Artículo de investigación científica

Study of some properties of cyanopyridine derivatives in solutions

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Summary

Some new cyanopyridine derivatives have been synthesized and their characterization was done by IR, ¹H NMR and mass spectral data. Further, some physicochemical properties such as density, refractive index, conductance etc. have been studied for these synthesized compounds, in different solvents at 308.15 K.

Key words: Cyanopyridine derivative, conductance, refractive index, density.

Resumen

Estudio de las propiedades de algunos derivados de cianopiridina en solución

Se sintetizaron algunos derivados de cianopiridina y se caracterizaron mediante IR, RMN ¹H y espectrometría de masa. Además, para los mismos compuestos se determinaron algunas propiedades fisicoquímicas tales como densidad, índice de refracción y conductancia, en diferentes solventes a 308,15 K.

Palabras clave: derivados de cianopiridina, conductancia, índice de refracción, densidad.

Introduction

The pyridine ring is an integral part of various natural products of therapeutic importance. It plays an important role in catalyzing both biological and chemical reactions [1]. Substituted cyanopyridines are known to act as intermediates in the pharmaceutical, dye, photo and agrochemical industries [2-4]. Further, Many fused cyanopyridines have drawn attention due to their wide spectrum biological activities [5-9]. Therefore, the synthesis of cyanopyridine derivatives continues to attract much interest in organic chemistry. However, best of our knowledge, very little work is known for their physicochemical properties.

In view of these observations and with a view to study physicochemical properties of this class of compounds, the present study includes synthesis and studies of some physicochemical properties such as density, refractive index and conductance of synthesized cyanopyridines in solutions.

Experimental

Equipments and Reagents used

1-naphthyl amine, acetic anhydride, POCl₃, malono nitrile, ammonium acetate and different substituted acetophenone used for the synthesis, were supplied from Spectrochem Pvt. Ltd. (Mumbai, India) and were used without any treatment.

The DMF and DMSO used were of AR grade supplied by Spectrochem Pvt. Ltd. (Mumbai, India) and were purified according to the standard procedure [10]. The distilled solvents were stored over molecular sieves. The purity of solvents were confirmed by GC-MS (SHIMADZU-Model No.-QP-2010) equipped with column (DB-5MS, 25 m in length, 0.20 mm internal diameter and 0.33 μ m film) and was found to be about 99.99%.

The pycnometer and Abbe refractometer were used for the measurement of density and refractive index of solutions of compounds respectively. For the measurement of conductance of solutions, Equip-tronics conductivity meter (Model No. 664) was used.

Synthesis

[A] Synthesis of N-(naphthalene-1-yl)acetamide: Equimolar mixture of 1-naphthyl amine and acetic anhydride in methanol was refluxed in water bath for 2-3 hrs using acetic acid as catalyst. The crude product was isolated and crystallized from absolute ethanol.

[B] Synthesis of 2-chloro benzo[h]quinoline-3-carbaldehyde: N-(naphthalene-1-yl) acetamide was added in a mixture of Vilsmeier-Haack reagent (prepared by drop wise addition of 6.5 ml POCl_3 in ice cooled 2 ml DMF) and refluxed for 27 hrs. The reaction mixture was poured into ice and kept for overnight followed by neutralization using sodium bicarbonate. The crude product was isolated and crystallized from ethanol. [C] Synthesis of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy-ohenyl)prop-2-en-1-one: To a well stirred solution of 2-chloro benzo[h]quinoline-3-carbaldehyde and p-methoxy-acetophenone in binary mixture of ethanol + DMF, 40% NaOH was added till the solution became basic. The reaction mixture was stirred for 48 hrs and the contents were poured into ice, acidified, filtered and crystallized from ethanol.

