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The Determination of the Physico-Chemical Properties of Nanoemulsion

Maurice O. Iwunze
Department of Chemistry, Morgan State University, MD 21251, USA

Abstract: Nanoemulsion is a heterogeneous fluid system that has been used in chemistry, biology and industry as a reaction medium and in medicine and allied sciences as a delivery vehicle for poorly water-insoluble biochemical compounds. It is made up of water-oil-surfactant and co-surfactant (usually a short chain alcohol). This fluid system has come of age and it is necessary that its physico-chemical properties be properly determined and documented. Such physico-chemical properties include dielectric constant, polarity, refractive index, viscosity, acidity, basicity and density. These properties are very important in designing a fruitful, effective and meaningful interpretation of chemical reactions and its utility. These are determined and documented in this work.

Key words: Nanoemulsion, effective dielectric constant, viscosity, reihardt dye, alcohols, surfactant.

1. Introduction

Nanoemulsion, (miniemulsion, as it is sometimes called) [1-4] is a heterogeneous system of oil-in-water dispersed by an amphiphilic compound (surfactant) and a co-surfactant, usually a short-chain alcohol. The mean oil droplet diameter of nanoemulsion ranges from 50 to 200 nanometers [5-17]. This heterogeneous system is known to exhibit unique properties [18, 19] and is used in all areas of science and technology: Its application includes solubilization of water-insoluble or poorly insoluble molecules [20-24], drug delivery [2, 6, 7, 9, 13, 20-25], pharmaceutical formulation [8, 9, 24], dermatology [11, 25-27] and a host of other applications. Many techniques have been used in producing a very kinetically stable nanoemulsion. Such techniques have varied from very sophisticated mechanical process [6] to ultrasonic room temperature [9, 14, 28], including Phase Inversion Temperature (PIT) Technique [14-17, 29]. The literature is replete of reviews [2, 5, 7, 9, 10, 12, 13, 19, 21, 22, 25, 26] detailing the formulation and usage of this unique system whose physico-chemical properties have not been adequately documented. It is the objective of this work, therefore, to obtain and document the useful physico-chemical parameters of this unique system to aid and to enhance in its use in efficient design of chemical reactions tailored for specific in application.

Corresponding author: Maurice O. Iwunze, professor, research fields: physical chemistry and analytical chemistry.

2. Experimental

2.1 Chemicals

Analytical reagent grade methanol and ethanol were obtained from Pharmco. Other alcohols (propanol, butanol and hexanol) were obtained from Sigma Aldrich in 95-98% purity. Reichardt dye $E_T(30)$ of 90% purity, tetradecane and 1-pentanol of 99% purity and cetylhexadecyltrimethylammonium bromide (CTAB) were obtained from Across Chemicals. All chemicals were used as received.

2.2 Nanoemulsion Preparation

Appropriate weight of CTAB and a measured volume of water were mixed together. To this mixture a known volume of n-tetradecane as oil was added with vigorous stirring. A calculated volume of co-surfactant (1-pentanol) was added drop-wise with vigorous mechanical stirring for about five minutes before transferring it to ultrasonic sonicator bath for about 7-10 more minutes. The solution so prepared was isotonic, clear and translucent. This solution was stable for a considerable length of time. The Table 1 shows the composition the compounds used in this work and their values in the make-up of the nanoemulsion described in this work.

2.3 Instruments

The instruments used in this work include Brookfield viscometer Model RDVD II+ for the viscosity determination; the VWR Conductance meter for the measurement of the solution conductance, the Abbe Digital refractometer for the determination of the refractive index; the digital PAAR density meter, model DMA 35 for density measurement and the Carry spectrophotometer model 1E for determination of the absorbance of the alcohols.

3. Results and Discussion

We show in Fig. 1 the SEM image of the 76% nanoemulsion prepared as discussed above.

The image was further analyzed for particle size distribution using the Image J program from Dune Sciences, Inc. [30]. The plot for this distribution is shown in Fig. 2. It can be seen that the plot peaked at 123.0 nanometers.

