Synthesis of some new D-mannose glycosides based 1,2,3-triazoles as urease inhibitors

Zeyad Kadhem oleiwi
Department of Pharmacy
Al-furat Al-awsat technical university
Kufa, Iraq

Authors Name/s per 2nd Affiliation (*Author*)
Department of Pharmacy
University of Kufa
Kufa, India

***Abstract*— Williamson etherification of (1) with propargyl bromide afforded the 1-O-propargyl-2,3:5,6-Di-O-isopropyli-dene α-D-mannofuranoside (2) in a very good yield . 1,3-Dipolar cycloaddition of (2) with four different aryl azides derivatives using click conditions gave four novel 1,2,3-triazole derivatives containing sugar moiety . The biological activity of synthesized compounds were tested against urease activity by immobilize this enzyme on the synthesized compounds. All of these compounds show inhibition activity of enzyme. Some of these compounds (T1) show high inhibition action on the enzyme activity, while (T2, T3, T4) show moderate effect on the activity.**

Keywords*— *D-mannose, glycoside , 1,2,3-triazole, urease, inhibitors

I. INTRODUCTION

Synthesis of some new heterocyclic compounds containing a carbohydrate moiety has great interest because of the possibility to obtain nucleosides and nucleosides analogues, which have, in some cases, therapeutic importance [1].Where significant efforts were devoted to the discovering of new routes for the synthesis of new heterocyclic compounds from carbohydrates and their derivatives [2]. The 1, 2, 3-triazole ring system has been the subject of considerable research mainly due to its usefulness in organic synthesis and also because of the pharmacological properties shown by some of its derivatives. [3] The 1, 2, 3-triazole moiety is a constituent part of many modified nucleosides or carbanucleosides with antiviral, anti-HIV or cytostatic activities [4-6].

II. EXPERIMENTAL PART

A. *Materials*

- Chemical reagents and starting materials were obtained from Ajax and Sigma-Aldrich Chemical.
- Instrumentations
- FT-IR spectra were recorded by using Fourier transformation infrared Shimadzu FT-IR-8400S infrared spectrophotometer by KBr disc, Faculty of Pharmacy University of Kufa.
- 1H NMR, 13C NMR were recorded by Bruker spectrometer, operating at (400MHZ) with (DMSO-d6). Measurements were made at Faculty of Science, Osmania University, India.
- TLC plates were used with an aluminum backing (0.2 mm, 60 F254).

B. *Synthesis of aryl azide derivatives (general procedure) (A1-A4) [7]*

An aniline derivative (1 eq) was dissolved in 10 mL of dilute HCl in a Round Bottomed flask. Reaction mass was cooled to (-10°C to -5°C). Sodium nitrite (1.2 eq) was added in small portions (4 portions) to the reaction mass by maintaining the temperature at -10°C to 0°C and maintained the reaction for 10 min. A solution of sodium azide (1.2 eq) was added in a drop wise manner to the reaction mixture at 0°C. The Reaction mixture was stirred for 10 min. at 0°C. The product was extracted by using chloroform followed by washing with water up to neutral pH. Organic layer was dried with anhydrous sodium sulfate and then the solvent removed to yield aryl azide derivatives. The material was used without further purification.

C. *Synthesis of 1-O-propargyl-2,3:5,6-Di-O-isopropyli-dene α-D-mannofuranoside (2) [8]*

2,3:5,6-Di-O-isopropylidene-α-D-manno furanose (1) (5.205 g, 20 mmol) was dissolved in DMF (30 mL) in a dry flask and to this solution was added crushed NaOH (1.6 g, 40 mmol). The contents stirred for (10 min) before propargyl bromide (2.85, 24mmol) was added dropwise. The reaction mixture was then allowed to stir for a further (24h.), gradually warming to RT. The reaction mixture was quenched with distilled water (50 mL) and extracted with diethyl ether (3×100 mL). The combined organic layer was washed with sat. NH4Cl (3×30 mL), distilled water, dried over Na2SO4, filtered and the solvent was evaporated to dryness under reduced pressure to yield a pale yellow oil (36) (85%), Rf = (0.67), (2:1) (hexane: EtOAc).

D. *Synthesis of 1,2,3-triazole derivatives of sugar via click chemistry (general procedure) (T1-T4) [9]*

A solution of propargyl ether (1.0 eq) in DMF(5mL) was added to the suspension of sodium ascorbate (1.2 eq) and CuSO4.5H2O (1.2 eq) in DMF (4mL).The mixture was stirred for (10 min) and to this was added an aryl azides derivatives (1.2 eq). The mixture was heated to 50°C with stirring for (10-48 h.). The reaction mixture was diluted with distilled water (30 mL), extracted with EtOAc (3×30 mL), the combined organic layers were washed with sat. NaCl (2× 20 mL), dried over Na2SO4, and evaporated to dryness under reduced pressure. The residue was flash chromatographed (silica gel, n-Hexane: Et2O) to yield the desired compounds as a yellow syrup (T1 – T4). (60-80) %.

E. Studying the biological activity of synthesized compounds [10]

1) Reagents for Urease activity: The following reagents which supported form ―biomerieux ®, urea kit.

a) Phosphate buffer PH=8 with concentration 50mM, sodium salicylate (26mM), sodium nitroprosside (3.35mM), EDTA (1mM).

b) Sodium hydroxide (0.5mM) and sodium hypochloride (24.8mM).

2) Phosphate Buffer (PH 7): 0.5L of 1M K2HPO4 at 174.18 g mol-1 = 87.09g .

0.5L of 1M KH2PO4 at 136.09 g mol-1 = 68.045g .

Preparation of 0.1 M potassium phosphate buffer at 25°C.