[D] Synthesis of 2-amino-4-(2-chlorobenzo[h]quinolin-3-yl)-6-(4-methoxy-phenyl) pyridine-3-carbonitrile(CP-1): A mixture of 3-(2-chlorobenzo[h]quinolin-3-yl)-1-(4-methoxy-phenyl) prop-2-en-1-one, malononitrile and ammonium acetate in ethanol was refluxed for 10-12 hrs. The content was poured on crushed ice. The product obtained was filtered, washed with water and crystallized from DMF.

Similarly, other substituted cyano pyridines have been prepared.

Figure 1 shows the reaction scheme. The structures of all the synthesized compounds were confirmed by IR, ¹H NMR and mass spectral data. The IR spectra were recorded by SHIMADZU-FTIR-8400 Spectrophotometer in the frequency range of 4000-400 cm⁻¹ by KBr powder method. The NMR spectra were recorded by BRUKER Spectrometer (400 MHz) using internal reference TMS and solvent CDCl₃/DMSO. The Mass spectra were recorded by GCMS-SHIMADZU-QP2010.

Table 1 shows the physical parameters of synthesized cyanopyridine compounds.

Sr. No.	Comp. Code	Mol. Wt. (g/mol)	M.F.	R	R _f * Value	M.P. (°C)	Yield %
1	CP-1	436.8	$C_{27}H_{17}ClN_4O$	4-OCH ₃ -C ₆ H ₄ -	0.59	221	70
2	CP-2	420.8	$C_{26}H_{17}ClN_4$	4-CH ₃ -C ₆ H ₄ -	0.56	180	68
3	CP-3	485.7	$C_{25}H_{14}BrClN_4$	4 -Br- C_6H_4 -	0.63	214	71
4	CP-4	421.8	$C_{25}H_{16}ClN_5$	$4-NH_2-C_6H_4-$	0.69	208	65
5	CP-5	451.8	$C_{25}H_{14}ClN_5O_2$	$4-NO_2-C_6H_4-$	0.64	187	69
6	CP-6	422.8	$C_{25}H_{15}ClN_4O$	3-OH-C ₆ H ₄ -	0.70	235	67
7	CP-7	441.3	$C_{25}H_{14}Cl_2N_4$	4-Cl-C ₆ H ₄ -	0.72	234	72
8	CP-8	451.8	$C_{25}H_{14}ClN_5O_2$	3-NO ₂ -C ₆ H ₄ -	0.62	201	63
9	CP-9	422.8	C ₂₅ H ₁₅ ClN ₄ O	4-OH-C ₆ H ₄ -	0.67	229	65
10	CP-10	406.8	$C_{25}H_{15}ClN_4$	H-C ₆ H ₄ -	0.49	162	73

Table 1. Physical constants of synthesized Cyanopyridine compounds.

*Ethyl acetate : Hexane: 3:7.



Figure 1. Reaction Scheme.

Physicochemical studies

Density and refractive index: The density and refractive index of all the synthesized cyanopyridine derivatives have determined in dimethylformamide and dimethyl sulfoxide solutions at 298.15 K. The density and refractive index were measured at definite temperature by pycnometer and Abbe refractometer respectively. The temperature was maintained by circulating water through jacket around the prisms of refractometer from an electronically controlled water bath (NOVA NV-8550 E). The uncertainty of temperature was \pm 0.1 °C and that of density and refractive index was \pm 0.0001 g/cm³ and 0.0005 respectively.

Conductance: For all the synthesized compounds, conductance is measured in dimethylformamide and dimethylsulfoxide solutions at 298.15 K. The conductance of each solution was measured by using Equip-tronics conductivity meter (Model No. 664) having a cell constant 0.98 cm⁻¹ at 298.15 K.

Results and discussion

In all 10 compounds were synthesized and IR, NMR and mass spectral data analysis confirmed their molecular structure. The IR, NMR and mass spectra of CP-1 are shown in Figures 2, 3 and 4 respectively. The spectral data are given below:

CP1: *IR (KBr, cm⁻¹)*: N-H: 3314, C=C: 1514, C≡N: 2195, C-Cl: 690.