Table 1 Chemicals used in the preparation of 76% nanoemulsion.

Component	Weight, g	Volume, mL	Percentage, %
Water	174.0	174.0	76.0
CTAB (Surfactant)	12.0	12.63	5.0
Oil (tetradecane)	14.0	18.25	6.0
Co-surfactant (n-pentanol)	29.90	31.80	13.0

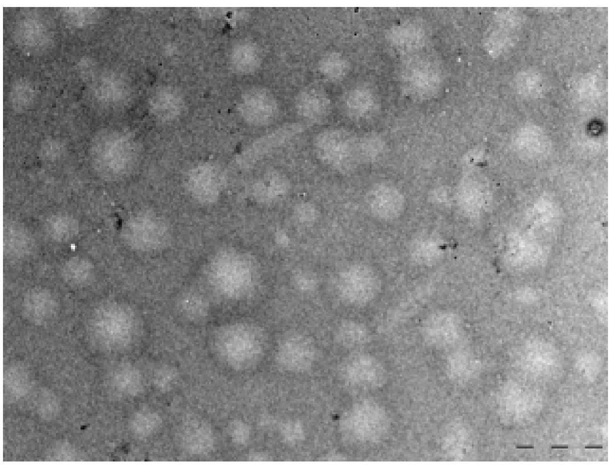


Fig. 1 SEM image of 76% nanoemulsion.

We used this value as the average diameter of the oil droplet in this preparation.

Reichardt dye (RD) also known as ET [30] (2, 6-Diphenyl-4-(2,4,6-triphenyl-1-pyridino)phenolate) is often used for polarity evaluation of solvents. This is because this compound is very sensitive to its environment. Its maximum wavelength shifts in accordance with the polarity of a given solvent. Fig. 3 is the chemical structure of this compound.

The equation that is often used to calculate the E_T (30) values is

$$E_T\ (30),\ \text{Kcal/mol} = 28591/\lambda_{max},\ \text{nm} \qquad (1)$$

λ_{max} in this equation is a characteristic maximum wavelength of E_T (30) in a given solvent.

Using the solvatochromic technique developed by Reichardt, Taft and other workers [31-37] the E_T (30) value of the alcohols used in this work (methanol through hexanol) were obtained in the 76% nanoemulsion. We show in Fig. 4 a typical absorbance of Rd solubilized in propanol and in the prepared nanoemulsion. A closer look will reveal that the maximum wavelength of the Reichardt's dye solubilized in 1-propanol is slightly shifted bathochromically compared to the RD solubilized in the 76% nanoemulsion. However, it was noticed that the observed shift is characteristic for all the alcohols

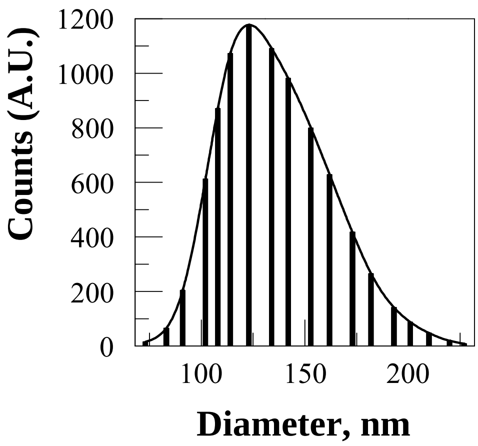


Fig. 2 Plot of the Size Distributon of Oil Droplet in 76% Emulsion.

