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Binding properties of coumarin phthalonitrile derivatives in methanol

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ABSTRACT

The complexation properties of coumarin phthalonitrile derivatives 1-3, towards some transition, heavy and lanthanide metal cations have been investigated in methanol by means of UV spectrophotometry and conductivity experiments. The stoichiometries of the complexes formed and their stability constants were resolved by digital processing of data. A binuclear M_2L (M = Metal, L = Ligand) species were formed and the profiles of affinity of ligands 1-3 towards transition metal cations illustrate their selectivity towards Cu^{2+}.

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1. Introduction

Several methods, both catalytic and non-catalytic, have been investigated in the production of aromatic dinitriles. Some substituted aromatic *o*-dinitriles are widely used in the synthesis of phthalocyanines [1], polymers, and intermediates in organic syntheses [2]. Most common methods of their synthesis include cyanation of aromatic halides [2-4], nucleophilic substitution of nitrophthalonitriles [5-12], Diels-Alder addition of fumaronitrile or dicyanoacetylene to substituted dienes and furans [13,14], and multistep synthesis involving the transformation of aromatic *o*-diacids via imides and diimides [15] to dinitriles [16-18]. Direct electrophilic aromatic substitution of aromatic *o*-dinitriles is generally not used due to the presence of two desactivating electron-withdrawing nitrile groups and the fact that these groups are susceptible to the hydrolysis during the strongly acidic conditions of these reactions. Coumarin derivatives are of interest because of their physiological, photodynamic, anticoagulant, spasmolytic, bacteriostatic and antitumor activity [19]. They are also extensively used as analytical reagents. Coumarins and their derivatives have been studied extensively for their complexation with metal ions [20,21].

Our interests in synthetic phthalocyanines led us to study the binding properties of a variety of multi-substituted phthalonitriles, *bis*-aromatic-*o*-dinitriles, naphthalene dicarbonitriles (5-Substituted-2,3-dicyanonaphthalenes) and phenanthrene-tetracarbonitriles [20-22].

The complexation of alkali, alkaline-earth, transition and heavy metal cations by ligands **1**, **2** and **3** (Scheme 1), in acetonitrile, were described previously by our team [22]. Mononuclear complexes ML were formed and high affinities of ligands **2** and **3** towards Rb^+ and Cu^{2+} were noticed. While in the case of alkaline-earth metal cations, the stability profile of ligands **1**, **2** and **3** are similar with a high affinity in favor of Ca^{2+} [22]. As a continuation of this work, the complexation of transition, heavy and some lanthanide metal cations, followed in methanol, is reported in this paper. The study was followed by means of spectrophotometry UV-Visible. Conductometric measurements were also used to obtain preliminary estimates of stoichiometries of complexes formed. The last part in this paper is dealing about liquid-liquid extraction of metallic picrate salts by coumarin derivatives **1-3** from water into dichloromethane.

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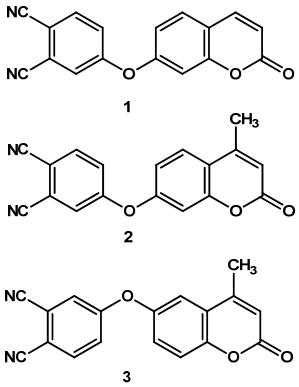

Scheme 1

2. Experimental

2.1. Synthesis

2.1.1. Synthesis of 4-(2-oxo-2H-chromen-7-yloxy)-phthalonitrile (1) [22]

4-Nitrophthalonitrile (2.25 g, 12.34 mmol) was dissolved in dry DMF (15 mL) under argon and 7-hydroxycoumarin (2.00 g, 12.34 mmol) was added. After stirring for 15 min at room temperature, finely ground anhydrous potassium carbonate (3.67 g, 26.6 mmol) was added in portions during 2 h with efficient stirring. The reaction mixture was stirred under argon atmosphere at room temperature for 24 h after which time, the ensuing mixture was poured into 100 mL iced water and the precipitate filtered off, washed with methanol and then dried. The crude product was chromatographered over a silica gel column using a mixture of $CHCl_3$:MeOH (100:5, *v*:*v*) as eluent, giving a powder of 4-(2-oxo-2*H*-chromen-7-yloxy)-phthalonitrile (**1**). Finally, the pure powder was dried in a vacuum. Color: White. Yield: 65%. M.p.: 223-225 °C . FT-IR (KBr, ν, cm^{-1}): 3061 (Ar-CH), 2225 (CN), 1587 (C=C), 1726 (C=O, Lactone and ester), 1483 (C-O-C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 6.50-8.18 (m, 8H, Ar-H+H2,3). ^{13}C NMR (150 MHz, DMSO-d_6, δ, ppm): 160.1, 159. 9, 157.4, 155.4, 144.1, 136.7, 130.8, 124.1, 123.9, 117.3, 116.5, 116.0, 115.5, 109.9, 108.0. Anal. calcd. for $C_{17}H_8N_2O_3$: C, 70.83; H, 2.780; N, 9.72. Found: C, 70.80; H, 2.70; N, 9.70%. MS (LCMS-MS, *m/z* (%)): 287.2 [M-H$^+$].