III. Estimation of Urease Activity

Urease activity is estimated by using end point method for the formation of ammonia per minutes. Urease catalyzed degradation of urea results in the formation of ammonia, which is determined by the Berthelot method (according to method of urea kit). The assay is simple, sensitive, stable and high-throughput adaptable The steps of the method are as follows:

- The blank of reaction consist of five hundred microliters of 1.65mg/ml of free or immobilize or dispersion jack bean urease (dispersion is solution from urease at concentration 1.65 was mixed with 2mg/ml of synthesized compounds) were mixed with a of solution which contain phosphate buffer PH 8 with concentration of 50 mM, sodium salicylate 26mM, sodium nitroprusside 3.35mM, EDTA 1mM).
- Twenty microliters of one concentration of urea (50 mg/dl) were mixed with 1 ml of blank, (enzyme and buffer) and then incubated for 5 minutes at room temperature.
- Two hundred microliters from alkaline reagent (consist of sodium hydroxide 0.5mM, sodium hypochloride 24.8mM) were added and the mixture incubated for 5 minutes, the absorbance was measured at 580 nm by spectrophotometer.
- Calibration curve was obtained from the absorbance of different concentration of ammonium sulfate
- Urease activity was determined through measurement released ammonia per minute at room temperature and PH 7.

IV. Results and Discussion

A. Synthesis of aryl azide derivatives

Compounds (A1-A4) were synthesized by treatment of an aromatic amines derivatives with hydrochloric acid and sodium nitrite to from diazoniume salts at (0-5)0C, followed by reaction of diazoniume salt with sodium azide at the same temperature.

FT-IR spectra of compounds (A1-A4), figures (8-14) showed the following bands at cm-1 (KBr) summarized in table (1).

TABLE I. FT-IR and percentage yield of compounds (A1-A3)

compound	FT-IR bands/cm $^{-1}$	Yield %
A1	3100 (υ C–H aromatic),2127 (υ N=N=N, of azide), 1579 (υ C=C aromatic), 1517 (υ O=N=O),1286(δ C–H aromatic,)	70%
A2	3066(υ C–H aromatic) 2106 (υ N=N=N, of azide), 1697 (υ C=O of carboxylic acid) ,1559(υ C=C aromatic), 1276(υ C–O of carboxylic acid)	72%
A3	3066(υ C–H aromatic),2113 (υ N=N=N, of azide),1642 (υ C=C aromatic)	55%
A4	3111(υ C–H aromatic),2983 (υC–H, CH_3),2123 (υ N=N=N, of azide),1716 (υ C=O of ester),1600(υ C=C aromatic),1278(υ C–O of ester)	63%

B. Synthesis of 1-O-propargyl-2,3:5,6-Di-O-isopropyli-dene α-D-mannofuranoside (1)

Williamson etherification of 2,3:5,6-Di-O-isopropyli-dene α-D-mannofuranoside with propargyl bromide in DMF as solvent and the presence of basic media (NaOH) produced the terminal alkyne (1) in very good yield (78%)

FT-IR spectrum of compound (1) showed the following bands at $\bar{\upsilon}$ cm^{-1}(KBr): 3267 ($\upsilon_{C-H,}$ **alkyne**), 2987($\upsilon_{C-H,}$ **CH_3**), 2941($\upsilon_{C-H,}$ **CH_2**), 2893($\upsilon_{C-H,}$ **CH**), 2121(**υ** $_{C\equiv C}$), 1452($\delta_{as.C-H,}$ **CH_3**), 1377($\delta_{s.C-H,}$ **CH_3**), 1216,1261($\upsilon_{C-O,}$ **C–O–C**), 1078($\upsilon_{C-O,}$ **C–O-H**).

FT-IR spectrum is a good evidence that the reaction happened successfully by disappearing the band at 3435 cm^{-1} and appearing sharp bands at (3253, 2115) cm^{-1} attributed to the terminal alkyne (C–H and C≡C) respectively.

^{1}H NMR spectrum, (400 MHz, DMSO-d_6) for the compound showed the following signals at δ (ppm): 1.24, 1.26, 1.33, 1.35 (s, 12H, 4C***H*** $_{3\ isopropylidene}$), 3.47 (t, J 2.4 Hz of C≡C **-H**),3.81 (dd, J7.2, 3.6 Hz, 1H, of C4-H), 3.88 (dd, *J 8.4*, 5.2 Hz, 2H, of C**H_2**-C≡C), 3.99 (d, *J* 6.4 Hz, 2H, 2 of C6-H), 4.22 (t, *J* 3.3 Hz, 1H, of C3-H), 4.43 (t, *J* 4.0 1H, of C2-H), 4.73 (dd, *J* 5.6,3.2 1H, of C2-H), 5. 70 (1H, of C1-H),

^{13}C NMR spectrum, (100MHz, DMSO-d_6) showed the following signals at δ (ppm): 25.29, 26.09[(2 × C(***C***H_3)$_2$],53.38, 80.19(**2C of** - C≡C) ,63.89(1C of **C**- C≡C –H) 66.62 (1C of C6), 69.59 (1C of C5), 74.34 (1C of C3), 79.02 (1C of C4), 82.05 (1C of C2), 105.36 (1C of C1), 112.26,115.75[(2 × ***C***(CH_3)$_2$].

C. Synthesis of 1-O{(4-nitrophenyl)-1H-1,2,3-triazole-4-yl}methyl]- 2,3:5,6-Di-O-isopropylidene α-D-mannofuranoside (T1)

Compound (T1) was synthesized by 1,3-dipolar cycloaddition reaction catalyzed with Cu(I) of propargyl ether D-mannofuranoside (1) and 4-azidnitrobenzene (A1) to produce a very good yield.

