A SYNTHESIS OF FUSED PYRIMIDINE MONO-*N*-OXIDES

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ABSTRACT *- An efficient synthesis of functionalized fused pyrimidine mono-N-oxide derivatives from the nitroaromatic compounds (involving the Vicarious Nucleophilic Substitution of Hydrogen and cyclocondensation of aromatic ortho-aminooximes with orthoesters) is described.*

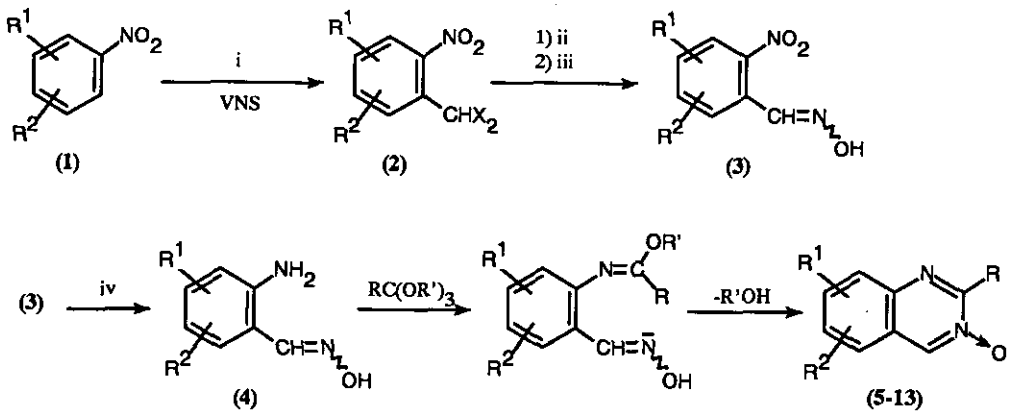
The *N*-oxide function - modifying considerably chemical properties of the parent ring system - is present in many heterocyclic moieties.[1] This functionality in many cases is responsible for high and specific biological activity of the corresponding *N*-oxides.[1,2] It has been also observed, that some alkaloids converted into *N*-oxide derivatives exhibit reduced toxicity, without decreasing their biological activity.[3] On the other hand a catalytic activity of N->O function was found, *e.g.* in ozonolysis of olefines,[4] *N*-oxidation of amines,[5] or other chemical transformations.[6] Therefore, since Polonovski[7] isolated the first naturally occurring heterocyclic *N*-oxide, generosine (a derivative of an eserine alkaloid), several studies on synthesis and structure-activity relationship of heterocyclic *N*-oxides have been reported.[1-3]

A general method of the preparation of these compounds - the direct *N*-oxidation[1,8] of the corresponding heterocyclic base, is practically inapplicable to the synthesis of the *mono-N*-oxide moieties of diazines or other polyazaarenes, as well as compounds possessing groups sensitive to oxidation, *e.g.* low valent sulphur. Another approach, the formation of the ring carrying the *N*-oxide group, by the cyclisation reaction[1,9-11] can be applied in such cases; however, it is a difficult task owing to limited availability of the suitable intermediates.

In this paper we report an efficient approach to the synthesis of fused pyrimidine *mono-N*-oxide derivatives. As starting materials in this methodology, the corresponding nitroaromatic compounds are used. A crucial step of this synthesis is the Vicarious Nucleophilic Substitution of Hydrogen reaction (VNS),[12] which can

serve for introduction of appropriate substituents into position *ortho*- to the nitro group; thus gives an opportunity for transformations leading to the cyclizable intermediates (see Schemes). Among others, the application of VNS has been found as an excellent tool for introduction the dihalomethyl groups[13] in the aromatic or heteroaromatic nitro-compounds. The hydrolysis of these dihalomethyl substituents in com-

Scheme 1



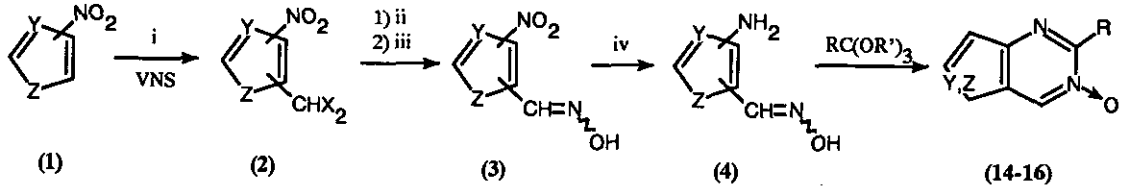
1 - 4*)	R^1	R^2
a	H	4-Cl
b	H	4-Ph
c	5,6-[-CH=CH-CH=CH-]	
d	5,6-[-N=CH-CH=CH-]	
e	5,6-[-CH=CH-CH=N-]	

Reaction conditions:

i) CHX_3 (X = Cl, Br) / t-BuOK, THF-DMF, -70°C
ii) $AgClO_4$, toluene-H_2O (or MeCN-H_2O), reflux, under argon or HCO_2H-H_2O ($ZnCl_2$ optionally), reflux, under argon
iii) NH_2OHxHCl, AcONa, MeOH-H_2O, room temperature, 24 h
iv) H_2, 10% Pd/C, EtOH, 20-40 psi, 2-6 h.

