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Synthesis of the BEAC4ND4 Ionophore from *p-t*-Butylcalix[4]arene Carboxylic Acid

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Abstract

The BEAC4ND4 ionophore has been successfully synthesized from *p-t*-butylcalix[4]arene carboxylic acid. The BEAC4ND4 ionophore was obtained in two steps of the synthesis reaction. The first step is the chlorination reaction of *p-t*-butylcalix[4]arene carboxylic acid with thionyl chloride in dry benzene solvent. The chlorination reaction product is *p-t*-butylcalix[4]arene acyl chloride in the form of the light brown viscous liquid with a yield of 78.25% and TLC (SiO_2, CH_3OH: CH_2Cl_2 = 1: 1 v/v, R_f = 0.65). The second step is the amidation reaction of ethyl 2-aminoacetate with *p-t*-butylcalix[4]arene acyl chloride in dry tetrahydrofuran solvent. The product of the amidation reaction is *p-t*-butylcalix[4]arene ethylesteramide or the BEAC4ND4 ionophore in the form of a white solid with the yield of 75.22%, a melting point of 314-316°C, and TLC (SiO_2, CH_3OH: CH_2Cl_2 = 1: 1 v/v, R_f = 0.75).

1. Introduction

Calix[4]-and-[6]arenes are only slightly soluble in organic solvents. The solubility can be increased by modifying the lower and upper rims of the calix[4]-and-[6]arenes. Modification of the lower rim with thioamide can increase the solubility of *p-t*-butylcalix[4]-and-[6]arenes in water and dichloromethane [1]. Modification of the top rim with sulfonates can increase the solubility of calix[4]-and-[6]arenes in methanol. Modification can not only increase solubility, but modification can also improve the properties and expand the applications of calix[4]-and-[6] arene. Modifications to the lower rim with ethers, esters, ketones, carboxylic acids, amides, and crown ethers [1] can produce ionophores with binding properties of Na^+, Cs^+, Ca^{2+}, Mg^{2+} [2], and Fe^{3+}, Ni^{2+} cations, which is very selective.

The lower rim of calix[4]-and-[6]arenes by esterification and etherification reactions of the hydroxyl groups on the lower rim are the most popular and extensively studied functionalization. Group modification on the lower rim of calix[4]-and-[6]arenes have been reported by researchers, such as tri(ethoxy carbonyl methoxy)tri(hydroxy)-calix[6]arene [3], hexa(ethylester)calix[6]-arene [4], tetrakis(ethoxy carbonyl methoxy) calix[4]arene, tetra-(carboxylic) calix[4]arene, tetra-(propenyl tetraester)calix[4]arene, and tetra(propenyltetracarboxylicacid)calix[4]-arene [5].

The functionalization of the upper rim of calix[4]-and-[6]arenes can be done by modifying *p-t*-butyl with other groups. The *p-t*-butyl group of calix[4]-and-[6]arenes can be removed by a Friedel-Crafts dealkylation reaction [6]. Furthermore, the new group may be bound to the *para* position through electrophilic aromatic substitution reactions. For example, the Friedel-Crafts dealkylation reaction of *p-t*-butylcalix[4]arene gives *p*-H-calix[4]arene. Electrophilic aromatic substitution reactions of *p*-H-calix[4]arene produces *para*-substituted calix[4]arenes with various *para*-substituents. The reaction of *p*-H-calix[4]arene with formaldehyde and dimethylamine (Mannich

Reaction) gives *p*-aminomethyl-calix[4]arene, which can be converted into the corresponding quaternary ammonium compounds by reaction with MeI. Attack of the ammonium salts by a nucleophile affords *p*-Nu-methylcalix[4]arenes. The *p*-H-calix[4]arene is alkylated with allyl bromide in the presence of a base to give the tetraallyl ether, which undergoes the Claisen rearrangement to give *p*-allylcalix[4]arene [7]. So, the combination of the lower rim modification reactions with some protection-deprotection strategies allows one, two, three, or four substituents (same or different) to be attached on the *para*-positions of calix[4]arenes.

Modification of functional groups of the upper and the lower rim of calix[4]-and-[6]arenes can produce ionophores [3, 6]. The OH group's modification reactions of the lower rim with ethylester produce BEC4ND1 and BEC6ND1 [2] ionophores. Modification reactions of the ethylester group of the lower rim with carboxylic acid produce BCAC4ND2 [8] and BCAC6ND2 [9] ionophores. Modification reactions of the *t*-butyl group of the upper rim with a tetramer or hexamer produces an ionophore that is selective to the cations of Rb, Sr, Cs, alkali metals, and alkaline earth metals [10].

This study aims to synthesize BEAC4ND4 ionophore from *p*-*t*-butylcalix[4]arene carboxylic acid. The BEAC4ND4 ionophore can be synthesized in two steps of the synthesis reaction. The first step is the chlorination reaction of *p*-*t*-butylcalix[4]arene carboxylic acid with thionyl chloride in dry benzene solvent. The second step is the amidation reaction of ethyl 2-aminoacetate with *p*-*t*-butylcalix[4]arene acyl chloride in dry tetrahydrofuran solvent.

