CHAPTER III

RESULTS AND DISCUSSION

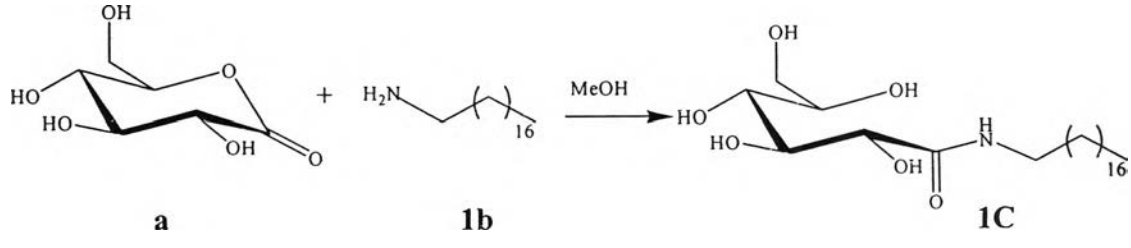
3.1 Characterization of gluconamide derivatives (1C-6C)

This research was focused on the syntheses and structure-activity relationships study of six gluconamides. Five compounds (**2C, 3C, 4C, 5C** and **6C**) were disclosed to be new substances based upon no report cited in chemical literature. The structures of all synthesized compounds were well characterized using spectroscopic techniques including IR and ^{1}H-NMR spectroscopy. The results are shown in Figures **A.1 – A.12 (Appendix A).**

N-Octadecyl–D-gluconamide (1C):

The methodology used to synthesize *N*-octadecyl–*D*-gluconamide **(1C)** was illustrated in Scheme 3.1. The product was white powder with 86% yield and had melting point 145-146 °C. According to IR spectrum (Figure A.1), the spectral pattern of N-H stretching of primary amide vibration around 3109-3627 cm^{-1}, C=O stretching vibration of gluconamide at 1510-1695 cm^{-1}, C-N stretching of aliphatic primary amide vibration at 1150-1050 cm^{-1}, and C-H vibration at 2831-2948 cm^{-1} were visualized.

The signals of the interlinking methylene group were clearly observed in ^{1}H-NMR (Figure A.2) as multiplet around δ 1.16-1.40 while the signal with 3H intensity of CH_3 was observed as triplet around δ 0.86 (J= 6.20 Hz). Two protons belonging to $NHCH_2$ were observed as triplet around δ 3.17 (J= 6.35 Hz) together with a singlet proton of NH was observed at δ 8.01. Another signal detected approximately δ 3.33-4.25 could be designated for gluconic protons.



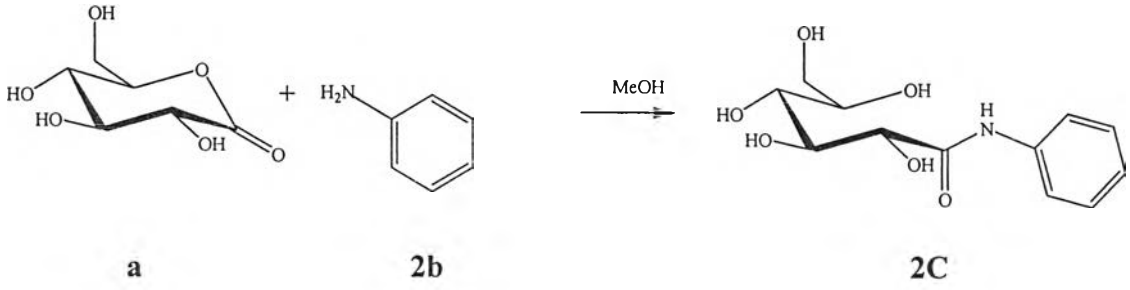
a **1b** **1C**

Scheme 3.1 General procedure for the synthesis of *N*-octadecyl–*D*-gluconamide (**1C**)

N-Phenyl–D-gluconamide (2C)

N-phenyl-*D*-gluconamide **(2C)** was obtained as white powder (52% yield), melting point 154-155 °C. According to the IR spectrum (Figure A.3), the spectral pattern of N-H stretching of primary amide vibration around 3324-3464 cm^{-1}, C=O stretching vibration of gluconamide at 1590-1695 cm^{-1}, C-H vibration at 2902-2995 cm^{-1}, Ar-H stretching vibration at 1500-1600 cm^{-1} and N-H stretching of aliphatic primary amide vibration at 670-750 cm^{-1} were observed.

