Preparation and Herbicidal Properties of Substituted Quinoline-2-carboxanilides

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Abstract: In this study a series of twenty-five substituted quinoline-2-carboxanilides were prepared. The procedures for synthesis of the compounds are presented. The compounds were tested for their activity related to inhibition of photosynthetic electron transport (PET) in spinach (*Spinacia oleracea* L.) chloroplasts. For all the compounds the structure-activity relationships (SAR) are discussed.

Keywords: quinoline-2-carboxanilides; PET inhibition; spinach chloroplasts; structure-activity relationships.

INTRODUCTION

A quinoline scaffold possesses unique physico-chemical properties and therefore it is present in many classes of biologically-active compounds [1-5]. A number of quinoline related compounds expressed antifungal, antibacterial and antituberculotic/antimycobacterial activity [4-13]. Some quinoline analogues showed also antineoplastic and antiviral activity [2,5,14-16]. In addition, according to the results reported recently, some new hydroxyquinoline derivatives also showed noteworthy herbicidal activities [9,11-14,17].
Both pharmaceuticals and pesticides are designed to target particular biological functions, and in some cases these functions overlap in their molecular target sites, or they target similar

processes or molecules. Modern herbicides express low toxicity against mammals. One of the reasons of such safety is the fact that mammals do not mostly have target sites of action. At present approximately 20 mechanisms of action of herbicides are known. It was determined that inhibitors of protoporphyrinogen oxidase (PROTOX), 4-hydroxyphenylpyruvate dioxygenase (HPPD) and glutamine synthetase (GS) inhibit these enzymes both in plants and mammals. However, the consequences of inhibition of the overlapping target site can be completely different for plants and animals. Therefore a compound that has lethal action on plants may be beneficial for mammals. Such chemical compounds are characterized by low toxicity on mammals as a result of quick metabolism and/or elimination of herbicide from the mammal system. Taking into consideration that mammals may also have molecular sites of action of herbicides, most pharmaceutical companies until recently had pesticide divisions, sometimes with a different name. All compounds generated by either division of the company were evaluated for both pesticide and pharmaceutical uses. Sometimes lead pesticides became pharmaceuticals and vice versa. However, little of this type of information was published and must usually be deduced from patent literature. One of the exceptions is fluconazole, a fungicide product discovered by the pharmaceutical sector that is now used as a pharmaceutical and patented as a crop production chemical [18-20].

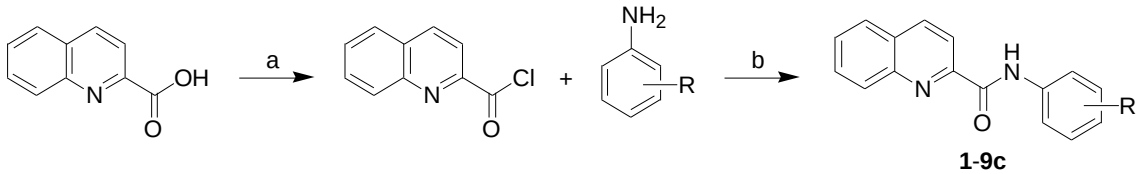
Over 50% of commercially available herbicides act by reversible binding to photosystem II (PS II), a membrane-protein complex in the thylakoid membranes, which catalyses the oxidation of water and the reduction of plastoquinone [21], and thereby inhibit photosynthesis [22-24]. Some organic compounds, possessing an amide (-NHCO-) group, e.g. substituted benzanilides [25-28], pyridine- and/or pyrazine-2-carboxylic acids [29,30-33] or a wide variety of compounds containing the quinoline system [34-36] were found to interact with tyrosine radicals Tyr_Z and Tyr_D which are situated in D_1 and D_2 proteins on the donor side of PS II. Due to this interaction, interruption of the photosynthetic electron transport occurred.

In the context of the previously-described azanaphtalenes [9,11-14,17] or various amides [26-28,30-32], new simple modifications of quinoline that can trigger interesting biological activity were investigated. The compounds were tested for their photosynthesis-inhibiting activity – the inhibition of photosynthetic electron transport in spinach chloroplasts (*Spinacia oleracea* L.). Relationships between the structure and the inhibitory activity related to inhibition of photosynthetic electron transport (PET) in spinach chloroplasts of the new compounds are discussed.

RESULTS AND DISCUSSION

All the studied compounds were prepared according to Scheme 1. Condensation of the chloride of quinoline-2-carboxylic acid with commercially available ring-substituted anilines yielded a series of twenty-five substituted amides **1**-**9c**.

Scheme 1. Synthesis of quinoline-2-carboxanilides **1**-**9c**: (a) $(COCl)_2$, (b) TEA, toluene.



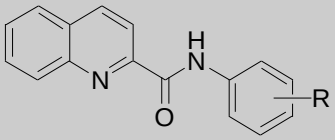
1-**9c**

R = H, OH, OCH_3, CH_3, F, Cl, Br, CF_3, NO_2

Hydrophobicities (log *P*/Clog *P*) of compounds **1**-**9c** were calculated using two commercially available programs (ChemDraw Ultra 10.0 and ACD/LogP). The program ChemDraw did not resolve the varying lipophilicity values of individual positional isomers; thus the same

log *P*/Clog *P* data were calculated for derivatives **a-c**. The results are shown in Table 1. Compounds show a wide range of lipophilicity with log *P* (ACD/LogP) from 2.15 (compound **2c**, 4-OH) to 4.25 (compound **8b**, 3-CF_3). Individual substituents in the anilide part of the discussed compounds also possess a wide range (from -0.39 to 1.72) of electronic properties expressed as Hammett's σ parameters [37,38].

Table 1. Calculated lipophilicities (log *P*/Clog *P*), electronic Hammett's σ parameters and IC_{50} [μmol/L] values related to PET inhibition in spinach chloroplasts of compounds **1-9c** in comparison with 3-(3,4-dichlorophenyl)-1,1-dimethylurea (DCMU) standard.



Comp.	R	log *P*/Clog *P* ChemOffice	log *P* ACD/LogP	PET inhibition IC_{50} [μmol/L]	σ [37]
1	H	3.35 / 3.6310	2.90 ± 0.34	85.1	0
2a	2-OH	2.96 / 3.1940	2.54 ± 0.36	16.3	-0.09
2b	3-OH	2.96 / 2.9640	2.55 ± 0.36	[a]	0.12
2c	4-OH	2.96 / 2.9640	2.15 ± 0.35	[a]	-0.37
3a	2-OCH_3	3.22 / 3.0147	2.80 ± 0.36	[a]	-0.39 [38]
3b	3-OCH_3	3.22 / 3.6047	3.06 ± 0.36	[a]	0.12
3c	4-OCH_3	3.22 / 3.6047	2.85 ± 0.36	[a]	-0.27
4a	2-CH_3	3.83 / 3.4800	3.36 ± 0.34	142.9	0.10
4b	3-CH_3	3.83 / 4.1300	3.36 ± 0.34	100.6	-0.07
4c	4-CH_3	3.83 / 4.1300	3.36 ± 0.34	[b]	-0.17
5a	2-F	3.50 / 3.2642	2.86 ± 0.44	98.1	0.47
5b	3-F	3.50 / 3.8642	3.38 ± 0.44	86.9	0.34
5c	4-F	3.50 / 3.8642	3.34 ± 0.44	75.3	0.06
6a	2-Cl	3.91 / 3.5842	3.41 ± 0.36	56.3	0.67
6b	3-Cl	3.91 / 4.4342	3.93 ± 0.37	91.9	0.37
6c	4-Cl	3.91 / 4.4342	3.89 ± 0.36	147.6	0.23
7a	2-Br	4.18 / 3.7042	3.58 ± 0.44	92.2	0.71
7b	3-Br	4.18 / 4.5842	4.10 ± 0.44	409.0	0.39
7c	4-Br	4.18 / 4.5842	4.06 ± 0.44	307.9	0.23
8a	2-CF_3	4.27 / 3.2218	4.09 ± 0.42	109.4	–
8b	3-CF_3	4.27 / 4.6718	4.25 ± 0.42	329.5	0.43
8c	4-CF_3	4.27 / 4.6718	3.91 ± 0.41	[a]	0.74
9a	2-NO_2	3.27 / 3.1072	3.15 ± 0.38	[b]	1.72
9b	3-NO_2	3.27 / 3.5672	3.28 ± 0.38	[b]	0.71
9c	4-NO_2	3.27 / 3.5672	3.36 ± 0.38	[b]	1.26
DCMU	–	–	–	1.9	–

