International Journal of Advanced Research in Chemical Science (IJARCS)
Volume 2, Issue 11, November 2015, PP 18- 26
ISSN 2349-039X (Print) & ISSN 2349-0403 (Online)
www.arcjournals.org

Bisamide and Tetrahydropyrimidine Sugar Surfactants Via Staudinger Reaction

Salih Mahdi Salman

Department of Chemistry-College of Medicine-University of Diyala
waamrs@yahoo.com

Abstract: *The Staudinger reaction enables an easy access to sugar amide glycolipids including monoamide and bisamide at the anomeric positions by substitute the hydroxyl group after preparing the target hydroxyl group and protect the other hydroxyl groups. It's possible to drive Staudinger reaction to cyclization reaction by control the solvent and the quantities of the reactants to produce tetrahydropyrimidine compounds instead of the double amide chains. This is considering as new methodology to synthesis tetrahydropyrimidine sugars. It is used to synthesis new sugar surfactants. Both bisamide and Tetrahydropyrimidine sugar are a new type of surfactants and are easily accessed as chemically pure compounds based from natural renewable resources e.g. sugar and fatty acids both are reasonable economic and environmental friendly.*

Keywords: *Tetrahydropyrimidine surfactants, Staudinger reaction, bisamide and biosurfactants*

1. INTRODUCTION

The major amphilphilic compounds of the cell membrane are characterized by a biantennary lipid structure comprising a single hydrophilic head group and two hydrophobic alkyl chains, which commonly are derived from fatty acids. A typical glycolipid structure involves a glycerol spacer linking two fatty acids and the carbohydrate[1-3], example structure A as shown in figure 1 utilizes a lactose head group, as saccharides with this core structure are frequently found in the nature[4,5]. Unlike the glycosidic linkage between the glycerol and sugar, the ester bonds between the polyol and the fatty acids are easily affected by hydrolysis under both acid and basic conditions. This sensitivity renders natural glycolipids non-favorable for delivery applications.

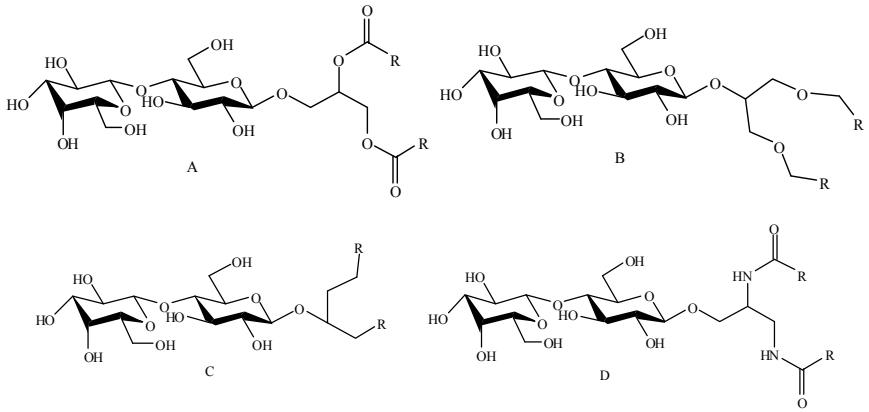

Figure1. *Structural Comparison of Natural and Synthetic bianternary glycolipids*

Several modifications have been suggested to increase the chemical stability of biatennary glycolipids. Examples involve replacement of the ester linkage by ethers6 figure 1 structure B or replacement of the entire diacyl glycerol by a branched alcohol chain7 figure 1 structure C. The aim of this work is to synthesize new glycolipid with enhanced chemical stability and close structural similarity to natural cell membrane lipids by replacement of the ester linkage with amide analogs for the development of a drug delivery system.

2. RESULTS AND DISCUSSIONS

2.1. Synthesis

In order to synthesis the bianternary glycolipids I previously developed a synthesis concept on glucose and lactose[8]. This concept started with peractylation of glucose and lactose with acetic

anhydride in presence of sodium acetate to give β-glucosepentaacetate and lactoseoctaacetate respectively[9-11]. A kinetic glycosylation applied with 1,3-dichloro-2-propanol and boron trifluoride diethyl etherate ($BF_3.Et_2.O$) in dichloromethane over a period of less 3h in order to control the stereoselectivity at the anomeric center give exclusively the dichloride derivatives for both sugar[12-14]. The latter was converted into diazide by sodium azide in DMF at 80 °C[15,16]. Final coupling of diazides with straight chain fatty acid chlorides (C_{12}) which is accessible by a simple treatment of dodecanoic acid with oxalyl chloride[17-19], applied triphenylphosphine in dichloromethane by Staudinger reaction furnished the biatennary glycolipids of glucose 1,3-Didodecanamido-2-propyl-β-D-glucopyranoside **[1]**[20-23] figure 2. While lactose diazide gave 2-undecyl-5-(4-O-β-D-galactopyranosyl-β-D-glucopyranosyl)-1,4,5,6-tetrahydro-pyrimidine **[2]** (figure 2) after deprotection[24,25], when we applied the same reaction and condition on both sugar.

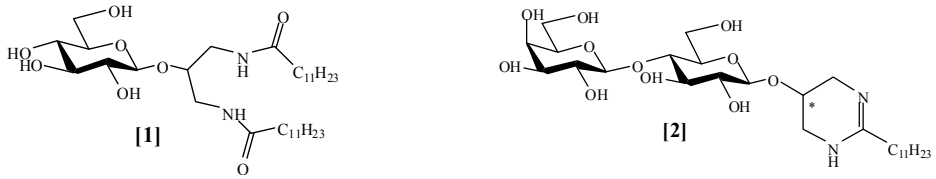

Figure2. *Bisamide glucose and tetrahydropyrimidine lactose surfactants*

The current study used the same synthesis scheme with some modification including using benzene as a solvent instead of dichloromethane and half equivalent of the fatty acid chloride with one equivalent of diazide glucose in order to drive the reaction to intermolecular cyclization to produced the monoantennary surfactant 2-undecyl-5-β-D-glucopyranosyl-1,4,5,6-tetrahydro-pyrimidine **[8]** as shown in figure 3. The latter was spectroscopically analyzed in both acetylated as well as the deprotected form. Structural identities are based on NMR spectra (^1H & ^{13}C), high-resolution mass spectrometry and elemental analysis.

