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AN APPROACH TO FUSED PYRIMIDINE DERIVATIVES *via* SCHIFF BASES OF AROMATIC *ortho*-NITROCARBALDEHYDES. AN INVESTIGATION OF SUBSTITUENT EFFECTS ON THE REACTION COURSE

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The synthesis of fused pyrimidines from the Schiff bases of aromatic ortho-nitrocarbaldehydes is reported. The Schiff bases after selective reduction of the nitro group on 10% Pd/C, followed by condensation of the amines formed with orthoesters, are transformed to the corresponding imidates. Heating of the latter in a sealed tube with an excess of ammonia (or with ammonia in ethanol) gives fused pyrimidines. The influence of various substituents in the aromatic ring of the imine moiety of the Schiff bases on the overall yield of fused pyrimidine derivatives has been investigated. Moderate electron-withdrawing groups gave the best results.

Keywords: fused pyrimidines, Schiff bases, catalytic hydrogenation.

Many simple fused pyrimidines (e.g., purines, pteridines) are biologically active themselves or are essential components of important natural substances such as nucleic acids. For example, a pyrimidine nucleus is embedded in a large number of alkaloids, drugs, antibiotics, agrochemicals, and antimicrobial agents [1], and since the early years of this century, several studies on the synthesis and structure-activity relationships of pyrimidine derivatives have been reported [1, 2]. The limiting factor for their preparation is the availability of starting materials [3-6].

In the previous papers [7-9] we have presented efficient syntheses of fused pyrimidines, starting with *ortho*-nitroarene carboxime derivatives or with *ortho*-(isocyanomethyl)nitroaromatic/nitroheteroaromatic compounds, which were readily available by Vicarious Nucleophilic Substitution of Hydrogen (VNS) [10]. On the other hand, the construction of the pyrimidine ring utilizing the Schiff bases of 4-nitroimidazole-5-carbaldehydes was also described [9]. In that case, a moderate influence of the X substituent in the aromatic ring of the imine moiety was observed on the total yield of fused pyrimidine ring formation.

Herein, an approach to the fused pyrimidine skeleton (*via* Schiff bases) is reported (for preliminary results see [11]), and investigations on two model compounds (**1a**, **1b**) are undertaken to explain how the character of the X substituent influences the reaction yield.

Aldehydes of type **1** on interaction with anilines **2** can be easily transformed into the Schiff bases **3**. The latter (in contrast to oximes [7, 9]), after simple transformations *via* aminoimines **4** to imidates **5**, were used in the cyclocondensation with ammonia (Scheme 1).

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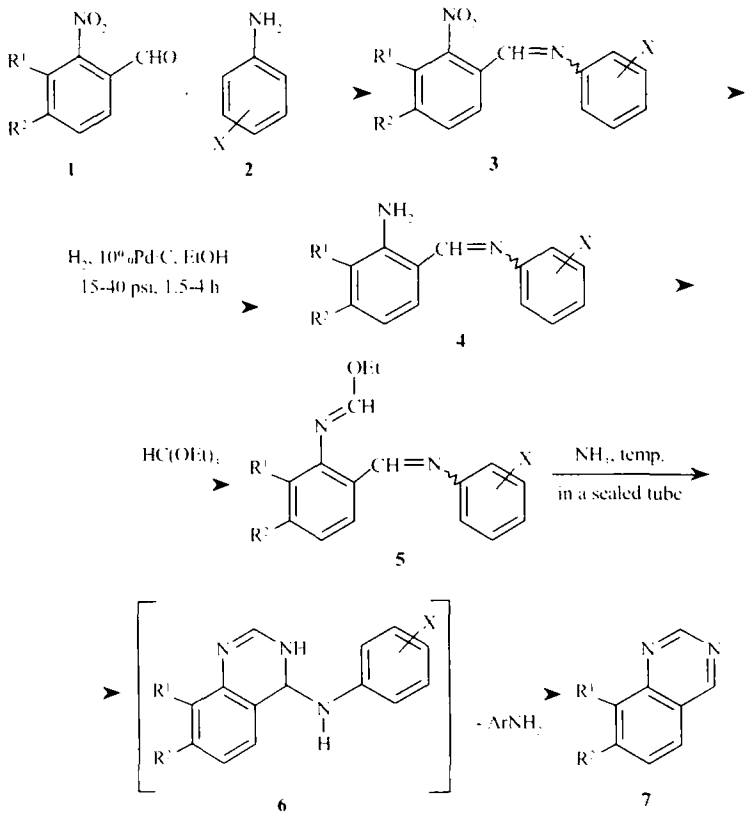
Scheme 1



In this approach, heating of imidates **5** in a sealed tube with an excess of ammonia (80-90°C, 8-12 h) or with a saturated solution of ammonia in ethanol gives fused pyrimidines **7**. Perhaps the first step of this cyclocondensation is the addition of the ammonia moiety to the carbon atom on the >C=N double bond of the Schiff base, and then intramolecular replacement of the OEt group by the amino group by addition-elimination to give intermediate **6**.