2. Methodology

2.1. Tools

The tools used are rotary vacuum evaporator (BUCHI Rotavapor™ series R-300), digital melting point apparatus (Electrothermal series IA9100), desiccator, analytical balance (Explorer Ohaus), measuring cup (Pyrex), chemical beaker (Pyrex), chamber, ball coolers, thermometers (100°C), heating mantles, funnels, and a set of reflux devices consisting of 100 mL three-neck round bottom flask. Spectrometers used are the FTIR Shimadzu series Prestige-21 and FTNMR Jeol series JNM-MY500.

2.2. Materials

The materials used are the raw material, *p*-*t*-butylcalix[4]arene carboxylic acid (synthesized), benzene (Merck), thionyl chloride (Merck), pyridine (Merck), tetrahydrofuran (THF) (Merck), ethyl ester amines (Merck), triethylamine (Merck), nitrogen gas (commercial), methanol (Merck), dichloromethane (Merck), anhydrous sodium sulfate (Na_2SO_4) (Merck), double distilled water (Onelab Waterone), and TLC plate. All reagents were in analytical grade.

2.3. Synthesis of the BEAC4ND4 Ionophore

p-*t*-Butylcalix[4]arene carboxylic acid (0.44 g, 0.5 mmol) in dry benzene (25 mL) was added $SOCl_2$ (5 mL) and 3 drops of pyridine. The mixture was stirred and refluxed under nitrogen at room temperature for 8 hours. The mixture was TLC tested every 2 hours to control the reaction results. The solution of *p*-*t*-butylcalix[4]arene acyl chloride (bp. 182°C) was separated from thionyl chloride (bp. 74.6°C) by distillation. The solution of *p*-*t*-butylcalix[4]arene acyl chloride is unstable, so this solution is used immediately without further purification.

The solution of *p*-*t*-butylcalix[4]arene acyl chloride (0.23 g, 0.2409 mmol) in dry THF (5 mL) was added dropwise to a solution of ethyl 2-aminoacetate (0.21 mL, 1.8328 mmol) and trimethylamine (0.21 mL, 2.227 mmol) in dry THF (10 mL) at atmospheric conditions nitrogen. The mixture was stirred with a magnetic stirrer for 24 hours at room temperature while flowing nitrogen gas. Every 8 hours, the mixture tested TLC to control the reaction results. Furthermore, the mixture was filtered, and the filtrate was concentrated with rotavapor at 66°C. The residue was dissolved in dichloromethane (10 mL), and the solution is washed with cold water (-5°C) (10 mL). Furthermore, the solution was dried with anhydrous Na_2SO_4. The product solution was filtered, and the solvent was evaporated with rotavapor at 39.6°C. The solids that formed were recrystallized with methanol and dichloromethane. The white solid formed is BEAC4ND4 ionophore. Furthermore, the BEAC4ND4 ionophore is dried in the desiccator and then characterized by TLC, melting point, FTIR, and FTNMR (^1H, ^{13}C). The temperatures used for the ^1H-NMR and ^{13}C-NMR measurements were 408°C and 406.5°C, respectively.

2.4. Determination of the BEAC4ND4 Ionophore Structure

The BEAC4ND4 ionophore structure was determined using spectroscopic techniques, namely FTIR and FTNMR 1-D (^1H and ^{13}C). The physical data of the BEAC4ND4 ionophore are yield of 75,22%; mp 314-316°C; TLC (SiO_2, $CH_3OH : CH_2Cl_2 = 1 : 1$ v/v, Rf = 0.75). The spectrum data of FTIR, ^1H and ^{13}C-NMR of the BEAC4ND4 ionophore are presented in the following description. FTIR (KBr) ν_{maks} (cm^{-1}): 1749.44 (esters C=O stretch), 1120.64 (C-O-C stretch in dialkyl ethers), 1242.16 (C-O-C stretch in alkyl aryl ethers), 1066.64 (R-C-O stretch in alkyl aryl ethers), 3055.24 and 3024.38 (CH stretch of unsaturated aromatic), 1633.71 (aromatic C=C stretch), 1201.65 (aromatic C-O stretch), 817.82 and 783.1 (CH out-of-plane deformation of disubstituted *para* aromatic), 3446.79 (NH stretch of secondary amides), 1645.28 (C=O stretch of secondary amides) (amide I band), 1479.4 (C-N stretch of secondary amides) (amide II band), 2960.73, 2906.73, and 2866.22 (CH stretch of $(CH_3)_3C$ saturated aliphatic), 1392.61 (CH stretch of CH_3 aliphatic), 1429.25 (CH stretch of CH_2 aliphatic); ^1H-NMR (500 MHz, $CDCl_3$) δ_H (ppm): 7.0380 [(s, 1**H**) (Ar**H**-22/24)], 4.3273 [(s, 2**H**) (C**H**$_2$O-2”)], 5.9762 [(s, 1**H**) (N**H**-1^)], 2.5419 [(s, 2**H**) (C**H**$_2$NH-1#)], 3.0034 [(q, 2**H**, *J* = 6.7 Hz) (OC**H**$_2$CH$_3$-1*)], 1.4423 [(t, 3**H**, *J* = 6.7 Hz) (OCH$_2$C**H**$_3$-2*)], 4.2428 [(d, 2**H**, *J* = 12.9 Hz) (ArC**H**$_2$Ar-2$_b$)], 3.4808 [(d, 2**H**, *J* = 12.9 Hz) (ArC**H**$_2$Ar-2$_a$)], 1.1985 [(s, 9**H**) (C(C**H**$_3$)$_3$-2’)]; ^{13}C-NMR (500 MHz, $CDCl_3$) δ_C (ppm): 172.1537 [(**C**O amides) (**C**-1”)], 42.4278 [**C**H$_2$ amides) (**C**-1#)], 170.7319 [(**C**O esters) (**C**-2#)], 62.3785 [(**C**H$_2$ esters) (**C**-1*)], 11.5713 [(**C**H$_3$ esters) (**C**-2*)], 146.8248 [(**C**O aryl) (**C**-25)], 144.5451