The signals of the aromatic protons were clearly detected in ^{1}H-NMR spectrum (Figure A.4) as triplet around δ 7.07 (1H, *J*= 7.21 Hz) and a triplet signal of Ar-H were observed at δ 7.30 (2H, *J*= 7.06 Hz). Other Ar-H were observed as triplet around δ 7.34 (2H, *J*= 7.82Hz) while 1H of NH was observed as singlet around δ 10.01. Another set of signals belonging to gluconic protons could be detected approximately δ 3.25-4.15.



a **2b** **2C**

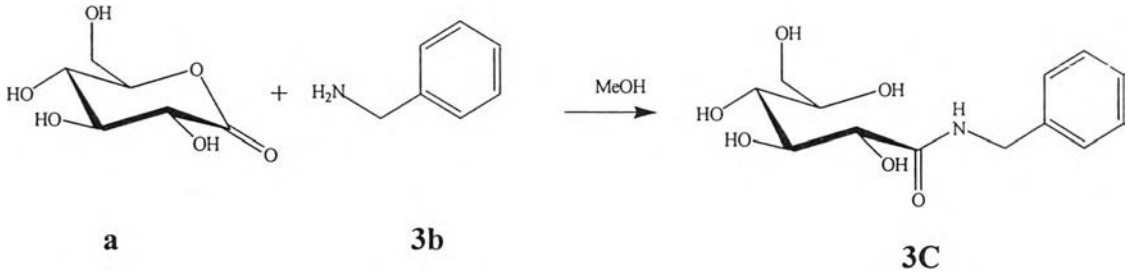
Scheme 3.2 General procedure for the synthesis of *N*-phenyl-*D*-gluconamide **(2C)**

N-Benzyl–D-gluconamide (3C)

The methodology used to synthesize *N*-benzyl -*D*-gluconamide **(3C)** was illustrated in Scheme 3.3. The white powder product was achieved in 72% yield with melting point of 158-159 °C. According to IR spectrum (Figure A.5), the spectral pattern of N-H stretching of primary amide vibration around 3257-3430 cm^{-1} and C=O stretching vibration of gluconamide at 1607-1683 cm^{-1} and that of Ar-H stretching vibration at 1488-1590 cm^{-1} and C-H vibration at 2868-2995 cm^{-1} were clearly detected.

The signals of the aromatic group were also clearly observed in ^{1}H-NMR spectrum (Figure A.6) as doublet around δ 7.28 (2H, *J*= 7.12 Hz) triplet around δ 7.31 (2H, *J*= 6.85 Hz) and another triplet around δ 7.25 (1H, *J*= 6.25 Hz). The signal

belonging to N-CH_2-Ar was observed as singlet around δ 4.32 and 1H of NH was observed as singlet around δ 8.19. Another set of signals detected approximately δ 3.45-4.35 could be designated for gluconic protons.



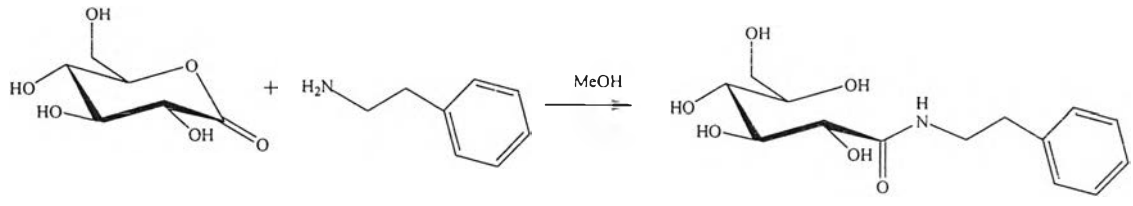
a 3b 3C

Scheme 3.3 General procedure for the synthesis of *N*-benzyl–*D*-gluconamide **(3C)**

N-Phenethyl–D-gluconamide (4C)

The similar methodology described for synthesizing **3C** was conducted for the preparation of *N*-phenethyl-*D*-gluconamide **(4C)** as illustrated in Scheme 3.4. The product was obtained as white power (83% yield) with melting point 166-167 °C. According to IR spectrum (Figure A.7), the N-H stretching vibration of primary amide was observed around 3109-3466 cm^{-1} and C=O stretching vibration of gluconamide was at 1655-1721 cm^{-1}. The Ar-H stretching vibration at 1524-1634 cm^{-1}, C-H vibration at 2856-2970 cm^{-1}, and N-H stretching of aliphatic primary amide vibration at 687-757 cm^{-1} were also visualized.