2.1.2. Synthesis of 4-(4-methyl-2-oxo-2H-chromen-7-yloxy)-phthalonitrile (2) [22]

The synthesis of compound **2** was similar to that of compound **1**, except 7-hydroxy-4-methylcoumarin (1.232 g, 7 mmol) was employed instead of 7-hydroxycoumarin. The amounts of the other reagents were: 4-nitrophthalonitrile, 0.865 g (5 mmol) and anhydrous potassium carbonate, 1.035 g (7.55 mmol). Color: Yellow. Yield: 75%. M.p.: 225-227 °C. FT-IR (KBr, ν, cm^{-1}): 3068 (Ar-CH), 2227 (CN), 1587 (C=C), 1724 (C=O, Lactone and ester), 1487 (C-O-C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.40 (s, 3H, CH_3), 7.42-8.30 (m, 7H, Ar-H+H3). ^{13}C NMR (150 MHz, DMSO-d_6, δ, ppm): 161.7, 159. 8, 153.2, 150.8, 149.8, 136.6, 125.0, 122.5, 122.2, 121.5, 119.1, 117.7, 117.0, 116.2, 115.7, 115.4, 108.6, 18.5. Anal. calcd. for $C_{18}H_{10}N_2O_3$: C, 71.52; H, 3.33; N, 9.27. Found: C, 71.50; H, 3.30; N, 9.20%. MS (LCMS-MS, *m/z* (%)): 301.2 [M-H$^+$].

2.1.3. Synthesis of 4-(4-methyl-2-oxo-2H-chromen-6-yloxy)-phthalonitrile (3) [22]

The synthesis of compound **3** was similar to that of compound **1**, except 6-hydroxy-4-methylcoumarin (1.232 g, 7 mmol) was employed instead of 7-hydroxycoumarin. The amounts of the other reagents were: 4-nitrophthalonitrile, 0.865 g (5 mmol) and anhydrous potassium carbonate, 1.035 g (7.55 mmol). Color: White. Yield: 70%. M.p.: 223-225 °C. FT-IR (KBr, ν, cm^{-1}): 3059 (Ar-CH), 2229 (CN), 1577 (C=C), 1720 (C=O, Lactone and ester), 1435 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 2.41 (s, 3H, CH_3), 6.48-8.12 (m, 7H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 161.7, 159.8, 153.2, 150.9, 150.0, 136.7, 125.0, 122.6, 122.4, 121.6, 119.1, 117.7, 117.1, 116.2, 115.7, 115.5, 108.7. Anal. calcd. for $C_{18}H_{10}N_2O_3$: C, 71.52; H, 3.33; N, 9.27, Found: C, 71.50; H, 3.30; N, 9.20%. MS (LCMS-MS, *m/z* (%)): 301.2 [M-H$^+$].

2.2. Instrumentations

Methanol (Riedel-de Haën for HPLC) and dichloromethane (Fluka, Purum) were commercial and used without further purification. The metal salts chosen were chlorides (Fluka, Purum). Melting points were determined using an Electro-thermal apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were carried on a Varian Gemini 400 (400 MHz) spectrometer using TMS as internal standard (δ = 0 ppm). IR spectra were recorded on a Perkin-Elmer 398 Spectrophotometer. MS were recorded on a LCMS-MS 8030 Shimadzu. Elemental analyses were performed on Perkin-Elmer 2400 elemental analyzer, and the values found were within ±0.3% of the theoretical values. The UV absorption spectra were recorded on a Perkin Elmer Lambda 11 spectrophotometer. The supporting electrolyte used in the stability constant determinations was NEt_4Cl (Acros Organics). The picrate salts employed in extraction were prepared as described in literature [23]. A conductivity measurement was made by using Cyber Scan PC510 conductivity meter. The conductivity cell constant is K = 0.9 cm.

