DOI: 10.1002/ejoc.201201006

One-Pot Synthesis of *N*-(Imidazo[1,2-*a*]pyridin-3-yl)- and *N*-(Imidazo[2,1-*b*][1,3]thiazol-5-yl)sulfonamides

Igor B. Rozentsveig,*[a] Valery Y. Serykh,[a] Gulnur N. Chernysheva,[a] Kirill A. Chernyshev,[a] Evgeniy V. Kondrashov,[a] Evgeny V. Tretyakov,[b] and Galina V. Romanenko[b]

Keywords: Synthetic methods / Domino reactions / Nucleophilic addition / Nitrogen heterocycles / Sulfonamides

The reaction of 2-aminopyridines or 2-aminothiazole with *N*-(2,2-dichloro-2-phenylethylidene)arensulfonamides affords the corresponding products of nucleophilic addition to the azomethine group, *N*-[2,2-dichloro-2-phenyl-1-(heteryl-amino)ethyl]sulfonamides, in good yields. The latter are easily cyclized to (imidazo[1,2-*a*]pyridin-3-yl)sulfonamides and (imidazo[2,1-*b*]thiazol-5-yl)sulfonamides in the presence of alkali, whereas the expected isomeric (imidazo[1,2-*a*]pyridin-2-yl)sulfonamides and (imidazo[2,1-*b*]thiazol-6-yl)sulfonamides are not formed. A one-pot two-stage method for the synthesis of target heterocyclic compounds without the isolation of intermediates has been developed. A tentative mechanism of the formation of annulated heterocyclic derivatives has been proposed.

Introduction

Heterocyclic compounds containing an imidazo[1,2-*a*]-pyridine moiety are widely applied in medicine[1] as somnifacient, sedative, and anxiolytic agents[1a–1c] (*alpidem*, *zolpidem*, *saripidem*), drugs and promising agents for treatment of gastroesophageal reflux and peptic ulcer diseases[2] (*zolimidine* and analogues), acute heart failure (*olprinone*), osteoporosis (minodronic acid derivatives),[3] diabetes,[4] herpes viruses,[5] and cancer.[6] Imidazo[1,2-*a*]pyridines act as receptor agonists or antagonists,[7] ferment inhibitors and modulators,[8] stimulators of neuroactive steroid synthesis in plasma and in the brain.[9] These properties are associated with a range of pharmacological activities, including anticonvulsant, anxiolytic, immunomodulating, and cardiovascular ones. Prospective radioligands for positron emission tomography for β-amyloid in Alzheimer's disease based on imidazo[1,2-*a*]pyridine derivatives have been widely reported.[10] Accordingly, the development of new methods for the preparation of imidazo[1,2-*a*]pyridines is urgent, because heterocycles of this type are pharmaceutically attractive. Furthermore, imidazopyridines serve as photoluminescent reagents,[11] ionic liquids,[12] ligands,[6] and key reagents in modern heterocyclic chemistry for the synthesis of diverse annulated structures.[10f,13]

The most generally applied methods for the synthesis of pharmaceutical imidazo[1,2-*a*]pyridines are based on the reactions of 2-aminopyridines with bromoaldehydes or bromoketones.[5,9a,9c,13a,14] New methods leading to functionalized imidazo[1,2-*a*]pyridines through *N*-(pyridin-2-yl)amidines have been recently reported.[15a,15b] Multi-component reactions[16] of 2-aminopyridine with aldehydes and isocyanides, nitrile, thiocyanates, imidazoline-2,4,5-trione or acetylene, cascade synthesis,[17] and palladium catalyzed C–C bond cross-coupling reactions[18] are very promising for the preparation of imidazo[1,2-*a*]pyridine derivatives. Synthetic approaches based on benzotriazoles,[19] pyridinium fluorides,[20] diazoketones,[21] oxothioamide,[22] and vicinal diols[23] are also known. A simple method is coupling of 2-aminopyridine with acetophenones in the presence of acids.[24]

The protocols described open up approaches to obtain a broad range of various imidazo[1,2-*a*]pyridines. However, described methods for the synthesis of imidazo[1,2-*a*]pyridines have disadvantages; high costs of reagents, labor intensive syntheses, low selectivity and difficulties optimizing reaction conditions for multigram quantities of products. In this regard, improving the range of methods available to chemists and technologists for the synthesis of imidazo[1,2-*a*]pyridines or related heterocyclic systems remains a challenge.

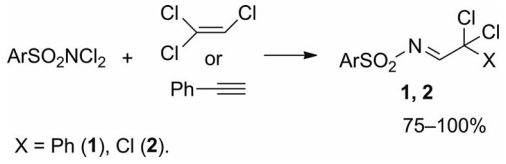
To develop a synthetic route for unknown *N*-(2,2,2-trichloroethyl)- and *N*-(2,2-dichloro-2-phenylethyl)sulfonamides as well as new derivatives of imidazo[1,2-*a*]pyridine

[a] A.E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences,
Favorsky Str. 1, Irkutsk 664033, Russian Federation
Fax: +7-3952-419346
E-mail: i_roz@irioch.irk.ru
Homepage: http://www.irkinstchem.ru
[b] International Tomography Center, Siberian Branch of the Russian Academy of Sciences,
Institutskaya Str. 3a, Novosibirsk 630090, Russia

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201201006.

and imidazo[2,1-*b*]thiazole containing pharmacophoric sulfonylamino groups we studied the reaction of 2-aminopyridines and 2-aminothiazole with *N*-(2,2-dichloro-2-phenylethylidene)- and *N*-(2,2,2-trichloroethylidene)arenesulfonamides **1** and **2**.

Imines **1** and **2** represent electron-deficient halogen-containing azomethines.[25] At present, these highly electrophilic reagents are available through synthetic methods based on free-radical reactions of *N*,*N*-dichlorosulfonamides with trichloroethylene or phenylacetylene[25,26] (Scheme 1). The ability of polyhalogenated *N*-sulfonylaldimines to react with various nucleophiles is used to design diverse acyclic and heterocyclic sulfonamide derivatives.[25,26b,27]

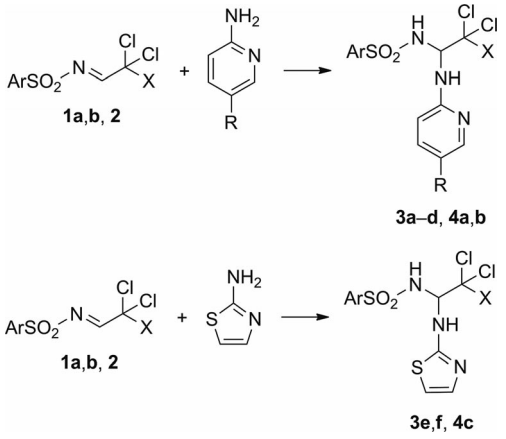


Scheme 1. Synthesis of imines **1** and **2** from *N*,*N*-dichlorosulfonamides.

It was found that the reaction of imines **1** and **2** with primary and secondary amines depends on the nature of the amine. Anilines and primary amines gave products arising from *N*-nucleophilic addition to the activated C=N group,[25] whereas more basic secondary amines led to the formation of amidine derivatives, which are the products of haloform cleavage.[25,26]

Results and Discussion

We have found that reactions of imines **1** and **2** with 2-aminopyridine, 2-amino-5-chloropyridine or 2-aminothiazole are efficient in all the solvents studied (Scheme 2, Table 1). The resulting corresponding products of nucleophilic addition of the aromatic amines to the activated C=N group were *N*-[2-polychloro-1-(2-pyridinylamino)ethyl]- or *N*-[2-polychloro-1-(1,3-thiazol-2-ylamino)ethyl]arenesulfonamides **3** and **4**. The reaction proceeds under mild conditions (room temperature, no catalyst) owing to the high electrophilicity of imines **1** and **2** resulting from the strong electron-withdrawing substituents. The best yields are achieved when the reaction is carried out in polar aprotic solvents [*N*,*N*-dimethylformamide (DMF), dioxane] in which the reagents are easy soluble. At the same time, for adducts **4** the experiment is less laborious when trichloroethylene is used. Imines **2** can be used without isolation from the resulting reaction mixture (Table 1, Entry 11). However, in this case the reaction time is 20 h.