FT-IR spectrum of compound (T1) showed the following bands at $\bar{\upsilon}$ cm^{-1} (KBr): 3114 ($\upsilon_{C-H,}$ **triazole**), 3099 ($\upsilon_{\mathbf{C-H\ of\ benzene}}$) 2989($\upsilon_{C-H,}$ **CH_3**), 2937($\upsilon_{C-H,}$ **CH_2**), 1616($\upsilon_{\mathbf{C=C}}$, **aromatic**), 1517 ($\upsilon_{O=N=O}$), 1458($\delta_{as.C-H,}$ **CH_3**), 1377 ($\delta_{s.C-H,}$ **CH_3**), 1263($\delta_{C-H\ aromatic,}$), 1211, 1161($\upsilon_{C-O,}$ **C–O–C**), 1161 ($\upsilon_{\mathbf{C-N}}$), 1080 (υ_{C-O}).

FT-IR spectrum is a good evidence that cycloaddition reaction happened successfully through disappearing the bands around υ (2127, 2121, 3267) cm^{-1} which is attributed to (-N3 ,**C≡C and** $\upsilon_{C-H,}$ **alkyne**) respectively.

^{1}H NMR spectrum, (400 MHz, DMSO-d_6) for the compound showed the following signals at δ (ppm): 1.24, 1.25, 1.31, 1.33 (s, 12H, 4C***H_3*** **isopropylidene**), 3.58 (m, 1H, of C4-H), 3.69 (d, *J* 6.4 Hz, 2H, 2 of C6-H), 4.49 (m, 1H, of C3-H), 4.58 (m, 1H, of C2-H), 4.73 (m 1H, of C2-H),4.78(m,2H of O-CH_2 of triazole) 5. 70 (1H, of C1-H),7.28-7.38(m , of aromatic and triazoles.

^{13}C NMR spectrum, (100MHz, DMSO-d_6) showed the following signals at δ (ppm): 22.26, 25.75[(2 × C(***C***H_3)$_2$], 62.60 (1C of C6), 64.69 (1C of C5), 76.09 (1C of C3),78.26(1C of OCH2C=C of triazol) 79.09 (1C of C4), 83.60 (1C of C2), 110.09 (1C of C1), 112.29,115.54[(2 × C(CH3)2],120.45,131.36,141.01,151.55161.57 (m C of aromatic carbon of benzene and triazole ring).

D. Synthesis of 1-O{(2-carboxyphenyl)-1H-1,2,3-triazole-4-yl}methyl]- 2,3:5,6-Di-O-isopropylidene α-D-mannofuranoside (T2

Compound (T2) was synthesized by 1,3-dipolar cycloaddition reaction catalyzed with Cu(I) of propargyl ether D-mannofuranoside (1) and 2-azidobenzoic acid (A2) to produce a very good yield

FT-IR spectrum , of compound (T2) showed the following bands at $\bar{\upsilon}$ cm^{-1} (KBr):3421($\upsilon_{\mathbf{O-H\ of\ carboxylic\ acid}}$) 3100 ($\upsilon_{C-H,}$ **triazole**), 3070 ($\upsilon_{\mathbf{C-H\ of\ benzene}}$) 2989($\upsilon_{C-H,}$ **CH_3**), 2939($\upsilon_{C-H,}$ **CH_2**),1707($\upsilon_{\mathbf{C=O\ of\ carboxylic\ acid}}$) 1687($\upsilon_{\mathbf{C=C}}$, **aromatic**), 1454($\delta_{as.C-H,}$ **CH_3**), 1377 ($\delta_{s.C-H,}$ **CH_3**), 1292($\delta_{C-H\ aromatic,}$), 1232, 1165($\upsilon_{C-O,}$ **C–O–C**), 1161 ($\upsilon_{\mathbf{C-N}}$), 1085 ($\upsilon_{\mathbf{C-O}}$).

FT-IR spectrum is a good evidence that cycloaddition reaction happened successfully through disappearing the bands around υ (2106, 2121, 3267) cm^{-1} which is attributed to (-N3 ,**C≡C and** $\upsilon_{C-H,}$ **alkyne**) respectively .

^{1}H NMR spectrum, (400 MHz, DMSO-d_6) for the compound showed the following signals at δ (ppm): 1.24, 1.25, 1.31, 1.33 (s, 12H, 4C***H_3*** **isopropylidene**), 3.58 (m, 1H, of C4-H), 3.68 (d, *J* 6.4 Hz, 2H, 2 of C6-H), 4.49 (m, 1H, of C3-H), 4.58 (m, 1H, of C2-H), 4.73 (m 1H, of C2-H),4.78(m,2H of O-CH_2 of triazole) 5. 56 (1H, of C1-H),7.28-7.38(m , of aromatic and triazoles) ,10.06(s,1H of COO**H**).

^{13}C NMR spectrum, (100MHz, DMSO-d_6) showed the following signals at δ (ppm): 25.29, 26.29[(2 × C(***C***H_3)$_2$], 62.36 (1C of C6), 64.64 (1C of C5), 76.19 (1C of C3),78.26(1C of OCH2C=C of triazol) 79.09 (1C of C4), 83.61 (1C of C2), 110.09 (1C of C1), 112.25,115.54[(2 × C(CH3)2],116.43,122.63,130.36,130.46,137.96,138.49,148.91 (m C of aromatic carbon of benzene and triazole ring),171.11(1C of **C**OOH).

E. Synthesis of 1-O{(2,4-dichlorophenyl)-1H-1,2,3-triazole-4-yl}methyl]- 2,3:5,6-Di-O-isopropylidene α-D-mannofuranoside (T3

Compound (T3) was synthesized by 1,3-dipolar cycloaddition reaction catalyzed with Cu(I) of propargyl ether D-mannofuranoside (1) and 1-azido-2,4-dichlorobenzene (A3) to produce a very good yield

FT-IR spectrum of compound (T3) showed the following bands at $\bar{\upsilon}$ cm^{-1} (KBr): 3143 ($\upsilon_{C-H,}$ **triazole**), 3091 ($\upsilon_{\mathbf{C-H\ of\ benzene}}$) 2987($\upsilon_{C-H,}$ **CH_3**), 2937($\upsilon_{C-H,}$ **CH_2**), 1672($\upsilon_{\mathbf{C=C}}$, **aromatic**), 1498($\delta_{as.C-H,}$ **CH_3**), 1377 ($\delta_{s.C-H,}$ **CH_3**), 1259($\delta_{C-H\ aromatic,}$), 1211, ($\upsilon_{C-O,}$ **C–O–C**), 1161 ($\upsilon_{\mathbf{C-N}}$), 1089 ($\upsilon_{\mathbf{C-O}}$).