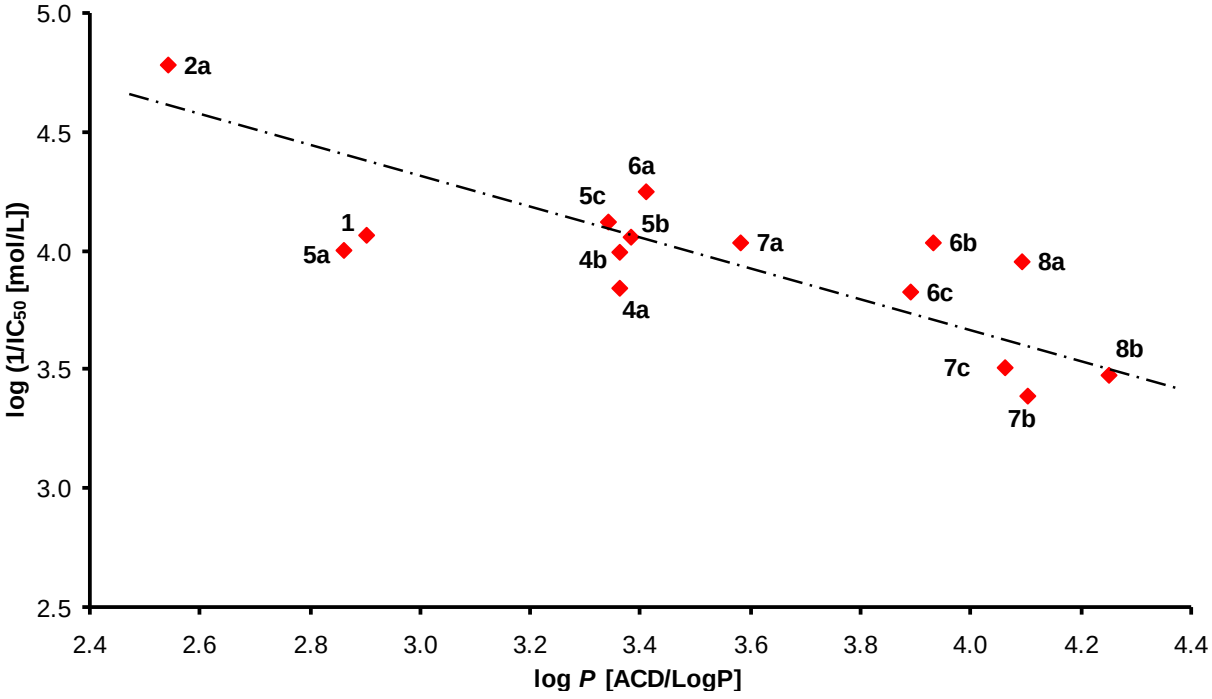
[a]precipitation during the experiment, [b]interaction with 2,6-dichlorophenol-indophenol (DCIPP)

The activity of the evaluated quinoline derivatives related to inhibition of photosynthetic electron transport (PET) in spinach (*Spinacia oleracea* L.) chloroplasts was moderate or low relative to the standard, see Table 1. The PET-inhibiting activity was expressed by negative logarithm of IC_{50} value (compound concentration in mol/L causing 50% inhibition of PET).

Compound **2a** (2-OH) expressed the highest PET-inhibiting activity (IC_{50} = 16.3 μmol/L), and compound **7b** (3-Br) expressed the lowest PET-inhibiting activity (IC_{50} = 409.0 μmol/L). Despite the relatively low inhibitory activity of the studied compounds, correlations between log ($1/IC_{50}$) and the lipophilicity or electronic properties of the individual anilide substituents in compounds **1**-**9c** were performed, see Fig. 1 and Fig. 2. Based on the obtained results it is not possible to decide, whether some of *ortho*-, *meta*- or *para*-positions are preferred from the point of view of PET-inhibiting activity. Nevertheless, according to Fig. 1 it can be stated that the dependence of PET-inhibiting activity on the lipophilicity expressed as log *P* (ACD/LogP) decreases with increasing lipophilicity and the lipophilicity of the compounds was decisive for PET inhibition:

$$\log (1/IC_{50}) = 5.952(\pm 0.406) - 0.559(\pm 0.113) \log P$$
$$r = 0.819,\ s = 0.211,\ F = 24.50,\ n = 14 \qquad (1)$$

Figure 1. Relationships between PET-inhibiting activity log ($1/IC_{50}$) [mol/L] in spinach chloroplasts and lipophilicity (log *P*) of studied compounds **1**-**9c**.

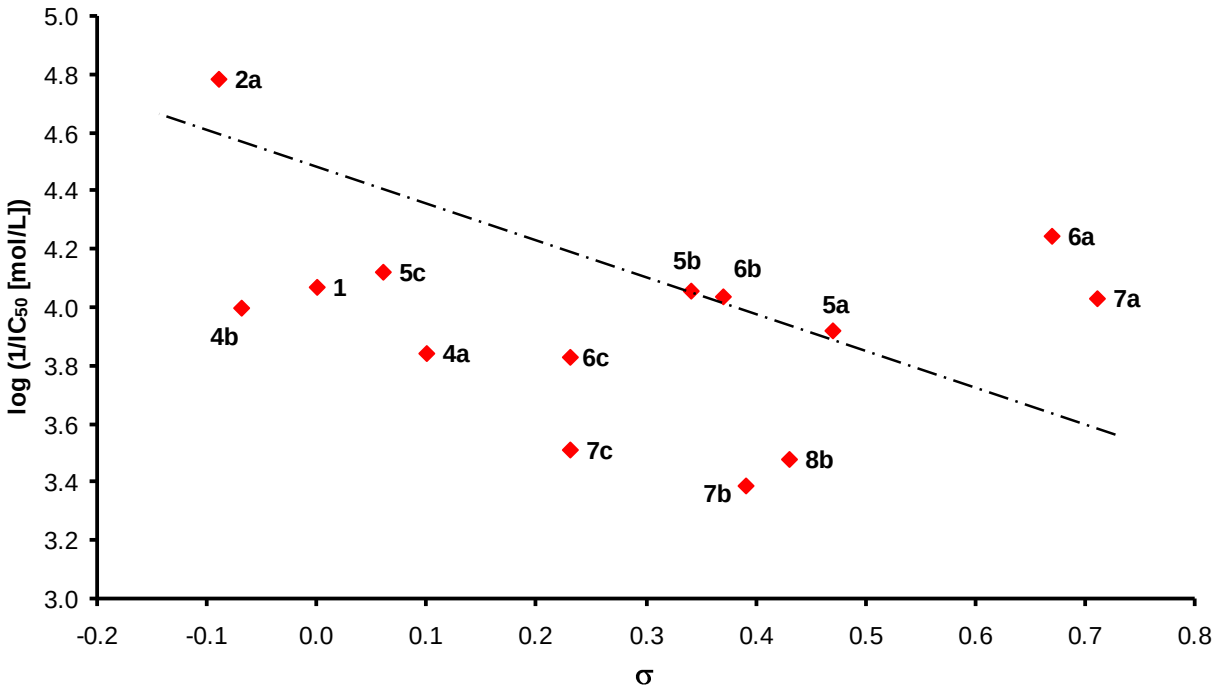


On the other hand, the biological activity was also affected by electronic σ properties of these anilide substituents, see Fig. 2. In general, the dependence of log ($1/IC_{50}$) on σ shows a similar trend as in case of lipophilicity, the activity decreases with increasing σ value. However, the importance of the lipophilicity of the anilide substituent was unambiguously much more significant for the inhibitory activity (IC_{50} [mol/L]) of the studied compounds than the electronic properties of the substituent, because introduction of σ into correlation equation (1) did not improve the results of statistical analysis:

$$\log (1/IC_{50}) = 5.938(\pm 0.424) - 0.549(\pm 0.121) \log P - 0.081(0.246)\sigma$$
$$r = 0.821,\ s = 0.219,\ F = 11.4,\ n = 14 \qquad (2)$$

The most active compound from the series was **2a** (R = 2-OH). The result indicates that PET inhibition can be associated with additional interaction of the phenol moiety with photosynthetic proteins. This compound can be understood as a bioisoster of 2-[(2-hydroxyphenylimino)methyl]quinolin-8-ol that expressed high herbicide effect [14].