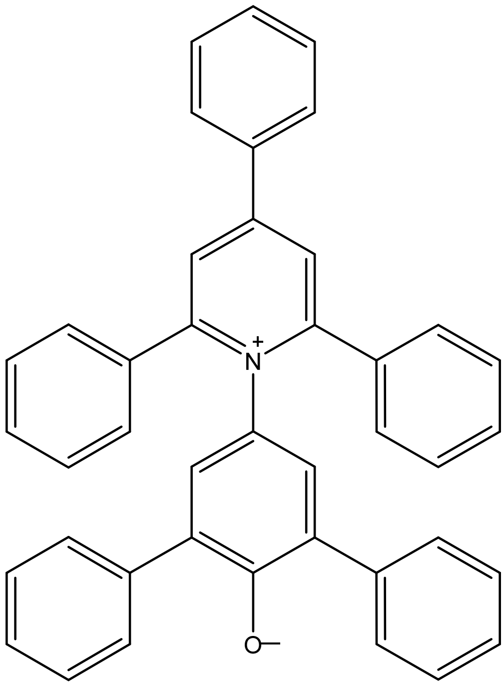
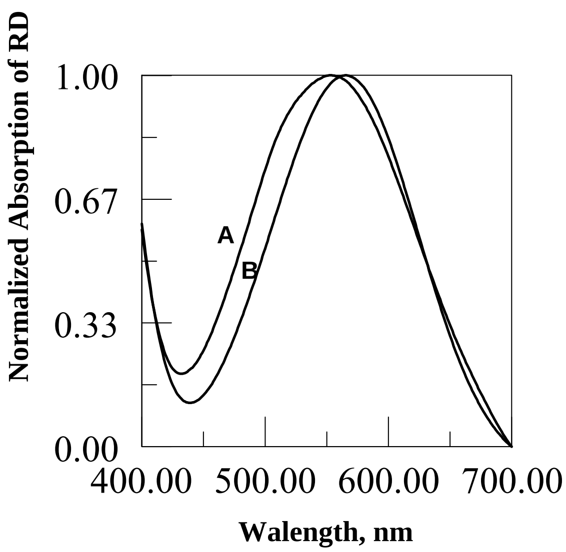


Fig. 3 Structure of Reichardt's Dye (E_T(30).



A- RD Solubilized in 76 % Nanoemulsion
B- RD Solubilized in Propaanol

Fig. 4 Plot of the absorbance spectrum of RD in 76% nanoemu and in propanol.

used. This observed shift is seen to be a function of the respective dielectric constant of a given alcohol. Table 2 gives the E_T(30) of the alcohols and their respective dielectric constants The values of the dielectric constants (ε) used were obtained from the Minnesota Solvent Descriptor Database [38].

When the observed E_T(30) values in 76% nanoemulsion are plotted as a function of the dielectric constants of the alcohols, a straight line curve is obtained as can be seen in Fig. 5.

The slope of this curve is 0.3356 and the intercept is 44.1086 with a correlation coefficient of 99.70%. Using these values the regression equation obtained is:

$$E_T\,(30) = 0.3356\varepsilon + 44.1086 \qquad (2)$$

From this equation the effective dielectric constant for each alcohol in E_T (30) is determined with the equation:

$$\varepsilon_f = (E_T\,(30) - 44.1086)/0.3356 \qquad (3)$$

In Eq. (3), ε_f stands for effective dielectric constant as defined by Zachariasse and his co-workers [39]. The E_T (30) is also a function of the polarity of the fluid system. We have used the Bakshiev equation F_2 (ε, n) [40] in this case to show that the observed E_T (30) is also linear with the relative polarity of some organic solvent as can be seen in Fig. 6.

Table 2 The calculated E_T (30) values of the alcohols and the dielectric constants.

Solvent number	Solvent	Dielectric constant (ε)	E_T (30), Kcal/mol
1	methanol	31.613	55.09
2	ethanol	24.852	52.61
3	propanol	20.521	50.69
4	butanol	17.332	49.81
5	pentanol	15.13	49.21
6	hexanol	12.51	48.79

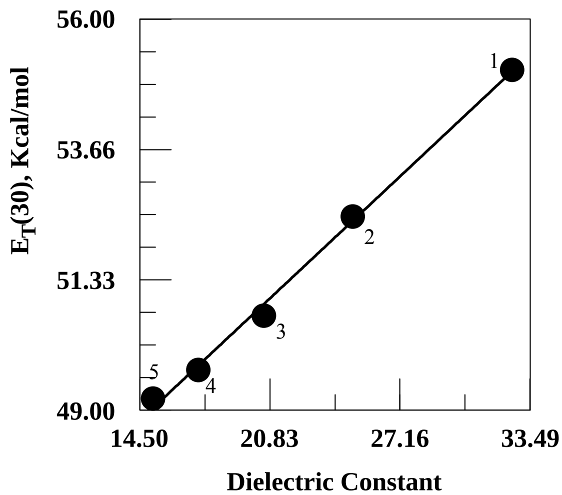


Fig. 5 Plot of ET(30) versus dielectric constants of alcohols.

