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IMPROVED METHOD FOR PREPARATION OF 4,5-DICHLOROPHTHALONITRILE AND SYNTHESIS OF 4-CHLORO-5-(R-AMINO)PHTHALONITRILES ON ITS BASIS

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4,5-dichlorophthalonitrile, N-nucleophiles, amines, S_NAr reaction, phthalocyanines, 4-chloro-5-(R-amino)phthalonitriles

Abstract. *The paper investigates the influence of the nature of N-nucleophiles on the reaction of activated aromatic nucleophilic substitution of chlorine atom in 4,5-dichlorophthalonitrile. The authors synthesised 4-chloro-5-(R-amino)phthalonitriles not described in the literature. They are promising compounds for the synthesis of phthalocyanines with increased organosolubility.*

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Introduction

Usually 4,5-Dichlorophthalonitrile is obtained by the four-step method proposed by D. Wörle [1-5], and used in S_NAr reactions with *O*-nucleophiles in the presence of base [6], while reactions with *N*-nucleophiles are much less common. There are few examples of 4,5-dichlorophthalonitrile interaction with secondary aliphatic amines in the literature. In [7], 4-chloro-5-(dimethylamino)phthalonitrile was obtained by interaction of 4,5-dichlorophthalonitrile with dimethylamine formed *in situ* from DMFA and triethylphosphite at 160 °C for 3 hours. However, under similar experimental conditions (without triethyl phosphite) using Na_2CO_3, K_2CO_3 or Cs_2CO_3, product formation with very low yields (14 to 26%) is usually observed with a total reaction time of 24 hours. According to the investigations, zinc phthalocyanine based on 4-chloro-5-(dimethylamino)phthalonitrile has a high fluorescence quenching efficiency when a solution of trinitrophenol and trinitrotoluene is added to this system. This may find potential application for explosives detection.

The synthesis of 4-chloro-5-(dihexylamino)phthalonitrile was also described previously [8]. In this case, only one chlorine atom was substituted for the dihexylamine fragment regardless of the choice of solvent (DMSO, THF, dimethylaminoethanol), the excess amount of *N*-nucleophile (twofold, fourfold, or eightfold excess), and the deprotonating agent used (K_2CO_3 or Na_2CO_3).

The authors of [9] prepared 4-chloro-5-morpholino-phthalonitrile and the corresponding octasubstituted phthalocyanine on the basis of 4,5-dichlorophthalonitrile and morpholine. They had good solubility in $CHCl_3$, CH_2Cl_2, THF, DMFA, DMSO and toluene, while the Bouguer-Lambert-Bera law was observed in THF in a certain concentration range. During the S_NAr reaction, the authors used morpholine and *n*-butylamine as *N*-nucleophiles. While the reaction with morpholine proceeded selectively with formation of the monosubstitution product without any complications (morpholine itself acts as the base and solvent), the reaction with the primary aliphatic amine resulted in the formation of an inseparable mixture of 7 compounds. Indeed, the authors failed to obtain 4,5-dimorpholinophthalonitrile: neither increasing the temperature nor adding excess morpholine did not lead to the desired result.

At the same time, the process proceeds selectively with the formation of 4-chloro-5-hexylaminophthalonitrile according to [10] in the case of *n*-hexylamine.

According to series of further studies [11], 4-chloro-5-morpholino-phthalonitrile can be used in a statistical condensation reaction with other phthalonitriles to synthesise A_3B-type phthalocyanines, with the *N*-containing substituent in the B fragment performing an auxochromic function. The introduction of an *N*-containing substituent at the periphery of the macrocycle always results in a significant bathochromic shift of the absorption and emission maximum.

Patent [12] describes the synthesis of promising aromatic and heteroaromatic carboxamides containing piperidine fragment. These compounds, according to the authors, can be used in the treatment of Parkinson's disease and other neurological diseases. One of the reported compounds was obtained by an aromatic nucleophilic substitution reaction between substituted piperidine and 4,5-dichlorophthalonitrile. The reaction was conducted in THF; triethylamine was used as a deprotonating agent, with the formation of a monosubstitution product only. Remarkably, the remaining chlorine atom was successfully substituted using $Pd_2(dba)_3$, the organophosphorus ligand "Xantphos" and Cs_2CO_3 to a 2-methoxynicotinamide moiety (the yield of the palladium-catalysed reaction was only 13%). This example shows the possibility of substituting a chlorine atom in 4-chloro-5-(R-amino)phthalonitrile, where R is alicyclic one in nature.

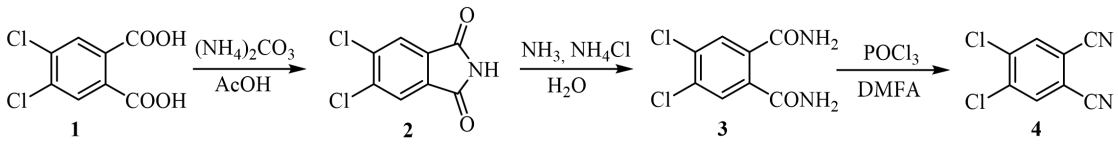
The use of 4,5-dichlorophthalonitrile in the S_NAr reaction with aromatic amines has not been described in the literature before.