Figure 2. Relationships between PET-inhibiting activity log ($1/IC_{50}$) [mol/L] in spinach chloroplasts and anilide substituent electronic Hammett's σ parameters of studied compounds **1**-**9c**.



EXPERIMENTAL

General

All reagents were purchased from Aldrich. Kieselgel 60, 0.040-0.063 mm (Merck, Darmstadt, Germany) was used for column chromatography. TLC experiments were performed on alumina-backed silica gel 40 F254 plates (Merck, Darmstadt, Germany). The plates were illuminated under UV (254 nm) and evaluated in iodine vapour. The melting points were determined on Boetius PHMK 05 (VEB Kombinat Nagema, Radebeul, Germany) and are uncorrected. Infrared (IR) spectra were recorded on a Smart MIRacle™ ATR ZnSe for Nicolet™ Impact 410 FT-IR Spectrometer (Thermo Scientific, USA). The spectra were obtained by accumulation of 256 scans with 2 cm^{-1} resolution in the region of 4000-600 cm^{-1}. All ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 MHz FT-NMR spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C, Bruker Comp., Karlsruhe, Germany). Chemicals shifts are reported in ppm (δ) using internal $Si(CH_3)_4$ as the reference with diffuse, easily exchangeable signals being omitted. Mass spectra were measured using a LTQ Orbitrap Hybrid Mass Spectrometer (Thermo Electron Corporation, USA) with direct injection into an APCI source (400 °C) in the positive mode.

Synthesis

General procedure for synthesis of carboxamide derivatives (**1**-**9c**): 2-Quinaldic acid (1 g, 5.8 mmol) was suspended in dry toluene (15 mL) at room temperature and oxalyl chloride (1 mL, 1.61 g, 12.7 mmol, 2.2 eq.) was added dropwise. The reaction mixture was stirred for 30 min at the same temperature and then DMF (2 drops) was added. The mixture was stirred for 24 h and then evaporated to dryness. The residue was washed with petroleum ether and used directly in the next step.

Into the solution of 2-quinaldic acid chloride in dry toluene (15 ml) triethylamine (4.5 mL, 2.92 g, 32.5 mmol) and corresponding substituted aniline (5.8 mmol) were added dropwise.

The mixture was stirred at room temperature for 24 h and then the solvent was removed under reduced pressure. The residue was extracted with $CHCl_3$. Combined organic layers were washed with water and saturated aqueous solution of $NaHCO_3$ and dried over anhydrous $MgSO_4$. The solvent was evaporated to dryness under reduced pressure. The crude product was recrystallized from isopropanol or EtOAc. The studied compounds **1-9c** are presented in Table 1.

N-phenylquinoline-2-carboxamide (**1**). Yield 32%; Mp. 139-140 °C (Mp. 139.5-140 °C [39]); ^{1}H-NMR (DMSO-d_6), δ: 10.75 (bs, 1H), 8.62 (d, *J*=8.3 Hz, 1H), 8.19-8.33 (m, 2H), 8.11 (d, *J*=7.5 Hz, 1H), 7.86-8.01 (m, 3H), 7.75 (ddd, *J*=8.1 Hz, *J*=7.0 Hz, *J*=1.3 Hz, 1H), 7.33-7.47 (m, 2H), 7.09-7.21 (m, 1H); ^{13}C-NMR (DMSO-d_6), δ: 162.71, 150.08, 145.88, 138.31, 138.22, 130.68, 129.35, 128.94, 128.78, 128.37, 128.15, 124.05, 120.29, 118.77; HR-MS: for $C_{16}H_{13}N_2O$ $[M+H]^+$ calculated 249.1022 m/z, found 249.1015 m/z.

N-(2-hydroxyphenyl)quinoline-2-carboxamide (**2a**) [40]. Yield 27%; Mp. 219-220 °C; ^{1}H-NMR (DMSO-d_6), δ: 10.67 (bs, 1H), 10.44 (bs, 1H), 8.63 (d, *J*=8.5 Hz, 1H), 8.44 (d, *J*=7.8 Hz, 1H), 8.29 (d, *J*=8.3 Hz, 1H), 8.15 (d, *J*=8.3 Hz, 1H), 8.10 (d, *J*=8.0 Hz, 1H), 7.88 (t, *J*=7.3 Hz, 1H), 7.73 (t, *J*=7.2 Hz, 1H), 7.00 (m, 2H), 6.89 (m, 1H); ^{13}C-NMR (DMSO-d_6), δ: 161.26, 149.65, 146.77, 145.74, 138.59, 130.91, 129.29, 129.08, 128.46, 128.22, 126.20, 124.29, 119.37, 119.26, 118.42, 114.84; HR-MS: for $C_{16}H_{13}N_2O_2$ $[M+H]^+$ calculated 265.0977 m/z, found 265.0983 m/z.

N-(3-hydroxyphenyl)quinoline-2-carboxamide (**2b**). Yield 52%; Mp. 154-155 °C; IR (Zn/Se ATR, cm^{-1}): 3338*w*, 2973*w*, 1760*m*, 1680*m*, 1605*w*, 1530*s*, 1504*s*, 1462*w*, 1425*m*, 1263*m*, 1235*m*, 1216*m*, 1171*w*, 1145*s*, 1096*m*, 1054*w*, 1002*w*, 964*w*, 908*m*, 879*w*, 841*m*, 773*s*, 754*s*, 685*m*, 665*m*; ^{1}H-NMR (DMSO-d_6), δ: 10.98 (bs, 1H), 8.62 (d, *J*=8.7 Hz, 1H), 8.20-8.36 (m, 3H), 8.06-8.18 (m, 1H), 7.87-7.97 (m, 2H), 7.71-7.83 (m, 2H), 7.54 (t, *J*=8.2 Hz, 1H), 7.18 (dd, *J*=8.0 Hz, *J*=1.8 Hz, 1H); ^{13}C-NMR (DMSO-d_6), δ: 163.05, 150.91, 149.86, 147.01, 145.90, 139.63, 138.29, 130.94, 129.99, 129.19, 128.49, 128.16, 121.35, 118.83, 117.99, 113.65; HR-MS: for $C_{16}H_{13}N_2O_2$ $[M+H]^+$ calculated 265.0977 m/z, found 265.0985 m/z.

N-(4-hydroxyphenyl)quinoline-2-carboxamide (**2c**) [41]. Yield 48%; Mp. 230-231 °C; ^{1}H-NMR (DMSO-d_6), δ: 10.34 (bs, 1H), 8.28-8.48 (m, 3H), 8.21 (d, *J*=8.5 Hz, 1H), 7.88-8.04 (m, 3H), 7.77-7.87 (m, 1H), 7.69 (m, 1H), 7.39 (d, *J*=9.0 Hz, 2H); ^{13}C-NMR (DMSO-d_6), δ: 162.11, 149.40, 147.23, 146.23, 137.94, 135.82, 130.84, 129.62, 129.45, 128.95, 127.60, 122.38, 120.66, 118.73; HR-MS: for $C_{16}H_{13}N_2O_2$ $[M+H]^+$ calculated 265.0977 m/z, found 265.0971 m/z.