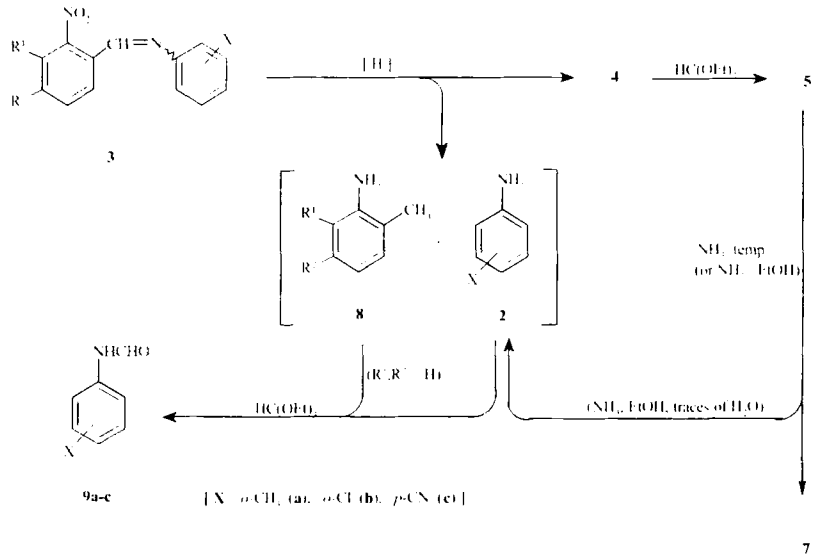
If this postulated reaction sequence operates as shown in Scheme 1, then the last step of this transformation must be the elimination of the arylamino moiety from the dihydro compound **6**. This could indeed be the case, as small amounts of these types of intermediates (see [9]) were identified by the MS method in the post-reaction mixtures along with the main products **7**. It is worth mentioning that the ArNH moiety, under basic conditions, is a rather poor leaving group. Hence, one can expect difficulties in the elimination step leading to the corresponding fused pyrimidine ring.

The transformations from imines **3** to pyrimidines **7**, due to the instability of the intermediates, were carried out step by step without the isolation of **4** and **5**. The reaction of the Schiff base, prepared from the 2-nitrobenzaldehyde (**1a**) and aniline (**2a**; X = H), afforded the fused pyrimidine **7a** in low overall yield (*ca* 5%). The use of naphthalene aldehyde (**1b**) and aniline derivatives (**2k**, **2l**, X = CH_3) gave the appropriate fused pyrimidine **7b** in moderate total yields (23% and 28%, respectively, Table 1). Similar results (21%) were obtained for the Schiff base **3br** prepared from the bulky trityl amine. One should expect the electron-withdrawing groups X in the aryl substituents to make the elimination **6** → **7** faster. An arylamine serving as a source of the good leaving group is needed to prepare the Schiff base, and a *para*-cyanoaniline (**2o**; X = *para*-CN) was selected to check this postulated substituent effect and to improve the yields of pyrimidine derivatives. Initially, it was found that the CN group was resistant to reduction under the catalytic conditions used for the transformation **3** → **4**. However, in the preliminary reaction, when the methyl substituent in the *para* position (Hammett constant: $\sigma_{para}(CH_3) = -0.170$ [12])

was replaced by the strong electron-withdrawing CN group (σ_{para}(CN) = 0.660 [12c]), the yield of the pyrimidine **7b** decreased dramatically (8%), while in the post-reaction mixture, the starting *para*-cyanoaniline (**2o**) and its N-formylated derivative were found (10-15%). Similar results were obtained, or no product was detected, for *ortho*-bromo (**3ab**), *ortho*-chloro (**3ac**), and *para*-phenylsulphonyl (**3af**) substituents as well for 2,4,6-tribromoaniline (**3ag**), 2,4-difluoroaniline (**3bp**), 2-aminopyridine (**3ai**), and 3-aminopyridine (**3aj**) moieties.

We tried to ascertain the influence of X-substitution on the reaction course, and it was found that the strong electron-withdrawing groups (i.e., X = CN, SO_2Ph, 2,4-difluoro-, etc.) increased the reactivity of the imine >C=N double bond; hence, under the reaction conditions used for the reduction of **3**, its hydrogenation (**3** → **8** + **2**) probably occurred, thus decreasing the overall yield. For example, after completion of the reaction sequence (treatment of the crude mixture after reduction of **3** with $HC(OEt)_3$, and cyclocondensation with ammonia), the N-formyl derivative of **9** (R^1,R^2 = H) was identified. This derivative (**9a**) must come from the "aldehyde part" of **3**, supporting the hypothesis of hydrogenation of the Schiff base in the early stage of this synthesis. Additionally, the degradation of the labile >C=N double bond (X = electron-withdrawing group) by NH_3, EtOH, or traces of water during the transformation **5** → **7** can compete with cyclocondensation, giving some amounts of aniline derivative **2**. Then, aniline derivative **2** as well as **8** can be partially formylated by the orthoester. All the discussed transformations are outlined in Scheme 2.

Scheme 2



The yields of fused pyrimidine **7b** (from the Schiff bases in naphthalene series) were higher as compared to **7a** from the benzo derivatives. This can be explained by the easier aromatization of the higher conjugated fused system. Hence, this method is limited for the synthesis of bicyclic fused pyrimidines. For this reason, for some cases in the benzene series (entries **ad**, **ae**, **ah**; Table 1) and in the thiophene series (entry **cr**), the transformations of imines **3** to fused pyrimidines were not realized.

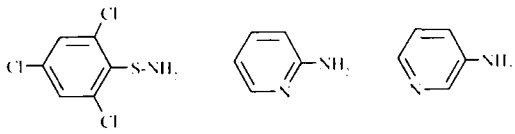
On the other hand, the best results were obtained in the naphthalene series in the case of the moderate electron-withdrawing groups: X = *para*-Br, σ = 0.232 [12] (imine **3bm**, 37%), X = *para*-Cl, σ = 0.227 [12] (imine **3bn**, 28%) or for X = Me; σ_{para} = -0.170, σ_{meta} = -0.069 [12] (imines **3bk**, **3bl**; 23% and 28%, respectively). Optimization of this transformation for the Schiff base **3bk** resulted in a yield of up to 39% product, and in the case of purine synthesis, described elsewhere [9], when X = *para*-Br, the use of this methodology resulted in an even higher product yield (47%) as compared to investigations on the model compounds presented in this paper.