*)Carbon atoms bearing NO_2 and NH_2 groups in compounds 1-4 were assigned 1.

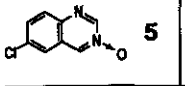
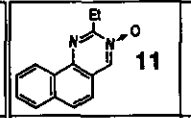
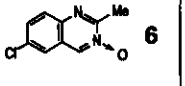
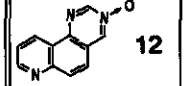
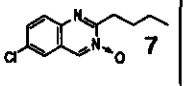
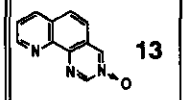
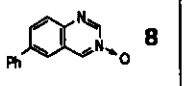
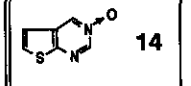
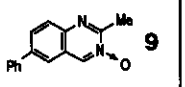
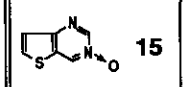
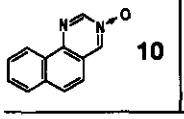
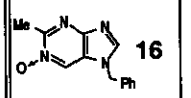
Scheme 2



1 - 4	Y	Z	Position of $NO_2(NH_2)$	Position of $CHX_2(CH=NOH)$
f	CH	S	2-	3-
g	CH	S	3-	2-
h	N	N-CH_2Ph	4-	5-

Reaction conditions *i) - iv)* - see Scheme 1.

Table: Fused Pyrimidine *mono-N*-Oxide Derivatives.

Products and **No**	Reaction cond. of **4** with orthoesters	Yield [%]	mp [°C] (solvent)	**Products** and **No**	Reaction cond. of **4** with orthoesters	Yield [%]	mp [°C] (solvent)
 **5**	24 h, room temperature	68	210-212 (Et_2O)	 **11**	3 weeks, room temperature	83	204-205 ($CHCl_3$-acetone)
 **6**	*85 h, room* temperature	60	186-187 ($CHCl_3$)	 **12**	17 h, reflux	90	260-265 ($CHCl_3$)
 **7**	1 week, room temperature	*44*	*103-107* ($CHCl_3$-MeOH)	 **13**	*60 h, room* temperature	*66*	>280 (decomp., $CHCl_3$)
 **8**	130 h, room temperature	87	270-273 (acetone)	 **14**	2 weeks, room temperature	22	semi-crystalline
 **9**	30 h, room temperature	93	205-208 ($CHCl_3$)	 **15**	2 weeks, room temperature	75	152-155 (acetone)
 **10**	2 weeks, room temperature	61	234-238 ($CHCl_3$)	 **16**	3 h, 100°C, in EtOH[a]	83	216-218 ($CHCl_3$-MeOH)

[a] The reaction was carried out in a sealed tube.

pounds **2a-h** to aldehydes and subsequent transformation into oximes **(3a-h)** gave intermediates for the preparation of *mono-N*-oxides of fused pyrimidine derivatives. Reduction of the nitro group in the *ortho*-nitroaldoximes **(3a-h)** led to the corresponding amino-derivatives **(4a-h)**. For this selective transformation of the NO_2 group only, catalytic hydrogenation was applied (20 - 40 psi, 10% Pd/C, EtOH, 2 - 6 h). These conditions are mild enough to prevent a partial dehalogenation of chlorine (compound **3a**) and also insensitive to catalytic inhibition - usually caused by bivalent sulphur (*e.g.* thiophene derivatives - **3 f,g**); thus they do not limit the preparation of the desired products. They have been found by us earlier, optimized and successfully used, already.[14,15] The reaction of aminooximes with diverse orthoesters (usually carried out at room temperature) provided a simple method for synthesis of the *mono-N*-oxides of pyrimidine derivatives. The higher temperature shortens the reaction time, in some cases however, decreases yields. This type of cyclisation has been known since 1957,[10] nevertheless, only a few examples of application of this method or its modifications has been described;[11] probably due to limited availability of the proper

intermediates **(4)**. The presented here approach, based on the VNS methodology, seems to be a fast, high-yielded, and easy way for their preparation. This method allows not only the selective introduction of N->O function into the desired position in the target compounds having more than one nitrogen atom, but can be also used for preparation of compounds in which some substituents are present, *e.g.* alkyl, aryl or halogens.