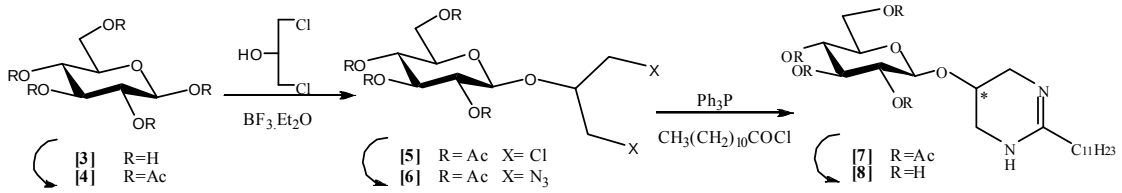

Figure3. *synthesis of 2-Undecyl-5-β-D-glucopyranosyl-1,4,5,6-tetrahydro-pyrimidine [8]*

^1H NMR of the acetylated surfactants **[7]** (figure 4) shows two signals for the (NH) of the tetrahydropyrimidine between δ 5.67 and δ 6.04 with integration for one proton, which indicate to two diastereomers for this surfactants. It confirms the formation of the tetrahydropyrimidine ring as it has a chiral center leading to two diastereomeric products with ratio of (80:20%). The protons for the sugar at acetylated oxygen appear between δ 5.00 (H-4) and δ 4.92 (H-2), while the anomeric signals (H-1) are found at δ 4.62. The non-acetylated sugar signal (H-5) are found between δ 3.9, while the primary (CH_2) of sugar (H-6) appear between δ 4.1 and δ 4.16. The protons of the methylene of the tetrahydropyrimidine ring are found between δ 3.68 and δ 3.45, while the chiral proton is found at δ 3.90. The values of the integration of the methyelen and methine as well as the difference in chemical shift for the two methyelen groups confirm the formation of the tetrahydropyrimidine. The acetate protons are found between δ 2.02 and δ 1.94. The protons of the alkyl chain appear between δ 2.10 (α-CH_2) and δ 0.81 (terminal CH_3). The integration of the bulk methylene signals at around δ 1.19 reflects the respective chain length of the surfactant (C_{12}).

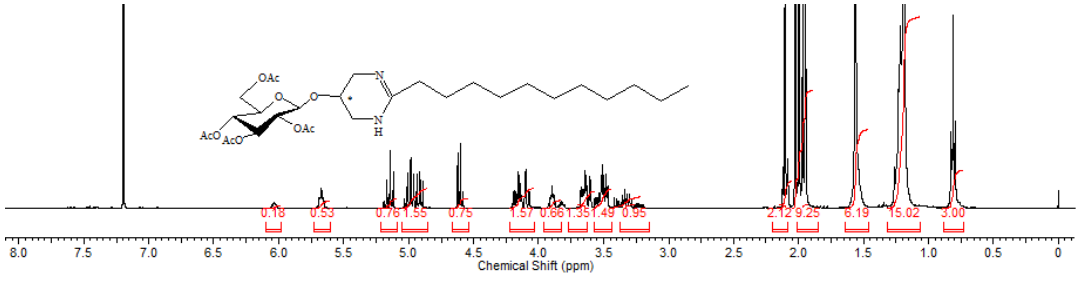

Figure4. *^1H NMR spectrum of 2-undecyl-5-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl-1,4,5,6-tetrahydro-pyrimidine [7]*

The ^{13}C NMR shows two signals for the tetrahydropyrimidine ring at δ 173.47 and δ 174. The signals of acetyl carbonyl are found between δ 170.59 and δ 169.42 The anomeric signal (C-1) are found at δ100.82. The carbons of the sugar at acetylated oxygen (C-2 to C-4) appear between δ 79.07 and δ 71.61, the non-acetylated sugar signal (C-5) is found around δ 68.24. The primary methyelen of the sugar ring (C6) appears at around δ 61.86. The carbons of the methylene of tetrahydropyrimidine are found at δ 43.93 and δ 40.62, while the chiral carbon appears at δ78.97. The alkyl chain carbons appear in between δ36.38 (α-CH_2) and δ 14.15 (terminal CH_3).

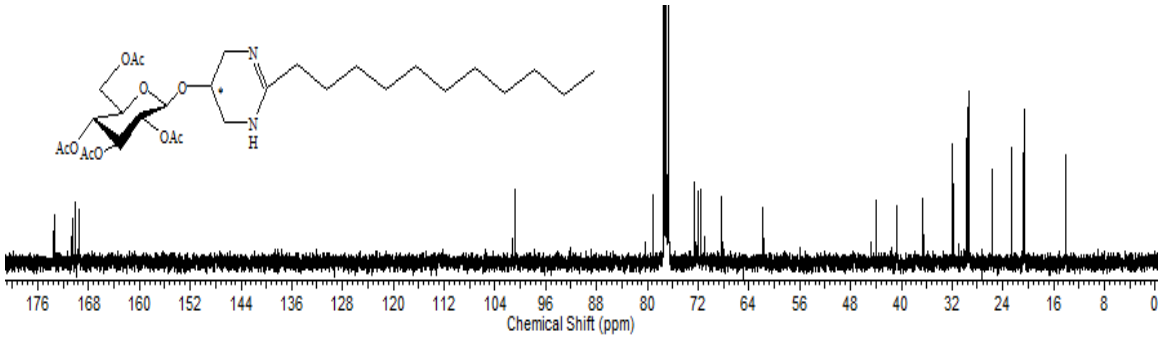

Figure5. *^{13}C NMR spectrum of 2-undecyl-5-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl-1,4,5,6-tetrahydro-pyrimidine [7]*

^{1}H NMR of the deacetylated surfactants shows the completely removal of the acetyl groups signals. The signals of amide disappeared due to ionic exchange because the using of methanol D as NMR solvent. Due to the absence of ester, the sugar hydrogen at (C-2 to C-4) are shifted upfield and appear between δ 3.76 to δ 3.31, which made some difficulties of the spectra analysis because of the peaks overlap. The anomeric signals (H-1) are found around δ 4.39. . The protons of the methylene of the tetrahydropyrimidine ring are found between δ 3.35 and δ 3.25, while the chiral proton is found at δ 3.8. The protons of the alkyl chain appear between δ 2.17 (α-CH_2) and δ 0.87 (terminal CH_3).