The signals of the aromatic group were clearly observed in ^{1}H-NMR spectrum (Figure A.8) as signals belonging to doublet around δ 7.28 (2H, *J*= 7.56 Hz). Other two signals belonging to Ar-H were detected as triplet around δ 7.31 (2H, *J*= 7.34 Hz) and triplet around δ 7.25 (1H, *J*= 7.02 Hz). Two protons of N-CH_2-Ar were observed as singlet around δ 4.32 together with a singlet proton of NH detected around δ 8.19. Another set of signals detected approximately δ 3.30-4.28 could be designated for gluconic protons.



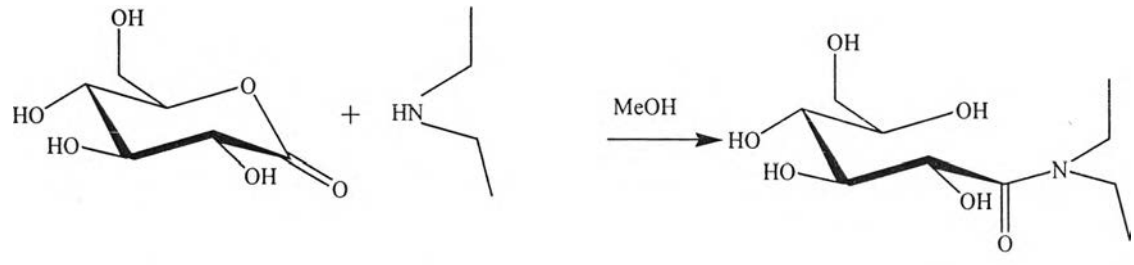
a **4b** **4C**

Scheme 3.4 General procedure for the synthesis of *N*-phenethyl-*D*-gluconamide (**4C**)

N,N-Diethyl-D-gluconamide (5C)

The preparation of *N,N*-diethyl-D-gluconamide **(5C)** was illustrated in Scheme 3.5. The product was yellowish oil with 41% yield. According to IR spectrum (Figure A.9), the spectral pattern of N-H stretching vibration of secondary amide was observed around 3330-3400 cm^{-1}, C=O stretching vibration of gluconamide at 1602-1690 cm^{-1} and that of C-H stretching vibration at 2750-2950 cm^{-1} were visualized.

The signals of the methylene group were clearly observed in ^{1}H-NMR spectrum (Figure A.10) as N-CH_2 were observed as singlet around δ 3.24 (4H) while CH_3 observed as triplet around δ 1.20 (4H, *J*= 7.26 Hz). The signals detected approximately δ 3.25-4.51 could be designated for gluconic protons.



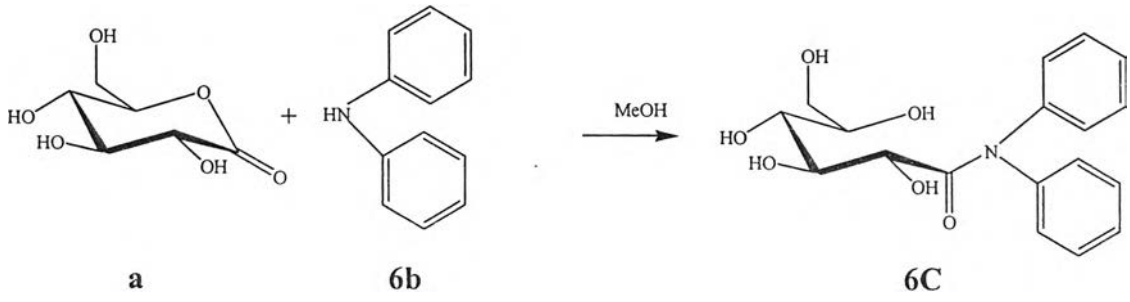
a **5b** **5C**

Scheme 3.5 General procedure for the synthesis of *N,N*-diethyl-D-gluconamide **(5C)**