Pure, isolated *mono-N*-oxides have to be stored at low temperature or used and analyzed directly after preparation because of the spontaneous transformations to deoxygenated compounds (*e.g.* for **16**) or to *bis-N*-oxides (*e.g.* for **6**) observed when kept at room temperature.

The examples of bicyclic and tricyclic fused pyrimidine *mono-N*-oxides obtained (among them purines, Table) demonstrate the general character of the presented method and a wide range of its applications. Taking into account a broad spectrum of the available starting nitroarenes, the presented method probably can receive much attention.

EXPERIMENTAL

Nmr spectra were recorded with a Varian GEMINI-200 spectrometer operating at 200 MHz for ^{1}H and 50 MHz for ^{13}C. Coupling constants *J* are expressed in hertz [Hz]. The assignment of the chemical shifts accompanied by asterisk*) or by double cross#) may be exchanged. The proton assignements in substituted quinolines (**3d**, **4d**) and their fused derivatives (**12**, **13**) were done based on the literature data[16] (usually coupling constants in heterocyclic ring are $J_{2,3}$ ~ 4.3 Hz and $J_{3,4}$ ~ 8.5 Hz). Mass spectra were measured with AMD 604 (AMD Intectra GmbH, Germany) spectrometer (electron impact and LSIMS methods). Melting points are uncorrected. Tlc analyses were performed on aluminium foil plates precoated with silica gel 60F 254 Merck. Silica gel 230-300 mesh (Merck AG) was used for column chromatography. The dihalomethylated compounds **2a-f** and all aldehydes prepared thereof were described in the literature.[13] Also, the preparation of aminooxime **4h** and its precursors was detaily described earlier.[14,15]

2-Dichloromethyl-3-nitrothiophene (2g). - To a vigorously stirred mixture of *t*-BuOK (3.96 g, 35.4 mmol) under argon in THF-DMF solvent system (2:1, 30 ml) cooled to -73°C, a solution of $CHCl_3$ (1.17 g, 9.8 mmol) and 3-nitrothiophene (1.20 g, 9.3 mmol) in DMF (3 ml) was added at -70 ÷ -68°C during a period *ca* 10 min. The stirring was continued for the next 1 min at -70°C and then the reaction mixture was quenched with acetic acid (2.6 g, *ca* 43 mmol) in MeOH (10 ml). The acidified mixture was poured into water with ice (400 ml). After extraction with CH_2Cl_2 (3x100 ml), the combined organic layers were washed with 20% aqueous K_2CO_3 (100 ml) and with water (3x100 ml), and dried over $MgSO_4$. The crude product **(2g)** was purified by column chromatography (eluent: from n-heptane/$CHCl_3$ (1:1) to $CHCl_3$). Yield - 1.70 g, 86%; mp 53°C ($CHCl_3$). - ^{1}H Nmr ($CDCl_3$): 7.72 (s, 1H, $CHCl_2$), 7.60 and 7.40 (2xd, J=5.7, 2H, H-4,5). - Ms, m/z (%): 215 (3), 213 (15), 211 (22), [isotopic $M^{+\cdot}$], 178 (47), 176 (100), 168 (9), 166 (19), 164 (12), 150 (30), 148 (95), 146 (33), 140 (13), 129 (19), 120 (38), 118 (98), 95 (59), 83 (18), 69 (15), 45 (72). - Anal. Calcd for $C_5H_3NO_2Cl_2S$: C 28.32, H 1.43, N 6.61, Cl 33.44, S 15.12. Found: C 28.46, H 1.49, N 7.04, Cl 32.96, S 15.15.