Information about 4-chloro-5- vegetarylamino-phthalonitriles is also absent in the literature. However, 4,5-dichlorophthalonitrile reacts with the following compounds: imidazole [13], 6-octyl- and 6-*tret*-butylpyrazole [14] (K_2CO_3 is taken as a base), carbazole and 3,6-di-*tret*-butylcarbazole [15], 3,6-dibromocarbazole [16] (CsF is taken as a base).

Therefore, development of methods for the synthesis of 4-chloro-5-(R-amino)phthalonitriles is an important task for obtaining new substituted phthalonitriles with potential biological activity, as well as phthalocyanines and other compounds containing imide, isoindoline and tetrazole fragments.

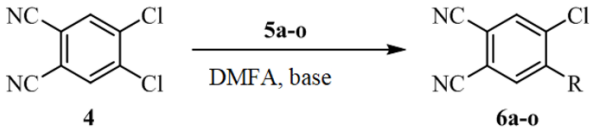
Main body

The classical synthesis of 4,5-dichlorophthalonitrile according to Wöhrle [1] provides only a satisfactory yield of the target product (49%). Therefore, we proposed a modification allows obtaining 4,5-dichlorophthalonitrile **4** in the third stage with a total yield of 72%. At the same time, 4,5-dichlorophthalimide **2** was obtained directly from 4,5-dichlorophthalic acid **1**; the use of ammonium chloride addition increased the yield of 4,5-dichlorophthalamide **3** in the second stage to 78%.



In this study we synthesised new 4-chloro-5-(R-amino)phthalonitriles. These compounds can be used for the preparation of phthalocyanines, potentially possessing a number of interesting properties from the practical viewpoint.

The aromatic nucleophilic substitution reaction between 4,5-dichlorophthalonitrile **4** and *N*-containing nucleophiles **5(a-o)** was conducted in DMFA for 0.5-19.5 h at 80-140 °C (depending on the nature of **5(a-o)**. Both potassium carbonate and triethylamine can be used as deprotonating agents. The choice of the base does not significantly affect the flow of the reaction.



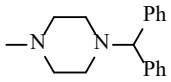
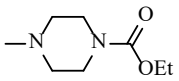
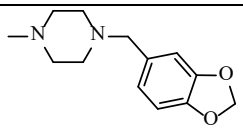
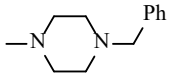
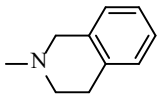
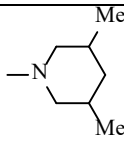
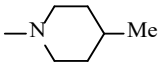
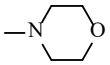
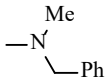
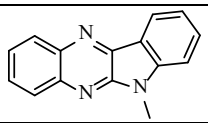
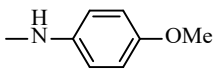
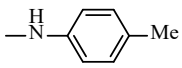
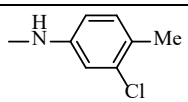
The target compounds **6(a-o)** were obtained with yields up to 57.5% (Table 1).

Indeed, the nature of the *N*-nucleophile appears to be the most important factor influencing the process. As might be expected, in the case of aromatic amines **5(m-o)**, the reaction could be conducted only under harsh conditions at 140 °C. The higher boiling tributylamine was used as a base; it favoured the continuous process under homogeneous conditions. Electron-donating substituents in the aromatic ring of anilines contribute to a faster reaction. At the same time, the introduction of electron acceptor groups, such as a halogen atom (in the case of **5o**), significantly increase the reaction time.

The structure and identity of all obtained compounds were confirmed by combined IR and NMR spectroscopy data. The structure of compounds **6(a-c, h)** was also proved by mass spectrometry.

Two singlets (δ^H 6.63-8.79 ppm) are located in the ^{1}H NMR spectra of the target compounds **6(a-o)** in the weak-field band, which correspond to the aromatic C(3,6)H protons of the phthalonitrile system. The **6(m-o)** 4-chloro-5-arylamino-phthalonitriles are characterised by a broadened singlet in the δ_H range of 8.66-8.80 ppm (Fig. 1).

Table 1. Time and conditions of the reaction of phthalonitrile production **6(a-o)**

No.	Coupling **6**	R	Time, h	Temperature, °C	Base	Yield, %
1	**a**		1.5	100	Et_3N	57.5
2	**b**		6	100	Et_3N	48
3	**c**		3	100	Et_3N	27
4	**d**		3	100	Et_3N	30
5	**e**		3	110	K_2CO_3	45
6	**f**		3	100	K_2CO_3	38
7	**g**		3	110	K_2CO_3	44
8	**h**		0.5	130	Et_3N	40
9	**i**		4	90	K_2CO_3	42
10	**j**		4.5	100	K_2CO_3	32
11	**k**		1.5	120	K_2CO_3	37
12	**l**		19.5	80	K_2CO_3	20
13	**m**		8.5	140	Bu_4N	16.5
14	**n**		11.5	140	Bu_4N	36.5
15	**o**		26	140	Bu_4N	20