N-(2-methoxyphenyl)quinoline-2-carboxamide (**3a**) [42]. Yield 37%; Mp. 111-112 °C; IR (Zn/Se ATR, cm^{-1}): 3382*w*, 1676*s*, 1596*m*, 1532*s*, 1485*w*, 1454*m*, 1426*m*, 1334*w*, 1288*w*, 1253*m*, 1138*m*, 1129*m*, 1093*w*, 1020*s*, 951*w*, 908*m*, 873*w*, 840*m*, 820*w*, 770*s*, 732*s*; ^{1}H-NMR (DMSO-d_6), δ: 10.68 (bs, 1H), 8.59 (d, *J*=8.5 Hz, 1H), 8.49 (d, *J*=7.8 Hz, 1H), 8.25 (d, *J*=8.5 Hz, 1H), 8.15 (d, *J*=8.5 Hz, 1H), 8.07 (d, *J*=8.3 Hz, 1H), 7.87 (t, *J*=7.3 Hz, 1H), 7.67-7.75 (m, 1H), 7.11 (d, *J*=4.0 Hz, 2H), 7.01 (dt, *J*=8.2 Hz, *J*=4.2 Hz, 1H), 3.98 (s, 3H); ^{13}C-NMR (DMSO-d_6), δ: 161.25, 149.34, 148.51, 145.62, 138.55, 130.82, 129.30, 129.06, 128.44, 128.14, 126.87, 124.25, 120.68, 118.84, 118.27, 110.91, 56.05; HR-MS: for $C_{17}H_{15}N_2O_2$ $[M+H]^+$ calculated 279.1134 m/z, found 279.1148 m/z.

N-(3-methoxyphenyl)quinoline-2-carboxamide (**3b**). Yield 47%; Mp. 117-118 °C; IR (Zn/Se ATR, cm^{-1}): 3352*w*, 1687*m*, 1589*m*, 1524*m*, 1503*m*, 1456*m*, 1425 *m*, 1334*w*, 1284*m*, 1203 *m*, 1157*m*, 1128*m*, 1049*s*, 906*w*, 876*m*, 854 *m*, 823 *w*, 798*w*, 762*s*, 740*s*, 685*m*; ^{1}H-NMR (DMSO-d_6), δ: 10.73 (bs, 1H), 8.58 (d, *J*=8.5 Hz, 1H), 8.19-8.32 (m, 2H), 8.07 (d, *J*=8.0 Hz, 1H), 7.82-7.96 (m, 1H), 7.65-7.79 (m, 2H), 7.59 (dd, *J*=8.0 Hz, *J*=1.0 Hz, 1H), 7.29 (t, *J*=8.2 Hz, 1H), 6.72 (dd, *J*=8.3 Hz, *J*=2.01 Hz, 1H), 3.78 (s, 3H); ^{13}C-NMR (DMSO-d_6), δ:

162.70, 159.61, 149.99, 145.88, 139.53, 138.23, 130.67, 129.61, 129.37, 128.97, 128.37, 128.16, 118.75, 112.47, 109.68, 105.91, 55.09; HR-MS: for $C_{17}H_{15}N_2O_2$ $[M+H]^+$ calculated 279.1134 m/z, found 279.1129 m/z.

N-(4-methoxyphenyl)quinoline-2-carboxamide (**3c**) [43]. Yield 53%; Mp. 130-131 °C; ^{1}H-NMR (DMSO-d_6), δ: 10.65 (bs, 1H), 8.57 (d, *J*=8.5 Hz, 1H), 8.24 (d, *J*=8.5 Hz, 2H), 8.07 (d, *J*=7.8 Hz, 1H), 7.82-7.95 (m, 3H), 7.63-7.78 (m, 1H), 6.97 (d, *J*=9.0 Hz, 2H), 3.75 (s, 3H); ^{13}C-NMR (DMSO-d_6), δ: 162.28, 155.80, 150.25, 145.90, 138.09, 131.47, 130.59, 129.32, 128.87, 128.22, 128.11, 121.85, 118.73, 113.87, 55.17; HR-MS: for $C_{17}H_{15}N_2O_2$ $[M+H]^+$ calculated 279.1134 m/z, found 279.1145 m/z.

N-(2-methylphenyl)quinoline-2-carboxamide (**4a**). Yield 40%; Mp. 100-101 °C; IR (Zn/Se ATR, cm^{-1}): 3334*w*, 1686*s*, 1587*s*, 1528*s*, 1498*M*, 1454*s*, 1427*s*, 1422 *m*, 1373*w*, 1305*m*, 1249*w*, 1201*w*, 1132*m*, 1091*w*, 1040*w*, 1013*w*, 981*w*, 954*m*, 932*w*, 907*m*, 872*m*, 842*s*, 793*w*, 765*s*, 750*s*, 731*s*, 681*s*; ^{1}H-NMR (DMSO-d_6), δ: 10.45 (bs, 1H), 8.60 (d, *J*=8.5 Hz, 1H), 8.24 (d, *J*=8.5 Hz, 1H), 8.17 (d, *J*=8.3 Hz, 1H), 8.08 (d, *J*=8.0 Hz, 1H), 7.95 (d, *J*=7.8 Hz, 1H), 7.83-7.91 (m, 1H), 7.69-7.77 (m, 1H), 7.22-7.31 (m, 2H), 7.08-7.16 (m, 1H), 2.37 (s, 3H); ^{13}C-NMR (DMSO-d_6), δ: 161.92, 149.67, 145.74, 138.35, 135.97, 130.72, 130.42, 130.01, 129.38, 129.01, 128.38, 128.11, 126.40, 124.96, 122.65, 118.49, 17.49; HR-MS: for $C_{17}H_{15}N_2O$ $[M+H]^+$ calculated 263.1184 m/z, found 263.1182 m/z.

N-(3-methylphenyl)quinoline-2-carboxamide (**4b**). Yield 43%; Mp. 82-83 °C; IR (Zn/Se ATR, cm^{-1}): 3355*w*, 1685*m*, 1592 *m*, 1527*s*, 1503*s* 1457*w*, 1424 *m*, 1300*w*, 1171*w*, 1125*m*, 908*w*, 852*m*, 773*s*, 740*w*, 690*s*; ^{1}H-NMR (DMSO-d_6), δ: 10.66 (bs, 1H), 8.61 (d, *J*=8.5 Hz, 1H), 8.25 (dd, *J*=7.9 Hz, *J*=5.40 Hz, 2H), 8.10 (d, *J*=8.0 Hz, 1H), 7.90 (t, *J*=7.5 Hz, 1H), 7.67-7.84 (m, 3H), 7.27 (t, *J*=7.7 Hz, 1H), 6.96 (d, *J*=7.3 Hz, 1H), 2.32 (s, 3H); ^{13}C-NMR (DMSO-d_6), δ: 162.54, 150.03, 145.88, 138.22, 138.20, 138.03, 130.68, 129.35, 128.94, 128.65, 128.35, 128.15, 124.75, 120.72, 118.70, 117.35, 21.23; HR-MS: for $C_{17}H_{15}N_2O$ $[M+H]^+$ calculated 263.1184 m/z, found 263.1191 m/z.

N-(4-methylphenyl)quinoline-2-carboxamide (**4c**). Yield 44%; Mp. 107-108 °C (Mp. 109.5-110 °C [39]); ^{1}H-NMR (DMSO-d_6), δ: 10.67 (bs, 1H), 8.59 (d, *J*=8.5 Hz, 1H), 8.18-8.30 (m, 2H), 8.08 (d, *J*=8.0 Hz, 1H), 7.79-7.94 (m, 3H), 7.72 (t, *J*=7.4 Hz, 1H), 7.18 (d, *J*=8.3 Hz, 2H), 2.27 (s, 3H); ^{13}C-NMR (DMSO-d_6), δ: 162.51, 150.17, 145.93, 138.21, 135.86, 133.09, 130.69, 129.39, 129.24, 128.94, 128.35, 128.18, 120.27, 118.77, 20.59; HR-MS: for $C_{17}H_{15}N_2O$ $[M+H]^+$ calculated 263.1184 m/z, found 263.1193 m/z.