TABLE 1. Intermediates and Products

R^1, R^2	X	Aldehyde	Aniline derivatives	Intermediates 3-6	Fused pyrimidines and yields (%)*
H, H	H	**1a**	**2a**	**aa**	**7a**, *ca* 5
H, H	*o*-Br	**1a**	**2b**	**ab**	**7a**, 3
H, H	*o*-Cl	**1a**	**2c**	**ac**	**7a**, traces
H, H	*m*-Br	**1a**	**2d**	**ad**	*[3]
H, H	*m*-Cl	**1a**	**2e**	**ae**	*[3]
H, H	*p*-SO_2Ph	**1a**	**2f**	**af**	**7a**,
H, H	2,4,6-trbromo	**1a**	**2g**	**ag**	**7a**,
H, H	2,4,6-trichloro	**1a**	**2'h***[2]	**ah**	*[3]
H, H	—	**1a**	**2'i***[2]	**ai**	**7a**, traces
H, H	—	**1a**	**2'j***[2]	**aj**	**7a**, 12
CH=CH CH=CH	*m*-CH_3	**1b**	**2k**	**bk**	**7b**, 23 [39]*[4]
CH=CH CH=CH	*p*-CH_3	**1b**	**2l**	**bl**	**7b**, 28
CH=CH CH=CH	*p*-Br	**1b**	**2m**	**bm**	**7b**, 37
CH=CH CH=CH	*p*-Cl	**1b**	**2n**	**bn**	**7b**, 28
CH=CH CH=CH	*p*-CN	**1b**	**2o**	**bo**	**7b**, 8
CH=CH CH=CH	2,4-difluoro-	**1b**	**2p**	**bp**	**7b**, 7
CH=CH CH=CH	—	**1b**	H_2N CPh_3 **2r**	**br**	**7b**, 21
2-Nitro-3-thiophenecarbaldehyde		**1c**	H_2N CPh_3 **2r**	**cr**	*[3]

* Calculated for the Schiff base 3 (3 steps).

*[2]



2'h **2'i** **2'j**

*[3] The transformations to pyrimidine derivatives were not realized due to decomposition in the earlier step.

*[4] [In brackets] optimized yield.

The ability to access fused pyrimidines is of great importance due to the biological activity of these systems. The approach *via* Schiff bases described herein can also be used for their preparation. The scope and limitations of this method were investigated: in particular, the influence of the X substituent on the overall reaction yield was examined, and we observed the best results for X = moderate electron-withdrawing groups. In this case, the approach presented can also be considered as a preparative method for the synthesis of polycyclic fused pyrimidines.

EXPERIMENTAL

General Methods. NMR spectra were recorded on a Varian Gemini-200 spectrometer (200 MHz for ^1H and 50 MHz for ^{13}C). Mass spectra were measured on an AMD 604 (AMD Intectra GmbH, Germany) spectrometer (electron impact and LSIMS (+) methods). Melting points are uncorrected. TLC analysis was performed on aluminum foil plates pre-coated with silica gel 60F 254 (Merck). Silica gel 200-300 mesh (Merck AG) was used for column chromatography.

The starting 1-nitronaphthalene-2-carbaldehyde (**1b**) and 2-nitrothiophene-3-carbaldehyde (**1c**) were prepared from the corresponding commercially available aromatic nitrocompounds according to the procedures described in the literature [13]. 2,4,6-Trichlorophenylsulfenamide (**2'h**) was prepared from 2,4,6-trichlorobenzenethiol sodium salt according to the typical procedure [14]. 4-(Phenylsulfonyl)aniline (**2f**) was obtained by catalytic reduction of 4-nitrophenyl phenyl sulfone (10% Pd/C, 20 psi, 3 h, in EtOH; quantitatively), mp 174-175°C (EtOH) (lit. mp 173-175°C [15a]) and *para*-cyanoaniline (**2o**) was obtained by catalytic reduction of *para*-nitrobenzonitrile (10% Pd/C, 40 psi, 2 h, in EtOH; quantitatively), mp 90-91°C (EtOH) (lit. mp 86°C [15b]). Aminopyridines (**2'i**, **2'j**), tritylamine (**2r**), and other aniline derivatives used are commercially available. 2,4-Difluoroaniline (**2p**) can be also obtained from 2,4-difluoronitrobenzene by catalytic reduction on 10% Pd/C (40 psi, 2 h, in EtOH). The Schiff bases **3** were prepared according to typical procedures [16, 17], optimized in our laboratory.

Preparation of Schiff Bases 3. General Procedures. Procedure A. - Aromatic aldehyde (**1a**, **1b**, **1c** respectively, 3.0 mmol), the proper aniline derivative (3.30 mmol), a catalytic amount of *p*-TsOH acid (2 mg, 0.01 mmol), and $Si(OEt)_4$ (15 ml) were dissolved in toluene (30 ml), and the reaction mixture was refluxed for 10-20 h, until the aldehyde disappeared (TLC monitoring; *n*-hexane–$CHCl_3$, 1 : 1). After cooling, the solvent and most of the $Si(OEt)_4$ were evaporated. The solid residue (after 2 days in refrigerator) was filtered off, washed with *n*-hexane, and recrystallized from chloroform–*n*-hexane (**3ab**, **3ac**, **3ad**, **3ae**, **3ag**, **3ah**, **3aj**, **3bo**), or the residue was purified by column chromatography (**3af**, **3ai**, **3bk**, **3br**, **3cr**; eluent: *n*-hexane–$CHCl_3$, 1 : 1) to give pure Schiff bases (mixtures of *E/Z*-isomers).