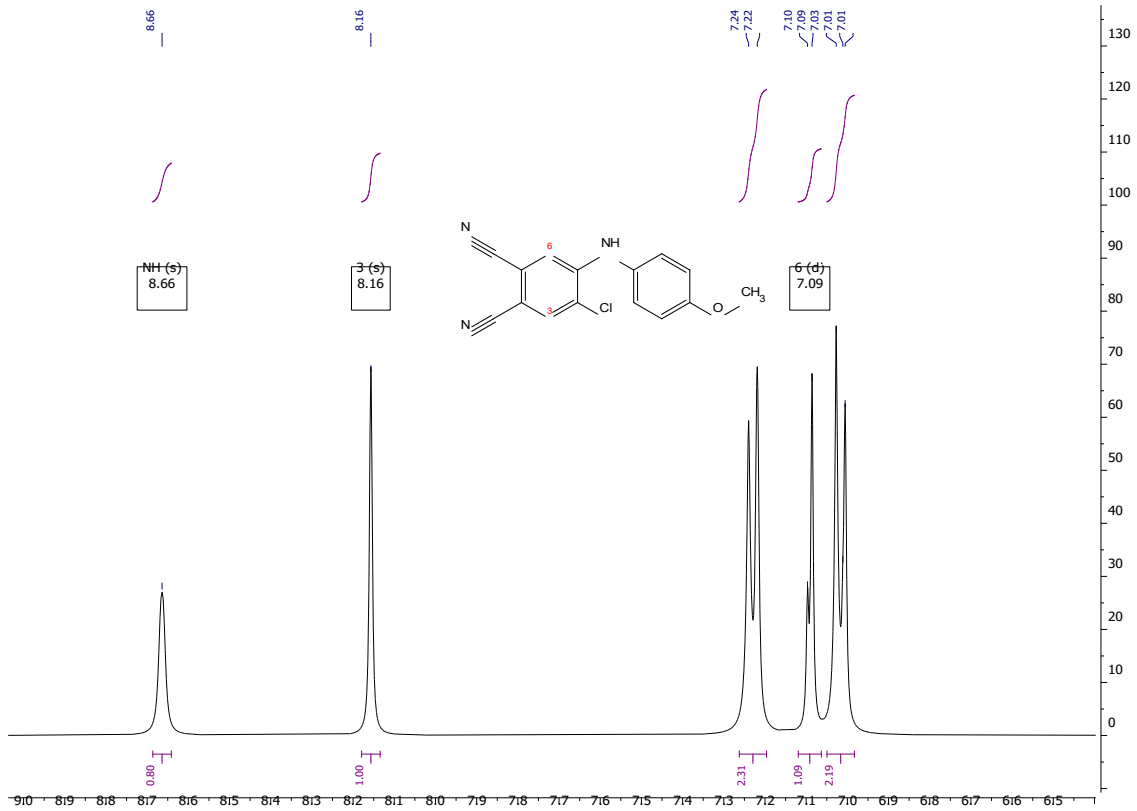


Fig. 1. Fragment of the ^{1}H NMR spectrum of compound **6m**

Both C(1,2)CN cyanogroup signals in the δ^{C} range of 115-116 ppm and C(4)Cl signal in the δ**C** range of 131.4-131.8 ppm can be observed in the $_{13}$C NMR spectra of 6(a-c) (Fig. 2).