Scheme 2. Formation of adducts **3a**–**f** and **4a**–**c** by the reaction of imines **1a**, **1b** and **2** with 2-aminopyridine, 2-amino-5-chloropyridine or 2-aminothiazole.

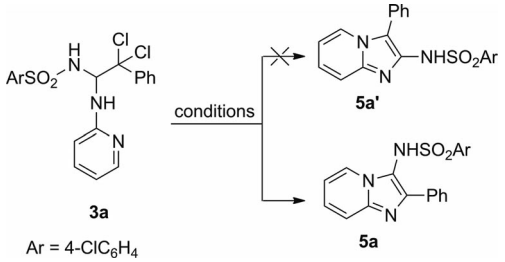
Adducts **3** and **4** are efficient precursors of imidazopyridine or imidazothiazole derivatives owing to the presence of exo- and endocyclic nitrogen atoms and a polychloromethyl group in the structure. So, we have studied their heterocyclization under different conditions with **3a** (Scheme 3).

It has been found that the heterocyclization of compound **3a** occurs in the presence of NaOH or KOH in 1,4-dioxane (Table 2, Entry 14) or in toluene (Table 2, Entry 16) and unexpectedly delivers 3-sulfonamido-2-phenylimidazo[1,2-*a*]pyridine (**5a**), instead of the anticipated 2-sulfon-

Table 1. Screening of solvents for the synthesis of adducts **3** and **4**.[a]

Entry	Imine **1**, **2**	X	Ar	Adduct **3**, **4**	R	Solvent	Yield [%][b]
1	**1a**	Ph	4-ClC_6H_4	**3a**	H	CCl_4	31
2	**1a**	Ph	4-ClC_6H_4	**3a**	H	ethyl acetate	47
3	**1a**	Ph	4-ClC_6H_4	**3a**	H	CH_3CN	76
4	**1a**	Ph	4-ClC_6H_4	**3a**	H	DMF	92
5	**1a**	Ph	4-ClC_6H_4	**3a**	H	1,4-dioxane	93
6	**1a**	Ph	4-ClC_6H_4	**3b**	Cl	1,4-dioxane	98
7	**1b**	Ph	4-MeC_6H_4	**3c**	H	1,4-dioxane	85
8	**1b**	Ph	4-MeC_6H_4	**3d**	Cl	1,4-dioxane	90
9	**1a**	Ph	4-ClC_6H_4	**3e**	–	1,4-dioxane	94
10	**1b**	Ph	4-MeC_6H_4	**3f**	–	1,4-dioxane	92
11	**2**	Cl	4-ClC_6H_4	**4a**	H	trichloroethylene[c]	51 (90)[d]
12	**2**	Cl	4-ClC_6H_4	**4a**	H	1,4-dioxane	93
13	**2**	Cl	4-ClC_6H_4	**4b**	Cl	1,4-dioxane	90
14	**2**	Cl	4-ClC_6H_4	**4c**	–	1,4-dioxane	88

[a] Conditions: Stirred imine **1** or **2** (3 mmol), aminopyridine or aminothiazole (3.4 mmol), in solvent (10 mL) for 4 h at room temp. [b] Isolated yield. [c] Without isolation of imine **2** from the reaction mixture. [d] Reaction time was 20 h.



Scheme 3. Synthesis of imidazo[1,2-*a*]pyridine **5a** from adduct **3a**.

amido-3-phenylimidazo[1,2-*a*]pyridine (**5a′**). Attempts to use other solvents or solvent-free conditions were unsuccessful or gave **5a** in lower yield. In the presence of potassium or sodium carbonate or triethylamine as base, the reaction does not take place (Table 2, Entries 2–7). Upon heating (Table 2, Entries 1, 3, 7, 10, 13) resinification increased, and was accompanied by cleavage and formation of 4-chlorobenzenesulfonamide in 15–70% yields. The highest yields of 4-chlorobenzenesulfonamide were obtained in the polar solvents DMF or dimethyl sulfoxide (DMSO).

Table 2. Effect of solvent, temperature and base on the yield of imidazo[1,2-*a*]pyridine **5a**.[a]

Entry	Solvent	Base	Temp. [°C]	Conversion of **3a** [%]	Yield of **5a** [%][b]
1	–	–	150	100[c]	0
2	DMF	K_2CO_3	25	8	0
3	DMF	K_2CO_3	50	78	0[d]
4	DMF	Na_2CO_3	25	5	0
5	DMF	$NaHCO_3$	25	2	0
6	DMF	Et_3N	25	17	0
7	DMF	Et_3N	50	91	0[d]
8	DMF	KOH	25	52	38
9	DMF	NaOH	25	45	41
10	DMF	NaOH	50	93	0[d]
11	Et_2O	NaOH	25	83	48
12	CH_3CN	NaOH	25	15	0
13	CH_3CN	NaOH	50	76	5[d]
14	1,4-dioxane	NaOH	25	100	91
15	1,4-dioxane	KOH	25	100	87
15	DMSO	NaOH	25	91	15
16	toluene	NaOH	25	100	85

[a] Adduct **3a** (3 mmol) and base (12 mmol) were stirred in solvent (5 mL) for 3 h. [b] Isolated yield. [c] Strong resinification. [d] The process was accompanied with formation of 4-chlorobenzenesulfonamide.

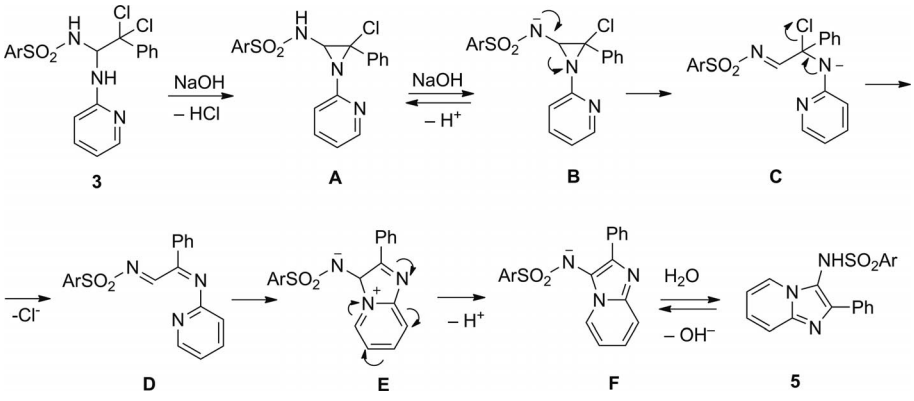
A tentative route for the formation of imidazopyridines can be rationalized as follow. The reaction is triggered by heterocyclization affording aziridine **A**, which is then transformed into anion **B**, followed by formation of intermediate **C** and diimine **D** as a result of the aziridine cycle opening and chlorine anion elimination. The heterocyclization involving the pyridine nitrogen atom and carbon atom of the azomethine group furnishes annulated structure **E** (Scheme 4). Subsequent aromatization owing to elimination of a proton from the 3-position leads to anion **F**, which is quenched by hydrolysis with water produced in the reaction mixture.

The reactivity research of adducts **3b**–**f** has shown that these products (similar to compound **3a**) give hitherto unknown 3-sulfonamido-2-phenylimidazo[1,2-*a*]pyridines **5b**–**d** or the corresponding derivatives of imidazo[2,1-*b*]thiazoles **6a** and **6b**.

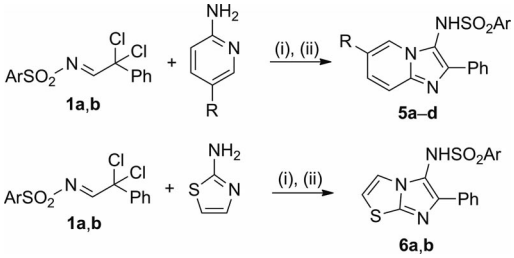
Under the conditions employed, we failed to synthesize the corresponding imidazopyridine derivatives from adducts **4a**–**c** prepared from chloral-imine **2**, and compounds **4a**–**c** were recovered unchanged. Under harsher conditions (application of base and above 100 °C), resinification of the reaction mixture took place.