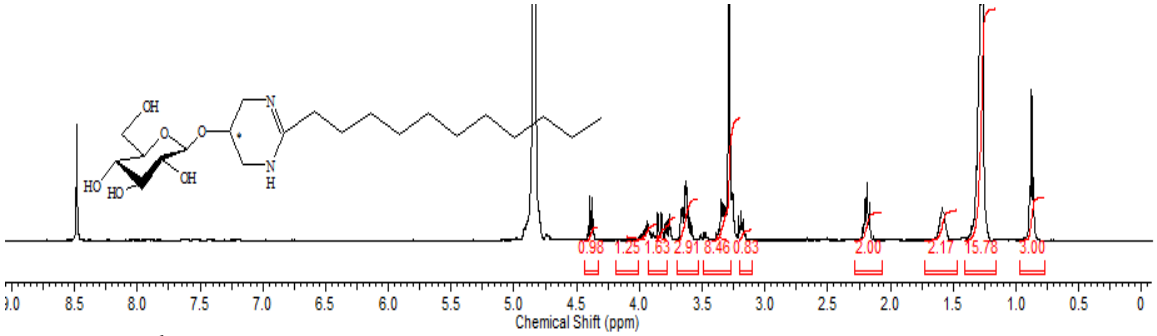

Figure6. *^{1}H NMR spectrum of 2-undecyl-5-β-D-glucopyranosyl-1,4,5,6-tetrahydro-pyrimidine [8]*

^{13}C NMR shows the signals for the tetrahydropyrimidine at about δ 175.33 and 168.84. The anomric carbon (C-1) found at about δ 103.81. Other sugar carbons appear between δ 78.75 and δ 70. The position of the primary carbons (C-6) is found at δ 61.29. The carbons of the linker are found at about δ 44.16 (CH_2N) and δ 40.22 (CH_2NH). The alkyl chain carbons appear in between 35.84 (α-CH_2) and 13.90 (terminal CH_3). For data analysis see the experimental part.

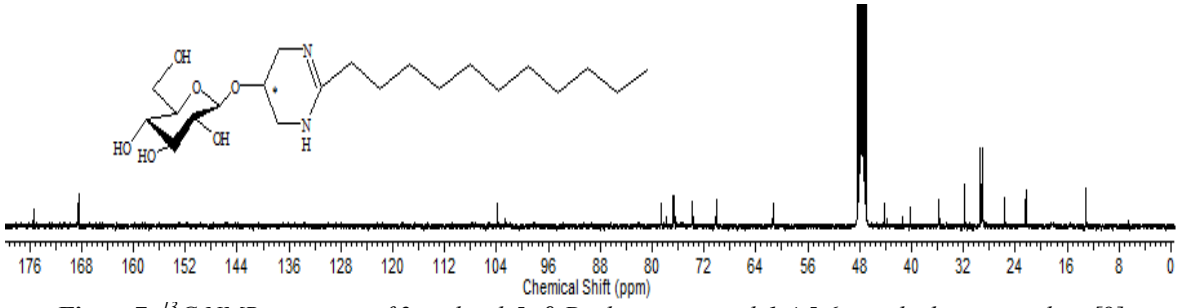

Figure7. *^{13}C NMR spectrum of 2-undecyl-5- β-D-glucopyranosyl-1,4,5,6-tetrahydro-pyrimidine [8]*

Another modified methodology was applied to synthesis the biatennary surfactant of lactose 1,3-didodecanamido-2-propyl-β-D-lactopyranoside **[14]** by applying benzene as solvent and two equivalents of dodecanoic chloride with one equivalent of lactose diazide as shown in figure 8.

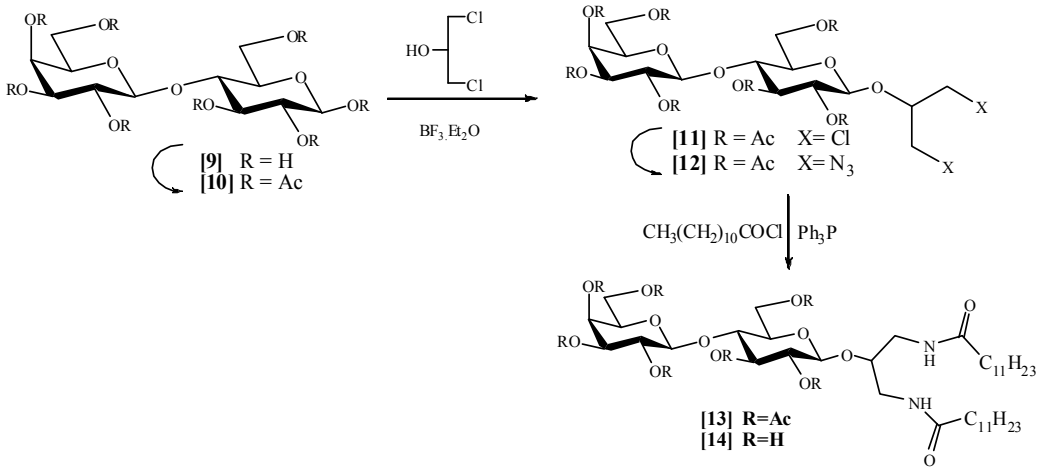

Figure8. *synthesis of 1,3-didodecanamido-2-propyl-β-D-lactopyranoside [14]*

^{1}H NMR of the acetylated oxygen of surfactant shows signals of the two amide protons at about δ 6.57 and δ 6.18. The anomeric protons signals (H-1, H-1') are found between δ 5.28 and δ 4.44. The protons for the sugar at acetylated oxygen appear between δ 5.04 (H-4') and δ 4.50 (H-2). The non-acetylated sugar signals (H-5/5') are found between δ 3.72 and δ 3.54, while the primary (CH_2) of sugar (H-6/6') appear between δ 3.85 and δ 3.58. The protons for the linker found at about δ 2.63 (OCH) and δ 2.63, 2.60 (CH_2N). The acetate protons are found between δ 2.14 and δ 1.90. The protons of the alkyl chain appear between δ 2.18 (α-CH_2) and δ 0.81 (terminal CH_3). The integration of the bulk methylene signals at around δ 1.19 reflects the respective chain length of the surfactant (C_{12}).