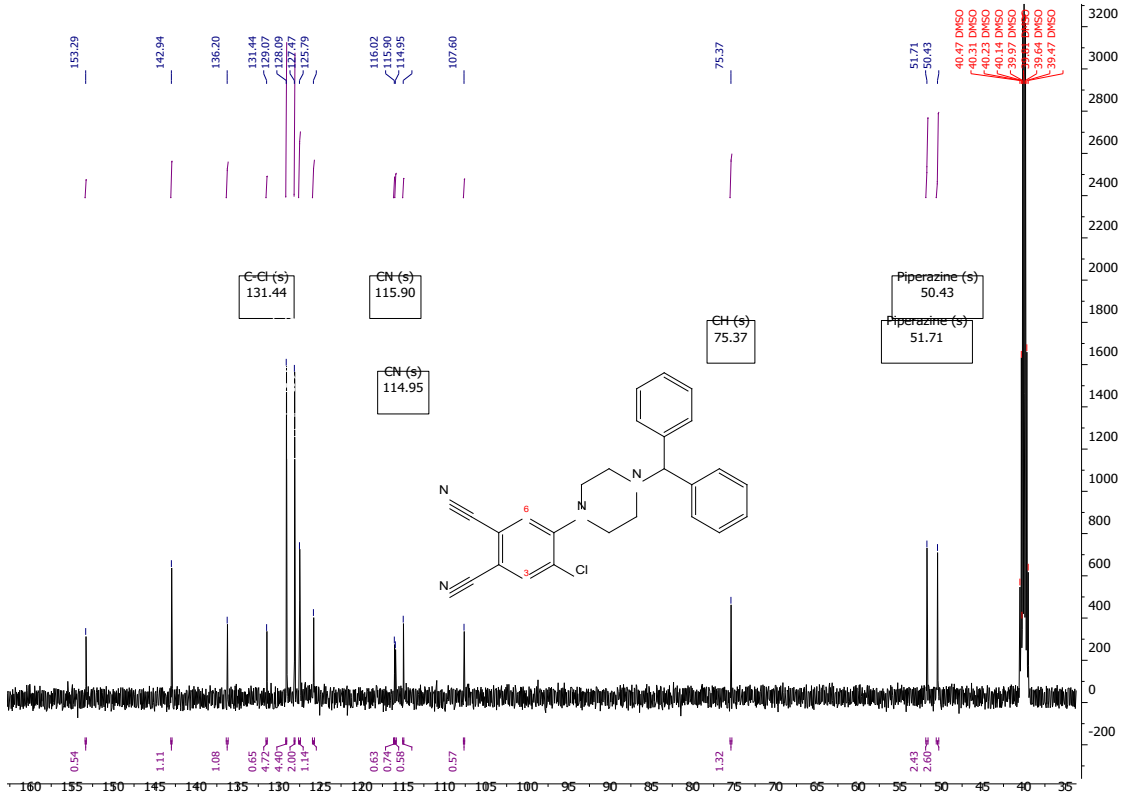


Fig. 2. Fragment of the ^{1}H NMR spectrum of compound **6a**

Both peaks corresponding to [M + 2]+, which intensity is approximately 30% of the $[M]^+$ peak, and peaks corresponding to $[M - {}^{35}Cl]^+$, $[M - {}^{37}Cl]^+$ can be observed in the mass spectra of compounds **6(a-c)**. This, in combination with NMR spectroscopy data, unambiguously indicates the presence of one chlorine atom in these compounds (Fig. 3).

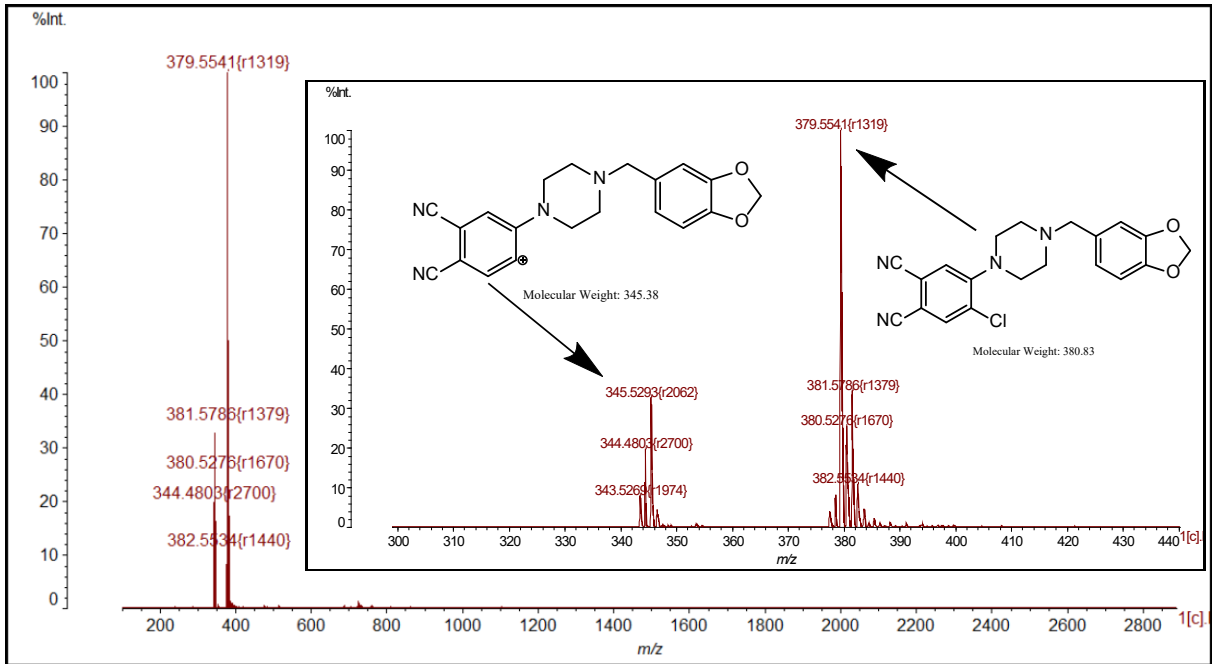


Fig. 3. Mass spectrum of compound **6c**

The reaction was monitored by thin layer chromatography on Silufol 254 UV plates. 4,5-Dichlorophthalic acid **1**, amines **5(a-o)**, DMFA, K_2CO_3, Et_3N, Bu_3N, $POCl_3$, AcOH, $(NH_4)_2CO_3$, 25% aqueous NH_3 solution, NH_4Cl are commercially available reagents. We recorded IR spectra in reflected light on a Spectrum Two PerkinElmer FT-IR spectrometer at 700-4000 cm^{-1}. We recorded the NMR spectra on a "Bruker DRX-400" (IOCh RAS, Moscow) for DMSO-d_6 solutions at 30 °C. As reference for the chemical shifts we used the signals of the residual solvent protons in ^1H NMR ($_\delta H$ = 2.50 ppm) and ^{13}C NMR (δ_C = 39.5 ppm). We used tetramethylsilane signal as a marker. Mass spectra were recorded on a Shimadzu Biotech AXIMA Confidence (Ivanovo State Chemical University, Ivanovo). Elemental analysis was conducted in the analytical laboratory of INEOS RAS, Moscow, on a PerkinElmer 2400. We determined the melting temperature using a Büchi M-560 melting point and boiling point apparatus.