[(**C**-*para* aryl) (**C**-23)], 127.8531 [(**C**-*ortho* aryl) (**C**-1/**C**-21)], 126.0980 [(**C**-*meta* aryl) (**C**-22/**C**-24)], 73.5713 [($ArOCH_2$-) (**C**-2”)], 34.1676 [(**C**(CH_3)$_3$) (**C**-1’)], 32.7750 [($C(CH_3)_3$) (**C**-2’)], and 31.5637 [($ArCH_2Ar$) (**C**-2/**C**-20)]. The position of the chemical shift value of ^{1}H and ^{13}**C**-NMR in the carbon framework of the BEAC4ND4 ionophore can be seen in Figure 1.

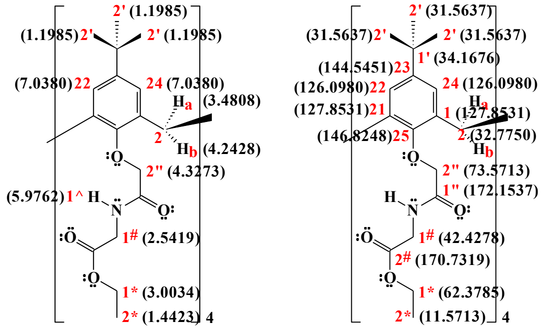

Figure 1. The position of the chemical shift value of ^{1}H-NMR (left) and ^{13}**C**-NMR (right) in the carbon framework of the BEAC4ND4 ionophore

3. Results and Discussion

The first step of the synthesis reaction of the BEAC4ND4 ionophore is the chlorination reaction of *p-t*-butylcalix[4]arene carboxylic acid with thionyl chloride in dry benzene (Figure 2). The *p-t*-butylcalix[4]arene acyl chloride was obtained in the form of the light brown viscous liquid with the yield of 78.25% and TLC (SiO_2, CH_3OH: CH_2Cl_2 = 1: 1 v/v, R_f = 0.65). R_f value of the synthesis product (0.65) is lower than the value of reactant R_f (0.91) (Figure 3). This is consistent with the expected where the synthesis product has a higher polarity than the reactant. The *p-t*-butylcalix[4]arene acyl chloride is not analyzed spectroscopically because the compound is highly reactive to water vapor.

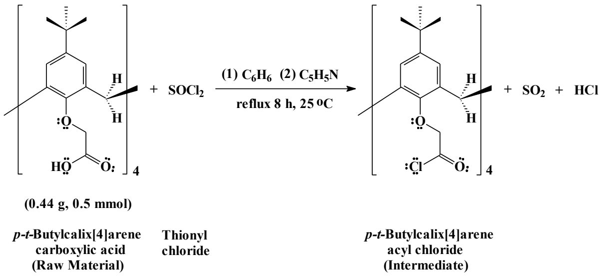

Figure 2. The chlorination reaction of *p-t*-butylcalix[4]arene carboxylic acid with thionyl chloride to form of the *p-t*-butylcalix[4]arene acyl chloride

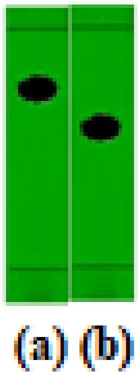

Figure 3. TLC (SiO_2, CH_3OH : CH_2Cl_2 = 1 : 1 v/v) test results: (a) *p-t*-butylcalix[4]arene carboxylic acid (R_f = 0.91); (b) *p-t*-butylcalix[4]arene acyl chloride (R_f = 0.65)

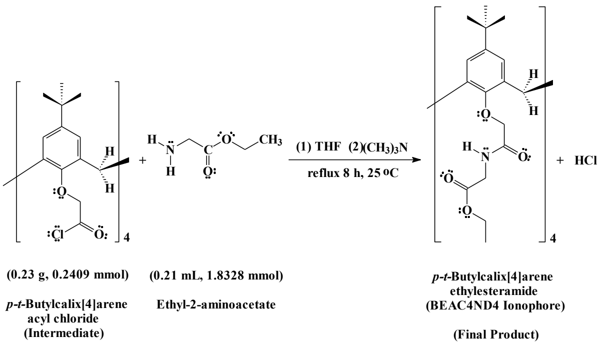

Figure 4. The amidation reaction of the *p-t*-butylcalix[4]arene acyl chloride with ethyl 2-aminoacetate to form the BEAC4ND4 ionophore