N-(2-fluorophenyl)quinoline-2-carboxamide (**5a**). Yield 30%; Mp. 116-117 °C; IR (Zn/Se ATR, cm^{-1}): 3328*w*, 1691*m*, 1615*m*, 1591*w*, 1530*s*, 1504*m*, 1477*w*, 1454*m*, 1428*m*, 1317*w*, 1247*w*, 1185*w*, 1126*m*, 1088*w*, 910*w*, 837*m*, 772*s*, 746*s*, 683*m*; ^{1}H-NMR (DMSO-d_6), δ: 10.48 (bs, 1H), 8.57 (d, *J*=8.5 Hz, 1H), 8.17-8.25 (m, 2H), 8.13 (d, *J*=8.5 Hz, 1H), 8.05 (d, *J*=8.0 Hz, 1H), 7.85 (t, *J*=7.3 Hz, 1H), 7.65-7.76 (m, 1H), 7.28-7.40 (m, 1H), 7.13-7.27 (m, 2H); ^{13}C-NMR (DMSO-d_6), δ: 162.00, 153.58 (d, $^1J_{FC}$=244 Hz), 148.95, 145.67, 138.39, 130.76, 129.24, 129.15 (d, $^2J_{FC}$=19.1 Hz), 128.45, 128.08, 125.70 (d, $^3J_{FC}$=11.0 Hz), 125.53 (d, $^3J_{FC}$=7.3 Hz), 124.63 (d, $^4J_{FC}$=3.7 Hz), 122.91, 118.37, 115.43 (d, $^2J_{FC}$=19.1 Hz); HR-MS: for $C_{16}H_{12}FN_2O$ $[M+H]^+$ calculated 267.0934 m/z, found 267.0950 m/z.

N-(3-fluorophenyl)quinoline-2-carboxamide (**5b**). Yield 38%; Mp. 126-127 °C; IR (Zn/Se ATR, cm^{-1}): 3343*w*, 1690*s*, 1588*m*, 1531*s*, 1504*m*, 1481*s*, 1409*s*, 1170*m*, 1137*m*, 899*m*, 841*s*, 791*m*, 768*s*, 738*m*, 682*s*; ^{1}H-NMR (DMSO-d_6), δ: 10.91 (bs, 1H), 8.58 (d, *J*=8.5 Hz, 1H), 8.16-8.31 (m, 2H), 8.08 (d, *J*=8.3 Hz, 1H), 7.95 (d, *J*=11.8 Hz, 1H), 7.86-7.92 (m, 1H), 7.79 (d, *J*=8.3 Hz, 1H), 7.68-7.75 (m, 1H), 7.35-7.49 (m, 1H), 6.96 (td, *J*=8.4 Hz, *J*=2.0 Hz, 1H); ^{13}C-NMR (DMSO-d_6), δ: 163.01, 162.15 (d, $^1J_{FC}$=241 Hz), 149.73, 145.86, 140.11 (d, $^3J_{FC}$=11.0 Hz), 138.18, 130.65, 130.31 (d, $^3J_{FC}$=9.5 Hz), 129.33, 128.97, 128.39, 128.12,

118.77, 116.15 (d, $^{4}J_{FC}$=2.9 Hz), 110.47 (d, $^{2}J_{FC}$=21.3 Hz), 107.09 (d, $^{2}J_{FC}$=26.4 Hz); HR-MS: for $C_{16}H_{12}FN_2O$ $[M+H]^+$ calculated 267.0934 m/z, found 267.0953 m/z.

N-(4-fluorophenyl)quinoline-2-carboxamide (**5c**) [41,43]. Yield 33%; Mp. 115-116 °C; ^{1}H-NMR (DMSO-d_6), δ: 10.83 (bs, 1H), 8.57 (d, *J*=8.3 Hz, 1H), 8.17-8.29 (m, 2H), 8.06 (d, *J*=8.0 Hz, 1H), 7.94-8.02 (m, 2H), 7.87 (td, *J*=7.7 Hz, *J*=1.3 Hz, 1H), 7.66-7.76 (m, 1H), 7.17-7.28 (m, 2H); ^{13}C-NMR (DMSO-d_6), δ: 162.76, 158.58 (d, $^{1}J_{FC}$=237 Hz), 150.03, 145.95, 138.18, 134.81 (d, $^{4}J_{FC}$=2.2 Hz), 130.67, 129.39, 128.98, 128.37, 128.17, 122.31 (d, $^{3}J_{FC}$=7.3 Hz), 118.83, 115.26 (d, $^{2}J_{FC}$=22.7 Hz); HR-MS: for $C_{16}H_{12}FN_2O$ $[M+H]^+$ calculated 267.0934 m/z, found 267.0954 m/z.

N-(2-chlorophenyl)quinoline-2-carboxamide (**6a**) [43]. Yield 39%; Mp. 130-131 °C; ^{1}H-NMR (DMSO-d_6), δ: 10.77 (bs, 1H), 8.58 (d, *J*=8.5 Hz, 1H), 8.43 (d, *J*=8.0 Hz, 1H), 8.21 (d, *J*=8.5 Hz, 1H), 8.10 (d, *J*=8.5 Hz, 1H), 8.05 (d, *J*=8.3 Hz, 1H), 7.85 (t, *J*=7.5 Hz, 1H), 7.64-7.75 (m, 1H), 7.54 (d, *J*=7.8 Hz, 1H), 7.39 (t, *J*=7.7 Hz, 1H), 7.10-7.24 (m, 1H); ^{13}C-NMR (DMSO-d_6), δ: 161.54, 148.70, 145.47, 138.50, 134.21, 130.75, 129.29, 129.20, 129.07, 128.46, 128.00, 127.88, 125.23, 123.38, 121.27, 118.15; HR-MS: for $C_{16}H_{12}ClN_2O$ $[M+H]^+$ calculated 283.0638 m/z, found 283.0652 m/z.

N-(3-chlorophenyl)quinoline-2-carboxamide (**6b**) [43]. Yield 46%; Mp. 127-128 °C; ^{1}H-NMR (DMSO-d_6), δ: 10.90 (bs, 1H), 8.58 (d, *J*=8.5 Hz, 1H), 8.18-8.31 (m, 2H), 8.15 (s, 1H), 8.07 (d, *J*=8.0 Hz, 1H), 7.82-7.97 (m, 2H), 7.66-7.78 (m, 1H), 7.40 (t, *J*=8.0 Hz, 1H), 7.11-7.23 (m, 1H); ^{13}C-NMR (DMSO-d_6), δ: 163.02, 149.67, 145.87, 139.85, 138.20, 133.12, 130.68, 130.36, 129.34, 128.98, 128.43, 128.14, 123.70, 119.82, 118.77; HR-MS: for $C_{16}H_{12}ClN_2O$ $[M+H]^+$ calculated 283.0638 m/z, found 283.0648 m/z.

N-(4-chlorophenyl)quinoline-2-carboxamide (**6c**). Yield 34%; Mp. 134-135 °C (Mp. 135-135.5 °C [39]); ^{1}H-NMR (DMSO-d_6), δ: 10.88 (bs, 1H), 8.58 (d, *J*=8.5 Hz, 1H), 8.17-8.30 (m, 2H), 8.08 (d, *J*=8.0 Hz, 1H), 8.01 (d, *J*=8.8 Hz, 2H), 7.84-7.93 (m, 1H), 7.68-7.77 (m, 1H), 7.43 (d, *J*=8.8 Hz, 2H); ^{13}C-NMR (DMSO-d_6), δ: 162.87, 149.85, 145.88, 138.16, 137.34, 130.65, 129.34, 128.95, 128.62, 128.37, 128.14, 127.69, 121.92, 118.78; HR-MS: for $C_{16}H_{12}ClN_2O$ $[M+H]^+$ calculated 283.0638 m/z, found 283.0631 m/z.