4,5-dichlorophthalimide (2). We assembled a distillation apparatus. We poured 135 g (1.4 mol) of ammonium carbonate into a 500 cm^3 flask, then we added 300 cm^3 of acetic acid, after which we added 150 g (0.64 mol) of 4,5-dichlorophthalic acid **1**. We heated the reaction mixture on a sand bath to boiling point and distilled off 250 cm^3 of acetic acid. Then we poured the remaining reaction mixture into 200 cm^3 of water. We filtered the precipitate formed, washed with water, dried in air at room temperature. Yield is 130g (94%). IR spectrum, ν/cm^{-1}: 3224 (NH), 1711 (C=O), 1533 (NH). NMR spectrum ^1H (400 MHz, δ, ppm, *J*/Hz): 8.05 (s, 2 H, C(4,7)H).

4,5-dichlorophthalamide (3). We loaded 725 cm^3 of 25% aqueous ammonia solution and 41 g (0.77 mol) of ammonium chloride followed by 123 g (0.57 mol) of 4,5-dichlorophthalimide 2 into a 2000 cm^3 flask provided with a magnetic stirrer and air cooler. The reaction was conducted for 2 h at 30 °C. When the reaction was finished, we cooled the flask with the formed precipitate **3** down to 5 °C. The precipitate was filtered off, washed with water, dried in air at room temperature. Yield is 106,2 g (78%). IR spectrum, ν/cm^{-1}: 1688 (C = O), 1651 (NH_2), 1120 (C_{Ar}–Cl). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 7.88 (s, 2 H, NH), 7.70 (s, 2 H, C(3,6)H), 7.50 (s, 2 H, NH).

4,5-dichlorophthalonitrile (4). We loaded 106.2 g (0.46 mol) of 4,5-dichlorophthalamide 3 and 685 cm^3 of DMFA into a 1000 cm^3 flask fitted with a magnetic stirrer. Then we slowly added 85.6 cm^3 (0.92 mol) of $POCl_3$ while stirring the reaction mass vigorously. We cooled the flask with the reaction mixture on a water bath without allowing the reaction mixture to be heated above 35 °C. We cooled the reaction mixture to 5 °C and filtered it. We poured the filtrate into 2800 cm^3 of water. We filtered off the white precipitate and washed it with water. Yield is 87,9 g (98%), T. melt. = 184-186 °C. IR spectrum, ν/cm^{-1}: 3085 (C_{Ar}–H), 2238 (CN), 1052 (C_{Ar}–Cl). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 8.60 (s, 2 H, C(3,6)H).

4-Chloro-5-(R-amino)phthalonitriles 6(a-o) (general methodology). We loaded 5 mmol of **4**, 6 mmol of **5(a-o)** and 10 cm^3 of DMFA into a flask equipped with a stirrer, a reflux condenser and a thermometer. After dissolution of the reagents under vigorous stirring, we added fine anhydrous K_2CO_3 (10 mmol) or triethylamine (20 mmol) or tributylamine (20 mmol) to the reaction mixture. We conducted the reaction at 80-140 °C for 0.5-19.5 h depending on the nature of **5(a-o)** (the reaction progress was monitored by TLC). When the reaction was complete, we cooled the contents of the flask to room temperature and poured it into 60 cm^3 of cold water. We filtered the precipitate **6(a-o)**, washed with excess water, then with isopropanol (twice 5 cm^3 each). We dried the precipitate at 60 °C. We obtained the target products **6(a-o)** in 16.5-57.5 % yield after recrystallisation from a suitable solvent.