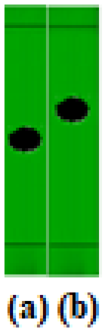

Figure 5. TLC (SiO_2, CH_3OH : CH_2Cl_2 = 1 : 1 v/v) test results: (a) *p-t*-butylcalix[4]arene acyl chloride (R_f = 0.65); (b) BEAC4ND4 ionophore (R_f = 0.75)

The second step is the amidation reaction of the *p-t*-butylcalix[4]arene acyl chloride with ethyl 2-aminoacetate in dry tetrahydrofuran to form the *p-t*-butylcalix[4]arene ethylesteramide or the BEAC4ND4 ionophore (Figure 4).

The synthesis product of the BEAC4ND4 ionophore was shaped white solid with a yield of 75.22%, a melting point of 314-316°C, and TLC (SiO_2, CH_3OH: CH_2Cl_2 = 1: 1 v/v, R_f = 0.75). R_f value of the synthesis product (0.75) is higher than the value of reactant R_f (0.65) (Figure 5). This is consistent with the expected where the BEAC4ND4 ionophore has a lower polarity than the reactant.

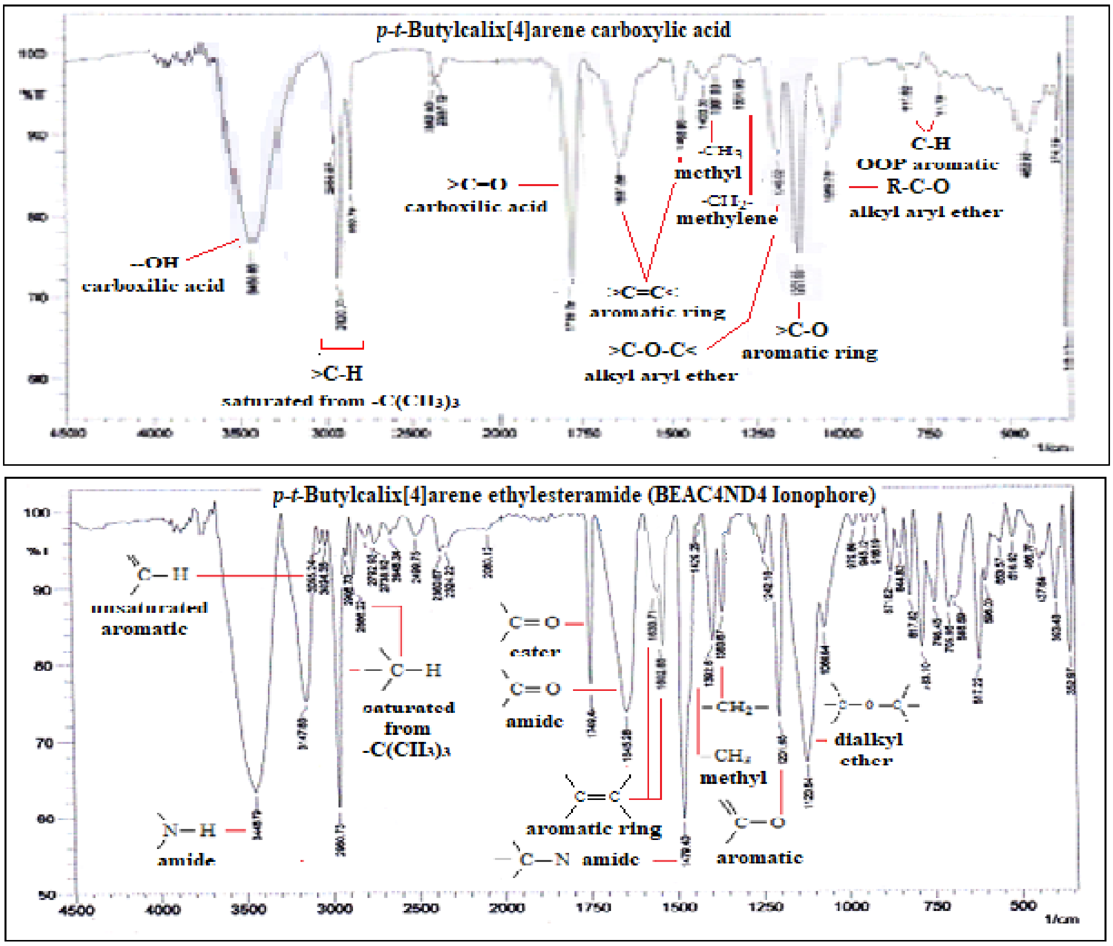

Figure 6. Comparison of the FTIR spectrum of *p-t*-butylcalix[4]arene carboxylic acid (raw material) (above) and the BEAC4ND4 ionophore (product) (under)