Procedure B. - To a solution of aromatic aldehyde (3.0 mmol) and aniline derivative (3.6 mmol) in toluene (30 ml), a catalytic amount of *p*-TsOH acid (10 mg, 0.06 mmol) was added, and the mixture was refluxed for *ca* 8 h (TLC monitoring; $CHCl_3$). After cooling and evaporation to dryness, the crude products were purified by chromatography (eluent: from *n*-hexane–$CHCl_3$, 5 : 1 to $CHCl_3$) to give a mixture of *E/Z*-isomers (products **3aa**, **3bl**, **3bm**, **3bn**, and **3bp** were obtained).

(*E/Z*)-N-(2-Nitrobenzylidene)aniline (3aa). Solid, yield 71%. ^{1}H NMR spectrum ($CDCl_3$): 8.95 (s, 1H, C<u>H</u>=N); 8.32 (d, J = 7.7 Hz, 1H, H-Ar); 8.09 (d, J = 8.1 Hz, 1H, H-Ar); 7.82-7.57 (m, 2H, H-Ar); 7.49-7.34 (m, 2H, H-Ar); 7.34-7.20 ppm (m, 3H, H-Ar). MS, m/z (I_{rel}, %): 226 (M^+, 46), 210 (15), 209 (100), 195 (6), 180 (13), 179 (76), 178 (29), 167 (10), 153 (38), 152 (55), 151 (16), 134 (6), 105 (12), 104 (11), 92 (12), 77 (57), 76 (15), 51 (23); HR-MS: found: 226.0763. $C_{13}H_{10}N_2O_2$. Calculated: 226.0742.

(*E/Z*)-N-(2-Nitrobenzylidene)-2-bromoaniline (3ab). Solid, yield 82%. ^{1}H NMR spectrum ($CDCl_3$): 8.98 (s, 1H, C<u>H</u>=N); 8.59-8.52 (m, 2H, H-Ar); 8.31 (dd, J = 7.7, 1.6 Hz, 1H, H-Ar); 8.11 (dd, J = 8.1, 1.4 Hz, 1H, H-Ar); 7.83-7.56 (m, 3H, H-Ar); 7.37 ppm (ddd, J = 8.1, 4.7, 0.8 Hz, 1H, H-Ar). MS, m/z (I_{rel}, %): 306 (29), 304 (29) [isotopic M^+], 290 (9), 289 (63), 288 (9), 287 (63), 260 (4), 259 (25), 258 (5), 257 (26), 208 (10), 195 (14), 181 (17), 180 (100), 179 (15), 178 (52), 177 (15), 167 (10), 158 (2), 157 (20), 156 (2), 155 (20), 152 (43), 151 (28), 134 (8), 104 (12), 91 (8), 77 (17), 76 (38), 75 (24), 63 (11), 51 (14), 50 (15). Found, %: C 51.06; H 2.77; N 9.05; Br 26.20. $C_{13}H_9BrN_2O_2$ (305.13). Calculated, %: C 51.17; H 2.97; N 9.18; Br 26.19.

(*E/Z*)-N-(2-Nitrobenzylidene)-2-chloroaniline (3ac). Solid, yield 90%. ^{1}H NMR spectrum ($CDCl_3$): 8.90 (s, 1H, C<u>H</u>=N); 8.38 (dd, J = 7.7, 1.6 Hz, 1H, H-Ar); 8.12 (dd, J = 8.1, 1.3 Hz, 1H, H-Ar); 7.83-7.61 (m, 2H, H-Ar); 7.47 (dd, J = 7.6, 1.6 Hz, 1H, H-Ar); 7.38-7.11 ppm (m, 3H, H-Ar). MS, m/z (I_{rel}, %): 262 (13) and 260 (45) [isotopic M^+], 245 (29), 243 (88), 215 (19), 213 (55), 208 (8), 195 (10), 179 (15), 178 (45), 177 (18), 167 (7), 152 (100), 151 (26), 139 (11), 134 (11), 126 (12), 113 (8), 111 (28), 104 (11), 89 (6), 77 (11), 76 (17), 75 (25), 63 (7), 51 (10), 50 (9). Found, %: C 59.87; H 3.19; N 10.68; Cl 13.43. $C_{13}H_9ClN_2O_2$ (260.68). Calculated, %: C 59.90; H 3.48; N 10.75; Cl 13.60.

(*E/Z*)-N-(2-Nitrobenzylidene)-3-bromoaniline (3ad). Solid, yield 86%. ^{1}H NMR spectrum ($CDCl_3$): 8.95 (s, 1H, C<u>H</u>=N); 8.31 (dd, J = 7.7, 1.7 Hz, 1H, H-Ar); 8.13 (dd, J = 7.9, 1.6 Hz, 1H, H-Ar); 7.85-7.64 (m, 2H) and 7.50-7.21 ppm (m, 4H) [H-Ar]. MS, m/z (I_{rel}, %): 306 (35) and 304 (36) [isotopic M^+], 290 (15), 289 (95), 288 (16), 287 (100), 274 (5), 260 (5), 259 (25), 258 (5), 257 (24), 208 (12), 195 (10), 180 (67), 179 (20), 178 (68), 177 (19), 167 (11), 158 (3), 157 (29), 156 (5), 155 (30), 152 (54), 151 (32), 134 (18), 119 (7), 104 (18), 77 (24), 76 (48), 75 (41), 63 (15), 51 (17), 50 (19), 39 (9). Found, %: C 51.14; H 2.77; N 9.13; Br 26.28. $C_{13}H_9BrN_2O_2$ (305.13). Calculated, %: C 51.17; H 2.97; N 9.18; Br 26.19.