2.3. Stability constant determination

The stability constants β_{xy} being the concentration ratios $[M_xL_y^{xn+}]/[M^{n+}]^x[L]^y$ (where M^{n+} = Metal ion, L = Ligand) were determined in methanol by UV-absorption spectrophotometry at 25 °C. The ionic strength has been maintained at 0.01 mol/L using Et_4NCl. The spectra of ligand solutions of concentrations ranging between 1×10^{-5} and 6×10^{-5} mol/L and increasing concentration of metal ion were recorded between 220 and 360 nm. Generally the metal to ligand ratio R at the end of the titration did not exceed 15 and the equilibriums were quasi-instantaneous for all the systems. Addition of the metal salts to the ligand induced spectra changes, large enough to allow the analysis of the resulting data using the program "Letagrop" [24]. Best values for the formation constants β_{xy} of the various complex species and their molar absorptive coefficients for various wavelengths, are deduced from the best fit between the experimental and calculated UV spectra.

The best fit is reflected by the lowest value of U (the sum of U values for all given lambda) corresponding to the square sum of a differences between experimental and calculated absorbances ($U = \sum (A_{cal} - A_{exp})^2$). The β_{xy} values correspond to the average of at least three independents experiments [24-26].

2.4. Extraction studies

The extraction methods of transition, silver and lanthanum metal picrates from water into dichloromethane, were performed according to a procedure described in the literature [27,28]. Equal volumes (5 mL) of neutral aqueous solution of metal picrate (3×10^{-4} mol/L) and CH_2Cl_2 solution of coumarins (3×10^{-4} mol/L) were mixed, magnetically shaken in a thermo-regulated water bath at 25 °C for 30 min, and then left standing for 2 to 6 h in order to obtain a complete separation of two phases.

Table 1. Stability constants (log $\beta_{21}\pm\sigma_{n-1}$) of M_2L complexes of transition, heavy and some lanthanide cations, in methanol, at 25 °C, I = 10^{-2} M.

Ligand	M:L	Mn^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Ag^{+}	Sn^{2+}	Hg^{2+}	La^{3+}	Sm^{3+}
1	2:1	-*	5.90±0.03	6.70±0.01	8.08±0.03	7.21±0.01	6.72±0.02	6.12±0.05	8.72±0.03	7.31±0.04	8.98±0.01
2	2:1	6.12±0.03	-	-	7.90±0.01	7.01±0.01	7.22±0.01	7.42±0.05	8.67±0.01	8.11±0.04	8.72±0.03
3	2:1	6.42±0.05	-	-	7.89±0.04	6.61±0.04	7.58±0.02	7.72±0.02	7.84±0.01	8.41±0.05	8.81±0.03

* Absorbance changes too small to enable satisfactory fitting.

The concentration of metal picrate remaining in the aqueous phase was determined from the absorbance *A* at 355 nm. The percentage extraction (%E) was derived from the following expression in which A_0 is the absorbance of the aqueous solution of a blank experiment without coumarins.

$$\%E = 100\ (A_0 - A)\ /\ A_0 \quad (1)$$

2.5. Conductimetric studies

Although the metal cation complexation by a neutral ligand is not expected to dramatically alter the molar conductivity of a cationic species, the measurement of conductance of a solution of ligand could be a useful for establishing the stoichiometry of complexes formed during a titration by a metal ion solution. Therefore, this procedure was followed to obtain preliminary estimates of the metal:ligand ratio in the complexes formed by coumarins **1**-**3** [29,30].

3. Results and discussion

3.1. Complexation by UV-visible spectrophotometer

The UV spectra of coumarins **1**-**3** have been recorded in methanol between 220 and 360 nm. Those of ligands **2** and **3** are almost similar and characterized by a maximum of absorption at 310 nm and a shoulder at 285 nm. For ligand **1**, the maximum of absorption appears at 260 nm while a smaller one appears at around 305 nm. A shoulder at 320 nm is also noticeable.

The complexation of metal cation is interpreted by a decrease of intensities. The spectra, at the end of titration, keep generally the same profile of starting spectrum of pure ligand. Moreover, isobestic points are observed at 243 nm in the case of ligand **2**/Sm^{3+} (Figure 1), at 252 nm for ligand **1**/Hg^{2+} and for ligand **2**/ Hg^{2+} and at 251 nm for ligand **3**/ Hg^{2+}.