Table 1. Interpretation of the FTIR spectrum of the *p-t*-butylcalix[4]arene carboxylic acid (raw material) and the BEAC4ND4 ionophore (product)

No	Frequency (cm^{-1}) and Intensities		Frequency Ranges (cm^{-1}) and Intensities*	Group or Class	Remarks
	Raw Material	BEAC4ND4 Ionophore			
1	3450.65 (vs)	-	3400-2400 (s)		OH stretch
2	1739.79 (vs)	-	1730-1700 (vs)	Carboxylic Acids RCOOH	C=O stretch
3	-	1749.44 (s)	1765-1720 (vs)	Esters RCOOR'	C=O stretch
4	-	1120.64 (vs)	1140-1110 (vs)	Ethers ROR'	C-O-C stretch in dialkyl ethers
5	1244.09 (s)	1242.16 (s)	1280-1220 (s)		C-O-C stretch in alkyl aryl ethers
6	1089.78 (s)	1066.64 (s)	1075-1020 (s)		R-C-O stretch in alkyl aryl ethers
7	-	3055.24 (w)	3159-3000 (m)	Aromatic ArH	C-H unsaturated stretching
8	-	3024.38 (w)			
9	1637.56 (s)	1633.71 (w)	1630-1430 (v)		C=C aromatic ring stretching
10	1201.65 (vs)	1201.65 (vs)	1300-1000 (s)		C-O aromatic ring stretching
11	817.82 (w)	817.82 (m)	900-650 (s)		Out-of-plane C-H deformation 1,4-disubstituted *para*
12	711.73 (w)	783.1 (s)			
13	-	3446.79 (vs)	3460-3400 (m)	Amides CONHR	N-H stretch of secondary amides
14	-	1645.28 (s)	1680-1640 (vs)		C=O stretch of secondary amides (amide I band)
15	-	1479.4 (vs)	1550-1460 (s)		C-N stretch of secondary amides (amide II bands)
16	2956.87 (w)	2960.73 (vs)	2970-2850 (s)	Aliphatic RH	C-H saturated stretching from $(CH_3)_3C$-
17	2920.23 (vs)	2906.73 (w)			
18	2850.79 (s)	2866.22 (w)			
19	1367.53 (w)	1392.61 (m)	1450-1375 (s)	*t*-Butyl$(CH_3)_3C$-	C-H stretch from CH_3-
20	1465.90 (w)	1429.25 (m)	1485-1450 (m)	Methylene -CH_2-	C-H stretch from -CH_2-

◦Notes: vs = *very strong*; v = *variable*; s = *strong*; m = *medium*; w = *weak*

*Sources: [11, 12, 13]

Comparison and interpretation of the FTIR spectrum of *p-t*-butylcalix[4]arene carboxylic acid (raw material) and the BEAC4ND4 ionophore (product) are shown in Figure 6 and Table 1. The FTIR spectrum of the *p-t*-butylcalix[4]arene carboxylic acid (raw material) shows strong absorption bands at 3450.65 cm^{-1} 1739.79 cm^{-1} derived from the OH and C=O stretches of carboxylic acids. These two strong absorption bands do not appear in the FTIR spectrum of the BEAC4ND4 ionophore. In contrast, the FTIR spectrum of the BEAC4ND4 ionophore showed strong absorption bands at 1749.44 cm^{-1} (C=O stretch), 1120.64 cm^{-1} (C-O-C stretch in dialkyl ethers), 3446.79 cm^{-1} (N-H stretch of secondary amides), 1645.28 cm^{-1} (C=O stretch of secondary amides [amide I band]),

and 1479.4 cm^{-1} (C-N stretch of secondary amides [amide II bands]). These five strong absorption bands do not appear in the FTIR spectrum of the raw material. This shows that OH and C=O groups of carboxylic acids in the raw material have been changed to C=O esters, C-O-C ether, C=O amide, and C-N amide groups in the BEAC4ND4 ionophore during the synthesis reaction.

This synthesis reaction's success is also supported by the ^{1}H-NMR spectrum data of the synthesis product. Comparison and interpretation of the ^{1}H-NMR spectrum of *p*-*t*-butylcalix[4]arene carboxylic acid (raw material) and the BEAC4ND4 ionophore (product) are shown in Figure 7 and Table 2.