N,N-Diphenyl –D- gluconamide (6C)

N,N-diphenyl-D-gluconamide **(6C)** was gained as violet powder 57% yield, melting point 178-179 °C. According to IR spectrum (Figure A.11), the spectral pattern of N-H stretching of secondary amide vibration around 3345-3476 cm^{-1} and C=O stretching vibration of gluconamide at 1661-1791 cm^{-1} and that of Ar-H stretching vibration at 1400-1524 cm^{-1} and C-H vibration at 2830-2970 cm^{-1} were visualized.

The signals of the aromatic group were clearly observed in ^{1}H-NMR spectrum (Figure A.12) as doublet around δ 7.26 (4H, *J*= 7.50 Hz), triplet around δ 7.24 (4H, *J*= 7.99 Hz) and singlet around δ 7.07 (2H). The signals detected approximately δ 3.35-4.21 could also be designated for gluconic protons.



a 6b 6C

Scheme 3.6 General procedure for the synthesis of *N,N*-diphenyl–D-gluconamide **(6C)**

The physical properties and spectroscopic data of synthesized compounds are summarized in Tables 3.1 and 3.2.

Table 3.1 Physical properties and % yield of synthesized gluconamides

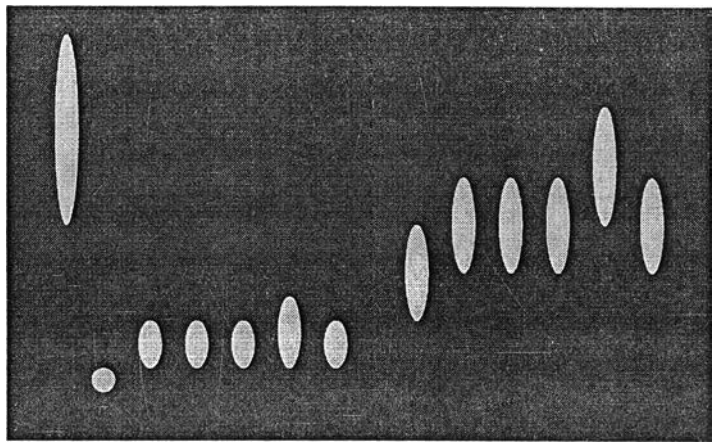
Compounds	Physical Property			% Yield
	Appearance	m.p. (°C)	MW	
1C	White powder	145-146	447.7	86
2C	White powder	154-155	271.3	52
3C	White powder	158-159	285.3	72
4C	White powder	166-167	299.3	83
5C	Yellowish oil	-	251.3	41
6C	Violet powder	178-179	347.5	57