¹*H NMR* (δ *ppm*): 3.83(s, 3H), 3.49 (s, 2H), 7.09-7.12(d, 2H), 7.5-7.54(t, 1H), 7.66-7.76(dd, 2H), 7.83-7.99(m, 2H), 8.07-8.10(m, 2H), 8.37(s, 1H), 8.51(d, 2H).

m/z: 436.8, 422, 402, 385, 357, 338, 295, 247, 226, 218, 151, 108, 92, 78.

CP2: *IR (KBr, cm⁻¹)*: N-H: 3348, C=C: 1518, C≡N: 2201, C-Cl: 699.

¹*H* NMR (δ ppm): 2.75 (s, 3H), 3.55 (s, 2H), 7.08-7.16(d, 2H), 7.59-7.63(t, 1H), 7.81-7.85(dd, 2H), 8.04-8.08(m, 2H), 8.15-8.19(m, 2H), 8.34(s, 1H), 8.63(d, 2H).

m/z: 420.8, 386, 369, 341, 295, 247, 218, 151, 108, 92, 78.

CP3: *IR (KBr, cm⁻¹):* N-H: 3332, C=C: 1512, C≡N: 2198, C-Cl: 709.

¹*H NMR* (δ *ppm*): 3.66 (s, 2H), 7.18-7.22(d, 2H), 7.51-7.67(t, 1H), 7.82-7.86(dd, 2H), 8.14-8.18(m, 2H), 8.38-8.44(m, 2H), 8.51(s, 1H), 8.63(d, 2H).

m/z: 485.7 470, 451, 433, 406, 295, 218, 151, 108, 92, 78.

CP4: *IR (KBr, cm⁻¹)*: N-H: 3318, C=C: 1524, C≡N: 2212, C-Cl: 718.

¹*HNMR* (δ *ppm*): 3.41 (s, 2H), 3.59(s, 2H), 7.01-7.06(d, 2H), 7.21-7.24(t, 1H), 7.61-7.64(dd, 2H), 7.83-7.94(m, 2H), 8.17-8.25(m, 2H), 8.31(s, 1H), 8.44(d, 2H).

m/z: 421.8, 407, 387, 370, 323, 295, 247, 218, 151, 108, 92, 78.

CP5: *IR (KBr, cm⁻¹)*: N-H: 3321, C=C: 1504, C≡N: 2208, C-Cl:695.

¹*H NMR* (δ *ppm*): 3.49 (s, 2H), 7.25-7.31(d, 2H), 7.59-7.61(t, 1H), 7.69-7.72(dd, 2H), 7.88-7.94(m, 2H), 8.17-8.23(m, 2H), 8.41(s, 1H), 8.56(d, 2H).

m/z: 451.8, 437, 435, 419, 417, 400, 353, 295, 247, 218, 151, 108, 92, 78.

CP6: *IR (KBr, cm⁻¹)*: OH: 3405, N-H: 3307, C=C: 1530, C=N: 2226, C-Cl: 702.

¹*HNMR* (δ *ppm*): 3.33(s, 2H), 4.05(s, 1H), 7.15-7.18(d, 2H), 7.59-7.61(t, 1H), 7.63-7.67(dd, 2H), 7.78-7.81(m, 2H), 8.12-8.17(m, 2H), 8.30(s, 1H), 8.39(d, 2H).

m/z: 422.8, 408, 405, 387, 371, 295, 212, 247, 218, 151, 108, 92, 78.

CP7: *IR (KBr, cm⁻¹)*: N-H: 3319, C=C: 1522, C=N: 2206, C-Cl: 698.

¹*H NMR* (δ *ppm*): 3.21(s, 2H), 7.29-7.33(d, 2H), 7.49-7.51(t, 1H), 7.55-7.59(dd, 2H), 7.69-7.75(m, 2H), 8.20-8.25(m, 2H), 8.39(s, 1H), 8.59(d, 2H).

m/z: 441.3, 408, 406, 390, 343,295, 247, 218, 151, 108, 92, 78.