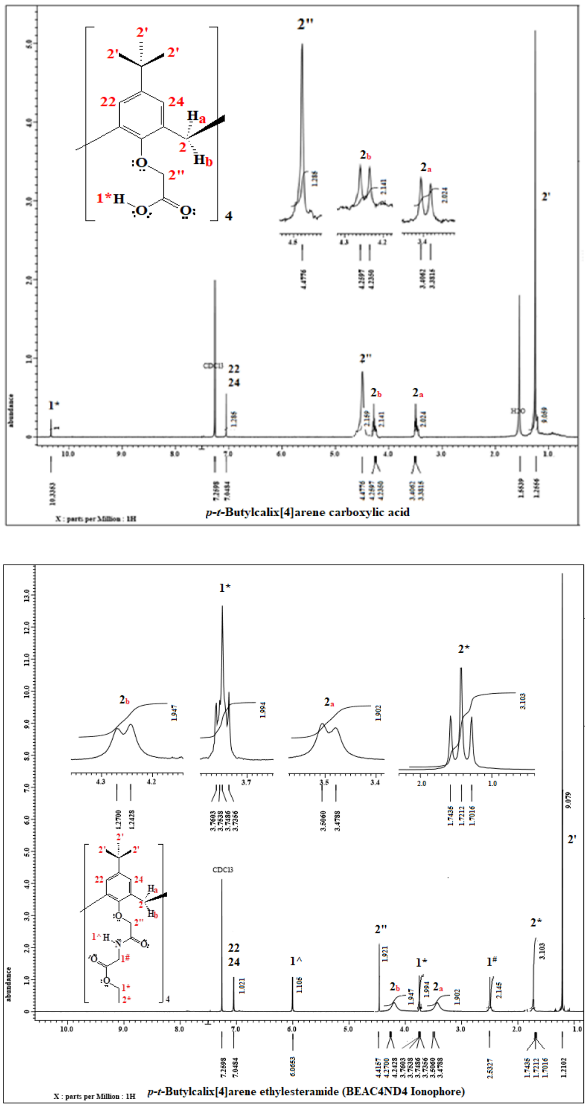

Figure 7. Comparison of the ^{1}H-NMR spectrum of *p*-*t*-butylcalix[4]arene carboxylic acid (raw material) (above) and the BEAC4ND4 ionophore (product) (below)

Table 2. Interpretation of the NMR (^{1}H, ^{13}C) spectrum of the *p*-*t*-butylcalix[4]arene carboxylic acid (raw material) and the BEAC4ND4 ionophore (product)

C Position	δ_C (ppm)		Groups	H Position	δ_H (ppm)		Groups
	Raw Material	BEAC4ND4 Ionophore			Raw Material	BEAC4ND4 Ionophore	
1, 21	127.8691	127.8531	**C**-*o* aryl		-	-	-
22, 24	126.1236	126.0980	**C**-*m* aryl	22, 24	7.0484 (2**H**, *s*)	7.0380 (2**H**, *s*)	Ar**H**
23	144.5516	144.5451	**C**-*p* aryl		-	-	-
25	146.8503	146.8248	**C**O aryl		-	-	-
1'	34.1932	34.1676	**C**$(CH_3)_3$		-	-	-
2'	31.5892	31.5637	$C(\mathbf{CH_3})_3$	2'	1.2556 (9**H**, *s*)	1.1985 (9**H**, *s*)	$C(CH_3)_3$
2_a, 2_b	30.2348	32.7750	Ar**C**H_2Ar	2_b	3.3939 (1**H**, *d*, *J* = 12.9 Hz)	3.4808 (1**H**, *d*, *J* = 12.9 Hz)	ArC$\mathbf{H_2}$Ar
				2_a	4.2474 (1**H**, *d*, *J* = 12.9 Hz)	4.2428 (1**H**, *d*, *J* = 12.9 Hz)	ArC$\mathbf{H_2}$Ar
1''	-	172.1537	**C**=O amides	1''	-	-	-
	170.3153	-	**C**=O carboxylic acids		10.3353 (1**H**, *s*)	-	CO_2**H**
2''	73.1351	73.5713	ArO**C**H_2-	2''	4.4776 (2**H**, *s*)	4.3273 (2**H**, *s*)	$\mathbf{CH_2}$O
				1^	-	5.9762 (1**H**, *s*)	N**H**
1#	-	42.4278	**C**H_2NH	1#	-	2.5419 (2**H**, *s*)	$\mathbf{CH_2}$NH
2#	-	170.7319	**C**=O esters		-	-	-
1*	-	62.3785	O**C**H_2CH_3	1*	-	3.0034 (2**H**, *q*, *J* = 6.7 Hz)	O$\mathbf{CH_2}CH_3$
2*	-	11.5713	OCH_2**C**H_3	2*	-	1.4423 (3**H**, *t*, *J* = 6.7 Hz)	$OCH_2\mathbf{CH_3}$