(*E/Z*)-N-(2-Nitrobenzylidene)-3-chloroaniline (3ac). Solid, yield 94%. ^{1}H NMR spectrum ($CDCl_3$): 8.95 (s, 1H, C<u>H</u>=N); 8.32 (dd, J = 7.7, 1.7 Hz, 1H, H-Ar); 8.14 (dd, J = 8.1, 1.3 Hz, 1H, H-Ar); 7.85-7.64 (m, 2H, H-Ar); 7.44-7.16 ppm (m, 4H, H-Ar). MS, m/z (I_{rel}, %): 262 (13) and 260 (40) [isotopic M^+], 245 (32), 243 (100), 229 (3), 215 (12), 213 (30), 208 (6), 195 (4), 178 (24), 177 (9), 152 (38), 151 (10), 134 (7), 113 (5), 111 (14), 104 (5), 77 (4), 76 (5), 75 (9), 63 (2), 51 (4). Found, %: C 59.31; H 3.20; N 10.46; Cl 12.43. $C_{13}H_9ClN_2O_2$ (260.68). Calculated, %: C 59.90; H 3.48; N 10.75; Cl 13.60.

(*E/Z*)-N-(2-Nitrobenzylidene)-4-(phenylsulfonyl)aniline (3af). Solid, unstable, yield *ca* 55%, it was directly used for the next steps; for crude product ^{1}H NMR and MS spectra were recorded. ^{1}H NMR spectrum ($CDCl_3$): 8.88 (s, 1H, C<u>H</u>=N); 8.26 (dd, J = 7.7, 1.7 Hz, 1H, H-Ar); 8.11 (dd, J = 8.0, 1.2 Hz, 1H, H-Ar); 8.04-7.94 (m, 4H, H-Ar); 7.82-7.66 (m, 2H, H-Ar); 7.64-7.51 (m, 3H, H-Ar); 7.35-7.27 ppm (m, 2H, H-Ar). MS, m/z (I_{rel}, %): 366 (M^+, 26), 350 (23), 349 (100), 334 (6), 319 (9), 195 (5), 180 (8), 179 (10), 178 (17), 166 (5), 152 (11), 151 (11), 134 (7), 125 (16), 104 (7), 77 (30), 51 (5).

(*E/Z*)-N-(2-Nitrobenzylidene)-2,4,6-tribromoaniline (3ag). Solid, yield 84%. ^{1}H NMR spectrum ($CDCl_3$): 8.80 (s, 1H, C<u>H</u>=N); 8.38 (dd, J = 7.6, 1.7 Hz, 1H, H-Ar); 8.17 (dd, J = 7.9, 1.3 Hz, 1H, H-Ar); 7.87-7.66 (m, 2H, H-Ar); 7.76 ppm (s, 2H, $C_6H_2Br_3$). MS, m/z (I_{rel}, %): 466 (11), 464 (30), 462 (30) and 460 (11) [isotopic M^+], 450 (5), 449 (22), 448 (11), 447 (58), 446 (12), 445 (63), 444 (3), 443 (22), 419 (6), 417 (15), 415 (15), 413 (6), 366 (2), 355 (5), 354 (2), 353 (9), 351 (4), 340 (47), 339 (15), 338 (100), 337 (11), 336 (61), 330 (10), 328 (11), 310 (10), 287 (3), 285 (3), 274 (3), 272 (3), 259 (6), 258 (6), 257 (20), 256 (4), 255 (15), 246 (5), 236 (6), 234 (13), 232 (7), 193 (6), 183 (6), 177 (20), 165 (8), 156 (3), 155 (17), 154 (4), 153 (16), 150 (15), 134 (11), 104 (15), 89 (7), 88 (7), 77 (12), 76 (10), 75 (14), 74 (17), 63 (7), 51 (10). Found, %: C 34.04; H 1.79; N 5.85; Br 51.33. $C_{13}H_7Br_3N_2O_2$ (462.92). Calculated, %: C 33.73; H 1.52; N 6.05; Br 51.78.

(*E/Z*)-N-(2-Nitrobenzylidene)-2,4,6-trichlorophenylsulfenamide (3ah). Solid, yield 65%. ^{1}H NMR spectrum ($CDCl_3$): 8.24 (s, 1H, C<u>H</u>=N); 8.08 (dd, J = 7.8, 1.6 Hz, 1H, H-Ar); 8.00 (dd, J = 8.2, 1.2 Hz, 1H, H-Ar); 7.70-7.46 (m, 2H, H-Ar); 7.54 ppm (s, 2H, $C_6H_2Cl_3$). MS, m/z (I_{rel}, %): 366 (<1), 364 (3), 362 (8) and 360 (8) [isotopic M^+], 282 (1), 280 (2), 252 (2), 229 (4), 227 (5), 225 (1), 214 (13), 213 (11), 212 (13), 211 (11) 190 (2), 180 (3), 178 (15), 176 (18), 149 (9), 133 (100), 119 (3), 103 (10), 91 (5), 79 (6), 65 (8), 51 (5). Found, %: C 42.92; H 1.84; N 8.00; Cl 29.64; S 9.07. $C_{13}H_7Cl_3N_2O_2S$ (361.63). Calculated, %: C 43.18; H 1.95; N 7.75; Cl 29.41; S 8.85.