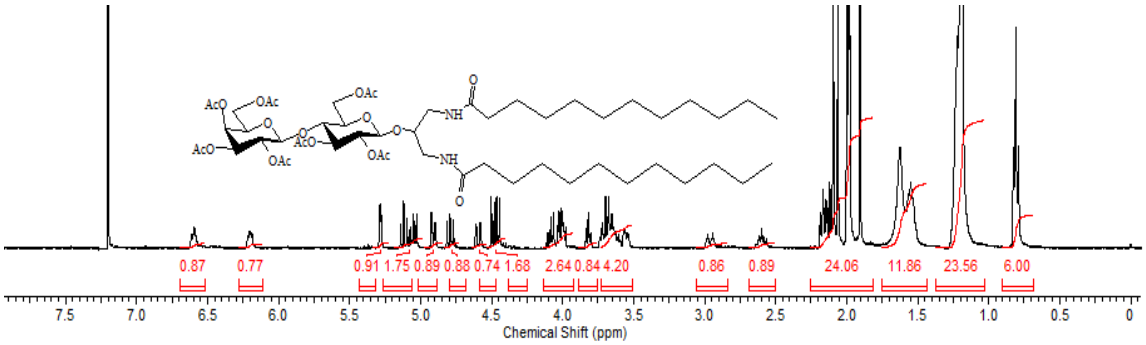

Figure9. *1H NMR spectrum of 1,3-didodecanamido 2,3,6,2',3',4',6'-hepta-O-acetyl-β-D-lactopyranoside [13]*

^{13}C NMR shows the signals of the two amide carbons at about δ 175 and δ 173.92 and the acetyl carbonyls between δ 170.53 and 168.96 The anomeric signals (C-1, C-1') are found at δ100.98 and δ100.59. The carbons of the sugar at acetylated oxygen (C-2 to C-4) appear between δ 71.81 and δ 70.00 the non-acetylated sugar signal (C-5) is found around δ 70.73. The primary methyelen of the sugar ring (C6/C6') appears at around δ 61.28 and δ 60.76. The carbons for the linker appear at about δ 39.46and δ 38.85. The alkyl chain carbons appear in between δ36.74 (α-CH_2) and δ 14.00 (terminal CH_3).

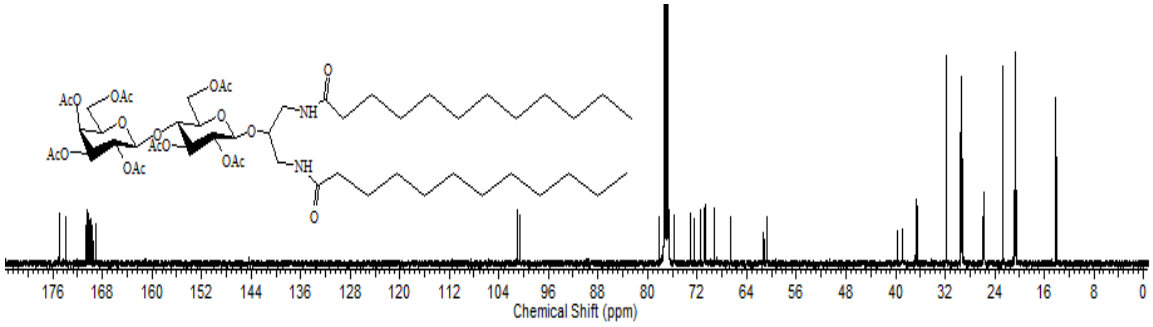

Figure10. *13C NMR spectrum of 1,3-didodecanamido 2,3,6,2',3',4',6'-hepta-O-acetyl-β-D-lactopyranoside [13]*

^{1}H NMR of the deacetylated surfactant shows the completely removal of the acetyl groups signals. Due to the absence of ester, the amide protons appear at δ 7.67 and δ 7.55. The sugar hydrogen at (C-2 to C-4') for both sugars domain are shifted upfield and appear between δ 3.77 to δ 3.15. The anomeric signals (H-1, H-1') are found around at δ 4.24 and δ 4.14. The protons for the linker located between δ 3.0 and δ 2.80 (CH_2N) and at δ 3.80 (OCH), respectively. The protons of the alkyl chain appear between δ 1.19 (α-CH_2) and δ 0.81 (terminal CH_3).