To optimize the protocol for the preparation of compounds **5a**–**d**, **6a** and **6b**, we selected conditions for a two-stage one-pot synthesis, which would exclude isolation of intermediate adducts **3a**–**f** (Scheme 5, Table 3). The first stage comprises the reaction of the starting azomethines **1a** and **1b** with aminopyridines or aminothiazole, further NaOH is added to the reaction mixture to accomplish the synthesis of target heterocycles **5a**–**d**, **6a** and **6b**.

To prove the relative positions of the sulfonamide fragment and benzene ring in the structure of compounds **5a**–**d**, **6a** and **6b**, we have accomplished the methylation reaction of these annulated heterocycles (Scheme 6, Table 4), because the presence of the methyl groups allows 2D NMR spectroscopic techniques for determination of relative positions of the substituents (see Supporting Information). Besides, methylated derivatives **7a**, **7b** and **8** readily form crys-



Scheme 4. A tentative route for the formation of imidazo[1,2-*a*]pyridines **5**.



Scheme 5. One-pot synthesis of imidazo[1,2-*a*]pyridines **5a**–**d** and imidazo[2,1-*b*]thiazoles **6a** and **6b**. (i) Imine **1** (3 mmol) and heterocyclic amine (3.4 mmol) were stirred in 1,4-dioxane (10 mL) at room temp. for 4 h; (ii) NaOH (12 mmol) was added and the reaction mixture was stirred for 4 h at room temp.

Table 3. Yields of imidazo[1,2-*a*]pyridines **5a**–**d** and imidazo[2,1-*b*]-thiazoles **6a** and **6b** obtained through a two-stage one-pot protocol without isolation of intermediate adducts **3a**–**f**.

Entry	Imine **1**	Ar	Product **5**, **6**	R	Yield [%][a,b]
1	**1a**	4-ClC_6H_4	**5a**	H	84
2	**1a**	4-ClC_6H_4	**5b**	Cl	97
3	**1b**	4-MeC_6H_4	**5c**	H	72
4	**1b**	4-MeC_6H_4	**5d**	Cl	60
5	**1a**	4-ClC_6H_4	**6a**	–	92
6	**1b**	4-MeC_6H_4	**6b**	–	67

[a] Calculated from starting imine **1**. [b] Isolated yield.

tals suitable for X-ray analysis (Figure 1) that makes it possible to establish unambiguously the structure of the heterocyclic compounds synthesized.

Table 4. Yields of methylation products **7a**, **7b**, **8** and **9**.

Entry	Ar	R	Product of methylation	Yield [%][a]
1	4-ClC_6H_4	H	**7a**	30
2	4-ClC_6H_4	H	**7b**	68
3	4-ClC_6H_4	Cl	**8**	87
4	4-ClC_6H_4	–	**9**	83

[a] Isolated yield.

It has been found that under the studied conditions, in the case of compounds **5b** and **6a**, sulfonamide nitrogen atom undergoes methylation even in the presence of excess MeI to afford monomethyl derivatives **8** and **9**. In the case of imidazopyridine **5a**, the reaction proceeds non-selectively

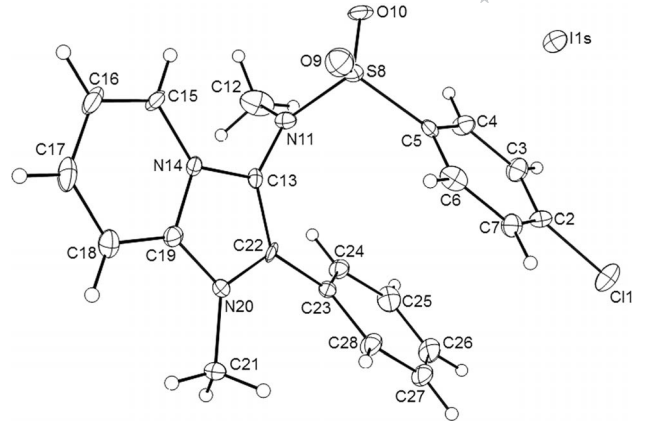
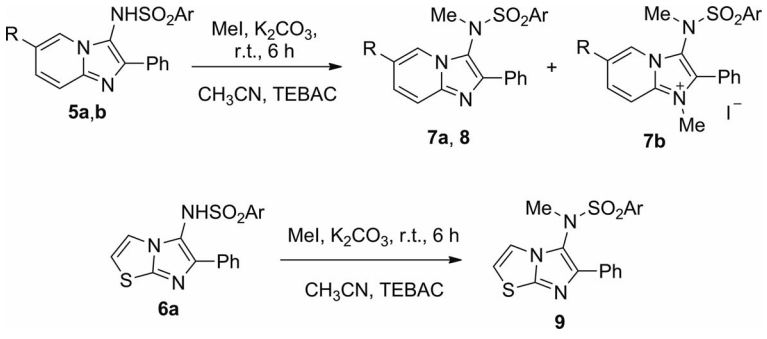


Figure 1. X-ray structure of compound **7b**.

to deliver a mixture of mono- and dimethylated derivatives **7a** and **7b** with the participation of both sulfonamide and one of endocyclic nitrogen atoms.

Conclusions

The reaction of *N*-sulfonylpolychloroacetaldimines with 2-aminopyridine, 2-amino-5-chloropyridine and 2-aminothiazole has been studied for the first time. It has been found that heterocyclic amines adds to electron-deficient imines at room temperature without catalysts to afford the corresponding adducts *N*-[2-polychloro-1-(2-aminopyridyl)ethyl]- and *N*-[2-polychloro-1-(1,3-thiazol-2-ylamino)-ethyl]arenesulfonamides. Heterocyclization of the adducts obtained to give imidazopyridine and imidazothiazole derivatives was investigated. It has been shown that the reaction unexpectedly leads to hitherto unknown (imidazo[1,2-*a*]pyridin-3-yl)sulfonamides and (imidazo[2,1-*b*]thiazol-5-yl)sulfonamides, whereas the expected isomeric (imidazo[1,2-*a*]pyridin-2-yl)sulfonamides and (imidazo[2,1-*b*]thiazol-6-yl)sulfonamides are not formed. A tentative reaction mechanism has been proposed. The one-pot method for the preparation of substituted 3-aminoimidazo[1,2-*a*]pyridines and 5-aminoimidazo[2,1-*b*]thiazoles bearing the protected amino group has been developed.



Scheme 6. Methylation of compounds **5a**, **5b** and **6a**.

Experimental Section

General Remarks: Imines **1a**, **1b**, and **2** were obtained by known methods.[22] All other reagents were reagent grade. The solvents were dried by standard procedures and distilled prior to use. NMR spectra were recorded with a Bruker DPX 400 spectrometer (^{1}H, 400.13 MHz; ^{13}C, 100.61 MHz) at 25 °C with hexamethyldisiloxane as an internal standard. IR spectra were recorded with a Bruker IFS-25 spectrophotometer in KBr. All melting points were measured with a Kofler micro hot stage apparatus. Elemental analyses were obtained by using a Thermo Finnigan Flash series1112 EA analyzer. Single-crystal diffraction data for the compounds were collected with a SMART APEX II CCD (Bruker AXS) automatic diffractometer (Mo-K_α, λ = 0.71073 Å, T = 240 K); an absorption correction was applied by using the Bruker SADABS program, version 2.10. The structures were solved by direct methods and refined by the full-matrix least-squares method in an anisotropic approximation for non-hydrogen atoms. The H atoms were calculated geometrically and used in riding model refinement. All structure solution and refinement calculations were carried out with SHELX-97 and Bruker SHELXTL Version 6.14 program packages.

General Procedure for Synthesis of Adducts 3 and 4: 2-Aminopyridine, 2-amino-5-chloropyridine or 2-aminothiazole (3.4 mmol) was added to a solution of imine **1** or **2** (2.8 mmol) in 1,4-dioxane (10 mL) and stirred with a magnetic stirrer for 4 h at room temp. After this time, the reaction mixture was diluted with water (100 mL), the precipitate was filtered, dried and washed with diethyl ether (50 mL).