4-Chloro-5-(4-benzhydrylpiperazin-1-yl)phthalonitrile (6a). Yield is 1.19 g (57.5%), *T* melt. = 201–203 °C. IR spectrum, ν/cm^{-1}: 3065 (C_{Ar}–H), 2811 (CH), 2236 (CN). Mass-spectrum, m/z ($I_{rel.}$, %): 413.48 (33) $[M + 2]^+$, 411.47 (100) $[M]^+$, 376.47 (34) [M – ^{35}Cl]. NMR spectrum ^{1}H (500 MHz, δ, ppm, *J*/Hz): 2.47 (t, 4 H, C(3',5')H, *J* = 4.6), 3.22 (t, 4 H, C(2',6')H, *J* = 4.6), 4.38 (s, 1 H, Ph_2CH), 7.21 (t. d, 2 H, CH_{Ph}, *J* = 7.4, 1.4), 7.30-7.33 (m, 4 H, CH_{Ph}), 7.46 (d. t., 4 H, CH_{Ph}, *J* = 8.2, 1.4), 7.78 (s, 1 H, C(6)H), 8.24 (s, 1 H, C(3)H). NMR spectrum ^{13}C (126 MHz, δ, ppm): 50.43 (2C), 51.71 (2C), 75.37, 107.60, 114.95, 115.90, 116.02, 125.79, 127.47 (2C), 128.09 (4C), 129.07 (4C), 131.44, 136.20, 142.94 (2C), 153.29. Found, %: C, 73.00; H, 5.22; N, 13.71. $C_{25}H_{21}ClN_4$. Calculated, %: C, 72.72; H, 5.13; N, 13.57. *M* = 412.92.

4-Chloro-5-(4-(ethoxycarbonyl)piperazin-1-yl)phthalonitrile (6b). Yield is 0.77 g (48%), *T* melt. = 163–165 °C. IR spectrum, ν/cm^{-1}: 3043 (C_{Ar}–H), 2985 (CH), 2229 (CN), 1685 (C=O). Mass-spectrum, m/z ($I_{rel.}$, %): 321 (27) $[M + 2]^+$, 319 (100) $[M]^+$. NMR spectrum ^{1}H (500 MHz, δ, ppm, *J*/Hz): 1.21 (t, 3 H, $COOCH_2C\underline{H}_3$, *J* = 7.2), 3.16 (t, 4 H, C(2',6')H, *J* = 5.0), 3.54 (t, 4 H, C(3',5')H, *J* = 5.0), 4.07 (qw, 2 H, $COOC\underline{H}_2CH_3$, *J* = 7.2), 7.82 (s, 1 H, C(6)H), 8.29 (s, 1 H, C(3)H). NMR spectrum ^{13}C (126 MHz, δ, ppm): 15.01, 51.71 (4C), 61.44, 108.20,

114.97, 115.81, 115.97, 126.30, 131.83, 136.21, 153.27, 155.07. Found, %: C, 56.40; H, 4.62; N, 17.41. $C_{15}H_{15}ClN_4O_2$. Calculated, %: C, 56.52; H, 4.74; N, 17.58. *M* = 319.

4-Chloro-5-(4-(4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl)phthalonitrile (6c). Yield is 0.51 g (27%), *T* melt. = 240-242 °C. IR spectrum, ν/cm^{-1}: 3035 (C_{Ar}–H), 2887 (CH), 2226 (CN), 1042 (C_{Ar}–Cl). Mass spectrum, m/z ($I_{rel.}$, %): 381.57 (34) $[M + 2]^+$, 379.55 (100) $[M]^+$, 345.55 (33) $[M - {}^{35}Cl]$, 343.52 (9) $[M - {}^{37}Cl]$. NMR spectrum ^{1}H (500 MHz, δ, ppm, *J*/Hz): 3.04-3.09 (m, 8 H, C(2',3',5',6')H), 4.12 (s, 2 H, C$\underline{H}_2$Ph), 6.05 (s, 2 H, OCH_2O), 6.94 (d, 1 H, C(4'')H, *J* = 7.7), 7.01 (d, 1 H, C(5'')H, *J* = 7.7), 7.21 (s, 1 H, C(7'')H), 7.89 (s, 1 H, C(6)H), 8.29 (s, 1 H, C(3)H). NMR spectrum ^{13}C (126 MHz, δ, ppm): 51.09 (4C), 60.31, 101.75 (2C), 108.34, 108.68 (2C), 115.02, 115.78, 115.91, 126.15 (2C), 131.62, 136.22 (2C), 147.81, 150.10. Found, %: C, 63.20; H, 4.62; N, 14.49. $C_{20}H_{17}ClN_4O_2$. Calculated, %: C, 63.08; H, 4.50; N, 14.71. *M* = 380.

4-Chloro-5-(4-benzylpiperazin-1-yl)phthalonitrile (6d). Yield is 0.51 g (30%), *T* melt. = 135–140 °C. IR spectrum, ν/cm^{-1}: 3041 (C_{Ar}–H), 2941 (CH), 2229 (CN), 1061 (C_{Ar}–Cl). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 2.54-2.56 (m, 4 H, C(3',5')H), 3.19 (t, 4 H, C(2',6')H, *J* = 4.8), 3.56 (s, 2 H, C$\underline{H}_2$Ph), 7.27 (t, 1 H, C(4'')H, *J* = 5.6), 7.34 (d, 4 H, C(2'',3'',5'',6'')H, *J* = 5.6), 7.77 (s, 1 H, C(6)H), 8.24 (s, 1 H, C(3)H). Found, %: C, 67.52; H, 5.13; N, 16.61. $C_{19}H_{17}ClN_4$. Calculated, %: C, 67.75; H, 5.09; N, 16.63.