CP8: *IR (KBr, cm⁻¹)*: N-H: 3311, C=C: 1515, C≡N: 2221, C-Cl: 712.

¹*H NMR* (δ *ppm*): 3.30(s, 2H), 7.33-7.37(d, 2H), 7.66-7.69(t, 1H), 7.75-7.80(dd, 2H), 7.77-7.83(m, 2H), 8.14-8.19(m, 2H), 8.27(s, 1H), 8.44(d, 2H).

m/z: 451.8, 438, 435, 419, 417, 353, 295, 247, 218, 151, 108, 92, 78.

CP9: *IR (KBr, cm⁻¹)*: OH: 3410, N-H: 3321, C=C: 1526, C≡N: 2208, C-Cl: 689.

¹*HNMR* (δ *ppm*): 3.32(s, 2H), 4.44(s, 1H), 7.31-7.34(d, 2H), 7.65-7.68(t, 1H), 7.71-7.75(dd, 2H), 7.81-7.86(m, 2H), 8.04-8.08(m, 2H), 8.23(s, 1H), 8.40(d, 2H).

m/z: 422.8, 408, 405, 371, 297, 213, 247, 218, 151, 108, 92, 78.

CP10: *IR (KBr, cm⁻¹)*: N-H: 3309, C=C: 1521, C≡N: 2218, C-Cl: 701.

¹*H NMR* (δ *ppm*): 3.23(s, 2H), 7.34-7.36(d, 2H), 7.60-7.63(t, 1H), 7.68-7.71(dd, 2H), 7.74-7.79(m, 2H), 8.09-8.13(m, 2H), 8.29(s, 1H), 8.39(d, 2H).

m/z: 406.8, 392, 371, 355, 308, 295, 247, 151, 108, 92, 78.



Figure 2. IR spectrum of CP-1.



Figure 3. NMR spectrum of CP-1. (It continues)



Figure 3. NMR spectrum of CP-1. (Continued)



Figure 4. Mass spectrum of CP-1.

The molecular formula, molecular weight, melting point, % yield and R_f values along with the solvent systems of all the compounds are given in Table 1.

Density and Refractive index

The density of solution is related to density of pure solvent, pure solute (i.e., synthesized compound) and their weight fractions by the following equation:

$$1/\rho_{12} = g_1/\rho_1 + g_2/\rho_2$$

where ρ_1 , ρ_2 and ρ_{12} are the density of pure solvent, pure solute (i.e., synthesized compound) and solution respectively. g_1 and g_2 are the weight fractions of solvent and solute respectively. The plot of $1/g_1\rho_{12}$ versus g_1/g_2 is shown in Figure 5 for CP-1.The slope of straight line gives $1/\rho_2$.



Figure 5. The plot of $(1/g_1\rho_{12})$ versus (g_1/g_2) for CP-1 in [A] DMF and [B] DMSO.

Further, the density of these compounds was also calculated using the following theoretical equation [11]:

$$\rho = KM/N_A \Sigma \Delta V_i$$

where ρ the density of the compound, K is packing fraction (0.599), M is the molecular weight of the compound, N_A is the Avogadro's number and ΔV_i is the volume increment of the atoms and atomic groups present in the compound. Table 2 shows the experimental and theoretical values of density. It is observed that there is deviation between experimental and theoretical density values and in different solvents, different density values are observed. This difference can be explained on the basis of interactions in solutions. In different solvents, different types of interactions exist with different solutes. This may change the volume thereby affecting the molecular weight of the compound, which ultimately affects the density. Thus, different density values in different solvents and deviation between experimental and theoretical density values suggest the presence of intermolecular interactions between solute and solvent molecules.