***N*-[2,2-Dichloro-2-phenyl-1-(2-pyridinylamino)ethyl]-4-chlorobenzenesulfonamide (3a):** Colorless needles, yield 1.22 g, 95%; m.p. 144–147 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 6.29 (m, 1 H, 3-H), 6.44 (m, 1 H, 5-H), 6.58–6.65 (m, 2 H, CH, NH), 7.17 (m, 1 H, 4-H), 7.20 (AA′BB′, 2 H, 2,6-H 4-ClC$_6$H$_4$), 7.30–7.39 (m, 3 H, 3,4,5-H C$_6$H$_5$), 7.58 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 7.72–7.78 (m, 3 H, 2,6-H C$_6$H$_5$, 6-H), 8.54 (m, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 68.5 (CH), 95.6 (CCl$_2$), 108.7 (C-3), 113.3 (C-5), 127.0 (C-2,6, C$_6$H$_5$), 127.8 (C-3,5, C$_6$H$_5$), 128.0 (C-2,6, 4-ClC$_6$H$_4$), 128.3 (C-3,5, 4-ClC$_6$H$_4$), 129.1 (C-4, C$_6$H$_5$), 136.4 (C-4), 136.7 (C-1, 4-ClC$_6$H$_4$), 139.4 (C-1, C$_6$H$_5$), 139.9 (C-4, 4-ClC$_6$H$_4$), 146.4 (C-6), 155.8 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1163, 1344 (SO$_2$), 1602 (C=N), 3209, 3250, 3399 (NH) cm^{-1}. C$_{19}$H$_{16}$Cl$_3$N$_3$O$_2$S (456.77): calcd. C 49.96, H 3.53, Cl 23.28, N 9.20, S 7.02; found C 50.06, H 3.51, Cl 23.32, N 9.15, S 7.09.

***N*-{2,2-Dichloro-1-[(5-chloro-2-pyridinyl)amino]-2-phenylethyl}-4-chlorobenzenesulfonamide (3b):** Colorless needles, yield 1.25 g, 98%; m.p. 160–163 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 6.35 (d, ^3J = 10.2 Hz, 1 H, 3-H), 6.47 (dd, ^3J = 9.2, 9.8 Hz, 1 H, CH), 6.97 (d, ^3J = 9.8 Hz, 1 H, NH), 7.24 (m, 3 H, 2,6-H 4-ClC$_6$H$_4$, 4-H), 7.28–7.38 (m, 3 H, 3,4,5-H C$_6$H$_5$), 7.60 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 7.70–7.73 (m, 3 H, 6-H, 2,6-H C$_6$H$_5$), 8.66 (d, ^3J = 9.2 Hz, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 68.7 (CH), 95.3 (CCl$_2$), 110.1 (C-3), 119.4 (C-5), 127.1 (C-2,6, C$_6$H$_5$), 127.9 (C-3,5, C$_6$H$_5$), 128.2 (C-2,6, 4-ClC$_6$H$_4$), 128.5 (C-3,5, 4-ClC$_6$H$_4$), 129.2 (C-4, C$_6$H$_5$), 136.2 (C-4), 137.0 (C-1, 4-ClC$_6$H$_4$), 139.2 (C-1, C$_6$H$_5$), 139.9 (C-4, 4-ClC$_6$H$_4$), 144.40 (C-6), 154.6 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1164, 1343 (SO$_2$), 1598 (C=N), 3274, 3233, 3377 (NH) cm^{-1}. C$_{19}$H$_{15}$Cl$_4$N$_3$O$_2$S (491.22): calcd. C 46.46, H 3.08, Cl 28.87, N 8.55, S 6.53; found C 46.58, H 3.12, Cl 28.81, N 8.49, S 6.57.

***N*-[2,2-Dichloro-2-phenyl-1-(2-pyridinylamino)ethyl]-4-methylbenzenesulfonamide (3c):** Colorless needles, yield 1.04 g, 85%; m.p. 137–140 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 2.17 (s, 1 H, CH$_3$), 6.27 (m, 1 H, 3-H), 6.43 (m, 1 H, 5-H), 6.50 (d, ^3J = 9.7 Hz, 1 H, NH), 6.61 (dd, ^3J = 9.4, 9.7 Hz, 1 H, CH), 6.94 (AA′BB′, 2 H, 3,5-H 4-CH$_3$C$_6$H$_4$), 7.17 (m, 1 H, 4-H), 7.34 (m, 3 H, 3,4,5-H C$_6$H$_5$), 7.45 (AA′BB′, 2 H, 2,6-H 4-CH$_3$C$_6$H$_4$), 7.73 (m, 2 H, 2,6-H C$_6$H$_5$), 7.77 (m, 1 H, 6-H), 8.23 (d, ^3J = 9.4 Hz, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 20.8 (CH$_3$), 68.5 (CH), 96.0 (CCl$_2$), 108.7 (C-3), 113.2 (C-5), 126.5 (C-3,5, 4-CH$_3$C$_6$H$_4$), 127.1 (C-2,6, C$_6$H$_5$), 127.8 (C-3,5, C$_6$H$_5$), 128.4 (C-2,6, 4-CH$_3$C$_6$H$_4$), 129.1 (C-4, C$_6$H$_5$), 136.3 (C-4), 138.3 (C-1, 4-CH$_3$C$_6$H$_4$), 139.4 (C-1, C$_6$H$_5$), 141.9 (C-4, 4-CH$_3$C$_6$H$_4$), 146.4 (C-6), 155.9 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1163, 1338 (SO$_2$), 1601 (C=N), 3240, 3364 (NH) cm^{-1}. C$_{20}$H$_{19}$Cl$_2$N$_3$O$_2$S (436.36): calcd. C 55.05, H 4.39, Cl 16.25, N 9.63, S 7.35; found C 55.15, H 4.42, Cl 16.31, N 9.57, S 7.39.

***N*-{2,2-Dichloro-1-[(5-chloro-2-pyridinyl)amino]-2-phenylethyl}-4-methylbenzenesulfonamide (3d):** Colorless needles, yield 1.20 g, 90%; m.p. 153–156 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 2.20 (s, 3 H, CH$_3$), 6.34 (d, ^3J = 8.7 Hz, 1 H, 3-H), 6.46 (dd, ^3J = 9.4, 9.5 Hz, 1 H, CH), 6.85 (d, ^3J = 9.4 Hz, 1 H, NH), 6.97 (AA′BB′, 2 H, 3,5-H 4-CH$_3$C$_6$H$_4$), 7.23 (d, ^3J = 8.7 Hz, 1 H, 4-H), 7.31–7.39 (m, 3 H, 4,5,6-H C$_6$H$_5$), 7.47 (AA′BB′, 2 H, 2,6-H 4-CH$_3$C$_6$H$_4$), 7.71 (m, 3 H, 6-H, 2,6-H C$_6$H$_5$), 8.39 (d, ^3J = 9.5 Hz, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 20.8 (CH$_3$), 68.7 (CH), 95.6 (CCl$_2$), 110.1 (C-3), 119.1 (C-5), 126.6 (C-3,5, 4-CH$_3$C$_6$H$_4$), 127.1 (C-2,6, C$_6$H$_5$), 127.8 (C-3,5, C$_6$H$_5$), 128.4 (C-2,6, 4-CH$_3$C$_6$H$_4$), 129.13 (C-4, C$_6$H$_5$), 136.0 (C-4), 138.2 (C-1, 4-CH$_3$C$_6$H$_4$), 139.3 (C-1, C$_6$H$_5$), 142.1 (C-4, 4-CH$_3$C$_6$H$_4$), 144.4 (C-6), 154.7 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1161, 1335 (SO$_2$), 1597 (C=N), 3268, 3367 (NH) cm^{-1}. C$_{20}$H$_{18}$Cl$_3$N$_3$O$_2$S (470.80): calcd. C 51.02, H 3.85, Cl 22.59, N 8.93, S 6.81; found C 50.27, H 3.91, Cl 22.49, N 8.88, S 6.87.