Table 3.2 Spectroscopic data of synthesized gluconamides

Product	Molecular Formula	IR (KBr,cm^{-1})	^{1}H-NMR (DMSO-d_6 δ (ppm))
1C	$C_{24}H_{49}O_6N$	3109-3627, 2831-2948 , 1510-1695 and 1150-1050	0.86 (t, J = 6.20 Hz, 3H, -CH_3), 1.16 – 1.40 (m, 32H, -$(CH_2)_{16}$-), 3.17 (t, J = 6.35 Hz, 2H,-$NHCH_2$-), 8.01 (s, 1H,- NH), 3.33-4.25 (m, 7H, -Gluconic)
2C	$C_{12}H_{17}O_6N$	3324-3464, 2902-2995, 1590-1695 and 670-750	10.01 (s,1H,-NH), 7.34 (d, J =7.34 Hz, 2H,Ar-H), 7.30 (t, J = 7.06 Hz, 2H, Ar-H), 7.07 (t, J = 7.21Hz, 1H,Ar-H) , 3.25-4.15 (m, 7H, -Gluconic)
3C	$C_{13}H_{19}O_6N$	3257-3430, 2868-2995, 1607-1683 and 1488-1590	4.32 (s, 2H, N-CH_2-Ar) , 7.25 (t, J = 6.25Hz ,1H, Ar-H), 7.28 (d, J= 7.12 Hz, 2H, Ar-H), 7.31 (t, J = 6.85 Hz, 2H, Ar-H), 8.19 (s, 1H,- NH) , 3.45-4.35 (m, 7H, -Gluconic)
4C	$C_{14}H_{21}O_6N$	3109-3466, 2856-2970, 1655-1721, 1524-1634 and 687-757	4.32 (s, 2H, N-CH_2-Ar) ,7.25 (t, J = 7.02 Hz, 1H, Ar-H), 7.28 (d, J = 7.56 Hz,2H, Ar-H), 7.31 (t, J= 7.34 Hz, 2H, Ar-H), 8.19 (s, 1H,- NH) , 3.30-4.28 (m, 7H, -Gluconic)
5C	$C_{10}H_{11}O_6N$	3300-3400, 2750-2950 and 1602-1690	1.20 (t, J = 7.26 Hz, 4H, -CH_3), 3.24 (s, 4H,N –CH_2), 3.25-4.51 (m, 7H, -Gluconic)
6C	$C_{18}H_{21}O_6N$	3345-3476, 2830-2970, 1661-1791 and 1400-1524	7.26 (d, J = 7.50 Hz, 4H,Ar-H), 7.24 (t, J = 7.99 Hz, 4H, Ar-H), 7.07 (s, 2H, Ar-H), 3.35-4.21 (m, 7H, -Gluconic)

3.2 Thin-Layer Chromatography (TLC)

Gluconamide derivatives were accomplished by protocol in chapter II. The chromatograms of gluconamide derivatives after spotted and dipped in Potassium permanganate solution the results are shown in Figure 3.1.



a 1b 2b 3b 4b 5b 6b 1C 2C 3C 4C 5C 6C

Figure 3.1 TLC chromatograms assay for gluconamide derivatives

Figure 3.1 shows the TLC of compounds by R_f values which substances have R_f values different compounds. After developing in 1 : 1 ethyl acetate : hexane saw a single spot of compounds : 1C (R_f = 0.4) , 2C (R_f = 0.5), 3C (R_f = 0.5), 4C (R_f = 0.5), 5C (R_f = 0.7) and 6C (R_f = 0.5). This is a good indication that the sample is pure.

3.3 Determination of surface tension

Surface tensions of surfactants were determined by KRUSS digital tensiometer, Model DSA 10, Germany. The results are shown in Tables 3.3 and Appendix B.1. The surface tension of surfactant solutions was studied and compared with that of pure water. When the concentrations of the synthesized surfactants were increased from 0.1% (w/v) to 1.0% (w/v), the surface tensions of **1C, 2C, 3C, 4C, 5C** and **6C** were decreased from 70.40 to 68.61, 66.83 to 64.23, 72.60 to 69.63, 67.84 to 59.87, 64.08 to 48.37 and 68.26 to 62.15, respectively.

Table 3.3 The surface tensions of surfactants **1C - 6C**

Compounds	Concentration		Surface tension
	%w/v	mM	(mN/m)
N- Octadecyl-D- gluconamide **(1C)**	0.1	2.234	70.40
	1.0	22.340	68.60
N- Phenyl - D- gluconamide **(2C)**	0.1	3.686	66.83
	1.0	36.860	64.23
N- Benzyl - D-gluconamide **(3C)**	0.1	3.505	72.60
	1.0	35.050	69.63
N- Phenethyl- D- gluconamide **(4C)**	0.1	3.341	67.84
	1.0	33.410	59.87
N, N- Diethyl- D- gluconamide **(5C)**	0.1	3.979	64.08
	1.0	39.790	48.37
N, N- Diphenyl -D-gluconamide **(6C)**	0.1	2.878	68.26
	1.0	28.780	62.15
Reference surfactant			
Pure water	-	-	73.00
NP4 (Nonylphenolethoxylates of 4 ethylene oxide)	0.1	3.788	30.00
NP40 (Nonylphenolethoxylates of 40 ethylene oxide)	0.1	0.504	45.00

The results indicated that the surface tension of all six synthesized surfactants at 0.1 and 1.0% (w/v) were lower than pure water (73 mN/m) and those of the solutions were decreased when the concentrations were increased from 0.1 to 1.0% (w/v). These results clearly demonstrated that all six surfactants (**1C-6C**) displayed a property of surfactant to decrease the surface tension.