3-Nitrothiophene-2-carbaldehyde. - The dichloromethylated derivative **2g** (297 mg, 1.40 mmol) was dissolved in toluene (15 ml); then water (1.2 ml) and $AgClO_4$ (722 mg, 3.48 mmol) were added. The mixture was refluxed under argon for 2 h. After cooling, AgCl was filtered off, washed with $CHCl_3$ and acetone,

and the filtrate was diluted with $CHCl_3$ to a volume of 50 ml and dried over Na_2SO_4. After chromatography (eluent: from $CHCl_3$/n-heptane (1:1) to $CHCl_3$) a pure *3-nitrothiophene-2-carbaldehyde* was obtained. Yield - 188 mg, 85%; mp 54-56°C ($CHCl_3$). - ^{1}H Nmr ($CDCl_3$): 10.52 (s, 1H, CHO), 7.70 (s, 2H, H-4,5). - ^{13}C Nmr ($CDCl_3$): 182.3 (CHO), 141.0, 132.3, 125.4, 124.1. - Ms, m/z (%): 157 (8, $M^{+\cdot}$), 140 (10), 127 (83), 113 (75), 110 (89), 99 (35), 82 (54), 77 (15), 73 (32), 71 (34), 55 (39), 45 (90), 39 (100). - Anal. Calcd for $C_5H_3NO_3S$: C 38.22, H 1.92, N 8.91, S 20.40. Found: C 38.34, H 1.84, N 8.73, S 20.54.

Preparation of 3a-g. General Procedure.

An aldehyde (2.5 mmole) was added to hydroxylamine hydrochloride (204 mg, 2.94 mmol) and sodium acetate (242 mg, 2.94 mmol) dissolved in methyl alcohol (28 ml) with water (3 ml). The mixture was stirred at room temperature until the substrate had dissapeared (*ca* 24 h). Then, the reaction mixture was evaporated to dryness and to the residue $CHCl_3$ (120 ml) was added. The suspension was dried over Na_2SO_4, the solvent was evaporated and the pure oximes **(3a-g)** were isolated by column chromatography (eluent: from $CHCl_3$ to $CHCl_3$/MeOH (20:1)).

5-Chloro-2-nitrobenzaldehyde oxime (3a), solid, 93% yield.
- ^{1}H Nmr ($CDCl_3$, main isomer in *E/Z* mixture): 8.68 (s, 1H, OH), 8.04 (d, J=8.8, 1H, H-5), 7.95 (d, J=2.3, 1H, H-2), 7.73 (s, 1H, CH-oxime), 7.51 (dd, J=8.8,2.3, 1H, H-6). - Ms, m/z (%): 202 (6) and 200 (15) [isotopic $M^{+\cdot}$], 185 (3), 183 (8), 171 (34), 169 (100), 154 (9), 152 (24), 136 (21), 127 (27), 125 (68), 113 (29), 99 (35), 90 (23), 75 (37), 63 (21), 50 (12); HR-ms calcd for $C_7H_5N_2O_3Cl$ - 199.9989, Found - 199.9987. - Anal. Calcd for $C_7H_5N_2O_3Cl$: C 41.92, H 2.51, N 13.97, Cl 17.68. Found: C 42.33, H 2.41, N 13.55, Cl 17.02.

2-Nitro-5-phenylbenzaldehyde oxime (3b), solid, 82% yield.
- ^{1}H Nmr ($CDCl_3$, *E/Z* mixture): 8.80 and 8.08 (2xs, OH - *E/Z*), 8.19 (d, J=8.6, H-3), 8.13 (d, J=1.9, H-6), 7.76 (dd, J=8.6,1.9, H-4), 7.68-7.42 (m, H-Ph and CH-oxime). - Ms, m/z (%): 242 (27, $M^{+\cdot}$), 224 (40), 211 (40), 195 (32), 194 (91), 178 (17), 177 (28), 167 (100), 166 (37), 152 (35), 151 (37), 140 (34), 139 (36), 127 (12), 115 (19), 102 (18), 63 (8), 51 (7); HR-ms calcd for $C_{13}H_{10}N_2O_3$ - 242.0691, Found - 242.0690. - Anal. Calcd for $C_{13}H_{10}N_2O_3$: C 64.46, H 4.16, N 11.56. Found: C 64.41, H 3.68, N 11.10.

1-Nitronaphthalene-2-carboxime (3c), solid, 95% yield.
- ^{1}H Nmr ($CDCl_3$, main isomer in *E/Z* mixture): 10.28 (s, OH), 8.19-7.51 (m, H-Ar and CH-oxime). - Ms, m/z (%): 216 (85, $M^{+\cdot}$), 198 (7), 185 (54), 169 (25), 168 (25), 153 (23), 152 (22), 141 (100), 140 (68), 129 (60), 126 (55), 115 (76), 114 (73), 89 (16), 77 (20), 63 (24), 51 (15), 39 (10); HR-ms calcd and found 216.0535 ($C_{11}H_8N_2O_3$). - Anal. Calcd for $C_{11}H_8N_2O_3$: C 61.11, H 3.73, N 12.96. Found: C 60.95, H 3.59, N 12.99.