(*E/Z*)-N-(2-Nitrobenzylidene)-2-aminopyridine (3ai). Solid, unstable, yield *ca* 14%, it was directly used for the next steps; for crude product ^{1}H NMR spectrum and MS spectra were recorded. ^{1}H NMR spectrum ($CDCl_3$): 9.56 (s, 1H, C<u>H</u>=N); 8.52 (ddd, J = 4.8, 1.9, 0.8 Hz, 1H, H-Ar); 8.34 (dd, J = 7.6, 1.6 Hz, 1H, H-Ar); 8.17-7.23 ppm (m, 6H, H-Ar). MS, m/z (I_{rel}, %): 227 (M^+, 17), 210 (55), 197 (18), 182 (40), 181 (84), 180 (48), 179 (33), 168 (43), 152 (37), 134 (7), 127 (15), 121 (42), 104 (26), 94 (30), 79 (51), 78 (100), 67 (16), 51 (30).

(*E/Z*)-N-(2-Nitrobenzylideno)-3-aminopyridine (3aj). According to Procedure A; solid, yield 94%. ^{1}H NMR spectrum ($CDCl_3$): 8.86 (s, 1H, C<u>H</u>=N); 8.40 (dd, J = 7.7, 1.6 Hz, 1H, H-Ar); 8.12 (dd, J = 8.1, 1.3 Hz, 1H, H-Ar); 7.83-7.61 (m, 3H, H-Ar); 7.42-7.33 (m, 1H, H-Ar); 7.18-7.08 ppm (m, 2H, H-Ar). MS, m/z (I_{rel}, %): 227 (M^+, 28), 210 (100), 180 (36), 179 (33), 154 (13), 153 (11), 134 (11), 127 (27), 104 (13), 78 (34), 63 (7), 51 (30). Found, %: C 63.32; H 3.86; N 18.64. $C_{12}H_9N_3O_2$ (227.22). Calculated, %: C 63.43; H 3.99; N 18.49.

(*E/Z*)-N-(1-Nitro-2-naphthylidene)-3-methylaniline (3bk). Solid, yield 58%. ^{1}H NMR spectrum ($CDCl_3$): 8.60 (s, 1H, C<u>H</u>=N); 8.36 and 8.05 (two d, J = 8.8 Hz, 2H, H-Ar); 8.00-7.93 (m, 1H, H-Ar); 7.89-7.82 (m, 1H, H-Ar); 7.75-7.63 (m, 2H, H-Ar); 7.38-7.04 (m, 4H, H-Ar); 2.41 ppm (s, 3H, CH_3). MS, m/z (I_{rel}, %): 290 (M^+, 80), 273 (100), 258 (10), 245 (20), 242 (23), 230 (25), 215 (19), 202 (49), 184 (5), 169 (14), 154 (11), 141 (8), 140 (7), 126 (11), 114 (10), 106 (12), 91 (27), 79 (5), 65 (15). Found, %: C 73.61; H 4.62; N 9.11. $C_{18}H_{14}N_2O_2$ (290.32). Calculated, %: C 74.47; H 4.86; N 9.65.

(*E/Z*)-N-(1-Nitro-2-naphthylideno)-4-methylaniline (3bl). Solid, yield 71%. ^{1}H NMR spectrum ($CDCl_3$): 8.60 (s, 1H, C<u>H</u>=N); 8.37 and 8.04 (two d, J = 8.6 Hz, 2H, H-Ar); 8.00-6.89 (m, 8H, H-Ar); 2.39 ppm (s, 3H, CH_3). MS, m/z (I_{rel}, %): 290 (M^+, 10), 273 (10), 259 (5), 258 (6), 245 (5), 243 (4), 230 (5), 215 (5), 202 (11), 195 (4), 194 (4), 169 (3), 149 (8), 107 (94), 106 (100), 92 (7), 91 (25), 79 (18), 77 (20), 65 (7), 63 (4), 53 (4), 51 (5), 39 (5). HR-MS: found: 290.1057. $C_{18}H_{14}N_2O_2$. Calculated: 290.1055.

(*E/Z*)-N-(1-Nitro-2-naphthylidene)-4-bromoaniline (3bm). Solid, yield 75%. ^{1}H NMR spectrum ($CDCl_3$): 8.56 (s, 1H, C<u>H</u>=N); 8.33 and 8.05 (two d, J = 8.7 Hz, 2H, H-Ar); 8.00-7.80 (m, 2H, H-Ar); 7.74-7.62 (m, 2H, H-Ar); 7.53 and 7.15 ppm (AA'XX', 4H, H-Ar). MS, m/z (I_{rel}, %): 356 (28) and 354 (28) [isotopic $M^{+\cdot}$], 339 (54), 337 (54), 326 (5), 325 (8), 324 (17), 323 (7), 322 (13), 309 (3), 308 (3), 258 (7), 245 (4), 244 (5), 243 (7), 231 (19), 230 (100), 229 (19), 228 (25), 227 (24), 217 (7), 216 (12), 215 (9), 203 (14), 202 (75), 201 (30), 200 (19), 189 (6), 185 (5), 184 (6), 183 (5), 169 (18), 157 (17), 155 (17), 154 (18), 153 (8), 142 (4), 141 (12), 140 (15), 127 (15), 126 (26), 115 (13), 114 (21), 113 (7), 107 (6), 101 (19), 100 (21), 88 (14), 87 (8), 76 (17), 75 (19), 63 (8), 58 (11), 51 (5), 50 (7), 44 (6), 43 (29), 39 (5). HR-MS: found: 354.0002. $C_{17}H_{11}N_2BrO_2$. Calculated: 354.0004.