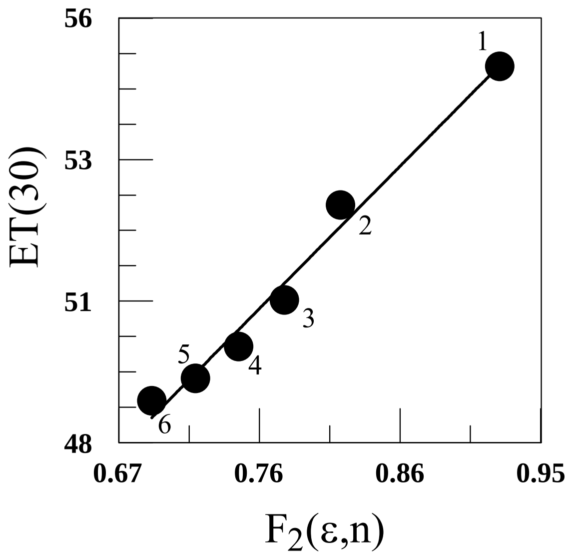


Fig. 6 Plot of $E_T(30)$ versus polarity index.

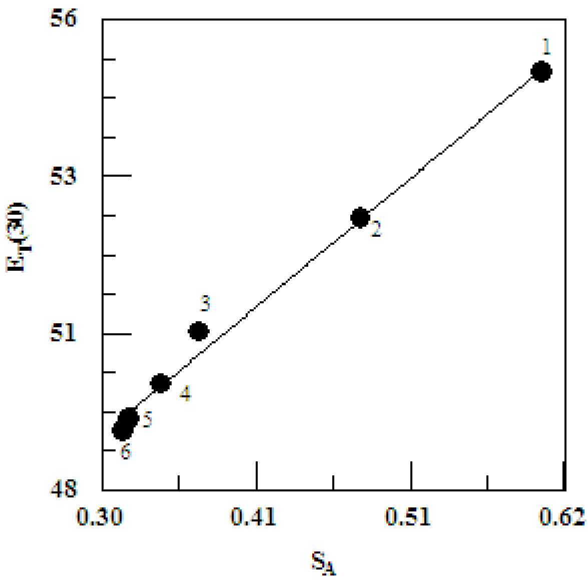


Fig. 7 Plot of $E_T(30)$ versus acidity parameter.

The $F_2(\varepsilon,n)$ is $F_2 = \left[\frac{\varepsilon - 1}{\varepsilon + 2} - \frac{n^2 - 1}{n^2 + 2}\right]\left(\frac{2n^2 + 1}{n^2 + 2}\right)$

Catalan et al. [41-46] in a series of studies showed the basicity and acidity of solvents. Using their methodology, the acidity (S_A) and basicity (S_B) of the prepared 76% nanoemulsion were determined. It was observed that these two parameters are also linear with the E_T (30) value. The plots that show this linearity are given in Figs. 7 and 8.

The observed/calculated physico-chemical properties of the oil in water nanoemulsion (76%) nanoemulsion are given in Table 3.

