts dried by anhydrous magnesium sulfate. Evaporation and the residue recrystallized from benzene to yield the pure product (7) (4g, 44.4%) as a white crystals, m.p (110-112°C).  $R_f$  (0.63) (benzene: methanol, 6:4) (v/v). FTIR (KBr,  $\text{cm}^{-1}$ ): 3080

(C-H<sub>ar.</sub>), 2839, 2677 (C-H<sub>ald.</sub>), 1689 (C=O<sub>ald.</sub>), 900-600  $\delta$ (C-H<sub>ar.</sub>) (O.O.P.). <sup>1</sup>HNMR (CDCl<sub>3</sub>):  $\delta$ (4.97) ppm (s, 1H, H<sub>4</sub>),  $\delta$  (7.28-8.17) ppm (m, 10H, aromatic),  $\delta$ (11.4) ppm (br, 1H, CHO). <sup>13</sup>CNMR (CDCl<sub>3</sub>):  $\delta$ (172.44) ppm (C=O),  $\delta$ (133.83) ppm (C-3),  $\delta$ (133.47) ppm (C-2),  $\delta$ (130.23-128.03) ppm (C<sub>ar.</sub>),  $\delta$ (77.46) ppm (C-4). The signal of aldehydic carbonyl was disappeared due to it which showed out of the scale.[6]

#### Synthesis of 5-C-dimethyl malonyl-pentulose- $\gamma$ -lactone-2,3-enedibenzoate (8)

The mixture of potassium hydroxide (1.9g, 34mmol) and dimethyl malonate (3.9ml, 34mmol) was stirred for 30 minutes, a solution of (7) (10g, 28.4mmol) in absolute ethanol (60ml) was added.

After stirring for 24 hours at room temperature, the TLC showed that the reaction was complete (benzene: methanol, 4:6) and the resulting mixture was filtered then the solvent was evaporated, the combined residue was washed with chloroform and then petroleum ether (60-80°C) to give (8) (10g, 72.7%) as a white crystals, m.p (dec.240°C), R<sub>f</sub> (0.65). FTIR (KBr, cm<sup>-1</sup>): 3402 (O-H), 3055 (C-H<sub>ar.</sub>), 2904 (C-H<sub>ali.</sub>), 1720 (C=O<sub>est.</sub>), 1581 (C=C<sub>ali.</sub>), 1450(C=C<sub>ar.</sub>), 1400-1000 (C-O), 900-600  $\delta$ (C-H<sub>ar.</sub>) (O.O.P.). <sup>1</sup>HNMR (DMSO):  $\delta$ (2.50) ppm (DMSO),  $\delta$ (2.72) ppm (d, 1H, CH malonate),  $\delta$ (3.16) ppm (s, 1H, OH),  $\delta$ (3.56-3.58) ppm (s, 6H, 2CH<sub>3</sub> malonate),  $\delta$ (7.14-8.86) ppm (m, 10H, aromatic). <sup>13</sup>CNMR (CDCl<sub>3</sub>):  $\delta$ (168.82) ppm (C=O),  $\delta$ (135.26) ppm (C-3),  $\delta$ (131.55) ppm (C-2),  $\delta$ (129.58,128.40) ppm (C<sub>ar.</sub>),  $\delta$ (51.63) ppm (C-4),  $\delta$ (44.67) ppm (C-5),  $\delta$ (40.78-39.11) ppm (C-6 and carbon 2CH<sub>3</sub> malonate).

#### Synthesis of pentulose- $\gamma$ -lactone-2,3-enedibenzoate barbituric acid (9) or thiobarbituric acid (10) or azhydrobarbituric acid (11)

To the solution of sodium methoxide (30.9mmol of sodium metal dissolved in absolute methanol (20ml)), dry urea or thiourea or guanidine hydrochloride (15.5mmol) was added, stirring at room temperature for 1 hour.

The compound (8) (5g, 10.3mmol) in absolute methanol (30ml) was added, stirring was continued at room temperature for 48 hours. The TLC showed that the reaction was complete (benzene: methanol, 4:6). The solvent was evaporated; the combined residue was washed with hot absolute ethanol to give (9), (10), and (11) respectively. The physical properties for prepared compounds showed in Table (1). The FTIR, <sup>1</sup>HNMR and <sup>13</sup>CNMR spectra data are given in Tables (2), (3) and (4).

## Results and Discussion

L-ascorbic acid (3) is one of the natural antioxidant present in biological system because of its activity to attack the free radicals and other reactive oxygen species, as the literatures points to the great role which ascorbic acid plays to prevent a number of disease and its importance in food industry.[7],[8]

One strategy allows the synthesis of compounds (9), (10) and (11) in (6) steps starting from L-ascorbic acid, scheme (1). The first step employs the protection of the hydroxyl groups at C-5 and C-6 positions in L- ascorbic acid with acetal formation leading to compound (4) using dry acetone in acidic media, following Salomon[9] method. This is followed by esterification of the hydroxyl groups at C-2 and C-3 positions with excess of benzoyl chloride in dry pyridine.