FT-IR spectrum is a good evidence that cycloaddition reaction happened successfully through disappearing the bands around υ (2113, 2121, 3267) cm^{-1} which is attributed to (-N3 ,**C≡C and** $\upsilon_{C-H,}$ **alkyne**) respectively .

^{1}H NMR spectrum, (400 MHz, DMSO-d_6) for the compound showed the following signals at δ (ppm): 1.24, 1.25, 1.31, 1.33 (s, 12H, 4C***H_3*** **isopropylidene**), 3.58 (m, 1H, of C4-H), 3.68 (d, *J* 6.4 Hz, 2H, 2 of C6-H), 4.49 (m, 1H, of C3-H), 4.58 (m, 1H, of C2-H), 4.73 (m 1H, of C2-H),4.78(m,2H of O-CH_2 of triazole) 4. 78 (1H, of C1-H),6.78 -7.29(m , of aromatic and triazoles).

^{13}C NMR spectrum, (100MHz, DMSO-d_6) showed the following signals at δ (ppm): 24.19, 25.21[(2 × C(***C***H_3)$_2$], 62.36 (1C of C6), 64.64 (1C of C5), 76.19 (1C of C3),78.26(1C of OCH2C=C of triazole) 79.09 (1C of C4), 83.61 (1C of C2), 110.09 (1C of C1), 112.25,115.54[(2 × C(CH3)2],116.43,122.63,130.36,130.46,137.96,138.96,146.61 (m C of aromatic carbon of benzene and triazole ring).

F. Synthesis of 1-O{(4-ethylbenzoatephenyl)-1H-1,2,3-triazole-4-yl}methyl]- 2,3:5,6-Di-O-isopropylidene α-D-mannofuranoside(T4

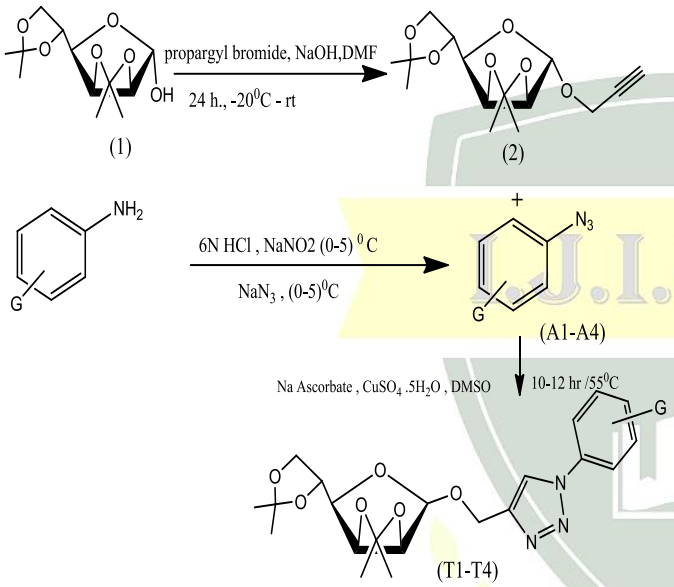
Compound (T4) was synthesized by 1,3-dipolar cycloaddition reaction catalyzed with Cu(I) of propargyl ether D-mannofuranoside (1) and ethyl 4-azidobenzoate (A4) to produce a very good yield

FT-IR spectrum of compound (T4) showed the following bands at $\bar{\upsilon}$ cm^{-1} (KBr): 3132 ($\upsilon_{C-H,}$ **triazole**), 3089 ($\upsilon_{\mathbf{C-H\ of\ benzene}}$) 2985($\upsilon_{C-H,}$ **CH_3**), 2943($\upsilon_{C-H,}$ **CH_2**),1714($\upsilon_{\mathbf{C=O\ of\ benzoate}}$) 1610($\upsilon_{\mathbf{C=C}}$, **aromatic**), 1519($\delta_{as.C-H,}$ **CH_3**), 1375 ($\delta_{s.C-H,}$ **CH_3**), 1278($\delta_{C-H\ aromatic,}$), 1215, ($\upsilon_{C-O,}$ **C–O–C**), 1166 ($\upsilon_{\mathbf{C-N}}$), 1093 ($\upsilon_{\mathbf{C-O}}$).

FT-IR spectrum is a good evidence that cycloaddition reaction happened successfully through disappearing the bands around υ (2123, 2121, 3267) cm^{-1} which is attributed to (-N3 ,**C≡C and** $\upsilon_{C-H,}$ **alkyne**) respectively .

^{1}H NMR spectrum, (400 MHz, DMSO-d_6) for the compound showed the following signals at δ (ppm): 1.22,1.23,1.24, 1.25, 1.31, 1.33,1.35 (4C***H*****$_3$** **isopropylidene** and CH_2CH_3 of ethyl group) 3.58 (m, 1H, of C4-H), 3.68 (d, *J* 6.4 Hz, 2H, 2 of C6-H), 4.49 (m, 1H, of C3-H), 4.58 (m, 1H, of C2-H), 4.73 (m 1H, of C2-H),4.78(m,2H of O-CH_2 of triazole) 5.06 (1H, of C1-H),6.73 -8.16(m , of aromatic and triazoles)

^{13}C NMR spectrum, (100 MHz, DMSO-d_6) showed the following signals at δ (ppm):12.16(C of ethyl group) 24.11, 25.27[(2 × C(***C***H_3)$_2$], 62.36 (1C of C6), 64.64 (1C of C5), 76.11 (1C of C3),78.26(1C of OCH2C=C of triazole) 79.01 (1C of C4), 83.61 (1C of C2), 108.46 (1C of C1), 114.36,115.64[(2 × C(CH3)2],130.31,130.66,130.36, 137.96, 146.11 (m C of aromatic carbon of benzene and triazole ring).166.46(1C of C=O).