5-Nitroquinoline-6-carboxime (3d), solid, quantitative yield.
- ^{1}H Nmr ($CDCl_3$/DMSO-d_6 - 5:1, main isomer in *E/Z* mixture): 11.84 (broad s, OH), 8.96 (dd, J=4.3,1.4, H-2), 8.23-8.18 (m, H-7,8 and CH-oxime), 8.10 (d, J=8.4, H-4), 7.61 (dd, J=8.4,4.3, H-3). - Ms, m/z (%): 217 (48, $M^{+\cdot}$), 199 (4), 186 (93), 170 (15), 169 (12), 153 (25), 142 (100), 130 (39), 127 (29), 116 (31), 115 (41), 101 (13), 89 (16), 75 (6), 63 (6), 50 (6); HR-ms calcd and found 217.0487 ($C_{10}H_7N_3O_3$). - Anal. Calcd for $C_{10}H_7N_3O_3$: C 55.30, H 3.25, N 19.35. Found: C 54.84, H 2.81, N 18.63.

8-Nitroquinoline-7-carboxime (3e), solid, 91% yield.
- ^{1}H Nmr ($CDCl_3$, *E/Z* mixture): 9.05-9.00 (m, 1H, H-2), 8.29-8.20 (m, 2H, H-4 and OH), 8.03, 7.94 (AB, J=9.0) and 8.02, 7.93 (AB, J=8.9) [2H, H-5,6 of *E/Z* isomers], 7.83 (broad s, 1H, CH-oxime), 7.60-7.51 (m, 1H, H-3). - Ms, m/z (%): 217 (32, $M^{+\cdot}$), 171 (100), 154 (24), 142 (40), 141 (47), 129 (45), 128 (52), 127 (32), 116 (57), 115 (30), 114 (29), 102 (18), 101 (19), 100 (18), 89 (29), 75 (15), 63 (22), 51 (14), 50 (15), 40 (13); HR-ms calcd for $C_{10}H_7N_3O_3$ - 217.0487, Found - 217.0489.

2-Nitrothiophene-3-carboxime (3f), solid, quantitative yield.
- ^{1}H Nmr ($CDCl_3$, main isomer in *E/Z* mixture): 8.95 (s, 1H, OH), 7.48 and 7.44 (AB, J=6.3, 2H, H-4,5), 7.27 (s, 1H, CH-oxime). - Ms, m/z (%): 272 (100, $M^{+\cdot}$), 155 (55), 142 (26), 141 (19), 138 (28), 126 (38),

113 (22), 111 (24), 109 (22), 97 (43), 85 (30), 82 (35), 70 (48), 64 (26), 57 (17), 52 (24), 45 (72), 39 (26). - Anal. Calcd for $C_5H_4N_2O_3S$: C 34.88, H 2.34, N 16.27, S 18.62. Found: C 35.17, H 2.30, N 16.40, S 18.63.

3-Nitrothiophene-2-carboxime (3g), solid, 96% yield (4 mmol scale; 80% of substrate was recovered). - ^{1}H Nmr (acetone-d_6, *E/Z* mixture), major isomer (72%): 12.20 (s, 1H, OH), 8.62 (d, J=0.8, 1H, CH-oxime), 7.82 (part of AB, coupling with CH-oxime, J=5.7,0.8, 1H), 7.73 (part of AB, J=5.7, 1H) [H-4,5]; minor isomer (28%): 11.26 (s, 1H, OH), 8.88 (s, 1H, CH-oxime), 7.64 (part of AB, J=5.7, 1H), 7.61 (part of AB, coupling with CH-oxime, J=5.7,0.6, 1H) [H-4,5]. - Ms, m/z (%): 172 (100, $M^{+\cdot}$), 155 (38), 142 (32), 141 (45), 138 (18), 125 (14), 113 (12), 111 (18), 109 (12), 97 (37), 96 (18), 85 (25), 84 (30), 82 (19), 81 (20), 76 (5), 71 (24), 70 (48), 64 (35), 58 (16), 57 (15), 55 (13), 45 (64), 39 (22). - Anal. Calcd for $C_5H_4N_2O_3S$: C 34.88, H 2.34, N 16.27, S 18.62. Found: C 35.07, H 2.23, N 15.98, S 18.38.

Catalytic Hydrogenation of 3a-g. General Procedure.

The nitro-compound was dissolved in ethanol (5-10 ml for 100 mg) and it was hydrogenated in Parr Apparatus (40 psi; for compound **3a** - 20 psi) using 10-30% of catalyst (10% Pd/C) during 2 - 6 h; the reaction was monitored on tlc, $CHCl_3$/MeOH - 20:1. After the reduction the catalyst was filtered off, washed with alcohol, and the solvent was evaporated to give crude products. In most cases for these crude products ^{1}H nmr and ms spectra were recorded.