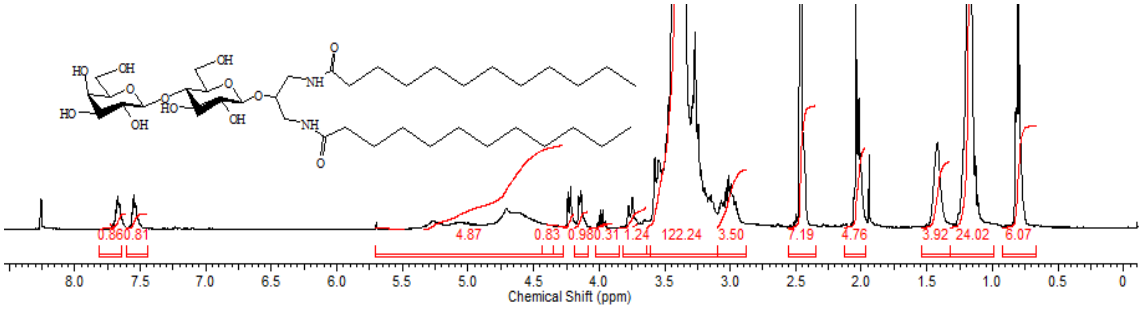

Figure 11: *1H NMR spectrum of 1,3-didodecanamid -β-D-lactopyranoside [14]*

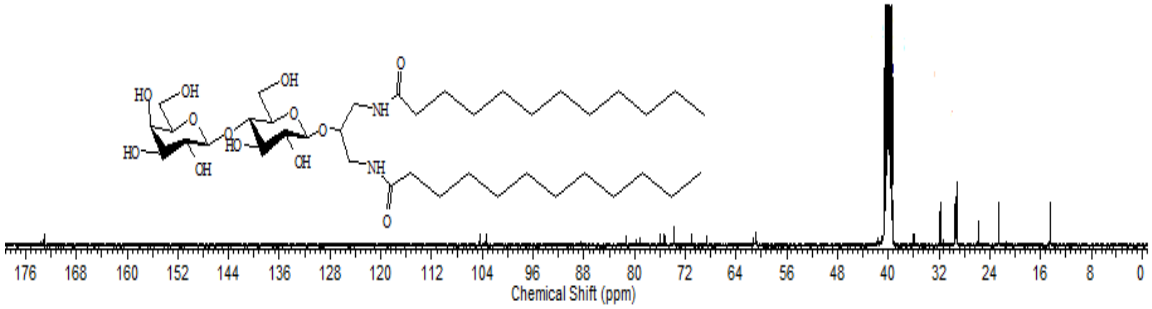

Figure 12. *1H NMR spectrum of 1,3-didodecanamido-β-D-lactopyranoside [14]*

^{13}C NMR shows the signals of the two amides carbon at about δ 173.30 and δ 173.13. The anomric carbons (C-1, C-1') found at about δ 104.44, δ 103.44. Other sugar carbons appear between δ 81.27 and δ 68.64. The position of the primary carbons (C-6, C6') is found between δ 61.21 and δ 60.91 Themethylene carbons of the linker appear between δ 36.00 and δ 35.84 reflecting the nitrogen substitution, while the methyne proton (OCH) is found at δ79.68. The alkyl carbon chains appear in between 31.81 (α-CH_2) and 14.40 (terminal CH_3). For detailed data analysis see the experimental part.

2.2. Physiochemical Properties

Both straight chain and cyclic chain surfactants show low solubility in water at room temperature and reasonable krafft temperature for surfactant **[8]** about (55 ºC) and high Krafft temperature more than (100 °C) for surfactant **[14].** Non surfactant shows a liquid crystals phase in OPM investigations at room temperature. The cyclic chain surfactant **[8]** shows both crystalline and hexagonal H_1 phases in contact with water as shown in (figure 13a). This reflects a significantly larger molecular surface area for the hydrated sugar compared to the single alkyl chain, while the double chains surfactant **[14]** exhibits a crystalline, cubic, and lamellar phases in contact with water (figure 13b). The exhibiting of the cubic phase makes the latter fit the target application for drug delivery.

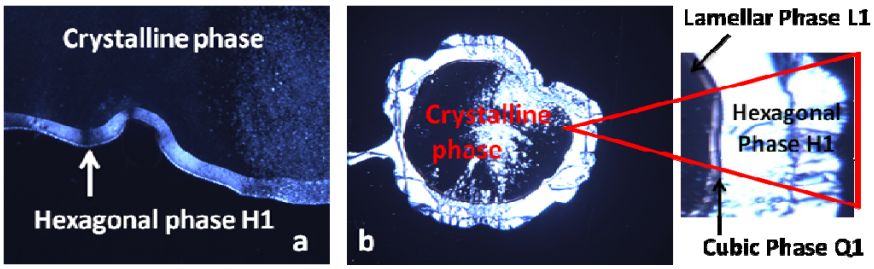

Figure 13: *OPM images for water penetrating of surfactants [8] and [14]*

The exhibition of crystalline thermotropic phase was confirmed by DSC which shows only two repeating peaks in heating cooling cycle referring to melting and re-crystalline of the surfactant. Figure 14 shows the DSC spectrum of compound **[14]**

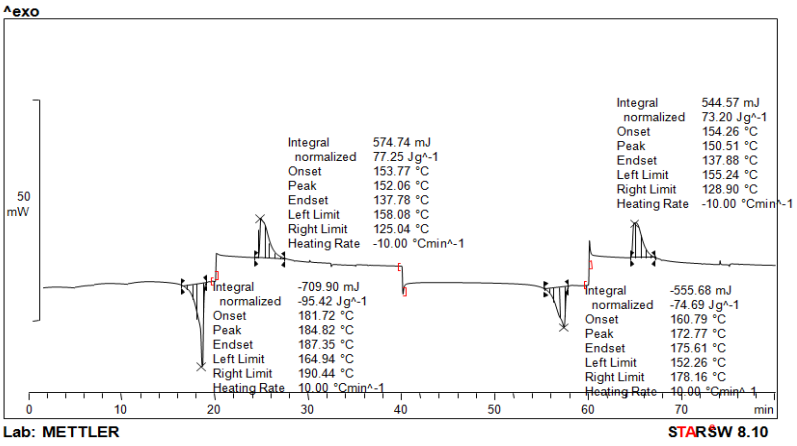

Figure14. *The DSC spectrum of compound [14]*

The critical micelle concentrations (CMC) were determined based on surface tension measurements carried out for the series of surfactant solutions with different concentrations. The CMC investigation was limited to the mono-antennary surfactants, as the bi-intermarry surfactant is extremely difficult to measure, due to the high Krafft temperature. The surface tensions and CMC for mono-antennary surfactant is about 30 mN/m at CMC 0.5 mmol/L (figure 15) , which is consistent with previously reported monosaccharide of this chain length[26] . This value makes the mono-antennary surfactant suitable for the target application as an oil-water emulsifier.