4-Chloro-5-(3,4-dihydroisoquinolin-2(1*H*)-yl))phthalonitrile (6e). Yield is 0.66 g (45%). IR spectrum, ν/cm^{-1}: 3061 (C_{Ar}–H), 2933 (CH), 2227 (CN), 1036 (C_{Ar}–Cl). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 2.99 (t, 2H, C(4')H, *J* = 5.8), 3.52 (t, 2 H, C(3')H, *J* = 5.8), 4.42 (s, 2 H, C(1')H), 7.16 (d.d, 1 H, C(7)H, *J* = 4.7, 2.4), 7.17–7.21 (m, 3H, C(5',6',8')H), 7.85 (s, 1 H, C(6)H), 8.28 (s, 1 H, C(3)H). Found, %: C, 69.46; H, 4.14; N, 14.37. $C_{17}H_{12}ClN_3$. Calculated, %: C, 69.51; H, 4.12; N, 14.30.

4-Chloro-5-(3,5-dimethylpiperidin-1-yl)phthalonitrile (6f). Yield 0.52 g (38%). IR spectrum, ν/cm^{-1}: 3051 (C_{Ar}–H), 2925 (CH), 2223 (CN), 1035 (C_{Ar}–Cl). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 0.72 (qw, 1H, C(3')H, *J* = 12.4), 0.88 (d, 6H, C(3',5')CH_3, *J* = 6.2), 1.70–1.84 (m, 3 H, C(5')H, C(4')H), 2.34 (t, 2H, C(2')H, *J* = 11.5), 3.45 (d.d, 2H, C(6')H, *J* = 11.5), 7.76 (s, 1 H, C(6)H, 8.22 (s, 1H, C(3)H). Found, %: C, 65.76; H, 5.84; N, 15.14. $C_{15}H_{16}ClN_3$. Calculated, %: C, 65.81; H, 5.89; N, 15.35.

4-Chloro-5-(4-methylpiperidin-1-yl)phthalonitrile (6g). Yield is 0.57 g (44%), *T* melt. = 156–160 °C. IR spectrum, ν/cm^{-1}: 3059 (C_{Ar}–H), 2982 (CH), 2217 (CN). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 0.95 (d, 3 H, C(4')CH_3, *J* = 6.5), 1.28 (t.t., 2 H, C(3')H, *J* = 12.5, *J* = 6.5), 1.51–1.59 (m, 1 H, C(4')H), 1.72 (d, 2 H, C(5')H, *J* = 12.5), 2.8 (t.d, 2 H, C(2')H, *J* = 12.5, 6.5), 3.47 (d, 2 H, C(6')H, *J* = 12.5), 7.75 (s, 1 H, C(6)H), 8.22 (s, 1 H, C(3)H). Found, %: C, 64.69; H, 5.47; N, 16.21. $C_{12}H_{10}ClN_3O$. Calculated, %: C, 64.74; H, 5.43; N, 16.18.

4-Chloro-5-(morpholin-4-yl)phthalonitrile (6h). Yield is 0.50 g (40%), *T* melt. = 171–176 °C. IR spectrum, ν/cm^{-1}: 3079 (C_{Ar}–H), 2991 (CH), 2218 (CN). Mass spectrum (EI, 70 eV), *m/z* (I_{rel} (%)): 249 (9) $[M + 2]^+$, 247 (27) $[M]^+$, 212 (31) $[M - {}^{35}Cl]^+$, 189 (100) $[M - {}^{35}Cl - CN + 2]^+$. NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 3.20 (d.d, 4 H, C(3',5')H, *J* = 4.2, *J* = 2.2), 3.77 (d.d, 4 H, C(2',6')H, *J* = 4.2, *J* = 2.2), 7.76 (s, 1 H, C(6)H), 8.11 (s, 1 H, C(3)H). NMR spectrum ^{13}C (126 MHz, δ, ppm): 50.39 (2C), 65.91 (2C), 106.75, 114.34, 115.22, 115.48, 125.91, 131.02,

135.82, 152.60. Found, %: C, 59.01; H, 4.13; N, 16.29. $C_{12}H_{10}ClN_3O$. Calculated, %: C, 58.19; H, 4.07; N, 16.97. *M* = 247. The characteristics obtained are consistent with those described in the literature [9].

4-Chloro-5-(azepan-1-yl)phthalonitrile (6i). Yield is 0.55 g (42%), *T*melt. = 93.2–94.5 °C. IR spectrum, ν/cm^{-1}: 3059 (C_{Ar}–H), 2935 (CH), 2216 (CN), 1032 (C_{Ar}–Cl). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 1.56–1.59 (m., 4 H, C(4',5')H), 1.80 (d., 4 H, C(3',6')H, *J* = 6.2), 3.50 (t, 4 H, C(2',7')H, *J* = 6.2), 7.63 (s, 1 H, C(6)H), 8.09 (s, 1 H, C(3)H). Found, %: C, 64.83; H, 4.89; N, 16.29. $C_{14}H_{14}ClN_3$. Calculated, %: C, 64.74; H, 5.43; N, 16.18.