2-Amino-5-chlorobenzaldehyde oxime (4a), solid.
- ^{1}H Nmr ($CDCl_3$, *E/Z* mixture): 10.38 and 7.76 (2xs, 1H, *E/Z*-OH), 6.87-6.31 (m, H-3,4,6, CH-oxime), 5.65 (broad s, NH_2). - Ms, m/z (%): 172 (5) and 170 (14) [isotopic $M^{+\cdot}$], 155 (6), 153 (17), 122 (100), 121 (45), 106 (27), 105 (40), 104 (63), 94 (25), 78 (36), 77 (29), 65 (9), 51 (7); HR-ms calcd for $C_7H_7N_2ClO$ - 170.0247, Found - 170.0246.

2-Amino-5-phenylbenzaldehyde oxime (4b), solid.
- ^{1}H Nmr ($CDCl_3$, main isomer in *E/Z* mixture): 8.32 (s, OH), 7.56-7.27 (m, H-Ar and CH-oxime), 6.78 (d, J=8.5, H-3), 5.54 (broad s, NH_2). - Ms, m/z (%): 212 (75, $M^{+\cdot}$), 195 (82), 194 (100), 180 (8), 168 (15), 167 (23), 166 (18), 152 (8), 139 (13), 115 (7), 84 (7); HR-ms calcd for $C_{13}H_{12}N_2O$ - 212.0950, Found - 212.0948.

1-Aminonaphthalene-2-carboxime (4c), solid.
- ^{1}H Nmr ($CDCl_3$, *E/Z* mixture): 8.39 (s, 0.68H, OH, one isomer of *E/Z* mixture), 7.91-7.19 (m, H-Ar and CH-oxime; OH of second isomer), 6.40 (broad s, 2H, NH_2). - Ms, m/z (%): 186 (100, $M^{+\cdot}$), 169 (87), 168 (43), 142 (15), 141 (13), 140 (23), 115 (29), 105 (8).

5-Aminoquinoline-6-carboxime (4d), solid.
- ^{1}H Nmr ($CDCl_3$/DMSO-d_6 - 5:1, one isomer only): 10.92 (s, 1H, OH), 8.70 (dd, J=4.2,1.3, 1H, H-2), 8.55 (d, J=8.6, 1H, H-4), 8.23 (s, 1H, CH-oxime), 7.37-7.12 (m, 3H, H-3,7,8), NH_2 - undetected. - Ms, m/z (%): 187 (78, $M^{+\cdot}$), 171 (27), 170 (100), 169 (32), 143 (20), 142 (40), 116 (21), 115 (23); HR-ms calcd and found - 187.0746 ($C_{10}H_9N_3O$).

8-Aminoquinoline-7-carboxime (4e), solid.
- ^{1}H Nmr ($CDCl_3$, *E/Z* mixture): 11.12 and 11.07 (2xs, OH of *E/Z* isomers), 8.95-7.00 (m, H-Ar and CH-oxime), NH_2 -undetected. - Ms, m/z (%): 187 (100, $M^{+\cdot}$), 171 (59), 170 (78), 155 (7), 143 (19), 142 (40), 128 (5), 116 (35), 115 (15), 89 (13); HR-ms calcd and found - 187.0746 ($C_{10}H_9N_3O$).

2-Aminothiophene-3-carboxime (4f) and ***3-aminothiophene-2-carboxime (4g)***; crude mixtures, directly used for the next steps without analysing.

Cyclocondensation.

The crude aromatic *ortho*-aminooxime (**4a-h**; 0.5 mmol) was suspended in the appropriate orthoester ($HC(OEt)_3$, $MeC(OEt)_3$, $EtC(OEt)_3$, n-$BuC(OMe)_3$; 2-3 ml) and the reaction mixture was stirred at room

*temperature until completion (exempt: **12** and **16**, see* Table). *The excess of the orthoester was removed* under reduced pressure and the product was chromatographed ($CHCl_3$ to $CHCl_3$/MeOH - 20:1 mixture as solvent system). Analytical samples were recrystallized (see Table).