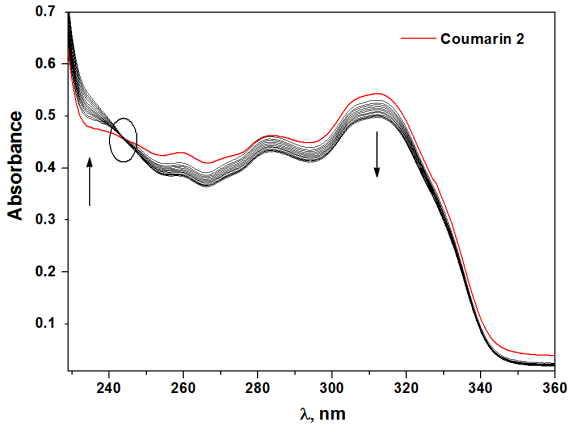

Figure 1. UV absorption spectra of complexation of Sm^{3+} by compound **2** in methanol, $C_L = 5\times10^{-5}$ M, $0 \le R_{M/L} \le 5$, at 25 °C.

The treatment of UV absorption spectra by letagrop allows us to find out the stoichiometries of different complexes formed by ligands **1**-**3** with transition, heavy and some lanthanide cations in methanol. Stability constants log β_{xy} were also calculated and collected in Table 1.

The complexes formed by coumarin derivatives **1**-**3** with all studied cations are binuclear species which imply an interaction between one ligand for two metals. In the first sequence of transition metals, very small variations of UV spectra didn't allow resolving the stoichiometries or stability constants of complexes formed with ligand **1**/Mn^{2+}, ligand **2**/Co^{2+}, ligand **3**/Co^{2+}, ligand **2**/Ni^{2+} and ligand **3**/Ni^{2+}. However, in other cases, the stability constants shift between 5.90 and 8.08 logarithmic units. The variation of the profiles of affinity of these ligands illustrates an increase of affinity from Mn^{2+} to Cu^{2+} and then a slightly decrease to Zn^{2+}. The high stabilities of coumarin derivatives **1**-**3** towards copper are previously observed in acetonitrile [22]. This result is following the Irving-Williams rules [31] which is dealing about an uniform increase in the stability of the complexes according to the following sequence: Ti < V < Cr < Mn < Fe < Co < Ni < Cu > Zn. This series illustrates that not only the trend depends on the ratio z/r (z = Charge of the metal ion, r = Radius of the metal ion), but also the large electrostatic contribution to complex formation [27,28]. Furthermore, the calculation of the selectivity $S_{(Cu^{2+}/Co^{2+})}$ ($S = 10^{(\log \beta_{21}(Cu2+) - \log \beta_{21}(Co2+))}$) in the case of ligand **1** prove a significant value which is close to 151.

In the case of heavy metals, the stability constants of **1**-**3** coumarins are varying between 6.12 and 8.72 logarithmic units. The profiles of stability of coumarins **2** and **3** are almost similar increasing from Ag^{+} to Hg^{2+}. A selectivity $S_{(Hg^{2+}/Sn^{2+})}$ around 400, is calculated for coumarin **1**. In the case of La^{3+} and Sm^{3+}, the binuclear complexes are very stables with stability constants shifting between 8 and 9 logarithmic units.

The open spatial structure of coumarins **1**-**3** and the soft base characters of both aromatic units and nitrogen could explain the formation of binuclear species with soft acids like transition, heavy metals and lanthanides. Moreover, the affinities of ligand **1**-**3** in methanol are lower than those in acetonitrile which is recognized by the effect of the solvation and the donor number of each solvent [32-34].

3.2. Complexation by conductometer

The conductometric studies were established in order to check the stoichiometry of complexes formed in some cases. The titration of the solution of coumarin derivatives in methanol were followed in the case of Sm^{3+} with ligand **3** and Zn^{2+} with ligand **2**. After plotting the conductance values according to the ratio $R = C_M/C_L$, a variation of the slopes are observable. The projection of the meeting point of both slopes corresponds to the stoichiometry of the complex formed after titration. Figure 2 illustrates the titration of coumarin **3** by Sm^{3+}. The projection shows the formation of complex M_2L, which confirms the stoichiometry found by spectrophotometry in same solvent: methanol. Same for coumarin **2**, its titration by Zn^{2+} confirms the formation of complex M_2L.

3.3. Extraction of metal picrates

The extraction of metal picrates from water into dichloromethane was studied with Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Ag^{+} and La^{3+}. The percentages of extraction (%E) are collected in Table 2.

Table 2. The extraction percentages (%E) of metal picrates from water into dichloromethane at 25 °C.