3.4 Determination of solubility

The solubility limits were carried out in three diverse solvents: water, ethanol and dodecane, which have different dielectric constant. Thus, solution in water ($\varepsilon_{25\,°C} = 80$), ethanol ($\varepsilon_{25\,°C} = 24$) and dodecane ($\varepsilon_{25\,°C} = 1.9$) were prepared to determine the solubility limit of the surfactants.The results are presented as shown in Table 3.4. Most of the surfactants have hydrophilic-lipophilic balance (HLB) values in the range of 8.0 to 14.2. It was apparent that the trend of aqueous solubility increased with an increased HLB value, whereas solubility in dodecane decreased with an increased HLB value.

N-octadeccy-D-gluconamide **(1C)** is a primary amide with low HLB and has low solubility in water. Thus, it can slightly be soluble in ethanol and dodecane. *N*-diethyl-D-gluconamide **(5C)** is a secondary amide with high HLB and has high solubility in water and ethanol but insoluble in dodecane. This observation could be explained that surfactants containing a primary amide as the connecting bond have lower aqueous solubilities than secondary amide. However, it is clear that the HLB value does not provide sufficient information for predicting the solubility. The general trend could however be expected and will be in accordance with the HLB concept. With the exceptions, compounds with high aqueous solubility but with low HLB values, share some common structural elements. They either possess a secondary amide bond instead of a primary amide bond, such as *N,N*- diphenyl - D-gluconamide **(6C)**. *N*-phenethyl-D-gluconamide **(4C),** *N*-phenyl-D-gluconamide **(2C)** and *N*-benzyl-D-gluconamide **(3C)** more soluble in water than **(1C)**. Thus, many surfactants may have the potential to act as good O/W emulsifiers and have rather high aqueous solubilities.

Table 3.4 Solubility limits for synthesized and selected surfactants in water, ethanol and dodecane

Compounds	Mw	HLB	Hydrophobic carbon atoms	Solubility limits (%w/v)		
				Aqueous	Ethanol	Dodecane
N- Octadeccyl-D- gluconamide **(1C)**	447.7	8.0	18	0.1	0.15 – 1	0.01 - 0.15
N- Phenyl - D- gluconamide **(2C)**	271.3	13.1	6	>1	0.15 – 1	< 0.01
N- Benzyl -D-gluconamide **(3C)**	285.3	12.5	7	>1	0.15 - 1	< 0.01
N- Phenethyl -D-gluconamide **(4C)**	299.3	11.9	8	>1	0.15 - 1	< 0.01
N,N- Diethyl- D- gluconamide **(5C)**	251.3	14.2	4	>1	>1	< 0.01
N,N- Diphenyl - D-gluconamide **(6C)**	347.5	10.3	12	>1	0.15 - 1	0.01 - 0.15
Reference surfactant						
NP 4 (Nonylphenolethoxylates of 4ethylene oxide)	264.0	4.6	15	0.15 - 1	>1	0.15 - 1
NP40 (Nonylphenolethoxylates of 40 ethylene oxide)	1986.0	18.0	15	>1	>1	< 0.01

3.5 Determination of wetting

The results of wetting determination are presented in Table 3.5. The contact angles of the synthesized surfactants were compared with commercial nonylphenol ethoxylates with 4 and 40 oxyethylene units (NP4, NP40) and pure water, with the defined reference values (5, 4 and 0 for NP4, NP40 and pure water, respectively). All gluconamides **1C- 6C** performed better wettability on nonpolar surface of parafilm than water, but poorer than those nonylphenols. Contact angles of gluconamides **1C- 6C** were decreased which were the characteristics of surfactant as would be explained below.