G1=4-NO_2,G2=2COOH,G3=2,4-Cl, G4=4 ethylbenzoate

Scheme(I) Synthetic methods of 1,2,3-triazole derivatives

V. STUDYING THE BIOLOGICAL ACTIVITY OF SYNTHESIZED COMPOUNDS

The biological activity of the synthesized compounds were tested against the activity of urease enzyme (which is catalyze urea to ammonia and carbon dioxide). The enzyme was immobilize on each one of synthesized compound by taking one concentration of each compound with enzyme and stirring the mixture for 10 min. The triazoles derivatives show different inhibition action toward the enzyme shown in the following figure (A).

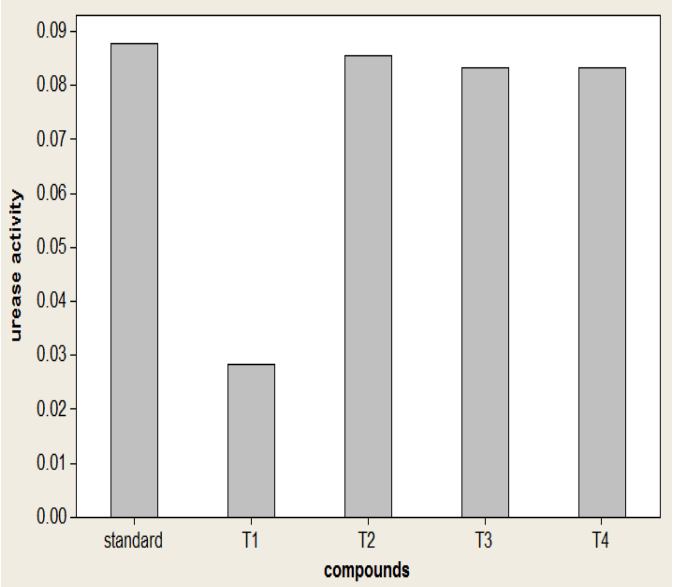


Fig. 1. The effect of synthesized compounds on urease activity.

Some of these compounds (T1) show high inhibition action on the enzyme activity, while (T2, T3, T4) show moderate effect on the activity.

The activities of enzyme with different compound were calculated from the amount of liberated ammonia per 5 min as shown in table (2).

TABLE II. SHOW THE AMOUNT OF LIBERATED AMMONIA AND ENZYME ACTIVITIES

	Name of compound	Absorbance	Ammonia concentration	Urease activity
1	standard	0.180	0.439	0.0878
2	T1	0.153	0.142	0.0284
3	T2	0.179	0.428	0.0856
4	T3	0.178	0.417	0.0834
5	T4	0.178	0.417	0.0834

- The amount of liberated ammonia were calculate from relationship

  (ammonia concentration = Absorbance-0.41/0.091)

  which is obtain from calibration curve. Fig.

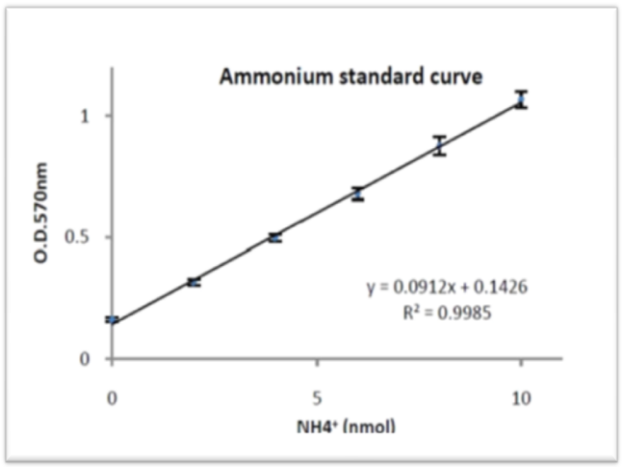


Fig. 2. Calibration curve for librated ammonia.

- The enzyme activity were calculate by relationship (Urease activity = amount of liberated ammonia /time) The time was 5 min.

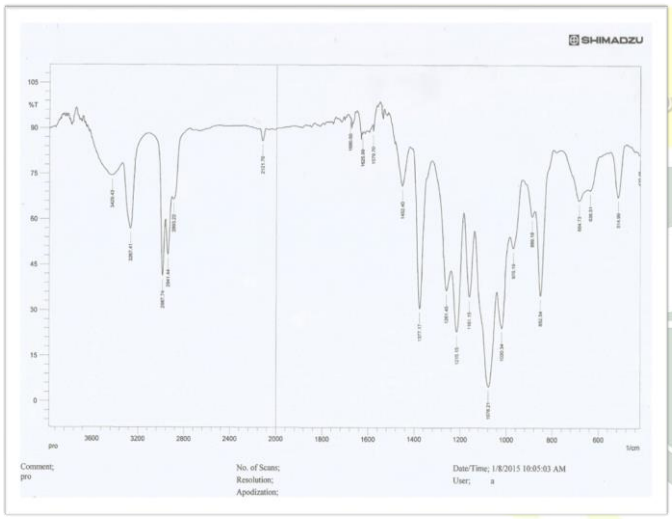


Fig. 3. FT-IR spectrum of compound (1).