We also compared the observed polarity of this nanoemulsion with the solvent polarity obtained by

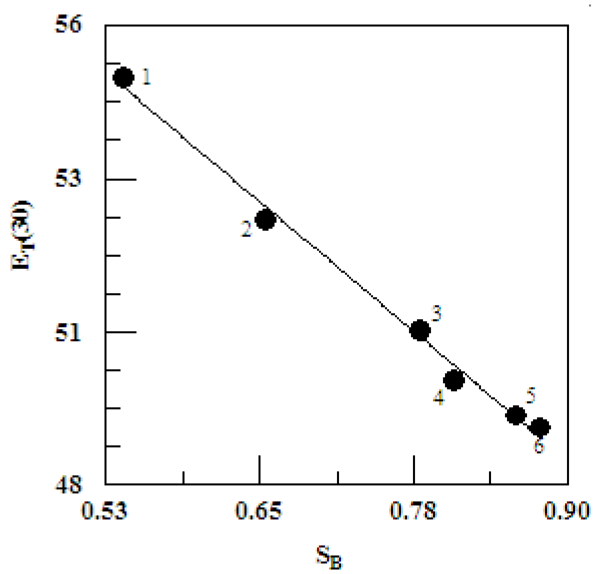


Fig. 8 Plot of $E_T(30)$ versus basicity parameter.

Table 3 The observed/calculated physico-chemical properties of 76% nanoemulsion.

Parameter	Value
E_T (30)	51.702 Kcal/mol
Effective dielectric constant, ε_f	22.59
Polarity	0.633
Refractive index, n	1.2631
Density	0.961 g/mL
Acidity parameter, SA	0.435
Basicity parameter, SB	0.721
Conductance	10.17 kμS
Viscosity, η	16.0 cP

Table 4 Comparison of the polarity of different solvents with the prepared nanoemulsion.

Compound	Polarity
Hexane	0.009
Benzene	0.111
Chloroform	0.259
DMF	0.385
DMSO	0.444
Acetonitrile	0.460
1-Propanol	0.617
Acetic acid	0.648
Glycerin	0.812
Water	1.000
76% nanoemulsion	0.633

other workers using different methods [47] as compiled by Prof. Steve Murov. This is given in Table 4.

It can be seen that the polarity of 76% nanoemusion prepared in this work is reasonably close to the polarity of 1-propanol as shown in Fig. 4.

4. Conclusion

We have shown in this work that the physico-chemical properties of nanoemulsion can be determined using RD and the values obtained are reasonably comparable to literature values. Also, nanoemulsion system is a very good solubilizing medium for molecules that are poorly soluble in water and is therefore usable in both pharmaceutical formulary, dermatology and a host of other applications.

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References

[1] Zhang Helgeson, M. E. 2016. "Colloidal Behavior of Nanoemulsions: Interactions, Structure and Rheology." *Current Opinion in Colloid & Interface Science* 25: 39-50.

[2] Lovelyn, C., Attama, A. A., and Biomaterials, J. 2001. *Nanobiotechnology* 2: 626-39.

[3] Asua, J. M. 2002. *Progress in Polymer Science* 27: 1283-346.

[4] Landfester, K. 2001. "Polyreactions in Miniemulsions." *Macromolecular Rapid Communications* 22 (12): 896-936.

[5] Gupta, A., Eral, B. B., Hatton, T. A., and Doyle, P. S. 2016. *Soft Matter* 12: 2826-41.

[6] Jaiswal, M., Dudhe, R., and Sharma, P. K. 2015. "Nanoemulsion: An Advanced Mode of Drug Delivery System." *3Biotech.* 5 (2): 123-7.

[7] Setya, S., Talegaonkar, S., and Razdan, B. K. 2014. "Nanoemulsions: Formulation Methods and Stability Aspects." *World Journal of Pharmacy and Pharmaceutical Sciences* 3 (2): 2214-28.

[8] Hamon, T. M., and Huang, J. 2014. *Drug Development* (October): 1-5.

[9] Solans, C., Esquena J., Forgirini, A. M., Uson, N., Morales, D., Izquierdo, P., Azemar, N., and Garcia-Celma, M. J. In *Adsorption and Aggregation of Surfactants in Solution*, edited by Mittal, K. L., and Dinesh, O. S. Marcel Dekker, inc. Chapter 25.

[10] Wu, Y., Li, Y. H., Gao, X. H., and Chen, H. D. 2013. "The Application of Nanoemulsion in Dermatology: An Overview." *J. of Drug Targeting* 21 (4): 321-7.