N-(2-bromophenyl)quinoline-2-carboxamide (**7a**). Yield 26%; Mp. 134-135 °C; IR (Zn/Se ATR, cm^{-1}): 3277*w*, 1689*s*, 1588*m*, 1579*m*, 1543*m*, 1530*s*, 1496*m*, 1440*m*, 1427*m*, 1302*w*, 1132*w*, 1204*m*, 908*w*, 842*m*, 768*s*, 736*m*, 698*m*; ^{1}H-NMR (DMSO-d_6), δ: 10.82 (bs, 1H), 8.60 (d, *J*=8.5 Hz, 1H), 8.44 (d, *J*=8.3 Hz, 1H), 8.23 (d, *J*=8.5 Hz, 1H), 8.13 (d, *J*=8.5 Hz, 1H), 8.07 (d, *J*=8.3 Hz, 1H), 7.87 (t, *J*=7.5 Hz, 1H), 7.64-7.77 (m, 2H), 7.44 (t, *J*=7.8 Hz, 1H), 7.10 (t, *J*=7.7 Hz, 1H); ^{13}C-NMR (DMSO-d_6), δ: 161.61, 148.71, 145.50, 138.60, 135.46, 132.58, 130.83, 129.26, 129.13, 128.55, 128.53, 128.08, 125.74, 121.39, 118.19, 114.08; HR-MS: for $C_{16}H_{12}BrN_2O$ $[M+H]^+$ calculated 327.0133 m/z, found 327.0138 m/z.

N-(3-bromophenyl)quinoline-2-carboxamide (**7b**). Yield 35%; Mp. 139-140 °C; IR (Zn/Se ATR, cm^{-1}): 3318*w*, 1687*m*, 1581*m*, 1519*m*, 1478*w*, 1408*m*, 1296*w*, 1124*m*, 1067*w*, 912*w*, 847*m*, 764*s*, 685*m*; ^{1}H-NMR (DMSO-d_6), δ: 10.89 (bs, 1H), 8.60 (d, *J*=8.3 Hz, 1H), 8.19-8.32 (m, 3H), 8.09 (d, *J*=8.0 Hz, 1H), 7.96 (d, *J*=7.5 Hz, 1H), 7.87-7.93 (m, 1H), 7.68-7.78 (m, 1H), 7.27-7.40 (m, 2H); ^{13}C-NMR (DMSO-d_6), δ: 163.02, 149.67, 145.86, 139.98, 138.21, 130.69, 130.67, 129.32, 128.97, 128.44, 128.14, 126.59, 122.66, 121.55, 119.14, 118.77; HR-MS: for $C_{16}H_{12}BrN_2O$ $[M+H]^+$ calculated 327.0133m/z, found 327.0143 m/z.

N-(4-bromophenyl)quinoline-2-carboxamide (**7c**). Yield 57%; Mp. 157-158 °C; IR (Zn/Se ATR, cm^{-1}): 3355*w*, 1693*s*, 1581*m*, 1522*s*, 1496*s*, 1423*w*, 1389*m*, 1305*w*, 1120*m*, 1095*w*, 1068*m*, 998*w*, 907*w*, 839*s*, 807*s*, 769*s*, 693*w*; ^{1}H-NMR (DMSO-d_6), δ: 10.84 (bs, 1H), 8.58 (d, *J*=8.5 Hz, 1H), 8.18-8.30 (m, 2H), 8.07 (d, *J*=8.3 Hz, 1H), 7.95 (d, *J*=8.8 Hz, 2H),

7.86-7.92 (m, 1H), 7.67-7.78 (m, 1H), 7.56 (d, *J*=8.8 Hz, 2H); ^{13}C-NMR (DMSO-d_6), δ: 162.86, 149.82, 145.87, 138.16, 137.74, 131.53, 130.64, 129.33, 128.94, 128.37, 128.12, 122.28, 118.77, 115.80; HR-MS: for $C_{16}H_{12}BrN_2O$ $[M+H]^+$ calculated 327.0133m/z, found 327.0129 m/z.

N-(2-trifluoromethylphenyl)quinoline-2-carboxamide (**8a**). Yield 32%; Mp. 120-121 °C; IR (Zn/Se ATR, cm^{-1}): 3316*w*, 1698*s*, 1590*s*, 1537*s*, 1498*w*, 1452*m*, 1423*m*, 1320*m*, 1288*m*, 1244*w*, 1202*w*, 1165*m*, 1124*m*, 1094*m*, 1054*m*, 1026*m*, 953*w*, 906*w*, 871*w*, 836*m*, 792*w*, 763*s*, 676*m*; ^{1}H-NMR (DMSO-d_6), δ: 10.78 (bs, 1H), 8.61 (d, *J*=8.3 Hz, 1H), 8.36 (d, *J*=8.3 Hz, 1H), 8.23 (d, *J*=8.3 Hz, 1H), 8.07 (t, *J*=8.3 Hz, 2H), 7.87 (t, *J*=7.5 Hz, 1H), 7.64-7.81 (m, 3H), 7.38 (t, *J*=7.7 Hz, 1H); ^{13}C-NMR (DMSO-d_6), δ: 162.05, 148.48, 145.53, 138.74, 135.14, 133.57, 131.01, 129.48 (q, $^2J_{FC}$=37 Hz), 129.21, 129.17, 128.68, 128.16, 126.41 (q, $^3J_{FC}$=5.1 Hz), 125.05, 124.10 (q, $^1J_{FC}$=274 Hz), 123.89 (q, $^3J_{FC}$=5.9 Hz), 118.31; HR-MS: for $C_{17}H_{12}F_3N_2O$ $[M+H]^+$ calculated 317.0902 m/z, found 317.0891 m/z.

N-(3-trifluoromethylphenyl)quinoline-2-carboxamide (**8b**). Yield 31%; Mp. 121-122 °C; IR (Zn/Se ATR, cm^{-1}): 3339*w*, 1692*s*, 1614*w*, 1536*m*, 1490*m*, 1424*w*, 1330*s*, 1223*w*, 1166*m*, 1109*s*, 1091*s*, 1065*m*, 952*w*, 933*w*, 874*s*, 844*m*, 08*s*, 771*s*, 744*w*, 698*s*; ^{1}H-NMR (DMSO-d_6), δ: 11.08 (bs, 1H), 8.59 (d, *J*=8.5 Hz, 1H), 8.46 (s, 1H), 8.17-8.31 (m, 3H), 8.08 (d, *J*=8.0 Hz, 1H), 7.89 (t, *J*=7.4 Hz, 1 H), 7.68-7.78 (m, 1 H), 7.61 (t, *J*=8.0 Hz, 1 H), 7.46 (d, *J*=7.5 Hz, 1H); ^{13}C-NMR (DMSO-d_6), δ: 163.26, 149.64, 145.90, 139.23, 138.21, 130.69, 129.86, 129.35 (q, $^2J_{FC}$=32 Hz), 129.34, 129.03, 128.45, 128.16, 124.20 (q, $^1J_{FC}$=273 Hz), 123.91, 120.24 (q, $^3J_{FC}$=3.7 Hz), 118.78, 116.61 (q, $^3J_{FC}$=3.7 Hz); HR-MS: for $C_{17}H_{12}F_3N_2O$ $[M+H]^+$ calculated 317.0902 m/z, found 317.0892 m/z.