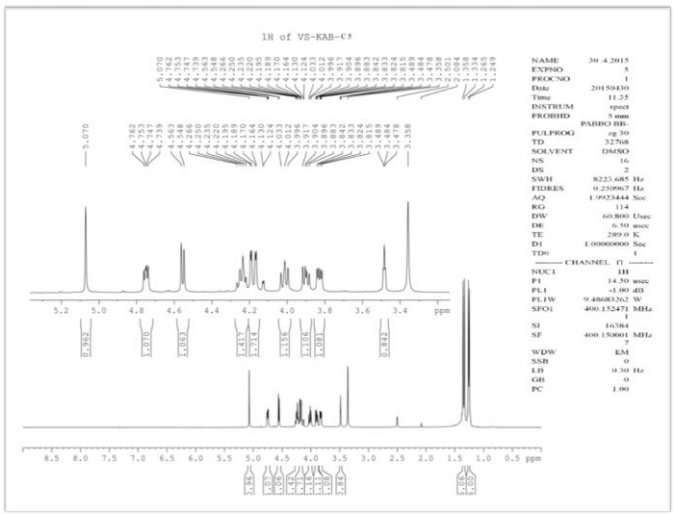


Fig. 4. H NMR spectrum of compound (1).

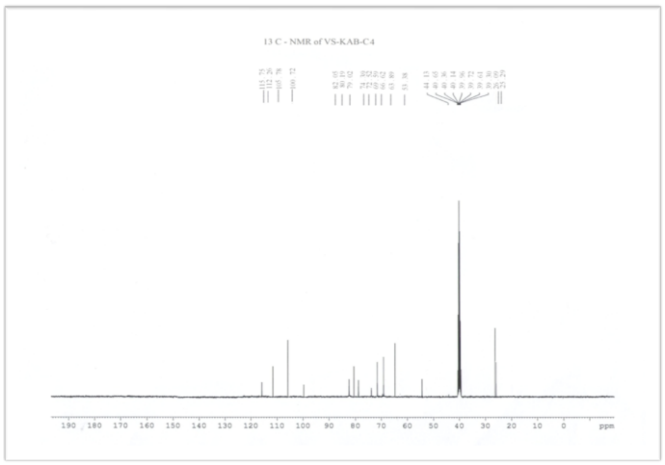


Fig. 5. ^{13}C NMR spectrum of compound (1).

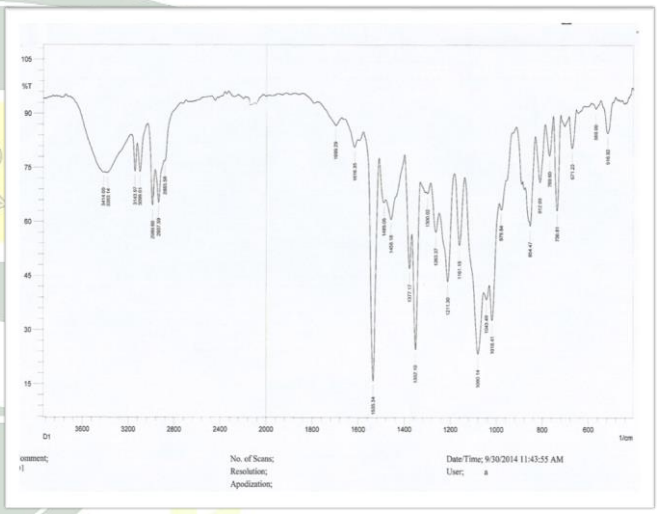


Fig. 6. FT-IR spectrum of compound (T1).

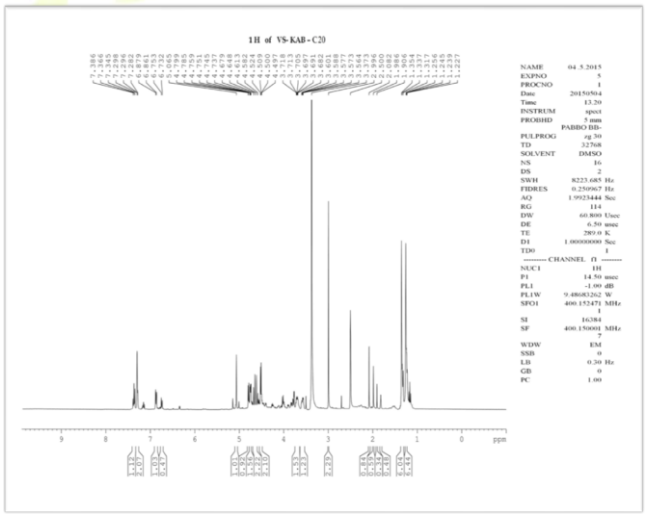


Fig. 7. ^{1}H NMR spectrum of compound (T1).

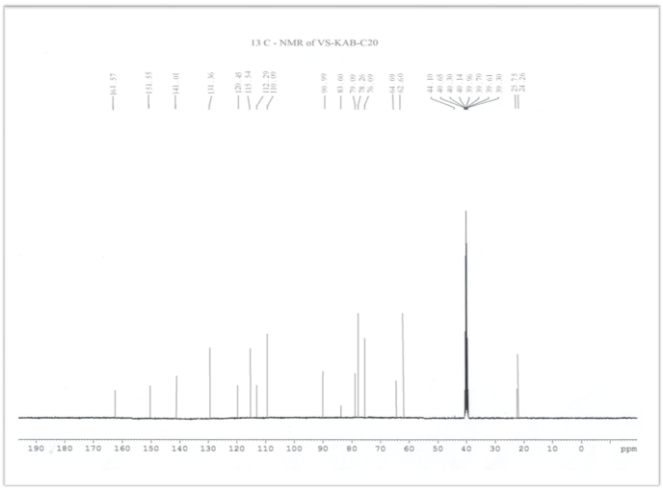


Fig. 8. ^{13}C NMR spectrum of compound (T1).