4-Chloro-5-(dimethylamino)phthalonitrile (6j). Yield is 0.33 g (32%). IR spectrum, ν/cm^{-1}: 3085 (C_{Ar}–H), 2946 (CH), 2864, 2814 ($N(CH_3)_2$), 2220 (CN), 1583 (C = C), 1061 (C_{Ar}–Cl). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 2.94 (s, 6H, $N(CH_3)_2$, 7.68 (s, 1 H, C(6)H), 8.17 (s, 1 H, C(3)H). NMR spectrum ^{13}C (100 MHz, δ, ppm.): 42.80 (2C), 106.22, 114.27, 115.34, 115.69, 122.90, 130.62, 135.85, 153.73. Found, %: C, 58.44; H, 3.89; N, 19.92. $C_{10}H_8ClN_3$. Calculated, %: C, 58.41; H, 3.92; N, 20.43. The characteristics obtained are consistent with those described in the literature [7].

4-Chloro-5-(benzyl(methyl)amino)phthalonitrile (6k). Yield 0.52 g (37%). IR spectrum, ν/cm^{-1}: 3070 (C_{Ar}–H), 2937 (CH), 2228 (CN). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 2.82 (s, 3H, NCH_3), 4.49 (s, 2H, NCH_2), 7.26-7.32 (m, 3H, CH_{Ph}), 7.35-7.38 (m, 2H, CH_{Ph}), 7.77 (s, 1H, C(6)H), 8.24 (s, 1H, C(3)H). Found, %: C, 68.16; H, 4.24; N, 14.97. $C_{16}H_{12}ClN_3$. Calculated, %: C, 68.21; H, 4.29; N, 14.91.

4-Chloro-5-(6H-indolo[2,3-b]quinoxalin-6-yl)phthalonitrile (3l). Yield is 0.38 g (20%), *T* melt. = 257–259 °C. IR spectrum, ν/cm^{-1}: 2238 (CN), 1051 (C_{Ar}–Cl). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 7.40 (d, 1 H, C(8)H, *J* = 8.0), 7.55 (t, 1 H, C(9)H, *J* = 8.0), 7.77 (br.d., 1 H, C(7)H, *J* = 8.0), 7.83 (m, 2 H, C(2,3)H), 8.03 (d, 1 H, C(1)H, *J* = 7.0), 8.33 (s, 1 H, C(6')H, *J* = 7.0), 8.49 (d, 1 H, C(4)H, *J* = 7.0), 8.79 (br.s., 1 H, C(3')H), 8.85 (br.s., 1 H, C(10)H). Found (%): C, 69.87; H, 2.81; N, 19.15. $C_{22}H_{10}ClN_5$. Calculated (%): C, 69.57; H, 2.65; N, 18.44.

4-Chloro-5-((4-methoxyphenyl)amino)phthalonitrile (6m). Yield is 0.23 g (16.5%), *T*melt. = 205–207 °C. IR spectrum, ν/cm^{-1}: 3335 (NH), 3079 (C_{Ar}–H), 2969 (CH), 2227 (CN). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 3.79 (s, 3 H, C(4)OCH_3), 7.02 (d, 2 H, C(3',5')H, *J* = 8.5), 7.09 (d, 1 H, C(6)H, *J* = 4.4), 7.23 (d, 2 H, C(2',6')H, *J* = 8.5), 8.16 (s, 1 H, C(3)H), 8.66 (br.s. 1H, NH). Found, %: C, 63.53; H, 3.47; N, 14.74. $C_{15}H_{10}ClN_3O$. Calculated, %: C, 63.50; H, 3.55; N, 14.81.

4-Chloro-5-[(4-methylphenyl)amino]phthalonitrile (6n). Yield is 0.49 g (36.5%), *T*melt. = 214,5–216 °C. IR spectrum, ν/cm^{-1}: 3339 (NH), 3072 (C_{Ar}–H), 2962 (CH), 2230 (CN). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 2.32 (br.s., 3H, C(4')CH_3), 7.21 (d, 5H, C(6)H, C(2',3',5',6')H, *J* = 16.1), 8.19 (br.s., 1H, C(3)H), 8.75 (br.s., NH). Found, %: C, 67.23; H, 3.62; N, 15.66. $C_{15}H_{10}ClN_3$. Calculated, %: C, 67.30; H, 3.77; N, 15.70.

4-Chloro-5-[(3-chloro-4-methylphenyl)amino]phthalonitrile (6o). Yield is 0.3 g (20%). IR spectrum, ν/cm^{-1}: 3328 (NH), 3067 (C_{Ar}–H), 2959 (CH), 2225 (CN). NMR spectrum ^{1}H (400 MHz, δ, ppm, *J*/Hz): 2.32 (s, 3H, C(4')CH_3), 7.21 (s, 1H, C(2')H), 7.37 (br.s., 2H, C(5',6')H), 7.43 (s, 1H, C(6)H), 8.23 (s, 1H, C(3)H), 8.80 (br.s., 1H, NH). Found, %: C, 59.52; H, 3.04; N, 13.84. $C_{15}H_9Cl_2N_3$. Calculated, %: C, 59.62; H, 3.00; N, 13.91.

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