The ^{1}H-NMR spectrum of the *p*-*t*-butylcalix[4]arene carboxylic acid (raw material) shows the presence of a signal at δ_H 10.3353 ppm (1**H**, *s*) derived from carboxylic acid protons (OH-1*). This signal is no longer found in the ^{1}H-NMR spectrum of the BEAC4ND4 ionophore. In contrast, the ^{1}H-NMR spectrum of the BEAC4ND4 ionophore shows the presence of several signals not found in the ^{1}H-NMR spectrum of the raw material. These signals are the amide (**N**H-1^) proton signal, which appears at δ_H 5.9762 ppm (1**H**, *s*), the methylene amide (CH_2NH-1#) proton signal, which appears at δ_H 2.5419 ppm (2**H**, *s*), the methylene ethoxy (OCH_2CH_3-1*) proton signal which appears at δ_H 3.0034 ppm (2**H**, *q*, *J* = 6.7 Hz), and the methyl ethoxy (OCH_2CH_3-2*) proton signal which appears at δ_H 1.4423 ppm (3**H**, *t*, *J* = 6.7 Hz). This shows that the OH group of raw material has been transformed into ethylesteramide in the BEAC4ND4 ionophore. Furthermore, the proton signals that appear on the BEAC4ND4 ionophore are the same as the raw material proton signals. These signals are the aryl (Ar**H**-22/24) proton signal that appears at δ_H 7.0380 ppm (1**H**, *s*), methylene methoxy (CH_2O-2'') proton signal that appears at δ_H 4.3273 ppm (2**H**, *s*), the methylene bridge proton signal, which is split into two, namely the methylene (ArCH_2Ar-2_a) bridge proton signal that appears at δ_H 4.2428 ppm (2**H**, *d*, *J* = 12.9 Hz) and the exo methylene (ArCH_2Ar-2_b) bridge proton signal which appears at δ_H 3.4808 ppm (2**H**, *d*, *J* = 12.9 Hz), and the highest-intensity singlet proton signal that appear at δ_H 1.1985 ppm (9**H**, *s*) originates from *tert*-butyl ($C(CH_3)_3$-2'). Thus, the signals that appear in the range of δ_H 0 - 7.0 ppm in the ^{1}H-NMR spectrum of the synthesized product are in accordance with the proton character of the BEAC4ND4 ionophore (Figure 8).

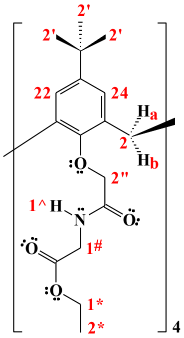

Figure 8. The proton character of the BEAC4ND4 ionophore

Comparison and interpretation of the ^{13}C-NMR spectrum of *p*-*t*-butylcalix[4]arene carboxylic acid (raw material) and the BEAC4ND4 ionophore (product) are shown in Figure 9 and Table 2. The analysis of the synthesis product with the ^{13}C-NMR spectrometer also corroborated the results of the FTIR and ^{1}H-NMR spectrum analysis above. The ^{13}C-NMR spectrum of the BEAC4ND4 ionophore showed a signal at δ_C 172.1537 ppm derived from carbon **C**-1" which binds to the **C**=O amide group. Whereas the **C**-1" carbon signal in the ^{13}C-NMR spectrum of the raw material appears as a **C**=O carboxylic acid group at δ_C 170.3153 ppm. This shows that the **C**=O carboxylic acid group on the raw material has been changed to the **C**=O amide group on the BEAC4ND4 ionophore. Furthermore, the ^{13}C-NMR spectrum of the BEAC4ND4 ionophore shows the presence of several signals not found in the ^{13}C-NMR spectrum of the raw material. These signals are the methylene amide (CH_2NH-1$^{\#}$) **C**-1$^{\#}$ signal, which appears at δ_C 42.4278 ppm, the carbonyl ester (**C**=O ester) **C**-2$^{\#}$ signal, which appears at δ_C 170.7319 ppm, the methylene ethoxy (OCH_2CH_3-1*) **C**-1* signal, which appears at δ_C 62.3785 ppm, and the methyl ethoxy (OCH_2CH_3-2*) **C**-2* signal which appears at δ_C 11.5713 ppm. This shows that the carbon framework of the BEAC4ND4 ionophore has increased by four atoms of C.

The other carbon signals in the ^{13}C-NMR spectrum of the BEAC4ND4 ionophore are the same as the raw material carbon signals. These signals are the signals of aryl carbon (**C**-aryl) atoms, scattered into four values of δ_C. First, the most *downfield* signal at δ_C 146.8248 ppm is the **C**-25 (**C**-aryl) atomic signal, which binds oxygen directly to the OCH_2CONHR group. Second, the signal that appears at δ_C 144.5451 ppm is the aryl **C**-23 atomic signal at the *para* (**C**-*para* aryl), which binds to the *t*-butyl group. Third, the signal that appears at δ_C 127.8531 ppm is the aryl **C**-1/**C**-21 atomic signal at the *ortho* (**C**-*ortho* aryl) position. Fourth, the signal that appears at δ_C 126.0980 ppm is the aryl **C**-22/**C**-24 atomic signal at the *meta* (**C**-*meta* aryl) position. Furthermore, the signals of carbon atoms appearing more *upfield* are signals from alkyl groups. The signal that appears at δ_C 73.5713 ppm is the **C**-2" atomic signal from methylene aryl ether carbon ($ArOCH_2$-). The signal that appears at δ_C 34.1676 ppm is the **C**-1' atomic signal from *t*-butyl *quarternary* carbon [-**C**$(CH_3)_3$]. The signal that appears at δ_C 32.7750 ppm is the (**C**-2/**C**-20) atomic signal from the methylene bridge carbon ($Ar\mathbf{C}H_2Ar$). The signal that appears at δ_C 31.5637 ppm is the C-2' atomic signal from *t*-butyl methyl carbon [-$C(CH_3)_3$]. Thus, the signals that appear in the range of δ_C 0 - 180.0 ppm in the ^{13}C-NMR spectrum of the synthesis product is in accordance with the carbon framework of the *p*-*t*-butylcalix[4]arene ethyl ester amide or the BEAC4ND4 ionophore (Figure 10).