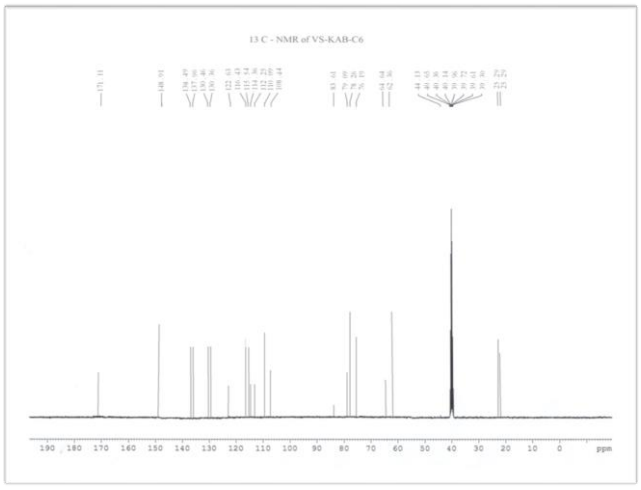


Fig. 11. ^{13}C NMR spectrum of compound (T2).

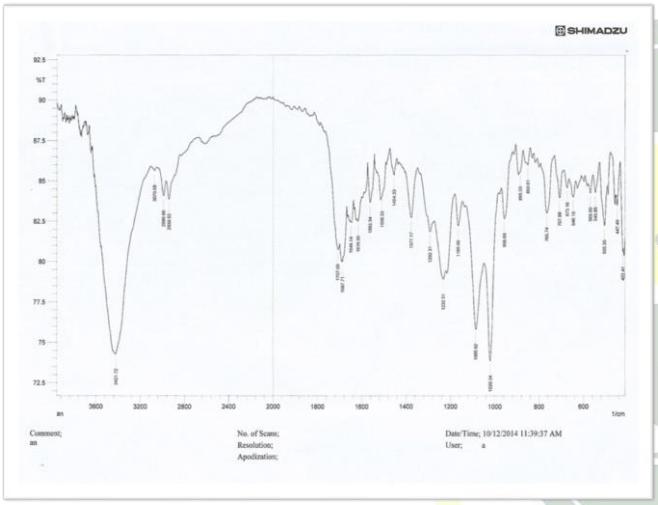


Fig. 9. FT-IR spectrum of compound (T2).

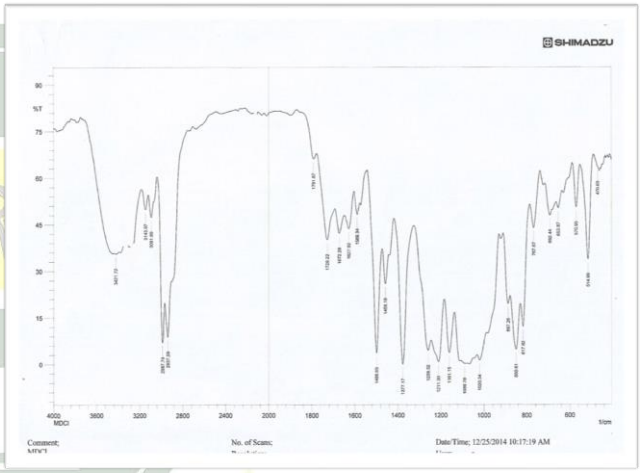


Fig. 12. FR-IR spectrum of compound (T3).

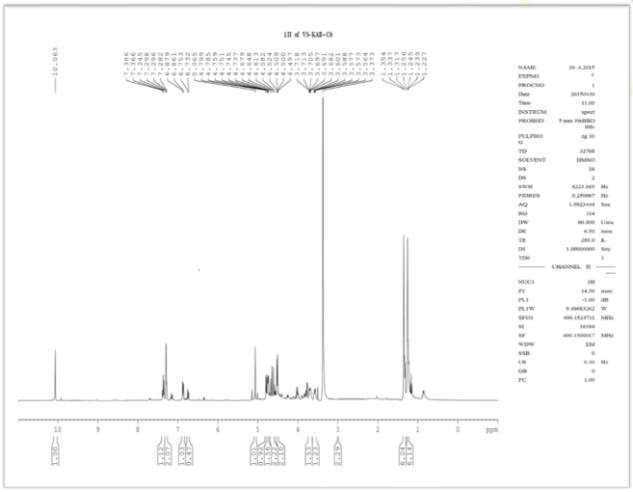


Fig. 10. ^{1}H NMR spectrum of compound (T2).

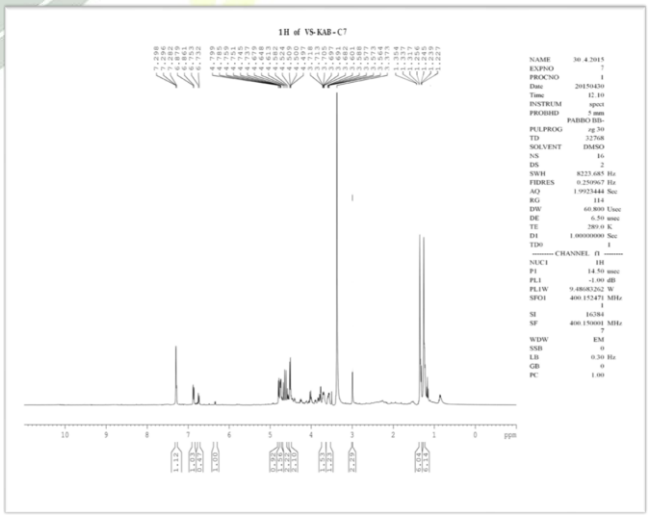


Fig. 13. ^{1}H NMR spectrum of compound (T3).