[11] Delmas, T., Piraux, H., Couffin, A. C., Texier, I., Vinet, F., Poulin, P., Cates, M. E., Bibette, J. 2011. "How to Prepare and Stabilize Very Small Nanoemulsions." *Langmuir* 27 (5): 1683-92.

[12] Rajalakshmi, R., Mahesh, K., and Kumar, C. K. A. 2011. "A Critical Review on Nano Emulsions." *International Journal of Innovative Drug Discovery* 1 (1): 1-8.

[13] Solans, C., Izquierdo, P., Nolla, J., Azemar, N., and Garcia-Celma, M. J. 2005. "Nano-Emulsions." *Current Opinions in Collid and Interface Science* 10: 102-10.

[14] Yang, H. J., Cho, W. G., and Park, S. N. 2009. "Stability of Oil-in-Water Nano-Emulsions Prepared Using the Phase Inversion Composition Method." *J. Industrial and Engineering Chemistry* 15: 331-5.

[15] Fernandez, P., Andre, V., Rieger, J., and Kuhnle, A. 2004. "Colloids and Surfaces A: Nano-emulsion Formation by Emulsion Phase Inversion." *Physico. Chem. Eng. Aspects* 251: 53-8.

[16] Tadros, T., Izquierdo, P. Esquena, J., and Solans, C. 2004. "Formation and Stability of Nanoemulsions." *Advances in Colloid and Interface Science* 108-109: 303-18.

[17] Izquierdo, P., Esquena, J., Tadros, Th. F., Dederen, C., Garcia, M. J., Azemar, N., and Solans, C. 2002. "Formation and Stability of Nano-Emulsions Prepared Using the Phase Inversion Temperature Method." *Langmuir* 18 (1): 26-30.

[18] Gutierrez, J. M., Gonzalez, C., Maestro, A., Sole, I., Pey, C. M., and Nolla, J. 2008. "Nano-emulsions: New Applications and Optimization of Their Preparation." *Current Opinions in Colloid and Interface Science* 13: 245-51.

[19] Mason, T. G., Wilking, J. N., Meleson, K., Chang, C. B., and Graves, S. M. 2016. "Nanoemulsions: Formation, Structure, and Physical Properties." *J. Phys: Condensed Matter* 18: R635-66.

[20] Zhang,Y., Shang, Z., Gao, C. G., Du, M., Xu. S., Song, H., and Liu, T. 2014. "Nanoemulsion for Solubilization, Stabilization, and in Vitro Release of Pterostilbene for Oral Delivery." *AAPS Pharm Sci Tech.* 15 (4), 1000-8.

[21] Thakur, A., Walia, M. K., and Kumar, S. L. 2013. "In

Enhancement of Bioavailability of Poorly Soluble Drugs: A Review." *H. Pharmacophore* 4 (1): 15-25.

[22] Debnath, S., and Satayanarayana, Kumar, V. 2001. *An International Journal of Advances in Pharmaceutical Sciences* 2 (2-3): 72-82.

[23] Shakeel, F., and Faisal, M. S. 2010. "Nano-emulsion: A Promising Tool for Solubility and Dissolution Enhancement Of Celecoxib." *Pharm. Dev. Technol.* 15 (1): 53-6.

[24] Tiwari, S. B., Shenoy, D. B., and Amiji, M. M. 2006. *NSTI-Nanotech.* 1: 475-8.

[25] Vadlapudi, A. D., and Mitra, A. K. 2013. "Nanomicelles: An Emerging Platform for Drug Delivery to the Eye." *Ther Deliv.* 4 (1): 1-3.

[26] Sutradhar, K. B., and Amin, Md. L. 2013. " Nanoemulsions: Increasing Possibilities in Drug Delivery." *European Journal of Nanomedicine*. 5 (2): 97-110.

[27] Chime, S. A., Kenechukwu, F. C., and Attama, A. A. INTECH. "Nanoemulsions—Advances in Formulation, Characterization and Applications in Drug Delivery." http://dx..doi.org/10.5772/15371.