Compounds **1C-6C** were investigated for the wetting on a nonpolar parafilm surface. On such a surface, there is a strong driving force for the surfactants to adsorb and diminish the unfavorable surface-water contact. The major driving force for the surfactants adsorption is the hydrophobic effect, which stems from the fact that water interacts more favorably with itself than with nonpolar molecules or surfaces. The equilibrium contact angle, θ, of the solution droplet on the surface is given by a balance of three interfacial tensions:

$$\gamma_{SV} - \gamma_{SL} = \gamma_{LV} \cos\theta$$

Where γ_{SV}, γ_{SL} and γ_{LV} are the surface tensions at the solid-vapor, solid- liquid and liquid-vapor interfaces, respectively. For a given solid surface, *i.e.*, a given value of γ_{SV}, the contact angle decreases as the surface tension of the solid-liquid interface is reduced. Also, if the contact angle is below 90°, a decrease in liquid-vapor interfacial tension reduces the contact angle. Thus, the solid-liquid and liquid–vapor interfacial tensions should be as low as possible to obtain a good wetting agent as shown in Figure 3.2.

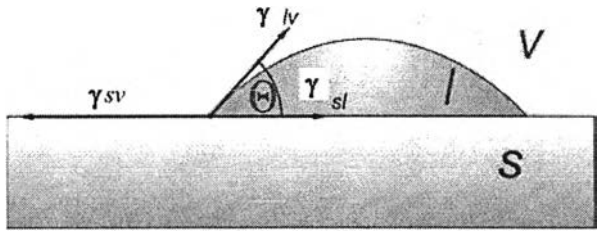


Figure 3.2 Contact angle

For a given solid surface, *i.e.*, a given value of γ_{SV}, the contact angle decreased as the surface tension of the solid-liquid interface reduced. The results demonstrated that six surfactants **1C-6C** showed a property of surfactant to decrease the surface tension.

Table 3.5 Wettability of surfactants on parafilm sheet

Compounds	Mw	Hydrophobic carbon atoms	Contact angle (θ)	Wettability (0-6 , 6 best)
N- Octadeccyl-D- gluconamide **(1C)**	447.7	18	76.5	0
N- Phenyl - D- gluconamide **(2C)**	271.3	6	71.0	0
N- Benzyl - D-gluconamide **(3C)**	285.3	7	77.0	0
N- Phenethyl -D-gluconamide **(4C)**	299.3	8	78.7	0
N,N- Diethyl- D- gluconamide **(5C)**	251.3	4	81.0	0
N,N- Diphenyl - D-gluconamide **(6C)**	347.5	12	80.5	0
Reference surfactant				
NP 4 (Nonylphenolethoxylates of 4ethylene oxide)	264.0	15	28. 1	5
NP40 (Nonylphenolethoxylates of 40 ethylene oxide)	1986.0	15	31.3	4
pure water	-	N/A	98.0	0

Table 3.5 and Figure 3.2 showed the relationship between contact angle and number of carbons in hydrophobic part of surfactant which the contact angle was increased when increasing the number of carbons in hydrophobic part of surfactant. The contact angle (θ) of surfactant (**2C**, **3C** and **4C**) were increased to 71.0, 77.0 and 78.7, respectively.