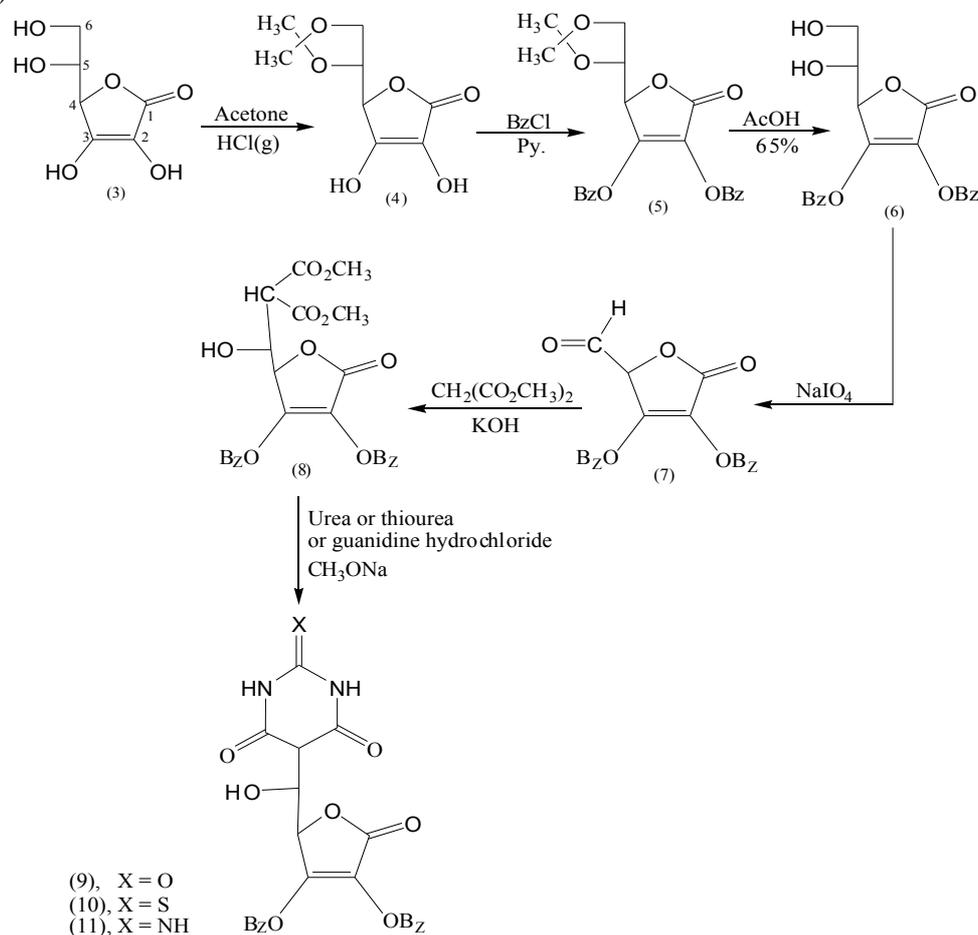
The FTIR spectra for compound (4) and (5) were confirmed the formation of compound (5) by disappearance of the bands for (O-H) of compound (4) and exhibited the band at (1662) cm<sup>-1</sup> for (C=O) of the ester in compound (5) spectrum.

In order to prepare aldehyde (7), the acetal moiety was cleaved under acidic condition[10] (65% acetic acid) for compound (5) to give (6) and oxidation of the product with sodium periodate to result (7), which gave a positive Tolen's test by the formation of a silver mirror.[11],[12] The FTIR spectra for compound (6) and (7) confirmed the formation of compound (7) by disappearance of the bands for (O-H) of compound (6) and exhibited the band at (1689) cm<sup>-1</sup> for (C=O) in compound (7) spectrum. The structure of (7) was confirmed

by  $^1\text{H NMR}$  which exhibited a signal at  $\delta(11.4)$  ppm for (CHO) and was characterised by  $^{13}\text{C NMR}$  and (U.V-Vis) spectrum which showed one peak at (295) nm ( $33898\text{ cm}^{-1}$ ) ( $\epsilon_{\text{max}} = 156\text{ molar}^{-1}\text{ cm}^{-1}$ ) assigned to ( $n \longrightarrow \pi^*$ ) transition.