***N*-[2,2-Dichloro-2-phenyl-1-(2-thiazolamino)ethyl]-4-chlorobenzenesulfonamide (3e):** Colorless needles, yield 1.22 g, 94%; m.p. 141–143 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 6.37 (dd, ^3J = 9.4, 9.6 Hz, 1 H, CH), 6.51 (d, ^3J = 3.3 Hz, 1 H, 4-H), 6.84 (d, ^3J = 3.3 Hz, 1 H, 5-H), 7.32 (AA′BB′, 2 H, 2,6-H 4-ClC$_6$H$_4$), 7.38 (m, 3 H, 3,4,5-H C$_6$H$_5$), 7.61 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 7.71 (m, 2 H, 2,6-H C$_6$H$_5$), 8.09 (d, ^3J = 9.6 Hz, 1 H, NH), 8.77 (d, ^3J = 9.4 Hz, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]-DMSO): δ = 72.0 (CH), 94.9 (CCl$_2$), 107.9 (C-4), 127.0 (C-2,6, C$_6$H$_5$), 128.0 (C-3,5, C$_6$H$_5$), 128.26 (C-2,6, 4-ClC$_6$H$_4$), 128.37 (C-3,5, 4-ClC$_6$H$_4$), 129.3 (C-4, C$_6$H$_5$), 136.9 (C-1, C$_6$H$_5$), 137.4 (C-5), 139.2 (C-1, 4-ClC$_6$H$_4$), 140.0 (C-4, 4-ClC$_6$H$_4$), 166.4 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1163, 1338 (SO$_2$), 1520 (C=N), 3228, 3358 (NH) cm^{-1}. C$_{17}$H$_{14}$Cl$_3$N$_3$O$_2$S$_2$ (462.80): calcd. C 44.12, H 3.05, Cl 22.98, N 9.08, S 13.85; found C 44.19, H 3.08, Cl 23.05, N 9.03, S 13.91.

***N*-[2,2-Dichloro-2-phenyl-1-(2-thiazolamino)ethyl]-4-methylbenzenesulfonamide (3f):** Colorless needles, yield 1.20 g, 92%; m.p. 155–158 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 2.25 (s, 3 H, CH$_3$), 6.40 (dd, ^3J = 9.7, 9.8 Hz, 1 H, CH), 6.51 (d, ^3J = 3.6 Hz, 1 H, 4-H), 6.87 (d, ^3J = 3.6 Hz, 1 H, 5-H), 7.06 (AA′BB′, 2 H, 3,5-H 4-CH$_3$C$_6$H$_4$), 7.34–7.39 (m, 3 H, 3,4,5-H C$_6$H$_5$), 7.49 (AA′BB′, 2 H, 2,6-H 4-CH$_3$C$_6$H$_4$), 7.71 (m, 2 H, 2,6-H C$_6$H$_5$), 8.02 (d, ^3J = 9.7 Hz, 1 H, NH), 8.49 (d, ^3J = 9.8 Hz, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 20.9 (CH$_3$), 72.0 (CH), 95.2 (CCl$_2$), 107.7 (C-4), 126.5 (C-3,5, 4-CH$_3$C$_6$H$_4$), 127.0 (C-2,6, C$_6$H$_5$), 127.9 (C-3,5, C$_6$H$_5$), 128.6 (C-2,6, 4-CH$_3$C$_6$H$_4$), 129.2 (C-4, C$_6$H$_5$), 137.4 (C-5), 138.4 (C-1, 4-CH$_3$C$_6$H$_4$), 139.2 (C-1, C$_6$H$_5$), 142.1 (C-4, 4-CH$_3$C$_6$H$_4$), 166.5 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1161, 1335 (SO$_2$), 1597 (C=N), 3268, 3367 (NH) cm^{-1}. C$_{18}$H$_{17}$Cl$_2$N$_3$O$_2$S$_2$ (442.38): calcd. C 48.87, H 3.87, Cl 16.03, N 9.50, S 14.49; found C 48.81, H 3.83, Cl 16.08, N 9.53, S 14.42.

***N*-[2,2,2-Trichloro-1-(2-pyridinylamino)ethyl]-4-chlorobenzenesulfonamide (4a):** Colorless needles, yield 1.08 g, 93%; m.p. 161–163 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 6.43 (m, 1 H, 5-H), 6.50–6.60 (m, 2 H, C H, 3-H), 6.96 (d, ^3J = 9.6 Hz, 1 H, NH), 7.27 (m, 3 H, 4-H, 2,6-H 4-ClC$_6$H$_4$), 7.65 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 7.88 (m, 1 H, 6-H), 8.95 (br. s, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 70.7 (CH), 102.0 (CCl$_3$), 109.0 (C-3), 114.0 (C-5), 128.3 (C-2,6, 4-ClC$_6$H$_4$), 128.5 (C-3,5, 4-ClC$_6$H$_4$), 136.8 (C-4), 137.1 (C-1, 4-ClC$_6$H$_4$), 139.5 (C-4, 4-ClC$_6$H$_4$), 146.5 (C-6), 155.7 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1163, 1341 (SO$_2$), 1603 (C=N), 3247, 3382 (NH) cm^{-1}. $C_{13}H_{11}Cl_4N_3O_2S$ (415.12): calcd. C 37.61, H 2.67, Cl 34.16, N 10.12, S 7.72; found C 37.58, H 2.70, Cl 34.20, N 10.17, S 7.77.

***N*-{2,2,2-Trichloro-1-[(5-chloro-2-pyridinyl)amino]ethyl}-4-chlorobenzenesulfonamide (4b):** Colorless needles, yield 1.13 g, 90%; m.p. 158–160 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 6.37 (dd, ^3J = 9.0, 9.7 Hz, 1 H, CH), 6.50 (d, ^3J = 9.4 Hz, 1 H, 3-H), 7.27 (d, ^3J = 9.0 Hz, 1 H, NH), 7.30 (AA′BB′, 2 H, 2,6-H 4-ClC$_6$H$_4$), 7.37 (dd, ^3J = 9.4, ^4J = 2.5 Hz, 1 H, 4-H), 7.67 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 7.87 (d, ^4J = 2.5 Hz, 1 H, 6-H), 9.06 (d, ^3J = 9.7 Hz, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 70.9 (CH), 101.5 (CCl$_3$), 110.3 (C-3), 120.0 (C-5), 128.3 (C-2,6, 4-ClC$_6$H$_4$), 128.5 (C-3,5, 4-ClC$_6$H$_4$), 136.6 (C-4), 137.3 (C-1, 4-ClC$_6$H$_4$), 139.5 (C-4, 4-ClC$_6$H$_4$), 144.5 (C-6), 154.4 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1168, 1330 (SO$_2$), 1601 (C=N), 3238, 3391 (NH) cm^{-1}. $C_{13}H_{10}Cl_5N_3O_2S$ (449.57): calcd. C 34.73, H 2.24, Cl 39.43, N 9.35, S 7.13; found C 34.68, H 2.26, Cl 39.48, N 9.37, S 7.19.

***N*-[2,2,2-Trichloro-1-(2-thiazolamino)ethyl]-4-chlorobenzenesulfonamide (4c):** Colorless needles, yield 1.04 g, 88%; m.p. 162–165 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 6.26 (dd, ^3J = 9.2, 9.5 Hz, 1 H, CH), 6.65 (d, ^3J = 3.5 Hz, 1 H, 4-H), 6.96 (d, ^3J = 3.5 Hz, 1 H, 5-H), 7.38 (AA′BB′, 2 H, 2,6-H 4-ClC$_6$H$_4$), 7.70 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 8.38 (d, ^3J = 9.2 Hz, 1 H, NH), 9.22 (d, ^3J = 9.5 Hz, 1 H, NHSO$_2$) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 74.0 (CH), 100.9 (CCl$_3$), 108.7 (C-4), 128.44 (C-2,6, 4-ClC$_6$H$_4$), 128.48 (C-3,5, 4-ClC$_6$H$_4$), 137.3 (C-1, 4-ClC$_6$H$_4$), 137.5 (C-5), 139.7 (C-4, 4-ClC$_6$H$_4$), 166.4 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1160, 1340 (SO$_2$), 1551 (C=N), 3292 (NH) cm^{-1}. $C_{11}H_9Cl_4N_3O_2S_2$ (421.14): calcd. C 31.37, H 2.15, Cl 33.67, N 9.98, S 15.23; found C 31.43, H 2.17, Cl 33.71, N 10.04, S 15.29.