(*E/Z*)-N-(1-Nitro-2-naphthylidene)-4-chloroaniline (3bn). Solid, yield 55%. ^{1}H NMR spectrum ($CDCl_3$): 8.57 (s, 1H, C<u>H</u>=N); 8.36 and 8.07 (two d, J = 8.5 Hz, 2H, H-Ar); 8.02-7.95 (m, 1H, H-Ar); 7.90-7.84 (m, 1H, H-Ar); 7.74-7.66 (m, 2H, H-Ar); 7.45-7.36 and 7.28-7.19 ppm (AA'XX', 4H, H-Ar). MS, m/z (I_{rel}, %): 312 (22) and 310 (63) [isotopic $M^{+\cdot}$], 296 (7), 295 (34), 294 (21), 293 (100), 280 (5), 278 (10), 265 (9), 263 (9), 258 (8), 251 (5), 236 (7), 231 (12), 230 (64), 229 (17), 228 (30), 227 (22), 216 (8), 203 (14), 202 (75), 201 (30), 200 (11), 184 (8), 170 (5), 169 (15), 154 (20), 153 (8), 141 (9), 140 (12), 139 (8), 129 (5), 128 (7), 127 (18), 126 (32), 114 (13), 113 (9), 111 (25), 100 (10), 75 (15), 63 (4), 51 (4). HR-MS: found: 310.0506. $C_{17}H_{11}N_2ClO_2$. Calculated: 310.0509.

(*E/Z*)-N-(1-Nitro-2-naphthylidene)-4-cyanoaniline (3bo). Solid, yield 84%. ^{1}H NMR spectrum ($CDCl_3$): 8.53 (s, 1H, C<u>H</u>=N); 8.32 and 8.08 (two d, J = 8.7 Hz, 2H, H-Ar); 8.02-7.66 (m, 6H, H-Ar); 7.34–7.25 ppm (part of AA'XX', 2H, H-Ar). MS, m/z (I_{rel}, %): 301 ($M^{+\cdot}$, 32), 284 (100), 253 (20), 242 (9), 228 (14), 227 (27), 201 (12), 184 (11), 169 (7), 154 (18), 140 (7), 126 (14), 114 (5), 102 (15), 75 (5). Found, %: C 71.06; H 3.17; N 13.56. $C_{18}H_{11}N_3O_2$ (301.30). Calculated, %: C 71.75; H 3.68; N 13.95.

(*E/Z*)-N-(1-Nitro-2-naphthylidene)-2,4-difluoroaniline (3bp). Semi-crystalline, unstable, yield *ca* 32%, it was used for the next steps; for crude product ^{1}H NMR spectrum and MS spectra were recorded. ^{1}H NMR spectrum ($CDCl_3$): 8.67 (s, 1H, C<u>H</u>=N); 8.38 and 8.07 (two d, J = 8.7 Hz, 2H, H-Ar); 8.01-7.95 (m, 1H, H-Ar); 7.91-7.84 (m, 1H, H-Ar); 7.75-7.65 (m, 2H, H-Ar); 7.30-7.16 (m, 1H, H-Ar); 7.02-6.88 ppm (m, 2H, H-Ar). MS, m/z (I_{rel}, %): 312 ($M^{+\cdot}$, 53), 296 (24), 295 (100), 280 (11), 267 (16), 265 (21), 264 (29), 263 (9), 259 (14), 253 (14), 245 (13), 239 (52), 238 (73), 220 (12), 219 (40), 189 (5), 184 (10), 171 (7), 169 (8), 156 (5), 155 (5), 154 (20), 141 (12), 140 (12), 128 (11), 127 (12), 126 (23), 115 (8), 113 (12), 97 (6), 85 (9), 71 (13), 69 (10), 63 (7), 57 (17), 55 (8), 43 (12), 41 (8).

(*E/Z*)-N-(1-Nitro-2-naphthylidene)tritylamine (3br). Solid, yield 42%. ^{1}H NMR spectrum ($CDCl_3$): 8.29 and 8.05 (two d, J = 8.6 Hz, 2H, H-Ar); 8.21 and 7.99 (two s, 1H, C<u>H</u>=N, *E/Z* isomers); 7.98-7.50 (m, 4H, H-Ar); 7.39-7.20 ppm (m, 15H, 3×Ph). MS, m/z (I_{rel}, %): 365 (<1, M-Ph), 347 (<1), 319 (<1), 257 (3), 244 (20), 243 (100), 228 (5), 215 (4), 165 (30), 77 (3). Found, %: C 80.02; H 4.65; N 6.08. $C_{30}H_{22}N_2O_2$ (442.52). Calculated, %: C 81.43; H 5.01; N 6.33.

(*E/Z*)-N-(2-Nitro-3-thienylidene)tritylamine (3cr). Solid, yield 61%. ^{1}H NMR spectrum ($CDCl_3$): 8.58 (s, 1H, C<u>H</u>=N); 7.86 and 7.46 (two d, J = 5.6 Hz, 2H, H-4,5); 7.39-7.20 ppm (m, 15H, 3×Ph). MS, m/z (I_{rel}, %): 398 ($M^{+\cdot}$, <1), 321 (<1), 288 (<1), 274 (<1), 243 (100), 228 (8), 165 (48), 77 (2). Found, %: C 72.71; H 4.48; N 6.11. $C_{24}H_{18}N_2O_2S$ (398.48). Calculated, %: C 72.34; H 4.55; N 7.03.