The other step was the formation of compound (8) from the reaction of an aldehyde (7) with dimethyl malonate. The FTIR spectrum of (8) showed the bands at ( $3402\text{ cm}^{-1}$  and ( $1720\text{ cm}^{-1}$ ) due to (O-H) and (C=O) of the ester respectively and disappearance of the band for (C=O) aldehydic. The structure of (8) was confirmed by the disappeared of a signal at  $\delta(11.4)$  ppm for (CHO) by  $^1\text{H NMR}$  and was characterised by  $^{13}\text{C NMR}$  and (U.V-Vis) spectrum which showed one peak at (297) nm ( $33670\text{ cm}^{-1}$ ) ( $\epsilon_{\text{max}} = 102\text{ molar}^{-1}\text{ cm}^{-1}$ ) assigned to ( $n \longrightarrow \pi^*$ ) transition.

In order to obtain our target compounds (9), (10) and (11), the cyclocondensation reaction of malonate (8) with urea, thiourea and guanidine hydrochloride in alkaline media (sodium methoxide) leads to these compounds. All FTIR spectra for these compounds exhibited disappearance of the band at ( $1720\text{ cm}^{-1}$ ) for (C=O) of the ester for compound (8) and displayed of the bands at ( $1662, 1597, 1643\text{ cm}^{-1}$ ) due to (C=O in CHCONH) for compounds (9), (10) and (11) respectively. The FTIR spectra of (9), (10) and (11) showed the bands at ( $1627\text{ cm}^{-1}$ , ( $1153\text{ cm}^{-1}$ ) and ( $1597\text{ cm}^{-1}$ ) due to (C=O in HNCONH), (C=S) and (C=N) respectively. The structures of these compounds were confirmed by  $^1\text{H NMR}$  and  $^{13}\text{C NMR}$ , which showed disappearance of the signals at  $\delta(3.56-3.58)$  ppm and  $\delta(40.78-39.11)$  ppm from  $^1\text{H NMR}$  and  $^{13}\text{C NMR}$  spectra for compound (8). The (U.V-Vis) spectra data are given in Table (5).



Scheme (1) the scheme of prepared compounds

## References

1. Cole, M. D. (2003) “*The Analysis of Controlled Substances*”, John Wiley and Sons, Ltd. Chapter 9: 139,140.
2. Al-Qase, A. H. J.(2000) M. Sc. Thesis, College of Education / Ibn-Al-Haitham, University of Baghdad
3. Fayad,A. A. (2008)Ph. D. Thesis, College of Education / Ibn-Al-Haitham, University of Baghdad
4. Khalafi-Nezhad ,A. and Hashemi,A. (2001) “Microwave Enhanced Knoevenagel Condensation of Barbituric Acid with Aromatic Aldehydes on Basic Alumina”, Iran. J. Chem. & Chem. Eng **20** (1):9-11.
5. Kidwai,M. ; Thakur ,R. and Mohan,R. (2005) “Ecofriendly Synthesis of Novel Antifungal (Thio) Barbituric Acid Derivatives” Acta Chim. Slov., **52**: 88-92.
6. Carey, F. A. (2006) “*Organic Chemistry*”, 6<sup>th</sup> Ed., the McGraw-Hill Companies, Inc., New York, pp. 767.
7. Beifuss,U.; Kunz ,O. and Aguado,G. P. (1999) *Synlett*, 147-149.
8. Beifuss,U. ; Kunz ,O. and Voss, G. (2000) “Regioselective Synthesis of 3-O-Alkyl Ethers of Ascorbic Acid without Protecting Groups in a Single Step”, *Tetrahedron*, **56**:357-363.
9. Salomon,L. L. (1963) *Experientia*, **19** (12): 619.
10. Gazivoda,T.; Wittine, K.; Lovric,I. ; Makuc, D.; Plavec, J.; Cetina, M. ; Mrvos-Sermek, D.; Suman,L. ; Kralj,M.; Pavelic, K. ; Mintas ,M. and Raic-Malic S. (2006)“Synthesis, structural studies, and cytostatic evaluation of 5,6-di-O-modified L-ascorbic acid derivatives”, *Carbohydr. Res.*, **341** (4):433-442.
11. Vogel, A. I. (1989) “*Vogel's Textbook of Practical Organic Chemistry*”, 5<sup>th</sup> Ed., John Wiley and Sons, Inc., New York, , pp. 1219.
12. Fieser ,L. F. and Williamson,K. L. (1983) “*Organic Experiments*”, 5<sup>th</sup> Ed., D. C. Heath and Company, the United States of America, , pp. 160-161.