Commente	Experimental I	Theoretical	
Compounds	DMF	DMSO	Density (g/cm ³)
CP-1	1.3641	1.2347	1.1673
CP-2	1.4624	1.3201	1.1517
CP-3	1.7806	1.3168	1.2990
CP-4	1.2361	1.3006	1.1928
CP-5	1.5218	1.3355	1.2354
CP-6	1.4378	1.3029	1.9530
CP-7	1.8005	1.2999	1.2162
CP-8	1.7737	1.3186	1.2350
CP-9	1.4689	1.2204	1.1884
CP-10	1.3939	1,1790	1,1665

Table 2. Experimental and calculated densities of compounds in DMF and DMSO solutions at 298.15 K.

The molar refraction of pure liquid and solutions can be determined according to Lorentz and Lorentz equations [12].

For pure liquid:

 $(MRD) = [(n^2 - 1)/(n^2 + 2)]M/\rho$

where n, M and ρ are refractive index, molecular weight and density of pure liquid respectively.

For solutions:

$$(MRD)_{12} = [(n^2_{12} - 1)/(n^2_{12} + 2)].(X_1M_1 + X_2M_2)/\rho_{12}$$

where n_{12} and ρ_{12} are refractive index and density of the solution respectively. X_1 and X_2 are the mole fractions and M_1 and M_2 are the molecular weight of the solvent and solute respectively.

Using these equations, the $(MRD)_2$ and refractive index of compounds in 0.1 M solutions were calculated and are given in Table 3.

		Solvents				
Compounds	DI	MF	DM	ISO		
	(MRD) ₂	n	(MRD) ₂	n		
CP-1	113.42	1.4360	145.92	1.4857		
CP-2	115.88	1.4341	150.18	1.4868		
CP-3	118.99	1.4361	132.03	1.4855		
CP-4	142.00	1.4365	149.70	1.4864		
CP-5	116.07	1.4331	134.83	1.4833		
CP-6	111.32	1.4324	137.24	1.4824		
CP-7	97.24	1.4322	127.63	1.4833		
CP-8	104.98	1.4329	130.48	1.4831		
CP-9	106.49	1.4321	135.37	1.4827		
CP-10	90.99	1.4308	134.54	1.4838		

Table 3. Calculated molar refraction and refractive index of 0.1 M solution of compounds in DMF and DMSO at 298.15 K.

Conductance

The measured conductance of all the compounds in DMF and DMSO was corrected by subtracting the conductance of pure solvent and are given in Tables 4 and 5 respectively. It is observed that conductance increases with concentration for both the solvents. Further, conductance is higher in DMF than that in DMSO.

Conc. (g/l)	κ.10 ⁵ (Ω) ⁻¹						
	CP-1	CP-2	CP-3	CP-4	CP-5		
0.000	2.40	2.40	2.40	2.40	2.40		
0.001	4.00	4.10	4.40	8.50	6.90		
0.002	4.30	4.30	4.90	8.80	8.10		
0.004	4.80	4.50	5.40	9.30	9.20		
0.006	5.30	4.90	6.00	9.80	9.90		
0.008	5.90	5.60	6.80	10.50	11.20		
0.010	6.80	6.30	7.60	11.40	12.80		
0.020	8.30	7.00	9.90	13.70	14.60		
0.040	10.80	8.50	17.50	16.70	24.90		
0.060	19.60	10.30	24.00	22.50	36.00		
0.080	25.00	13.30	29.90	26.70	47.40		
0.100	30.00	15.50	35.30	31.50	57.90		
	CP-6	CP-7	CP-8	CP-9	CP-10		
0.001	5.60	6.50	8.40	5.50	4.50		
0.002	5.90	6.80	8.50	5.80	5.10		
0.004	6.90	7.20	8.70	6.60	5.70		
0.006	7.60	8.00	9.10	7.30	6.40		
0.008	9.50	9.10	9.50	8.80	7.90		
0.010	10.30	10.60	11.60	9.90	8.60		
0.020	14.20	15.10	12.80	13.70	11.10		

Table 4. The measured conductance (κ) of synthesized compounds in DMF at 298.15 K.