Metal	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	La^{3+}	Ag^{+}
Ionic radius, Å	0.75	0.69	0.73	0.75	1.03	1.15
1	26	28	47	31	40	18
2	<1	<1	34	29	45	22
3	<1	<1	36	27	45	29

Generally, the values are not high although the presence of a soft base site as nitrogen in coumarins **1**-**3**. However, the extraction power increases for Cu^{2+} and La^{3+} as shown on Figure 3. The highest value is noticed for Cu^{2+} with ligand **1**, in harmony with the complexation results. It is clear from the Figure 3 that the profile of extraction is not proportional to the ionic radius. It is rather depending on the coordination of the transition metal in the complexes.

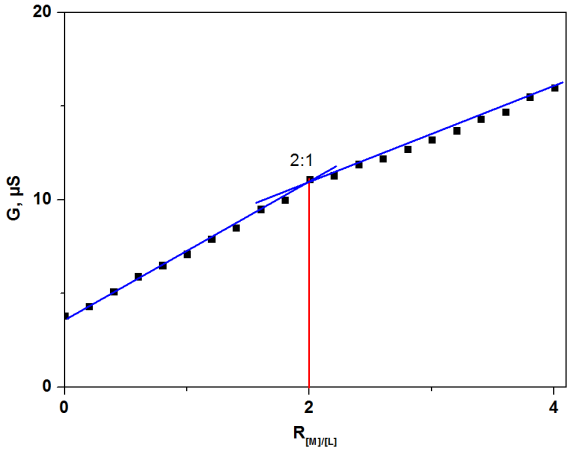

Figure 2. Conductometric titration in the case of ligand **3** with Sm^{3+} (C_L = 3.8× 10^{-5} mol/L) in methanol.

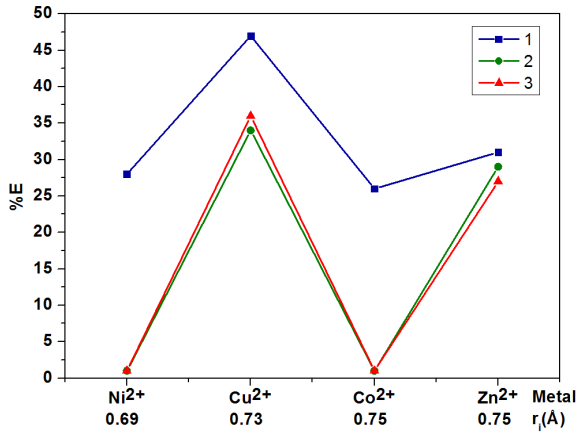

Figure 3. Trends of the extraction percentages (%E) for some salt metal picrates from water into dichloromethane.

4. Conclusion

In conclusion, the binding properties of new coumarin phtalonitrile derivatives **1**-**3** have been studied towards some transition, heavy and lanthanide metal cations in methanol by means of UV spectrophotometry absorption and conductivity methods. The last technique confirms the stoichiometry M_2L found by UV-Visible spectrophotometry. High affinity, in complexation and extraction studies, towards Cu^{2+} was detected and a selectivity $S_{(Cu^{2+}/Co^{2+})}$ around 151 was calculated for ligand **1**. This behavior towards Cu^{2+} was perceived previously in acetonitrile with same coumarin derivatives [22].

Furthermore, the formation of ML and the high affinity of ligand **1**-**3** in acetonitrile are probably interpreted by the transformation of the open spatial structure of ligands to an enwrapped structure creating a small cavity, encapsulating inside the metal [32-34]. To highlight this suggestion, a further study elaborated by ^{1}H NMR needs to be done to follow the variations of chemical shifts. Whereas, the formation of M_2L in methanol leads us to think about the open structure of ligands kept after complexation of both metals where one of them is probably located between the two aromatic units while the second cation is attracted by two nitrogens.