General Procedure for the Synthesis of Imidazopyridines 5 and Imidazothiazoles 6: 2-Aminopyridine, 5-chloro-2-aminopyridine or 2-aminothiazole (3.4 mmol) was added to a solution of imine **1** (2.8 mmol) in 1,4-dioxane (10 mL) and stirred with a magnetic stirrer for 4 h at room temp. Then sodium hydroxide (11.2 mmol) was added to the reaction mixture and stirred for an additional 5 h at room temp. The reaction mixture was then diluted with water (100 mL), acidified with hydrochloric acid (pH 3), the precipitate was filtered, dried and washed with diethyl ether (50 mL).

***N*-(2-Phenylimidazo[1,2-*a*]pyridine-3-yl)-4-chlorobenzenesulfonamide (5a):** Colorless needles, yield 0.90 g, 84%; m.p. 218–221 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 7.02 (m, 1 H, 6-H), 7.15 (m, 3 H, 3,4,5-H C$_6$H$_5$), 7.23 (AA′BB′, 2 H, 2,6-H 4-ClC$_6$H$_4$), 7.36 (m, 1 H, 7-H), 7.41 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 7.55–7.62 (m, 3 H, 2,6-H C$_6$H$_5$, 8-H), 8.31 (m, 1 H, 5-H) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 112.7 (C-6), 113.4 (C-3), 116.8 (C-8), 124.0 (C-5), 126.3 (C-7), 126.9 (C-2,6, C$_6$H$_5$), 127.4 (C-4, C$_6$H$_5$), 127.9 (C-3,5, C$_6$H$_5$), 128.4 (C-3,5, 4-ClC$_6$H$_4$), 129.1 (C-2,6, 4-ClC$_6$H$_4$), 132.4 (C-1, C$_6$H$_5$), 138.1 (C-1, 4-ClC$_6$H$_4$), 138.4 (C-4, 4-ClC$_6$H$_4$), 139.7 (C-2), 142.5 (C-8a) ppm. IR (KBr): $\tilde{\nu}$ = 1167, 1351 (SO$_2$), 1650 (C=N) cm^{-1}. $C_{19}H_{14}ClN_3O_2S$ (383.85): calcd. C 59.45, H 3.68, Cl 9.24, N 10.95, S 8.35; found C 59.55, H 3.64, Cl 9.30, N 10.89, S 8.41.

***N*-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridine-3-yl)-4-chlorobenzenesulfonamide (5b):** Colorless needles, yield 1.13 g, 97%; m.p. 232–235 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 7.22–7.32 (m, 5 H, 3,4,5-H C$_6$H$_5$, 2,6-H 4-ClC$_6$H$_4$), 7.47 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 7.67 (m, 2 H, 2,6-H C$_6$H$_5$), 7.69 (dd, ^3J = 9.5, ^4J = 1.5 Hz, 1 H, 7-H), 7.82 (d, ^3J = 9.5 Hz, 1 H, 8-H), 8.51 (d, ^4J = 1.5 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 114.5 (C-3), 116.1 (C-8), 121.5 (C-6), 122.5 (C-5), 127.2 (C-2,6, C$_6$H$_5$), 128.2 (C-3,5, C$_6$H$_5$), 128.5 (C-3,5, 4-ClC$_6$H$_4$), 128.6 (C-4, C$_6$H$_5$), 129.0 (C-1, C$_6$H$_5$), 129.1 (C-2,6, 4-ClC$_6$H$_4$), 130.1 (C-7), 137.5 (C-1, 4-ClC$_6$H$_4$), 137.8 (C-2), 138.5 (C-4, 4-ClC$_6$H$_4$), 139.2 (C-8a) ppm. IR (KBr): $\tilde{\nu}$ = 1172, 1341 (SO$_2$), 1653 (C=N) cm^{-1}. $C_{19}H_{13}Cl_2N_3O_2S$ (418.30): calcd. C 54.56, H 3.13, Cl 16.95, N 10.05, S 7.66; found C 54.36, H 3.16, Cl 16.88, N 10.12, S 7.59.

***N*-(2-Phenylimidazo[1,2-*a*]pyridine-3-yl)-4-methylbenzenesulfonamide (5c):** Colorless needles, yield 0.73 g, 72%; m.p. 169–172 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 2.20 (s, 3 H, CH$_3$), 6.99 (AA′BB′, 2 H, 2,6-H 4-CH$_3$C$_6$H$_4$), 7.23 (m, 2 H, 3,5-H C$_6$H$_5$), 7.31 (m, 1 H, 4-H C$_6$H$_5$), 7.35–7.40 (m, 3 H, 3,5-H 4-CH$_3$C$_6$H$_4$, 6-H), 7.64 (m, 2 H, 2,6-H C$_6$H$_5$), 7.80 (m, 1 H, 7-H), 7.87 (m, 1 H, 8-H), 8.55 (m, 1 H, 5-H) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 20.9 (CH$_3$), 113.7 (C-8), 114.7 (C-3), 115.7 (C-5), 125.1 (C-6), 126.6 (C-3,5, 4-CH$_3$C$_6$H$_4$), 127.4 (C-2,6, C$_6$H$_5$), 127.5 (C-1, C$_6$H$_5$), 128.3 (C-3,5, C$_6$H$_5$), 128.9 (C-4, C$_6$H$_5$), 129.5 (C-2,6, 4-CH$_3$C$_6$H$_4$), 131.6 (C-7), 134.2 (C-2), 136.2 (C-1, 4-CH$_3$C$_6$H$_4$), 139.4 (C-8a), 143.7 (C-4, 4-CH$_3$C$_6$H$_4$) ppm. IR (KBr): $\tilde{\nu}$ = 1162, 1340 (SO$_2$), 1650 (C=N) cm^{-1}. $C_{20}H_{17}N_3O_2S$ (363.43): calcd. C 66.10, H 4.71, N 11.56, S 8.82; found C 65.97, H 4.77, N 11.49, S 8.78.

***N*-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridine-3-yl)-4-methylbenzenesulfonamide (5d):** Colorless needles, yield 0.67 g, 60%; m.p. 204–207 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 2.21 (s, 3 H, CH$_3$), 7.03 (AA′BB′, 2 H, 2,6-H 4-CH$_3$C$_6$H$_4$), 7.28–7.38 (m, 3 H, 3,4,5-H C$_6$H$_5$), 7.41 (AA′BB′, 2 H, 3,5-H 4-CH$_3$C$_6$H$_4$), 7.75 (m, 2 H, 2,6-H C$_6$H$_5$), 7.90 (dd, ^3J = 9.5, ^4J = 1.8 Hz, 7-H), 7.95 (d, ^3J = 9.5 Hz, 1 H, 8-H), 8.46 (d, ^4J = 1.8 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 20.9 (CH$_3$), 114.5 (C-8), 115.5 (C-3), 123.1 (C-6), 123.2 (C-5), 126.5 (C-1, C$_6$H$_5$), 126.7 (C-3,5, 4-CH$_3$C$_6$H$_4$), 127.5 (C-2,6, C$_6$H$_5$), 128.5 (C-3,5, C$_6$H$_5$), 129.5 (C-4, C$_6$H$_5$), 129.7 (C-2,6, 4-CH$_3$C$_6$H$_4$), 132.9 (C-7), 134.4 (C-2), 136.1 (C-1, 4-CH$_3$C$_6$H$_4$), 137.6 (C-8a), 144.2 (C-4, 4-CH$_3$C$_6$H$_4$) ppm. IR (KBr): $\tilde{\nu}$ = 1168, 1333 (SO$_2$), 1653 (C=N) cm^{-1}. $C_{20}H_{16}ClN_3O_2S$ (397.88): calcd. C 60.38, H 4.05, Cl 8.91, N 10.56, S 8.06; found C 60.51, H 4.01, Cl 8.97, N 10.61, S 8.11.