**Table (1) :Physical properties for prepared compounds (9), (10) and (11)**

| Comp . No. | Formula                                                         | Molecular weight (g/mol) | Weight of product (g) | Yield % | M.p °C or dec. | Physical state    | R <sub>f</sub> |
|------------|-----------------------------------------------------------------|--------------------------|-----------------------|---------|----------------|-------------------|----------------|
| 9          | C <sub>23</sub> H <sub>16</sub> O <sub>10</sub> N <sub>2</sub>  | 480                      | 3.57                  | 72      | 210(dec.)      | White solid       | 0.52           |
| 10         | C <sub>23</sub> H <sub>16</sub> O <sub>9</sub> N <sub>2</sub> S | 496                      | 3                     | 60      | 225(dec)       | Yellow solid      | 0.60           |
| 11         | C <sub>23</sub> H <sub>17</sub> O <sub>9</sub> N <sub>3</sub>   | 479                      | 4.25                  | 86      | 205(dec.)      | Pale-yellow solid | 0.33           |

**Table (2): Infrared spectra data (wave number  $\nu$ )  $\text{cm}^{-1}$  of the compounds (9), (10) and (11)**

| Compound | $\nu(\text{N-H})$ and<br>$\nu(\text{O-H})$ | $\nu(\text{C=O})$ in<br>(CHCONH,<br>HNCONH) | $\nu(\text{C=N})$ | $\nu(\text{C-N})$ | $\nu(\text{C=S})$ |
|----------|--------------------------------------------|---------------------------------------------|-------------------|-------------------|-------------------|
| 9        | 3471(s)                                    | 1662(s)<br>1627(s)                          | -                 | 1346(w)           | -                 |
| 10       | 3383(s)                                    | 1597(s)                                     | -                 | 1392(s)           | 1153(m)           |
| 11       | 3421(br)                                   | 1643(m)                                     | 1597(s)           | 1334(w)           | -                 |

Where: s = strong, m = medium, w = weak, br = broad

**Table (3):  $^1\text{H}$ NMR data for the compounds (9), (10) and (11) measured in  $\text{D}_2\text{O}$  with tetramethyl silane (TMS) as internal standard and chemical shift in ppm ( $\delta$ )**

| Compound | Functional group                 | $\delta(\text{ppm})$ |
|----------|----------------------------------|----------------------|
| 9        | d, 1H, CH malonate               | 3                    |
|          | d, 1H, lactone ring $\text{H}_4$ | 4.70-4.78            |
|          | m, 10H, aromatic                 | 7.25-7.73            |
| 10       | d, 1H, CH malonate               | 3                    |
|          | t, 1H, CH-OH                     | 3.22                 |
|          | d, 1H, lactone ring $\text{H}_4$ | 4.69                 |
|          | m, 10H, aromatic                 | 7.32-7.76            |
| 11       | d, 1H, CH malonate               | 3                    |
|          | t, 1H, CH-OH                     | 3.23                 |
|          | d, 1H, lactone ring $\text{H}_4$ | 4.70-4.78            |
|          | m, 10H, aromatic                 | 7.34-7.77            |

**Table (4):  $^{13}\text{C}$ NMR data for the compounds (9), (10) and (11) measured in  $\text{CDCl}_3$  and chemical shift in ppm ( $\delta$ )**

| Compound | Functional group           | $\delta$ (ppm) |
|----------|----------------------------|----------------|
| 9        | C=O in HNCONH              | 177.53         |
|          | C=O in CHCONH              | 175.65         |
|          | C=O in ester, lactone ring | 164.53         |
|          | C-3                        | 136.14         |
|          | C-2                        | 131.63         |
|          | C, aromatic                | 131.24-127.85  |
|          | C-4                        | 61.24          |
|          | C-5, C-6                   | 47.85          |
| 10       | C=O                        | 161.70         |
|          | C-3                        | 136.00         |
|          | C-2                        | 131.20         |
|          | C, aromatic                | 128.73, 128.25 |
| 11       | C=NH                       | 177.43         |
|          | C=O in CHCONH              | 175.76         |
|          | C=O in ester, lactone ring | 163.31         |
|          | C-3                        | 136.18         |
|          | C-2                        | 131.25         |
|          | C, aromatic                | 128.75, 128.29 |
|          | C-4                        | 48.88          |
|          | C-5, C-6                   | 47.71          |

**Table (5): Electronic spectra data for the compounds (9), (10) and (11)**

| Compound | $\lambda_{\text{max}}$ nm | Wave number $\text{cm}^{-1}$ | $\epsilon_{\text{max}}$ $\text{molar}^{-1} \text{cm}^{-1}$ | Assignment                  |
|----------|---------------------------|------------------------------|------------------------------------------------------------|-----------------------------|
| 9        | 294                       | 34013                        | 66                                                         | $n \longrightarrow \pi^*$   |
| 10       | 257                       | 38910                        | 140                                                        | $\pi \longrightarrow \pi^*$ |
|          | 291                       | 34364                        | 195                                                        | $n \longrightarrow \pi^*$   |
| 11       | 232                       | 43103                        | 15                                                         | $\pi \longrightarrow \pi^*$ |
|          | 297                       | 33670                        | 192                                                        | $n \longrightarrow \pi^*$   |