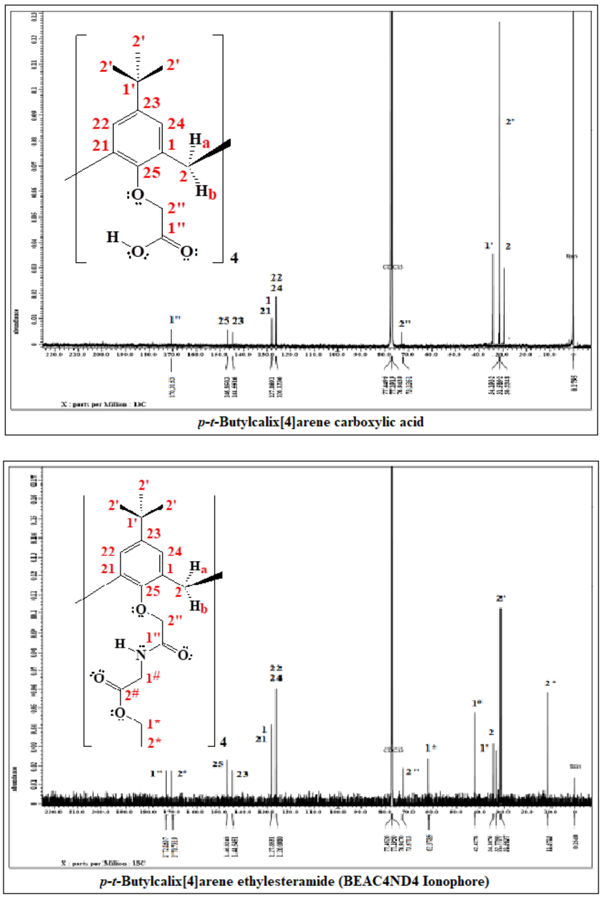

Figure 9. Comparison of the ^{13}C-NMR spectrum of *p*-*t*-butylcalix[4]arene carboxylic acid (raw material) (above) and the BEAC4ND4 ionophore (product) (under)

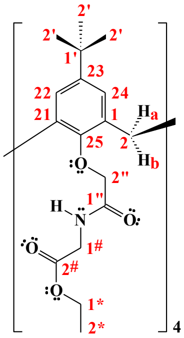

Figure 10. The carbon framework of the BEAC4ND4 ionophore

The conformational form of the BEAC4ND4 ionophore can be easily identified by their ^{1}H and ^{13}C-NMR spectrum, mainly through the bridging methylene groups' patterns. If the chemical shift of the methylene proton is close to (4.2 ± 1 ppm) and (3.4 ± 1 ppm), then the conformations of calix[4]arenes are *cone* [14, 15, 16, 17]. The ^{1}H-NMR spectrum of the BEAC4ND4 ionophore (Table 2) shows that the methylene bridge proton (ArC**H**$_2$Ar) absorption band appears as two *doublets* on δ_H 4.2428 ppm and δ_H 3.4808 ppm. These absorption bands' pattern indicates that the conformation of the BEAC4ND4 ionophore is a *cone* (Figure 11). If the chemical shift for the methylene carbon is near 31 ppm, two adjacent aryl groups are synced to each other [14, 15, 16, 17]. The ^{13}C-NMR spectrum of the BEAC4ND4 ionophore (Figure 9) shows that the carbon absorption band from the methylene bridge group (Ar**C**H$_2$Ar) appear at δ_C 32.7750 ppm (≈ 31 ppm). This means that the orientation of two adjacent aryl groups is *syn* (a plot) to each other (Figure 11).

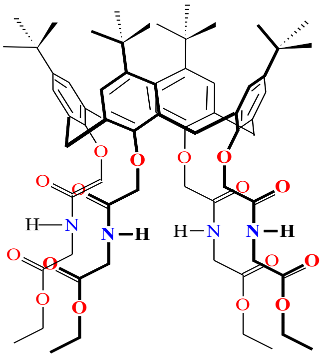

Figure 11. Cone conformation of the BEAC4ND4 ionophore

4. Conclusion

The BEAC4ND4 ionophore has been successfully synthesized from *p*-*t*-butylcalix[4]arene carboxylic acid. The BEAC4ND4 ionophore was obtained in two steps of the synthesis reaction, namely the chlorination and amidation reaction. The chlorination reaction product is *p*-*t*-butylcalix[4]arene acyl chloride in the form of the light brown viscous liquid with a yield of 78.25% and TLC (SiO_2, CH_3OH: CH_2Cl_2 = 1: 1 v/v, R_f = 0.65). The product of the amidation reaction is *p*-*t*-butylcalix[4]arene ethylesteramide or the BEAC4ND4 ionophore in the form of a white solid with the yield of 75.22%, a melting point of 314-316°C, and TLC (SiO_2, CH_3OH: CH_2Cl_2 = 1: 1 v/v, R_f = 0.75).

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