(5): - ^{1}H Nmr (acetone-d_6): 8.99 and 8.90 (2xs, 2H, H-2,4), 7.98 (d, J=9.0, 1H, H-8), 7.96 (broad s, 1H, H-5), 7.74 (dd, J=9.0,2.2, 1H, H-7). - Ms, m/z (%): 182 (38) and 180 (100) [isotopic $M^{+\cdot}$], 166 (13), 164 (40), 154 (18), 152 (70), 150 (60), 137 (22), 125 (44), 123 (32), 117 (15), 110 (17), 100 (9), 90 (16), 75 (18), 63 (26), 50 (8); HR-ms calcd for $C_8H_5N_2ClO$ - 180.0090, Found - 180.0087.

(6): - ^{1}H Nmr ($CDCl_3$): 8.83 (s, 1H, H-4), 7.81 (d, J=9.1, 1H, H-8), 7.39 (d, J=9.1, 1H, H-7), 7.02 (s, 1H, H-5), 2.85 (s, 3H, CH_3). - Ms, m/z (%): 196 (10) and 194 (29) [isotopic $M^{+\cdot}$], 177 (62), 160 (43), 159 (29), 136 (57), 135 (76), 134 (100), 107 (71), 71 (52), 58 (62), 44 (48), 42 (52); HR-ms calcd for $C_9H_7N_2ClO$ - 194.0247, Found - 194.0273.

(7): - ^{1}H Nmr ($CDCl_3$): 8.89 (s, 1H, H-4), 8.16-7.63 (m, 3H, H-Ar), 3.23 (t, J=7.4, CH_2), 2.00-1.40 (m, 2xCH_2), 1.00 (t, J=7.2, CH_3). - Ms, m/z (%): 236 (1, $M^{+\cdot}$), 235 (1), 221 (36), 220 (18), 219 (100), 207 (13), 196 (6), 194 (18), 191 (13), 178 (30), 164 (13), 152 (7), 150 (7), 75 (5); HR-ms calcd and found for $C_{12}H_{13}N_2ClO$ - 236.0717. - Anal. Calcd for $C_{12}H_{13}N_2ClOx3/2H_2O$: C 54.65, H 6.12, N 10.62. Found: C 54.70, H 6.23, N 10.24.

(8): - ^{1}H Nmr ($CDCl_3$): 8.51 (d, J=2.2, 1H, H-4), 8.48 (s, 1H, H-2), 8.07 (dd, J=8.6,2.2, 1H, H-7), 7.89 (d, J=8.6, 1H, H-8), 7.74-7.40 (2xm, 6H, H-5 and H-Ph). - Ms, m/z (%): 222 (100, $M^{+\cdot}$), 206 (31), 195 (40), 194 (66), 167 (25), 166 (23), 152 (22), 140 (20), 139 (27), 115 (8), 102 (13), 76 (6); HR-ms calcd for $C_{14}H_{10}N_2O$ - 222.0793, Found - 222.0797.

(9): - ^{1}H Nmr ($CDCl_3$): 8.95 (s, 1H, H-4), 8.00 (s, 1H, H-5), 7.82-7.30 (m, 7H, H-7,8 and H-Ph), 2.90 (s, 3H, CH_3). - Ms, m/z (%): 236 (10, $M^{+\cdot}$), 220 (100), 194 (14), 193 (20), 177 (7), 152 (51), 102 (35), 76 (23), 63 (7), 44 (7); HR-ms calcd for $C_{15}H_{12}N_2O$ - 236.0950, Found - 236.0948. - Anal. Calcd for $C_{15}H_{12}N_2O$: C 76.25, H 5.12, N 11.86. Found: C 75.96, H 5.17, N 11.49.

(10): - ^{1}H Nmr ($CDCl_3$): 9.17 and 8.88 (2xd, J=2.2, 2H, H-2,4), 9.10-9.03 (m, 1H, H-10), 7.97 and 7.55 (2xd, J=8.8, 2H, H-5,6), 7.97-7.90 and 7.85-7.74 (2xm, 3H, H-7,8,9). - Ms, m/z (%): 196 (100, $M^{+\cdot}$), 180 (54), 169 (15), 168 (54), 153 (10), 141 (19), 140 (35), 139 (16), 126 (19), 114 (16), 63 (9); HR-ms calcd for $C_{12}H_8N_2O$ - 196.0637, Found - 196.0633. - Anal. Calcd for $C_{12}H_8N_2O$: C 73.46, H 4.11, N 14.28. Found: C 73.44, H 3.87, N 14.09.