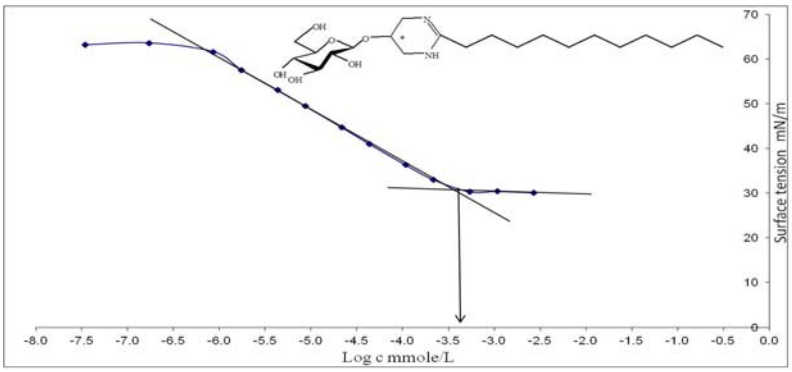

Figure15. *Surface tension investigation for the surfactant [8]*

3. EXPERIMENTAL

3.1. General procedures

Melting temperatures were determined using a manual melting point apparatus and are uncorrected. Optical rotations were measured at 589 nm in 10 cm cells at room temperature. NMR spectra were recorded on Jeol and Bruker spectrometers at 400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively. Assignments of ^{13}C-signals are based on HMQC spectra. High-resolution mass spectra were recorded on an LC–MS system, applying MeOH/water eluents. Phase transition temperatures were determined by DSC in replicated heating–cooling cycles at a heating/cooling rate of 10 °C min^{-1}. Lyotropic phases were investigated using the contact penetration technique under OPM observation[27,28]. The determination of Krafft points applied heating 20 mL samples of the surfactant in water at a concentration of about 10% above the CMC in an oil bath under moderate stirring until the mixture re cleared. Critical micelle concentrations were determined by surface tension measurements. The intersection of the concentration dependent and the high concentration independent region in the plot of the surface tension versus the logarithmic concentration determines the CMC. Surface tension measurements were measured at rt in 5 replicates with a standard deviation below 0.1 mN m^{-1}.

3.2. Glycosylation

Sugar β-peracetate (5 mmol) and 1,3-dichloro-2-propanol (6 mmol) were dissolved in anhydr. CH_2Cl_2 (50 mL) and treated with BF_3 x Et_2O (6 mmol). The reaction mixture was kept for about 3 h at rt before it was quenched with water. The organic layer was separated, washed with water and aqueous $NaHCO_3$, dried over $MgSO_4$, and concentrated. The crude product was purified by crystallization from EtOH to provide **[5]** and **[11]**, respectively, in about 50% yield.

3.3. Substitution to introduce azides

A solution of 1,3-dichloro-propylglycoside **[5]** or **[11]** (1 mmol) in DMF (25 mL) was treated with NaN_3 (6 mmol) and the suspension was heatedto80 ºC for 24h. After cooling to rt the reaction mixture was diluted with water and extracted with CH_2Cl_2.The organic layer extract was washed with water and aqueous $NaHCO_3$, dried over $MgSO_4$ and concentrated. Recrystallization of the crude product from ethanol furnished **[6]** and **[12]** respectively, in about75% yield.

3.4. Staudinger reaction

To a solution of the diazide (2 mmol) in benzene (40 mL) was added triphenylphosphine (1.25 g, 4.8 mmol). After the gas evolution has ceased a solution of the acid chloride (1.6 mmol for glucose diazide and 3.2 (mmol) for lactose diazide) in benzene (5 mL) was added drop-wise at rt. The reaction was left to stir at rt for 7–15 h, by which it had become cloudy. The solid was removed by filtration and the solution was washed with aqueous $NaHCO_3$ and dried over $MgSO_4$. After removal of the solvent the crude product was purified by chromatography on silica using ethyl acetate and acetone 6:1 to furnish compounds **[7]** and **[13]**.

3.5. Deacetylation

The carbohydrate **[7]** and **[13]** was dissolved in MeOH and treated with a catalytic amount of NaOMe. The reaction was left to complete over night at rt, before neutralization with Amberlite 120 (H+). The resin was filtered off and the solvent was evaporated to provide the surfactants [**8]** and **[14]** in practical quantitative yield.

3.6. 2-undecyl-5-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1,4,5,6-tetrahydro-pyrimidine [7]

Compound **[6]** (1.50 g, 3.17 mmol) was coupled with octonyl chloride according to the procedure 3.1.4 to yield 1.00 g, (67%) of compound **[7]** as white crystals. Mp 120 ºC. $[\alpha]_D^{25}$- 55 (c 0.15, CHC_{l3}). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.04, 5.67 (2 ddt, 1H, 1:4, NH),, 5.14 (ddt, H-3), 5.00 (ddt, H-4), 4.92 (dd, H-2), 4.62 (d, H-1), 4.16 (dd, H- 6A), 4.10 (dd, H-6B), 3.90 (m, H-5), 3.64 (ddd, NCH_2-A), 3.48 (ddd, NCH_2-B),3.34 (mc,1H,OCH), 2.12 (2 t, 2H, α-CH_2), 2.02, 2.00, 2.97, 1.94 (4 s, 3X 3H, Ac), 1.56 (mc, 4H, β CH_2), 1.19 (mc, 16H, bulk-CH_2), 0.81 (2 t, 3H, CH_3); ^{3}J1,2 = 8.0, ^{3}J2,3 = 9.5, ^{3}J3,4 = 9.5, ^{3}J4,5 = 10.0, ^{3}J5,6A = 2.5, ^{3}J5,6B = 4.5, ^{2}J6 = 12.0, ^{3}JCH$_2$,CH = 5.0, ^{3}JCH$_2$,NH = 5.0, ^{2}JCH$_2$ = 15.0, ^{3}JCH$_2$,CH = 8.0, ^{3}JCH$_2$,NH = 5.0, ^{2}JCH$_2$ = 15.0 Hz. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.47 (C=N), 170.60, 170.16, 169.47, 169.42 (C=O),100.81 (C-1), 78.99 (CH), 72.85 (C-3), 72.02 (C-5), 71.65 (C-2), 66.29 (C-4), 61.87 (C-6), (44.81), 43.95 (CH_2N), (41.62), 40.47 (CH_2NH),36.65, 36.50 (αCH_2), 31.94 (2 GO^{-2}), 29.61 (2), 29.36 (2) (bulk-CH_2), 25.65, (β), 22.68 (GO^{-1}), 20.77, 20.71, 20.58 (2) (Ac), 14.11 (GO). Elemental analysis for C29H48N2O10: C, 348.31(59.57%); H, 48.38(8.27%); N, 28.01 (4.79%);O, 159.99(27.36%) found: C, 348.306 (59.57%); H, 48.376 (8.27%); N,28.006 (4.789%) ; O, 159.986(27.36%).