N-(4-trifluoromethylphenyl)quinoline-2-carboxamide (**8c**) [41,44]. Yield 43%; Mp. 147-148 °C; ^{1}H-NMR (DMSO-d_6), δ: 11.02 (bs, 1H), 8.59 (d, *J*=8.3 Hz, 1H), 8.26 (d, *J*=8.5 Hz, 1H), 8.23 (d, *J*=8.3 Hz, 1H), 8.19 (d, *J*=8.5 Hz, 2H), 8.08 (d, *J*=8.0 Hz, 1H), 7.86-7.93 (m, 1H), 7.69-7.77 (m, 3H); ^{13}C-NMR (DMSO-d_6), δ: 163.27, 149.63, 145.88, 141.95, 138.23, 130.69, 129.38, 129.03, 128.48, 128.14, 125.96 (q, $^3J_{FC}$=3.7 Hz), 124.39 (q, $^1J_{FC}$=271 Hz), 124.00 (q, $^2J_{FC}$=32 Hz), 120.29, 118.81; HR-MS: for $C_{17}H_{12}F_3N_2O$ $[M+H]^+$ calculated 317.0902 m/z, found 317.0890 m/z.

N-(2-nitrophenyl)quinoline-2-carboxamide (**9a**). Yield 29%; Mp. 181-182 °C (Mp. 179.5-180 °C [39]); ^{1}H-NMR (DMSO-d_6), δ: 12.55 (bs, 1H), 8.75 (d, *J*=8.5 Hz, 1H), 8.60 (d, *J*=8.3 Hz, 1H), 8.17-8.28 (m, 2H), 8.09 (dd, *J*=13.9, 8.4 Hz, 2H), 7.86-7.95 (m, 1H), 7.78-7.85 (m, 1H), 7.70-7.77 (m, 1H), 7.34 (t, *J*=7.8 Hz, 1H); ^{13}C-NMR (DMSO-d_6), δ: 162.61, 148.50, 145.57, 138.55, 137.44, 135.73, 133.47, 130.94, 129.20, 129.16, 128.70, 128.09, 125.80, 123.97, 121.77, 118.38; HR-MS: for $C_{16}H_{12}N_3O_3$ $[M+H]^+$ calculated 294.0879 m/z, found 294.0888 m/z.

N-(3-nitrophenyl)quinoline-2-carboxamide (**9b**). Yield 30%; Mp. 189-190 °C; IR (Zn/Se ATR, cm^{-1}): 3305*w*, 1687*m*, 1620*w*, 1591*w*, 1529*m*, 1496*w*, 1427*m*, 1344*m*, 1202*w*, 1128*m*, 1068*w*, 939*w*, 291*m*, 837*m*, 798*m*, 773*s*, 733*s*, 675*s*; ^{1}H-NMR (DMSO-d_6), δ: 11.14 (bs, 1H), 8.95 (t, *J*=1.9 Hz, 1H), 8.57 (d, *J*=8.5 Hz, 1H), 8.34 (dd, *J*=8.0 Hz, *J*=1.0 Hz, 1H), 8.16-8.28 (m, 2H), 8.06 (d, *J*=8.0 Hz, 1H), 7.83-7.99 (m, 2H), 7.69-7.77 (m, 1H), 7.64 (t, *J*=8.2 Hz, 1H); ^{13}C-NMR (DMSO-d_6), δ: 163.35, 149.40, 147.88, 145.85, 139.56, 138.16, 130.64, 129.94, 129.30, 128.99, 128.44, 128.10, 126.34, 118.74, 118.34, 114.54; HR-MS: for $C_{16}H_{12}N_3O_3$ $[M+H]^+$ calculated 294.0879 m/z, found 294.0871 m/z.

N-(4-nitrophenyl)quinoline-2-carboxamide (**9c**) [43,44]. Yield 29%; Mp. 227-228 °C; ^{1}H-NMR (DMSO-d_6), δ: 11.29 (bs, 1H), 8.64 (d, *J*=8.5 Hz, 1H), 8.18-8.35 (m, 6H), 8.12 (d, *J*=8.0 Hz, 1H), 7.88-7.99 (m, 1H), 7.78 (d, *J*=7.8 Hz, 1H); ^{13}C-NMR (DMSO-d_6), δ: 163.61, 149.43, 145.88, 144.58, 142.77, 138.38, 130.83, 129.40, 129.11, 128.68, 128.21, 124.81,

120.17, 118.92; HR-MS: for $C_{16}H_{12}N_3O_3$ $[M+H]^+$ calculated 294.0879 m/z, found 294.0870 m/z.

Lipophilicity calculations

Log *P*, *i.e.* the logarithm of the partition coefficient for *n*-octanol/water, was calculated using the programs CS ChemOffice Ultra ver. 11.0 (CambridgeSoft, Cambridge, MA, USA) and ACD/LogP ver. 1.0 (Advanced Chemistry Development Inc., Toronto, Canada). Clog *P* values (the logarithm of *n*-octanol/water partition coefficient based on established chemical interactions) were generated by means of CS ChemOffice Ultra ver. 11.0 (CambridgeSoft, Cambridge, MA, USA) software. The results are shown in Table 1.

Study of inhibition photosynthetic electron transport (PET) in spinach chloroplasts

Chloroplasts were prepared from spinach (*Spinacia oleracea* L.) according to Masarovicova and Kralova [45]. The inhibition of photosynthetic electron transport (PET) in spinach chloroplasts was determined spectrophotometrically (Genesys 6, Thermo Scientific, USA), using the artificial electron acceptor 2,6-dichlorophenol-indophenol (DCIPP) according to Kralova *et al*. [46], and the rate of photosynthetic electron transport was monitored as photoreduction of DCPIP. The measurements were carried out in phosphate buffer (0.02 mol/L, pH 7.2) containing sucrose (0.4 mol/L), $MgCl_2$ (0.005 mol/L) and NaCl (0.015 mol/L). The chlorophyll content was 30 mg/L in these experiments and the samples were irradiated (~100 W/m^2) from 10 cm distance with a halogen lamp (250 W) using a 4 cm water filter to prevent warming of the samples. The studied compounds were dissolved in DMSO due to their limited water solubility. The applied DMSO concentration (up to 4%) did not affect the photochemical activity in spinach chloroplasts. The inhibitory efficiency of the studied compounds was expressed by IC_{50} values, *i.e.* by molar concentration of the compounds causing 50% decrease in the oxygen evolution rate relative to the untreated control. The comparable IC_{50} value for a selective herbicide 3-(3,4-dichlorophenyl)-1,1-dimethylurea, DCMU (Diurone®) was about 1.9 μmol/L [47]. The results are summarized in Table 1.

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REFERENCES

1. Palmer, M.H. The Structure and Reactions of Heterocyclic Compounds. Edward Arnold Publishers Ltd., London, 1967, pp.104-144.
2. Finley, K.T. Quinolines and Isoquinolines. *In*: Van Nostrand's Encyclopedia of Chemistry. John Wiley & Sons Inc., New York, 2005.
3. Quinolines and Isoquinolines. Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 21., 5th ed. John Wiley & Sons Inc., New York, 2007.
4. Roth, H.J.; Fenner, H. *Arzneistoffe* 3rd Ed.; Deutscher Apotheker Verlag: Stuttgart, Germany, 2000; pp. 51–114.
5. Mitková, L. Quinoline Derivatives: Their Preparation and Biological Activity. Diploma Thesis. Department of Chemical Drugs, Faculty of Pharmacy, University of Veterinary and Pharmaceutical Sciences Brno, 2009.
6. Harris, C.R.; Thorarensen, A. *Curr. Med. Chem.* **2004**, *11*, 2213.