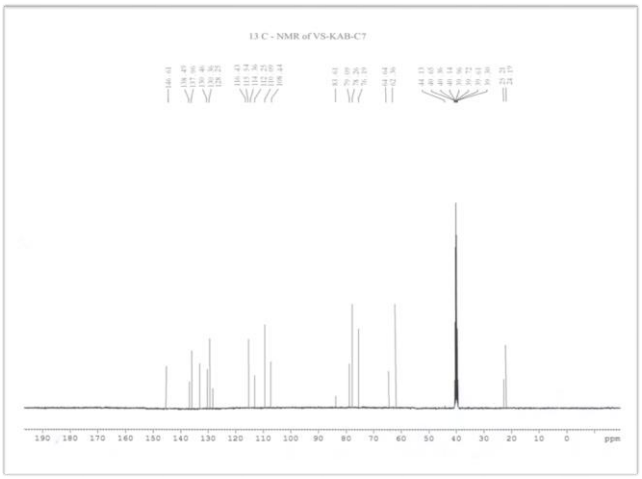


Fig. 14. ^{13}C NMR spectrum of compound (T3).

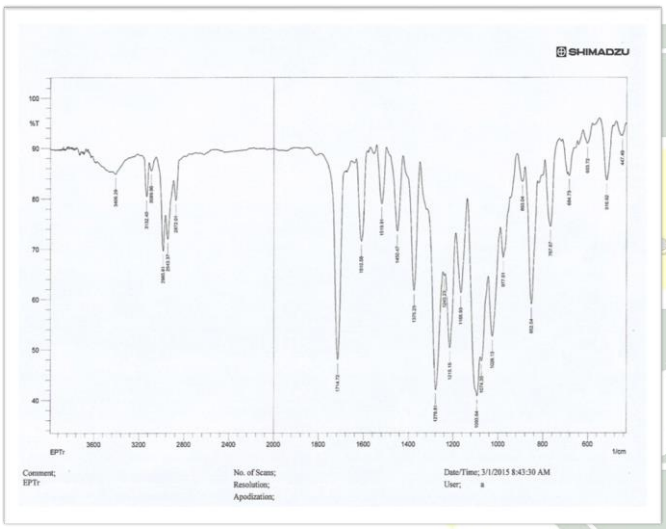


Fig. 15. FT-IR spectrum of compound (T4).

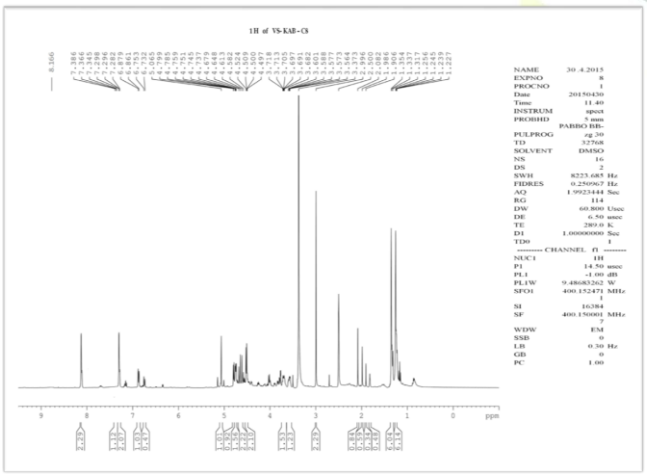


Fig. 16. ^{1}H NMR spectrum of compound (T4).

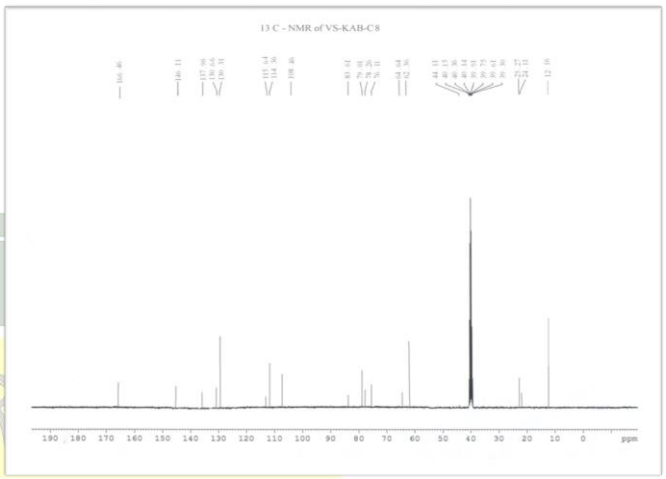


Fig. 17. ^{13}C NMR spectrum of compound (Z4).

REFERENCES

[1] Martins M. Alho , D'Accorso N.B., Molecules, 2000, 5, 381-382.

[2] Geert J. Boons , Karl J. Hale "organic synthesis with carbohydrates " 1st.ed. Sheffield Academic Press: (2000).

[3] Jagerovic, N.; Gómez de la Oliva, C.; Goya, P.; Dordal, A.; Cuberes, R. Eur. Pat. Appl. 0380290, 2006.

[4] Xia, Y.; Liu, Y.; Wan, J.; Wang, M.; Rocchi, P.; Qu, F.; Iovanna, J. L.; Peng, L. J. Med. Chem. 2009, 52, 6083–6096.

[5] Pérez-Castro, I.; Caamaño, O.; Fernández, F.; García, M. D.; López, C.; De Clercq, E. Org. Biomol. Chem. 2007, 5, 3805–3813

[6] Kiss, L.; Forro, E.; Fulop, F. Lett. Org. Chem. 2011, 8, 220–228

[7] Davinder Prasad, Nisha Aggarwal , Rajesh Kumar et al., indian journal of chemistry , 2012, 51B, 731-738 .

[8] Adnan I.Mohammed, Narjis H. Mansoor. ,Jalal H. Mohammed, Kerbala Journal of Pharmaceutical Sciences , 2013, 6 , 179-195 .

[9] Adnan I. Mohammed, Zaid H. Abood, Atheer H. Oda , Tetrahedron Letters ,2012, 53 , 5081–5083 .

[10] Muneer K. Khudair , M.Sc. thesis,2013, university of kufa ..