3.7. 2-undecyl-5- β-D-glucopyranosyl-1,4,5,6-tetrahydro-pyrimidine [8]

Compound **[7]** (1.5 g, 2.57 mmol) was deacetylated according to the procedure 3.1.5 to furnish 1.00 g, (94%) of compound **[8].** Mp 145 ºC. $[\alpha]_D^{25}$ + 0.16 (c 0.15, CH_3OH). ^{1}H NMR (400 MHz, CD_3OD) δ = 4.39 (d, H-1), 3.95 (dd, H-6A), 3.83 (dd, H-6B), 3.76 (ddd,H-3) 3.87-3.58 (m, 3H, H-2, H-4, H-5,)3.35-3.25,(mc ,4H , CH_2N), 3.80 (mc, OCH), 2.17 (2 t, 4H, αCH_2), 1.59 (mc, 4H, βCH_2), 1.32 (m, 16H, bulk-CH_2), 0.88 (t, 3H, CH_3); ^{3}J1,2 = 8.0, ^{3}J2,3 = 9.0, ^{3}J5,6A = 1.5, ^{3}J5,6B =5.0, ^{2}J6 = 11.5 Hz. ^{13}C NMR (100 MHz, CD_3OD) δ = 168.49 (C=N), 103.82 (C-1), 78.58 (C-3), 76.74,76.57 (C-5, CH), 73.71 (C-2), 70.10 (C-4), 61.30 (C-6), 44.17, 40.23 (2CH_2N), 35.72 (α), 31.73 (GO^{-2}), 29.41, 29.3, 29.14 , 29.02 (bulk-CH_2), 25.64 (β), 23.66 (GO^{-1}), 13.10 (GO). HRMS: $[M+H]^+$ calcd. For C39H74N2O13: 779.5264 found: 779.5142 618.4763.

3.8. 1,3-didodecanamido 2,3,6,2',3',4',6'-hepta-O-acetyl-β-D-lactopyranoside [13]

Compound **[11]** (1 g, 1.31 mmol) was coupled with dodecanoyl chloride according to the procedure 3.1.4 to yield 1,05 g, (75%) of compound **[13]** as white crystals. Mp 189 ºC. $[\alpha]_D^{25}$- 25 (c 0.15, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.57, 6.18 (2 t, 2H, NH),5.28 (d, 1H,H-1), 5.11 (ddd,1H, H-4'), 5.04 (ddt,1H, H-3), 4.93 (dd,1H, H-2'), 4.79 (dd,1H, H-3'), 4.50 (dd,1H, H-2), 4.44 (ddd, 1 H, H-1'), 4.06 (dd, H-6/6'A) 4.00 (dd, H-6'/6A),3.82 (dd, H6/ 6'B),3.82 (dd, H-6'/6B), 3.72-3.65 (m, 5H, CH, H-5'),3.62 (dd~t,1H, H-4), 3.54 (m, 1H, H-5),2.95 (ddd, CH_2N-B) 2.60 (Mc 1H.CH_2N-A), 2.14 (mc, 2H, αCH_2), 2.09, 2.06, 2.00, 199, 1.98(2), 1.90. (7 s, 21H, Ac), 1.55 (mc, 2H, βCH_2), 1.19 (mc, 32H,

bulk-CH_2), 0.81 (t, 3H, CH_3); ^{3}J1,2 = 8.0, ^{3}J2,3 = 9.0, ^{3}J3,4 = 9.0, ^{3}J4,5 = 9.0, ^{3}J1',2' = 8.0, ^{3}J2',3' = 10.0, ^{3}J3',4' = 3.0, ^{3}J4',5' 61 Hz. ^{13}C NMR(100 MHz, $CDCl_3$) δ = 174.98, 173.92 (CONH),170.53, 170.38, 170.15, 169.12, 170.90, 169.57, 168.96 (C=O), 100.98. 100.59 (C-1, C-1'), 78.09 (CH), 75.81 (C-4), 73.10 (C-3), 72.46 (C-3'), 71.50, (C-2), 70.91 (C-3'),70.73 (C-5'), 69.16 (C-2'), 66.69 (C-4'), 61.28 , 60.76 (C-6, C-6'), 39.46, 38..85 (CH_2N),(CH_2NH), 36.74,36.49 (α), 31.85 x2 (CH_2^{-2}), 29.45, 29.34, 29.32, 29.31, 28.25 (bulk-CH2), 25.82, 25.68 (β), 22.66x2 (CH_2^{-1}), 20.93, 20.77, 20.74, 20.64x3, 20.61,(Ac), 14.10 (CH_2). Elemental analysis for C53H88N2O20: C, 636.57(59.31%); H, 88.70(8.26%); N, 28.01(2.61%); O, 319.99(29.81%) found: C, 636.564(59.31%); H, 88.693(8.26%); N, 28.005(2.609%).

3.9. 1,3-didodecanamido-β-D-lactopyranoside [14]

Compound **[13]** (0.5 g, 0.58 mmol) was deacetylated according to the procedure 3.1.5 to furnish (0.34 g. 94%) of compound **[14].** Mp 181ºC. $[\alpha]^{25}$ +0.15 (c 0.15, CH_3OH). ^{1}H NMR (400 MHz, DMSO) δ = 7.67, 7.55 (2 CONH), 5.45-4.40 (m, 7OH), 4.22, 4.14^D(2 d d, 2H, H-1 & H-1'), 3.77– 3.18 (m, 17H), 3.50 (mc, 1H. CH), 2.04 (mc, 2H, αCH_2), 1.42 (mc, 2H, βCH_2), 1.19 (mc, 32H, bulk-CH_2), 0.81 (t, 3H, CH_3); ^{3}J1,2 = 8.0/7.5, ^{3}J1',2' = 7.5/ 8.0 Hz. ^{13}C NMR(100 MHz,) δ = 173.29,173.13 (2 CONH), 104.44, 103.44 (C-1, C-1', 81.24 (C-4). 79.90 (C-5),79.17 (C-3),76.05 (C-2), 76.05 (C-3'), 75.14 (C-5'),2x73.75 (C-2', CH),68.51 (C-4'), 61.20 (C-6), 60.91 (C-3), 5.99, 35.88 (αCH_2), 31.81 (CH_2^{-2}), 29.43, 29.35, 29.20, 30.20 (bulk-CH_2), 2x25.77 (β), 22.66 (CH_2^{-1}), 14.49 (CH_2). HRMS: $[M+H]^+$ calcd. For C21H40N2O6: 417.2959 found: 417.2831.