7. Andries, K.; Verhasselt, P.; Guillemont, J.; Gohlmann, H.W.; Neefs, J.M.; Winkler, H.; Van Gestel, J.; Timmerman, P.; Zhu, M.; Lee, E.; Williams, P.; de Chaffoy, D.; Huitric, E.; Hoffner, S.; Cambau, E.; Truffot-Pernot, C.; Lounis, N.; Jarlier, V. *Science* **2005**, *307*, 223.
8. Vangapandu, S.; Jain, M.; Jain, R.; Kaur, S.; Singh, P.P. *Bioorg. Med. Chem.* **2004**, *12*, 2501.
9. Jampilek, J.; Dolezal, M.; Kunes, J.; Buchta, V.; Kralova, K. *Med. Chem.* **2005**, *1*, 591.
10. Musiol, R.; Jampilek, J.; Buchta, V.; Niedbala, H.; Podeszwa, B.; Palka, A.; Majerz-Maniecka, K.; Oleksyn, B.; Polanski, J. *Bioorg. Med. Chem.* **2006**, *14*, 3592.
11. Jampilek, J.; Musiol, R.; Pesko, M.; Kralova, K.; Vejsova, M.; Carroll, J.; Coffey, A.; Finster, J.; Tabak, D.; Niedbala, H.; Kozik, V.; Polanski, J.; Csollei, J.; Dohnal, J. *Molecules* **2009**, *14*, 1145.
12. Jampilek, J.; Musiol, R.; Finster, J.; Pesko, M.; Carroll, J.; Kralova, K.; Vejsova, M.; O'Mahony, J.; Coffey, A.; Dohnal, J.; Polanski, J. *Molecules* **2009**, *14*, 4246.
13. Musiol, R.; Jampilek, J.; Nycz, J.E.; Pesko, M.; Carroll, J.; Kralova, K.; Vejsova, M.; O'Mahony, J.; Coffey, A.; Mrozek, A.; Polanski, J. *Molecules* **2010**, *15*, 288.
14. Musiol, R.; Jampilek, J.; Kralova, K.; Richardson, D.R.; Kalinowski, D.; Podeszwa, B.; Finster, J.; Niedbala, H.; Palka, A.; Polanski, J. *Bioorg. Med. Chem.* **2007**, *15*, 1280.
15. Podeszwa, B.; Niedbala, H.; Polanski, J.; Musiol, R.; Tabak, D.; Finster, J.; Serafin, K.; Wietrzyk, J.; Boryczka, S.; Mol, W.; Jampilek, J.; Dohnal, J.; Kalinowski, D.; Richardson, D.R. *Bioorg. Med. Chem. Lett.* **2007**, 17, 6138.
16. Mrozek-Wilczkiewicz, A.; Kalinowski, D.; Musiol, R.; Finster, J.; Szurko, A.; Serafin, K.; Knas, M.; Kamalapuram, S.K.; Kovacevic, Z.; Jampilek, J.; Ratuszna, A.; Rzeszowska-Wolny, J.; Richardson, D.R.; Polanski, J. *Bioorg. Med. Chem.* **2010**, *18*, 2664.
17. Musiol, R.; Tabak, D.; Niedbala, H.; Podeszwa, B.; Jampilek, J.; Kralova, K.; Dohnal, J.; Finster, J.; Mencel, A.; Polanski, J. *Bioorg. Med. Chem.* **2008**, *16*, 4490.
18. Shaner, D.L. *Pest. Manag. Sci.* **2004**, *60*, 17.
19. Delaney, J.; Clarke, E.; Hughes, D.; Rice, M. *Drug Discov. Today* **2006**, *11*, 839.
20. Duke, S.O. *Weed Sci.* **2010**, *58*, 334.
21. Draber, W.; Tietjen, K.; Kluth, J.F.; Trebst, A. *Angewandte Chemie* **1991**, *3*, 1621.
22. Tischer, W.; Strotmann, H. *Biochim. Biophys. Acta* **1977**, *460*, 113.
23. Trebst, A.; Draber, W. *Structure activity correlations of recent herbicides in photosynthetic reactions*. In *Advances in Pesticide Science*; Greissbuehler H. Ed.; Pergamon Press: Oxford, 1979; pp. 223–234.
24. Bowyer, J.R.; Camilleri, P.; Vermaas, W.F.J. In *Herbicides, Topics in Photosynthesis*, vol. 10. Baker N.R., Percival M.P. Eds.; Elsevier: Amsterdam, 1991; pp. 27–85.
25. Kralova, K.; Sersen, F.; Kubicova, L.; Waisser, K. *J. Trace Microprobe Techn.* **2000**, *18*, 251-256.
26. Otevrel, J.; Mandelova, Z.; Pesko, M.; Guo, J.; Kralova, K.; Sersen, F.; Vejsova, M.; Kalinowski, D.; Kovacevic, Z.; Coffey, A.; Csollei, J.; Richardson, D.R.; Jampilek, J. *Molecules* **2010**, *15*, 8122.
27. Imramovsky, A.; Pesko, M.; Kralova, K.; Vejsova, M.; Stolarikova, J.; Vinsova, J.; Jampilek, J. *Molecules* **2011**, *16*, 2414.
28. Imramovsky, A.; Pesko, M.; Monreal-Ferriz, J.; Kralova, K.; Vinsova, J.; Jampilek, J. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 4564.
29. Miletin, M.; Hartl, J.; Dolezal, M.; Odlerova, Z.; Kralova, K.; Machacek, M. *Molecules*, **2000**, *5*, 208.

30. Dolezal, M.; Palek, L.; Vinsova, J.; Buchta, V.; Jampilek, J.; Kralova, K. *Molecules* **2006**, *11*, 242.
31. Dolezal, M.; Cmedlova, P.; Palek, L.; Vinsova, J.; Kunes, J.; Buchta, V.; Jampilek, J.; Kralova, K. *Eur. J. Med. Chem.* **2008**, *43*, 1105.
32. Dolezal, M.; Zitko, J.; Osicka, Z.; Kunes, J.; Vejsova, M.; Buchta, V.; Dohnal, J.; Jampilek, J.; Kralova, K.. *Molecules* **2010**, *15*, 8567.
33. Dolezal, M.; Kralova, K. *Synthesis and evaluation of pyrazine derivatives with herbicidal activity*. In *Herbicides, Theory and Applications*; Soloneski S.; Larramendy, M.L. Eds.; InTech: Rijeka, 2011; pp.581–610.
34. Imperial Chemical Industries Ltd. Ger. Offen. 2,322,143 (December 13, 1973).
35. Mitsubishi Petrochemicals Co. Ltd. Jpn. Kokai 77,72,821 (June 17, 1977).
36. American Cyanamid Company Ltd. US Patent 5625068 (April 29, 1997).
37. Norrington, F.E.; Hyde, R.M.; Williams, S.G.; Wotton, R. *J. Med. Chem.* **1975**, *18*, 604.
38. Takahata, Y.; Chong, D.P. *Int. J. Quantum Chem.* **2005**, *103*, 509.
39. Davis, J.D.W., Jr. *J. Org. Chem.* **1959**, *24*, 1691.
40. Dzadzic, P.M.; Bastic, B.L.; Piletic, M.V. *Glasnik Hemijskog Drustva Beograd* **1971** *36*, 137.
41. Zymogenetics, Inc. & Osteoscreen, Inc. & University of Texas. PCT Int. Appl. WO 1997015308 A1 (May 1, 1997).
42. Chan, L.; Jin, H.; Stefanac, T.; Wang, W.; Lavallee, J.F.; Bedard, J.; May, S. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2583.
43. Schaefer, W.; Neubert, P. *Tetrahedron* **1969**, *25*, 315.
44. Kiselyov, A. S. *Tetrahedron Lett.* **2005**, *46*, 4851.
45. Masarovicova, E.; Kralova, K. *Approaches to measuring plant photosynthesis activity*. In *Handbook of Photosynthesis* 2nd Ed.; Pessarakli M. Ed.; Taylor & Francis Group: Boca Raton, London-New York-Singapore, 2005; pp. 617–656.
46. Kralova, K.; Sersen, F.; Sidoova, E. *Chem. Pap.* **1992**, *46*, 348.
47. Fedke, C. *Biochemistry and Physiology of Herbicide Action*. Springer Verlag: Berlin-Heidelberg-New York, 1982.