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References

[1]. Leznoff, C. C. Phthalocyanines; properties and applications, Vol. 1, VCH, New York. 1989.
[2]. Ellis, G. P.; Romney-Alexander, T. M. *Chem. Rev.* **1987**, *87*, 779-794.
[3]. Chambers, M. R. I.; Widdowson, D. A. *J. Chem. Soc. Perkin Trans. I* **1989**, 1365-1366.
[4]. Takagi, K.; Sakakibara, Y. *Chem. Len*. **1989**, 1957-1965.
[5]. Kelle, T. M.; Price, T. R.; Griffith, J. R. *Synthesis* **1980**, 613-622.
[6]. Marullo, N. P.; Snow, A. W. *ACS Symp. Ser*. **1982**, *14*, 325-337.
[7]. Siegl, W. O. *J. Heterocycl. Chem.* **1981**, *18*, 1613-1618.
[8]. Leznoff, C. C.; Marcuccio, S. M.; Creenberg, S.; Lever, A. B. P.; Tomer. K. B. *Can. J. Chem*. **1985**, *63*, 623-632.
[9]. Leznoff, C. C.; Terekhov, D. S.; McArthur, C. R.; Vigh, S.; Li, J. *Can. J. Chem*. **1995**, *73*, 435-443.
[10]. Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, *8*, 627-630.
[11]. Sonogashira, K.; Tohoa, Y.; Haginara. H. *Tetrahedron Lett.* **1975**, *16*, 4467-4470.
[12]. Marcuccio, S. M.; Svirskaya, P. I.; Greenberg, S.; Lever, A. B. P.; Leznoff, C. C.; Tomer. K. B. *Can. J. Chem.* **1985**, *63*, 3057-3069.
[13]. Kovshev, E.; Puchnova, V. A.; Luk'yanets. E. A. *Zh. Org. Khim*. **1971**, *7*, 369-379.
[14]. Cook, M. J.; Daniel, M. F.; Harrison, K. J.; McKeown, N. B.; Thomson. A. J. *J. Chem. Soc. Chem. Commun*. **1987**, *14*, 1086-1088.
[15]. McClelland, R. A.; Seaman, N. E.; Duff, J. M.; Branston. R. E. *Can. J. Chem*. **1985**, *63*, 121-128.
[16]. Drew, H. D. K.; Kelly, D. B. *J. Chem. Soc*. **1941**, 637-641.
[17]. Rasmussen, C. R.; Gardocki, J. F.; Plampin, J. N.; Twardzik, B. L.; Reynolds, B. E.; Molinari, A. J.; Schwartz, N.; Bennetts, W. W.; Price, B. E.; Marakowski, J. *J. Med. Chem.* **1978**, *21*, 1044-1054.
[18]. Campagna, F.; Carotti, A.; Cassini, G. *Tetrahedron Lett.* **1977**, *18*, 1813-1815.
[19]. Hall, T. W.; Greenberg, S.; McArthur, C. R.; Khouw B.; Leznoff. C. C. *Nouv. J. Chim*. **1982**, *6*, 653-658.
[20]. Sardari, S.; Mori, Y.; Horita, K.; Micetich, R. G.; Nishibe S.; Daneshtalab, M. *Bioorg. Med. Chem*. **1999**, *7*, 1933-1940.
[21]. Singh, H. B. *Acta Cienc. Indica. Ser. Chem*. **1980**, *6*, 88-91.
[22]. Medyouni, R.; Naouali, O.; Hamdi, N.; Zagrouba, F.; Baklouti, L. *J. Adv. Chem*. **2015**, *11*, 3512-3518.
[23]. Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M. J.; Egberink, R. J. M.; Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767-2777.
[24]. Sillen, G.; Warnquist, B. *Ark. Kemi*. **1968**, *31*, 377-390.
[25]. Naouali, O.; Soleiman, H.; Baklouti, L. *Eur. J. Chem.* **2014**, *5*, 339-342.
[26]. Thabet, W.; Baklouti, L.; Zieba, R.; Parola, S. *J. Inclusion. Phenom.* **2012**, *73*, 135-139.
[27]. Pedersen, C. *J. Am. Chem. Soc*. **1970**, *92*, 386-391.
[28]. Frensdorff, H. K. *J. Am. Chem. Soc*. **1971**, *93*, 4684-4686.
[29]. Ben Othman, A.; Abidi, R.; Baklouti, L.; Vicens, J. *Org. Chem. Ind. J.* **2005**, *1*, 38-43.

[30]. Ben Othman, Baklouti, L.; A.; Abidi, R.; Vicens, J. *Lett. Org. Chem.* **2007**, *4*, 339-343.
[31]. Irving, H.; Williams, R. J. P. *J. Chem. Soc.* **1953**, 3192-3210.
[32]. Gutmann, V. The Donor Acceptor Approach to Molecular Interactions, Plenum Press, New York, 1978.
[33]. Naouali, O.; Frija, R.; Elgabsi, W.; Hamdi, N.; Baklouti, L. *Med. J. Chem.* **2014**, *3*, 1057-1065.
[34]. Naouali, O.; Boubakri, L.; Hamdi, N.; Baklouti, L. *Asian J. Adv. Basic Sci.* **2015**, *3*, 186-193.