[28] Harwansh, R. K., Patra, K. C., Pareta, S. K. Singh, J., and Rhman, M. A. 2011. "Nanoemulsions as Vehicles for Transdermal Delivery of Glycyrrhizin." *Brazilian J. Pharmaceutical Sciences* 47 (4): 769-78.

[29] Hashtjin, A. M., and Abbasi, S. J. 2015. "Optimization of Ultrasonic Emulsification Conditions for the Production of Orange Peel Essential Oil Nanoemulsions." *Food Sci. Technol.* 52 (5): 2679-89.

[30] Dune Sciences Inc., www.dunesciences.com.

[31] Reichardt, C. 2004. "Pyridinium N-phenolate Betaine Dyes as Empirical Indicators of Solvent Polarity: Some New Findings." *Pure Appl. Chem.* 76 (10): 1903-19.

[32] Laglante, A. F., Spadi, M., and Bruno, T. J. 2000. *J. Chem. Eng. Data.* 45: 382-5.

[33] Lobaugh, J., and Rossky, P. J. 2000. "Solvent and Intramolecular Effects on the Absorption Spectrum of Betaine-30." *J. Phys. Chem. A* 104: 899-907.

[34] Reichardt, C. 1994. "Solvatochromic Dyes as Solvent Polarity Indicators." *Chem. Rev.* 94: 2319-58.

[35] Kosower, E. M., Dodiuk, H., Tanizawa, K., Ottolenghi, M., and Orbach, N. 1975. "Intramolecular donor-acceptor systems. Radiative and Non-Radiative Processes for the Exited States of 2-N-Arylamino-6-Naphthalenesulfonates." *J. Am. Chem. Soc.* 97 (8): 2167-77.

[36] Kamlet, M. J., and Taft, R. W. 1976. "The Solvatochromic Comparison Method. I. The Beta-Scale of Solvent Hydrogen-Bond Acceptor (HBA) Basicities." *Ibid* 98 (2): 377-83.

[37] Taft, R. W., and Kamlet, M. J. 1976. "The Solvatochromic Comparison Method. 2. The Alpha-Scale of Solvent Hydrogen-Bond Donor (HBD) Acidities." *Journal of the American Chemical Society* 98 (10): 2886-94.

[38] Winget, P., Dolney, D. M., Gisen, D. J., and Cramer, C. J. 1999. *Minnesota Solvent Descriptor Database.*

[39] Zachariasse, K. A., Phuc, N. V., and Kozanklowkz, B. J. 1981. "Investigation of Micelles, Micro-Emulsions, and Phospholipid-Bilayers with the Pyridinium N-Phenolbetaine ET(30), a Polarity Probe for Aqueous Interfaces." *Phys. Chem.* 85: 2676-83.

[40] Bakshiev, N. G. 1964. "Universal Intermolecular Interactions and Their Effect on the Position of the Electronic Spectra of Molecules in Two Component Solutions." *Opt. Spektrosk.* 16: 821-32.

[41] Jayabharathi, J., Ramanathan, P., Thanikachalaam, V., and Arunpandiyan, A. 2014. "Kamlet-Taft and Catalán Solvatochromism of Some π-Expanded Phenanthrimidazole Derivatives-DFT Analysis." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 133: 201-6.

[42] Catalan, J. et al. http://www.uam.es/personal_pdi/scienclas/catalan/sa.htm.

[43] Catalan, J. http://www.uam.es/personal_pdi/scienclass/catalan/sb.btm

[44] Catalan, J. http://www.uam.es/personal_pdi/scienclass/catalan/spp.htm.

[45] Catalan, J., and Diaz, C. 1997. *Liebigs Ann.* 1941-9.

[46] Catalan, J., Diaz, C., Lopez, V., Perez, P., de Paz, J. L. G., and Rodriguez, J. G. 1996. *Ibid*. 1785-94.

[47] https://www.murov.info//orgsolvents..html