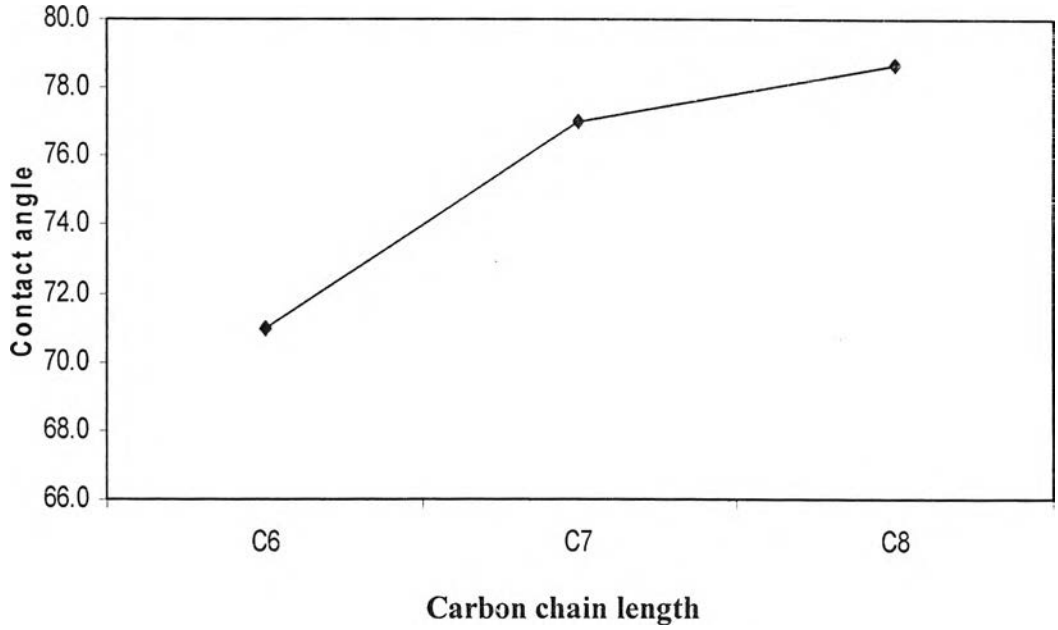


Figure 3.3 Contact angle of surfactant as a function of carbon chain length

3.6 Determination of foaming

The foamability and foam stability of the surfactants in this thesis was studied by foaming test. The foamability, the ability to produce foam under given conditions. The initial amount of foam was produced immediately after agitation. The foam stability is estimated by studying the remaining foam volume after 1 minute and were compared with two references nonylphenol ethoxylates NP-4 with processing low solubility and foamability but NP-40 with high solubility and foamability. The results are displayed in Table 3.6.

Table 3.6 Foaming properties of synthesized and reference surfactants

Compounds	Mw	Hydrophobic carbon atoms	Foaming volume		Aqueous Solubility (wt / vol %)
			(mm immediately)	(mm after 1 min)	
N- Octadeccyl-D- gluconamide **(1C)**	447.7	18	0	0	0.1
N- Phenyl-D- gluconamide **(2C)**	271.3	6	3 ± 0.5	0	>1
N- Benzyl -D-gluconamide **(3C)**	285.3	7	0.5 ± 0.5	0	>1
N- Phenethyl -D-gluconamide **(4C)**	299.3	8	0.5 ± 0.5	0	>1
N,N- Diethyl- D- gluconamide **(5C)**	251.3	4	3 ± 0.5	0	>1
N,N- Diphenyl - D-gluconamide **(6C)**	347.5	12	4 ± 0.5	0	>1
Reference surfactant					
NP 4 (Nonylphenolethoxylates of 4ethylene oxide)	264.0	15	10	8	0.15 - 1
NP40 (Nonylphenolethoxylates of 40 ethylene oxide)	1986.0	15	>30	>30	>1

From the results in Table 3.6, the foamability of surfactants was low. The foamability of surfactants **2C, 5C**, and **6C** having a high solubility were better than those of **1C**, **3C** and **4C**. However, these surfactants are vary soluble in water. Comparing the results derived from the synthesized surfactants with the two reference nonylphenol ethoxylates which show a maximal foamability the synthesized surfactants **2C**, **5C**, and **6C** are poorer foamability while **3C** and **4C** showed no foamability.

Conclusions from the data in Table 3.6, in the view point of foamability, *i.e.*, the foam volume, immediately formed after the mechanical agitation has stopped, is low for surfactants with low solubility and increasing of the bulky hydrophobic part. Because of the packing of the surfactant at the interface can't pack into a flat monolayer, which it is expected that the highest foam stability that can be achieved is when the packing of the surfactant at the interface is close to unity since in such a case the surfactant readily pack into flat monolayer as shown in Figure 3.4.

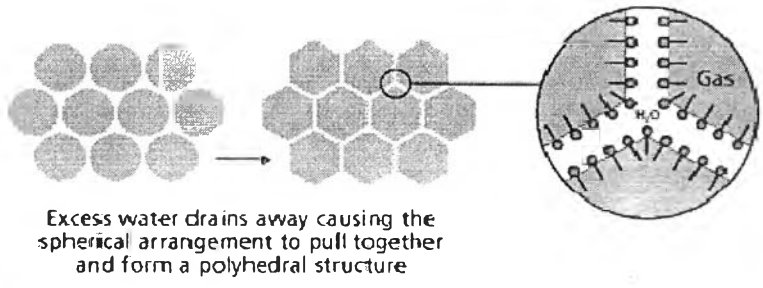


Figure 3.4 Foam stabilization