Catalytic Hydrogenation of Schiff Bases 3. The Schiff base **3** dissolved in ethanol (*ca* 5 ml for 100 mg) was hydrogenated in a Parr apparatus using *ca* 20 mg of catalyst (10% Pd/C): **3aa**, **3ab**, **3ac**, **3ai**, **3bk**, **3br** - 20 psi, 2.5 h; **3af**, **3aj** - 20 psi, 1.5 h; **3ag** - 15 psi, 3 h; **3bo** - 30 psi, 2 h: **3bl**, **3bn**, **3bm**, **3bp** - 40 psi, 4 h. The reactions were monitored by TLC ($CHCl_3$). After the reduction, the catalyst was filtered off and washed with methanol. The solvent was evaporated to give the desired products **4**. These crude products were used for the next steps.

For the crude imine **4aa** ^{1}H NMR spectrum and LSIMS (+) spectra were recorded. ^{1}H NMR spectrum ($CDCl_3$): 8.56 (s, 1H, C<u>H</u>=N); 7.63-6.86 (m, 5H, H-Ar); 6.69-6.41 (m, 4H, H-Ar); 4.98 (broad s, 2H, NH_2). LSIMS (+), m/z (I_{rel}, %): 197 (M+1, 11).

Transformation of Imines 4 to Fused Pyrimidines. The above crude imines **4** (*ca* 100 mg) were suspended in triethyl orthoformate (5 ml) and the mixture was refluxed until the reaction was completed (*ca* 15-20 h; TLC monitoring, $CHCl_3$). The excess of the orthoester was removed under reduced pressure and the residue (crude imidates **5**) was dissolved in dried liquid ammonia (2 ml; in a sealed tube). The reaction mixture

was heated for 8-12 h at 80-90°C (the critical temperature for NH_3, 132°C under pressure 111.5 atm, not alowing to reach). Then the sealed tube was cooled to -50°C, opened, and the ammonia was evaporated to give crude products **7a**, **7b**. They were purified by column chromatography (eluent: from $CHCl_3$ to $CHCl_3$–MeOH, 20:1). Yields are given in Table 1.

Quinazoline (7a); mp 45-46°C (*n*-hexane) (lit. mp 47-48°C [18]). ^{1}H NMR spectrum ($CDCl_3$): 9.41 (s, 1H, H-2); 9.34 (s, 1H, H-4); 8.10-8.03 (m, 1H, H-8); 7.99-7.88 (m, 2H, H-Ar); 7.67 ppm (ddd, J = 8.3, 6.8, 1.3 Hz, 1H, H-Ar). ^{13}C NMR spectrum ($CDCl_3$): 160.2, 155.2, 149.9, 134.1, 128.3, 127.9, 127.1, 125.0 ppm. MS, m/z (I_{rel}, %): 130 (M^+, 100), 103 (60), 76 (28), 50 (14).

Benzo[*h*]quinazoline (7b); mp 101-102°C (*n*-hexane) (lit. mp 102-103°C [19]). ^{1}H NMR spectrum ($CDCl_3$): 9.47 (s, 1H, H-2); 9.35 (s, 1H, H-4); 9.30-9.22 (m, 1H, H-Ar); 7.96-7.70 (m, 3H, H-Ar); 7.90 and 7.72 ppm (two d, J = 8.9 Hz, 2H, H-5,6). ^{13}C NMR spectrum ($CDCl_3$): 158.2, 155.4, 150.3, 135.2, 130.3, 129.2, 128.1, 127.7, 127.6, 124.7, 123.2, 122.8 ppm. MS, m/z (I_{rel}, %): 180 (M^+, 100), 153 (27), 126 (47), 118 (3), 90 (4), 76 (5), 63 (12).

N-(*ortho*-Tolyl)formamide (9a). Semi-crystalline, *ca* 95% purity. ^{1}H NMR spectrum ($CDCl_3$): 8.73-8.10 (m, *ca* 3H, NHCHO and its tautomers, *E/Z*; 1H of H-Ar); 7.58-7.05 (m, *ca* 3H, H-Ar); 2.30 ppm (s, 3H, CH_3). MS, m/z (I_{rel}, %): 135 (M^+, 30), 121 (100), 107 (13), 106 (35), 93 (45), 77 (7), 75 (7), 66 (23), 51 (6), 39 (10).

N-(2-Chlorophenyl)formamide (9b). Semi-crystalline, *ca* 90% purity. ^{1}H NMR spectrum ($CDCl_3$): 9.12-8.41 (m, 2H, CHO and its tautomers, *E/Z*; 1H of H-Ar); 7.90-6.88 ppm (m, *ca* 4H, H-Ar and NH). MS, m/z (I_{rel}, %): 157 (12) and 155 (38) [isotopic M^+], 129 (24), 127 (72), 120 (100), 106 (5), 100 (11), 99 (12), 92 (33), 91 (16), 73 (7), 65 (29), 52 (8), 39 (14).

N-(4-Cyanophenyl)formamide (9c); mp 186-190°C ($CHCl_3$) (lit. mp 189-190°C [20]). ^{1}H NMR spectrum ($CDCl_3$): 8.45 (s, 1H, CHO); 7.80-7.60 ppm (AA'XX', 4H, H-Ar); NH - undetected. MS, m/z (I_{rel}, %): 147 (M+1, 7), 146 (M^+, 63), 119 (12), 118 (100), 117 (7), 91 (51), 90 (13), 64 (12), 63 (9).

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