***N*-(6-Phenylimidazo[2,1-*b*]thiazol-5-yl)-4-chlorobenzenesulfonamide (6a):** Colorless needles, yield 0.95 g, 92%; m.p. 229–231 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 7.13–7.20 (m, 3 H, 3,4,5-H C$_6$H$_5$), 7.29 (AA′BB′, 2 H, 2,6-H 4-ClC$_6$H$_4$), 7.37 (d, ^3J = 4.4 Hz, 1 H, 3-H), 7.48 (AA′BB′, 2 H, 3,5-H 4-ClC$_6$H$_4$), 7.50 (m, 2 H, 2,6-H C$_6$H$_5$), 7.67 (d, ^3J = 4.4 Hz, 1 H, 2-H) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 114.7 (C-3), 114.9 (C-3), 118.6 (C-2), 126.2 (C-2,6, C$_6$H$_5$), 127.3 (C-4, C$_6$H$_5$), 127.9 (C-3,5, C$_6$H$_5$), 128.5 (C-3,5, 4-ClC$_6$H$_4$), 129.1 (C-2,6, 4-ClC$_6$H$_4$), 131.4 (C-1, C$_6$H$_5$), 137.9 (C-1, 4-ClC$_6$H$_4$), 138.1 (C-4, 4-ClC$_6$H$_4$), 139.7 (C-6), 146.7 (C-7a) ppm. IR (KBr): $\tilde{\nu}$ = 1165, 1345 (SO$_2$) cm^{-1}. $C_{17}H_{12}ClN_3O_2S_2$ (389.87): calcd. C 52.37, H 3.10, Cl 9.09, N 10.78, S 16.45; found C 52.41, H 3.14, Cl 9.15, N 10.71, S 16.52.

***N*-(6-Phenylimidazo[2,1-*b*]thiazol-5-yl)-4-methylbenzenesulfonamide (6b):** Colorless needles, yield 0.70 g, 67%; m.p. 199–202 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 2.24 (s, 3 H, CH$_3$), 7.10–7.53 (m, 11 H, 2-H, 3-H, Ar), 10.60 (br. s, 1 H, NHSO$_2$) ppm. ^{13}C NMR

(100.61 MHz, [D$_6$]DMSO): δ = 20.9 (CH_3), 114.4 (C-3), 115.4 (C-5), 118.5 (C-2), 126.2 (C-2,6, C_6H_5), 126.6 (C-3,5, 4-$CH_3C_6H_4$), 127.2 (C-4, C_6H_5), 127.9 (C-3,5, C_6H_5), 129.5 (C-2,6, 4-$CH_3C_6H_4$), 131.6 (C-1, C_6H_5), 136.4 (C-1, 4-$CH_3C_6H_4$), 139.5 (C-6), 143.52 (C-4, 4-$CH_3C_6H_4$), 146.6 (C-7a) ppm. IR (KBr): $\tilde{\nu}$ = 1164, 1343 (SO_2) cm^{-1}. $C_{18}H_{15}N_3O_2S_2$ (369.46): calcd. C 58.52, H 4.09, N 11.37, S 17.36; found C 58.66, H 4.03, N 11.41, S 17.29.

General Procedure for the Methylation of Imidazopyridines 5a and 5b, and Imidazothiazole 6a: Methyl iodide (4.8 mmol) was added to a stirred mixture of imidazopyridine **5a** and **5b**, or imidazothiazole **6a** (2.4 mmol), potassium carbonate (7.2 mmol), triethylbenzylammonium chloride (0.24 mmol) and acetonitrile (10 mL). The reaction mixture was stirred with a magnetic stirrer for 6 h at room temp. Then the solvent was removed under reduced pressure, the residue was washed with water (100 mL), dried and washed with diethyl ether (50 mL). To isolate compounds **7a** and **7b** the mixture of **7a** and **7b** was washed with acetone (50 mL). The insoluble residue was filtered off (compound **7a**); evaporation of the filtrate gave compound **7b**.

4-Chloro-*N*-methyl-*N*-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide (7a): Yellow cube crystals, yield 0.30 g, 30%; m.p. 151–154 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 3.51 (s, 3 H, NCH_3), 7.02 (m, 1 H, 6-H), 7.18–7.26 (m, 3 H, 3,4,5-H C_6H_5), 7.39 (m, 3 H, 7-H, 2,6-H 4-ClC_6H_4), 7.51 (m, 2 H, 2,6-H C_6H_5), 7.57 (AA′BB′, 2 H, 3,5-H 4-ClC_6H_4), 7.63 (m, 1 H, 8-H), 8.14 (m, 1 H, 5-H) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 37.9 (NCH_3), 112.9 (C-6), 117.1 (C-8), 117.2 (C-3), 123.9 (C-5), 126.4 (C-7), 126.7 (C-2,6, C_6H_5), 127.7 (C-4, C_6H_5), 128.1 (C-3,5, 4-ClC_6H_4), 128.8 (C-3,5, C_6H_5), 129.4 (C-2,6, 4-ClC_6H_4), 132.4 (C-1, C_6H_5), 137.2 (C-1, 4-ClC_6H_4), 138.6 (C-4, 4-ClC_6H_4), 140.2 (C-2), 142.5 (C-8a) ppm. IR (KBr): $\tilde{\nu}$ = 1160, 1350 (SO_2) cm^{-1}. $C_{20}H_{16}ClN_3O_2S$ (397.88): calcd. C 60.38, H 4.05, Cl 8.91, N 10.56, S 8.06; found C 60.45, H 4.11, Cl 8.95, N 10.47, S 8.11.

3-{[(4-Chlorophenyl)sulfonyl]methylamino}-1-methyl-2-phenylimidazo[1,2-*a*]pyridin-1-ium Iodide (7b): Yellow cube crystals, yield 0.88 g, 68%; m.p. 157–159 °C. ^{1}H NMR (400.13 MHz, [D$_6$]-DMSO): δ = 3.49 (s, 3 H, SO_2NCH_3), 3.76 (s, 3 H, NCH_3), 7.32–7.42 (m, 6 H, 2,3,5,6-H C_6H_5, 2,6-H 4-ClC_6H_4), 7.54 (m, 3 H, 3,5-H 4-ClC_6H_4, 4-H C_6H_5), 7.74 (m, 1 H, 6-H), 8.23 (m, 1 H, 7-H), 8.40 (m, 1 H, 8-H), 8.86 (m, 1 H, 5-H) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 32.4 (NCH_3), 39.45 (SO_2NCH_3), 111.8 (C-8), 118.0 (C-6), 120.2 (C-3), 123.2 (C-1, C_6H_5), 126.2 (C-5), 128.7 (C-3,5, C_6H_5), 128.9 (C-3,5, 4-ClC_6H_4), 129.5 (C-2,6, 4-ClC_6H_4), 130.0 (C-2,6, C_6H_5), 130.6 (C-4, C_6H_5), 135.0 (C-2, C-7), 135.5 (C-1, 4-ClC_6H_4), 137.8 (C-8a), 139.0 (C-4, 4-ClC_6H_4) ppm. IR (KBr): $\tilde{\nu}$ = 1158, 1350 (SO_2) cm^{-1}. $C_{21}H_{19}ClIN_3O_2S$ (539.82): calcd. C 46.73, H 3.55, Cl 6.57, N 7.78, S 5.94; found C 46.79, H 3.59, Cl 6.51, N 7.81, S 5.97.

***N*-(6-Chloro-2-phenylimidazo[1,2-*a*]pyridin-3-yl)-*N*-methyl-4-chlorobenzenesulfonamide (8):** Yellow cube crystals, yield 0.93 g, 87%; m.p. 200–203 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 3.54 (s, 3 H, NCH_3), 7.22–7.28 (m, 3 H, 3,4,5-H C_6H_5), 7.41 (AA′BB′, 2 H, 2,6-H 4-ClC_6H_4), 7.43 (dd, ^3J = 9.4, ^4J = 1.6 Hz, 1 H, 7-H), 7.52–7.59 (m, 4 H, 2,6-H C_6H_5, 3,5-H 4-ClC_6H_4), 7.68 (d, ^3J = 9.4 Hz, 1 H, 8-H), 8.12 (d, ^4J = 1.6 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 38.1 (CH_3), 117.9 (C-3), 118.1 (C-8), 119.9 (C-6), 121.9 (C-5), 126.7 (C-2,6, C_6H_5), 127.3 (C-7), 128.0 (C-4, C_6H_5), 128.2 (C-3,5, C_6H_5), 128.8 (C-3,5, 4-ClC_6H_4), 129.5 (C-2,6, 4-ClC_6H_4), 132.0 (C-1, C_6H_5), 137.1 (C-1, 4-ClC_6H_4), 138.8 (C-4, 4-ClC_6H_4), 140.9 (C-2), 141.3 (C-8a) ppm. IR (KBr): $\tilde{\nu}$ = 1162, 1360 (SO_2) cm^{-1}. $C_{20}H_{15}Cl_2N_3O_2S$ (432.32): calcd. C 55.56, H 3.50, Cl 16.40, N 9.72, S 7.42; found C 55.33, H 3.46, Cl 16.47, N 9.66, S 7.48.