4. CONCLUSION

Two series of surfactants were synthesized by coupling of sugar azide with fatty acid chloride using the Staudinger reaction. Two different sugars were used, i.e. the monosaccharides glucose as well as the disaccharides lactose. Applied fatty acids involve straight hydrocarbon chains (C12) were acquired from commercial resources. The physicochemical properties of these surfactants were investigated by optical polarizing microscope (OPM), differential scanning calorimetry (DSC) and systematic surface tension measurements.

The Staudinger reaction enables easy access to bisamide linked biantennary surfactants with close structural similarity to natural glycol-glycerolipids, provided the carbohydrate does not give rise to sterical hindrance. In case of the latter, an intra-molecular cyclization of a monoamide leads to a tetrahydropyrimidine linked mono-antennary surfactant instead. Amide analogs of glyco-glycero lipids exhibit very high Krafft temperatures. This may affect their potential use in a vesicular delivery system, as formulation requires high temperature treatments. The problem might, however, be solved by applying surfactant blends rather than single compounds. The phase behaviour of the biantennary amide surfactants in contact with water indicates the material as promising for the target application, due to the expression of a cubic phase, which is an important feature for supposed fusion of the vesicle with a cellular membrane.

REFERENCES

[1] Mannock, D. A.; Lewis, R. N.; Mcelhaney, R. N. *European Biophysics Journal* 1990, *30*, 537.

[2] Mannock, D. A.; Lewis, R. N.; Mcelhaney, R. N. *Chemistry and Physics of Lipids* 1990, *55*.

[3] Sauvageau, J.; Lagutin, J.; Sims, I. M.; Stocker, B. L.; Timmer, M. S. *Carbohyrate Research* 2012, *357*, 151.

[4] Choi, J. S.; I.Lee, D.; K.Lee, W.; Kim, D.; Choi., H. D.; Son, B. W. *Bulletin of the Korean Chemical Society* 1992, *20*.

[5] Gill, G. H.; H. Hong; C.Choe, J.; Kim, Y. H. *Bulletin of the Korean Chemical Society* 2003, *24*, 1163.

[6] Minamikawa, H.; Murakami, T.; Hato, M. *Chemistry and Physics of Lipids,* 1994, *72*, 111.

[7] Hashim, R.; Hashim, H. H.; N. Z. Rodzi; D.Hussen, R. S.; Heidelberg, T. *Thin Solid Films* 2006, *509*, 27.

[8] Salman, S. M.; Heidelberg, T.; Tajuddin, H. A. B. *Carbohyrate Research* 2013, *375*, 55.

[9] Cochran, M. A., University of Toronto, 2011.

[10] Hanessian, S.; Ducharme, D.; Massé, R.; Capmau, M. L. *Carbohydrate Research* 1978, *63*, 265.

[11] Sani, F. A.; Heidelberg, T.; Hashim, R.; Farhanullah *Colloids and surfaces B: Biointerfaces* 2012, *97*, 196.

[12] Fischer, E. *Berichte der deutschen chemischen Gesellschaft* 1916, *49*, 548.

[13] Khan, R.; Mufti, K. S.; R.Jenner, M. *Carbohydrate Research* 1978, *65*, 109.

[14] Dahmén, J.; Frejd, T.; Grönberg, G.; Lave, T.; Magnusson, G.; Noori, G. *Carbohydrate Research* 1983, *116*, 303.

[15] Carvalho, I.; Andrade, P.; Campo, V. L.; Guedes, P. M. M.; Sesti-Costa, R.; Silva, J. S.; Schenkman, S.; Dedola, S.; Hille, L.; Rejzek, M.; Nepogodiev, S. A.; Field, R. A. *Bioorganic & Medicinal Chemistry* 2010, *18*, 2412.

[16] Li, S.; Cai, X. M. M.; Li, Z. *Synthesis Communications* 2006, *36*, 637.

[17] Daubert, B. F.; Fricke, H. H.; Longgenecker, H. E. *Journal of American Chemical Society* 1943, *65*, 2142.

[18] Quinn G., J.; Sampugna, J.; Jensen, R. J. *Journal of the American Oil Chemists' Society* 1967, *44*, 439.

[19] Bauer, S. T. *Journal of the American Oil Chemists' Society* 1946, *23*, 1.

[20] Dedola, S.; Hughes, D. L.; Nepogodiev, S. A.; Rejzek, M.; Field, R. A. *Carbohydrate Research* 2010, *345*, 1123.

[21] Anjos, J. V. d.; Sinou, D.; Meloc, S. J. d.; Srivastava, R. M. *Carbohydrate Research* 2007, *342*, 2440.

[22] Park, B. S. R.; Jeon, H. B.; Kim, K. S. *Tetrahedron Letters* 2006, *47*, 5105.

[23] Tornøe, C. W.; Christensen, C.; Meldal, M. *The Journal of Organic Chemistry* 2002, *67*, 3057.

[24] Zemplen, G.; Gereces, A.; Hadacsy, I. *Berichte der deutschen chemischen Gesellschaft* 1936, *69B*, 1827.

[25] Neto, V.; Granet, R.; Krausz, P. *Tetrahedron* 2010, *66*, 4633.

[26] Abe, A.; Asakura, K.; Osanai, S. *Journal of Surfactants and Detergent* 2004, *7*, 297.

[27] Minden, H. M. V.; Brandenburg, K.; Seydel, K.; Koch, J. H. M.; Garamus, V.; Willumeit, R.; Vill, V. *Chemistry and Physics of Lipids* 2000, *106*, 157.

[28] Milkereti, G.; Brandenburg, K.; Gerber, S.; Koch, M. H. J.; Morr, M.; Andra, J.; Sydel, U.; Vill, V. *Chemistry and Physics of Lipids* 2005, *135*, 15.

AUTHOR'S BIOGRAPHY

Associate Professor **Dr. Salih Mahdi Salman,** obtained both bachelor's and master's degree of science in organic chemistry from the University of Baghdad and completed his Ph.D. at the University of Malaya under supervision of Associate Professor Thorsten Heidelberg and Hariul Anuar Tajuddin in 2013. Currently he is a lecturer at the department of chemistry, Faculty of Medicine, University of Diyala in Iraq. His interest area is organic synthesis.