(It continues)

Conc.	κ.10 ⁵ (Ω) ⁻¹					
(g/l)	CP-6	СР-7	CP-8	CP-9	CP-10	
0.040	18.10	28.30	27.30	17.90	21.50	
0.060	21.70	31.70	35.10	21.40	29.70	
0.080	27.70	38.30	46.70	27.80	36.90	
0.100	35.00	44.50	53.00	35.10	43.10	

Table 4. The measured conductance (κ) of synthesized compounds in DMF at 298.15 K. (Continued)

Table 5. The measured conductance (κ) of synthesized compounds in DMSO at 298.15 K.

Conc.	$\kappa.10^{5}(\Omega)^{-1}$					
(g/l)	CP-1	CP-2	CP-3	CP-4	CP-5	
0.000	0.20	0.20	0.20	0.20	0.20	
0.001	2.70	2.50	2.70	3.50	5.30	
0.002	2.90	3.00	3.70	3.80	5.60	
0.004	3.20	3.10	4.69	4.20	6.30	
0.006	3.70	3.20	4.10	4.70	7.40	
0.008	4.30	3.30	5.90	5.30	9.90	
0.010	5.10	4.10	6.90	5.80	11.20	
0.020	7.90	5.60	8.30	6.20	13.50	
0.040	9.50	7.20	9.80	7.50	15.90	
0.060	11.30	8.30	12.40	9.70	17.30	
0.080	13.60	9.80	14.80	11.20	19.60	
0.100	16.30	12.00	17.90	13.90	21.90	
	CP-6	CP-7	CP-8	CP-9	CP-10	
0.001	5.30	6.30	7.60	5.10	4.30	
0.002	5.50	6.60	7.90	5.40	4.90	
0.004	5.90	7.20	8.40	5.90	5.70	

(It continues)

Conc. (g/l)	κ.10 ⁵ (Ω) ⁻¹					
	CP-6	CP-7	CP-8	CP-9	CP-10	
0.006	6.50	7.90	9.10	6.50	6.50	
0.008	7.50	8.80	10.50	7.80	7.80	
0.010	9.30	9.60	12.10	9.10	9.60	
0.020	12.20	11.70	13.80	12.70	12.10	
0.040	14.10	13.50	15.10	17.90	21.50	
0.060	20.10	15.70	18.70	20.90	30.10	
0.080	25.70	18.60	20.70	26.80	37.00	
0.100	31.00	20.50	24.30	33.90	42.90	

Table 5. The measured conductance (κ) of synthesized compounds in DMSO at 298.15 K. (*Continued*)

From these conductance values, equivalent conductance was calculated which are shown in Figures 6 and 7 for DMF and DMSO respectively. It is obvious from these figures that for all the compounds, the equivalent conductance increases uninterruptedly with decreasing concentration. However, the nature of plots suggests that the studied compounds behave as weak electrolytes in studied solvents.



Figure 6. The equivalent conductance (λ_C) versus \sqrt{C} of compounds in DMF. (*It continues*) 272



Figure 6. The equivalent conductance (λ_c) versus \sqrt{C} of compounds in DMF. (*Continued*)



Figure 7. The equivalent conductance (λ_c) versus \sqrt{C} of compounds in DMSO. (It continues)



Figure 7. The equivalent conductance (λ_c) versus \sqrt{C} of compounds in DMSO. (*Continued*)

CONCLUSION

The different density values in different solvents and deviation between experimental and theoretical density values suggest the presence of intermolecular interactions between solute and solvent molecules. The refractive index of 0.1 N solutions of all the derivatives is found to be different in both the solvents. The conductance increases with concentration for both the solvents for all the compounds. Further, conductance is higher in DMF than that in DMSO. In both the selected solvents, compounds behave as weak electrolytes.

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