(11): - ^{1}H Nmr ($CDCl_3$): 9.08-9.01 (m, 1H, H-10), 8.84 (s, 1H, H-4), 7.89-7.66 (m, 4H, H-Ar), 7.43 (d, J=9.0, 1H, H-5 or H-6), 3.31 (q, J=7.4, 2H, CH_2), 1.53 (t, J=7.4, 3H, CH_3). - Ms, m/z (%): 224 (26, $M^{+\cdot}$), 208 (42), 207 (100), 180 (19), 179 (11), 168 (6), 153 (8), 152 (10), 140 (6), 127 (8), 126 (13); HR-ms calcd for $C_{14}H_{12}N_2O$ - 224.0950, Found - 224.0952. - Anal. Calcd for $C_{14}H_{12}N_2O$: C 74.98, H 5.39, N 12.49. Found: C 74.83, H 5.33, N 12.42.

(12): - ^{1}H Nmr ($CDCl_3$): 9.31 (dm, J=8.3, 1H, H-10), 9.19 (d, J=2.0, 1H, H-2[*]), 9.11 (dd, J=4.4,1.7, 1H, H-8), 8.94 (d, J=2.0, 1H, H-4[*]), 8.23 (d, J=9.2, 1H, H-6[#]), 7.82 (d, J=9.2, 1H, H-5[#]), 7.72 (dd, J=8.3,4.4, 1H, H-9). - Ms, m/z (%): 197 (100, $M^{+\cdot}$), 181 (59), 169 (28), 168 (16), 154 (23), 142 (33), 140 (16), 127 (23), 115 (24), 114 (16), 100 (9), 88 (10), 63 (9), 50 (9); HR-ms calcd for $C_{11}H_7N_3O$ - 197.0589, Found - 197.0591.

(13): - ^{1}H Nmr ($CDCl_3$/DMSO-d_6 -15:1): 9.01 (s, 1H, H-2[*]), 8.98 (dd, J=4.3,1.6, 1H, H-9), 8.86 (s, 1H, H-4[*]), 8.12 (d, J=8.0, 1H), 7.80 (d, J=8.8, 1H), 7.58-7.46 (m, 2H) [H-Ar]. - Ms, m/z (%): 197 (100, $M^{+\cdot}$), 196 (22), 181 (25), 180 (12), 170 (25), 169 (12), 154 (40), 142 (40), 141 (13), 140 (69), 127 (14), 115 (9), 114 (11), 113 (13), 100 (7), 87 (5), 75 (4), 63 (8), 50 (4); HR-ms calcd for $C_{11}H_7N_3O$ - 197.0589, Found - 197.0586. - Anal. Calcd for $C_{11}H_7N_3O$: C 67.00, H 3.58, N 21.31. Found - C 66.58, H 3.32, N 21.29.

(14): - ^{1}H Nmr ($CDCl_3$): 8.94 and 8.87 (2xs, 2H, H-2,4), 7.77 and 7.25 (2xd, J=6.0, 2H, H-5,6). - Ms, m/z (%): 152 (100, $M^{+\cdot}$), 136 (56), 109 (37), 97 (38), 85 (31), 83 (29), 73 (79), 60 (58), 57 (55), 43 (48); HR-ms calcd for $C_6H_4N_2OS$ - 152.0044, Found - 152.0051.

(15): - ^{1}H Nmr ($CDCl_3$): 8.98 (d, J=1.8, 1H, H-2[*]), 8.91 (dd, J=1.8,0.8, 1H, H-4[*]), 7.90 (d, J=5.5, 1H, H-6[#]), 7.52 (dd, J=5.5,0.8, H-7[#]). - Ms, m/z (%): 152 (79, $M^{+\cdot}$), 136 (100), 135 (14), 124 (28), 109 (43), 97 (23), 83 (12), 82 (18), 70 (18), 64 (10), 57 (11), 45 (55); HR-ms calcd and found - 152.0044 ($C_6H_4N_2OS$).

(16): - ^{1}H Nmr ($CDCl_3$): 8.43 (s, 1H, H-6), 8.22 (s, 1H, H-8), 7.44-7.38 and 7.25-7.19 (2xm, 5H, H-Ph), 5.31 (s, 2H, CH_2), 2.80 (s, 3H, CH_3). - ^{13}C Nmr ($CDCl_3$): 156.1, 151.3, 148.3, 132.9, 129.6, 129.5 (2xC), 129.3, 127.5 (2xC), 123.4, 50.5 (CH_2), 20.1 (CH_3). - Ms, m/z (%): 240 (7, $M^{+\cdot}$), 225 (6), 224 (30), 223 (14), 162 (35), 161 (54), 149 (22), 106 (15), 91 (100), 86 (37), 84 (49), 65 (20), 59 (25), 42 (36); HR-ms calcd for $C_{13}H_{12}N_4O$ - 240.1011, Found - 240.1010; LSIMS(+): 241 (M+H, 100), 91 (99).

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