4-Chloro-*N*-methyl-*N*-(6-phenylimidazo[2,1-*b*]thiazol-5-yl)benzenesulfonamide (9): Yellow cube crystals, yield 0.80 g, 83%; m.p. 167–169 °C. ^{1}H NMR (400.13 MHz, [D$_6$]DMSO): δ = 3.42 (s, 3 H, NCH_3), 7.20–7.23 (m, 3 H, 3,4,5-H, C_6H_5), 7.30 (d, ^3J = 4.5 Hz, 1 H, 3-H), 7.44–7.48 (m, 5 H, 2-H, 2,6-H 4-ClC_6H_4, 2,6-H C_6H_5), 7.61 (AA′BB′, 2 H, 3,5-H 4-ClC_6H_4) ppm. ^{13}C NMR (100.61 MHz, [D$_6$]DMSO): δ = 37.9 (NCH_3), 114.0 (C-3), 118.6 (C-2), 118.9 (C-5), 126.0 (C-2,6, C_6H_5), 127.3 (C-4, C_6H_5), 128.1 (C-3,5, C_6H_5), 128.9 (C-3,5, 4-ClC_6H_4), 129.5 (C-2,6, 4-ClC_6H_4), 132.6 (C-1, C_6H_5), 136.7 (C-1, 4-ClC_6H_4), 138.7 (C-4, 4-ClC_6H_4), 141.3 (C-6), 147.6 (C-7a) ppm. IR (KBr): $\tilde{\nu}$ = 1160, (SO_2) 1350 cm^{-1}. $C_{18}H_{14}ClN_3O_2S_2$ (403.90): calcd. C 53.53, H 3.49, Cl 8.78, N 10.40, S 15.88; found C 53.42, H 3.44, Cl 8.83, N 10.45, S 15.83. H 3.49 C 53.53 N 10.40 O 7.92 S 15.88 Cl 8.78.

CCDC-878862, -878863 and -878864 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of all compounds, crystal data and details of X-ray experiments for compounds **7a**, **7b and 8**.

Acknowledgments

This research was supported by the Russian Foundation for Basic Research (grant number 12-03-31762).

[1] a) S. M. Hanson, E. V. Morlock, K. A. Satyshur, C. Czajkowski, *J. Med. Chem.* **2008**, *51*, 7243–7252; b) A. N. Jain, *J. Med. Chem.* **2004**, *47*, 947–961; c) N. Hsu, S. K. Jha, T. Coleman, M. G. Frank, *Behav. Brain Res.* **2009**, *201*, 233–236.

[2] a) L. Almirante, L. Polo, A. Mugnaini, E. Provinciali, P. Rugarli, A. Biancotti, A. Gamba, W. Murmann, *J. Med. Chem.* **1965**, *8*, 305–312; b) K. Munson, R. Garcia, G. Sachs, *Biochemistry* **2005**, *44*, 5267–5284; c) A. M. Palmer, B. Grobbel, C. Jecke, C. Brehm, P. J. Zimmermann, W. Buhr, M. P. Feth, W.-A. Simon, W. Kromer, *J. Med. Chem.* **2007**, *50*, 6240–6264.

[3] C. Enguehard-Gueiffier, A. Gueiffier, *Mini-Rev. Med. Chem.* **2007**, *7*, 888–899.

[4] T. A. Engler, J. R. Henry, S. Malhotra, B. Cunningham, K. Furness, J. Brozinick, T. P. Burkholder, M. P. Clay, J. Clayton, C. Diefenbacher, E. Hawkins, Ph. W. Iversen, Y. Li, T. D. Lindstrom, A. L. Marquart, J. McLean, D. Mendel, E. Misener, D. Briere, J. C. O'Toole, W. J. Porter, S. Queener, J. K. Reel, R. A. Owens, R. A. Brier, Th. E. Eessalu, J. R. Wagner, R. M. Campbell, R. Vaughn, *J. Med. Chem.* **2004**, *47*, 3934–3937.

[5] K. S. Gudmundsson, B. A. Johns, *Org. Lett.* **2003**, *5*, 1369–1372.

[6] N. Margiotta, R. Ostuni, R. Ranaldo, N. Denora, V. Laquintana, G. Trapani, G. Liso, G. Natile, *J. Med. Chem.* **2007**, *50*, 1019–1027.

[7] a) S. C. Goodacre, L. J. Street, D. J. Hallett, J. M. Crawforth, S. Kelly, A. P. Owens, W. P. Blackaby, R. T. Lewis, J. Stanley, A. J. Smith, P. Ferris, B. Sohal, S. M. Cook, A. Pike, N. Brown, K. A. Wafford, G. Marshall, J. L. Castro, J. R. Atack, *J. Med. Chem.* **2006**, *49*, 35–38; b) A. Li, M. G. Johnson, J. Liu, X. Chen, X. Du, J. T. Mihalic, J. Deignan, D. J. Gustin, J. Duquette, Z. Fu, L. Zhu, A. P. Marcus, P. Bergeron, L. R. McGee, J. Danao, B. Lemon, T. Carabeo, T. Sullivan, J. Ma, L. Tang, G. Tonn, T. L. Collins, J. C. Medina, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 688–693; c) R. R. Singhaus, R. C. Bernotas, R. Steffan, E. Matelan, E. Quinet, P. Nambi, I. Feingold, C. Huselton,

A. Wilhelmsson, A. Goos-Nilsson, J. Wrobel, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 521–525.

[8] a) C. E. McKenna, B. A. Kashemirov, K. M. Błazewska, I. Mallard-Favier, C. A. Stewart, J. Rojas, M. W. Lundy, F. H. Ebetino, R. A. Baron, M. L. Kirsten, J. E. Dunford, M. C. Seabra, J. L. Bala, M. S. Marma, M. J. Rogers, F. P. Coxon, *J. Med. Chem.* **2010**, *53*, 3454–3464; b) G. Tresadern, J. M. Cid, G. J. Macdonald, J. A. Vega, A. I. Lucas, A. Garcia, E. Matesanz, M. L. Linares, D. Oehlrich, H. Lavreysen, I. Biesmans, A. A. Trabanco, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 175–179.

[9] a) N. Denora, V. Laquintana, M. G. Pisu, R. Dore, L. Murru, A. Latrofa, G. Trapani, E. Sanna, *J. Med. Chem.* **2008**, *51*, 6876–6888; b) V. Laquintana, N. Denora, A. Lopedota, H. Suzuki, M. Sawada, M. Serra, G. Biggio, A. Latrofa, G. Trapani, G. Liso, *Bioconjugate Chem.* **2007**, *18*, 1397–1407; c) G. Trapani, V. Laquintana, N. Denora, A. Trapani, A. Lopedota, A. Latrofa, M. Franco, M. Serra, M. G. Pisu, I. Floris, E. Sanna, G. Biggio, G. Liso, *J. Med. Chem.* **2005**, *48*, 292–305.

[10] a) L. Cai, J.-S. Liow, S. S. Zoghbi, J. Cuevas, C. Baetas, J. Hong, H. U. Shetty, N. M. Seneca, A. K. Brown, R. Gladding, S. S. Temme, M. M. Herman, R. B. Innis, V. W. Pike, *J. Med. Chem.* **2008**, *51*, 148–158; b) L. Cai, R. B. Innis, V. W. Pike, *Curr. Med. Chem.* **2007**, *14*, 19–52; c) L. Cai, F. T. Chin, V. W. Pike, H. Toyama, J. S. Liow, S. S. Zoghbi, K. Modell, E. Briard, H. U. Shetty, K. Sinclair, S. Donohue, D. Tipre, M. P. Kung, C. Dagostin, D. A. Widdowson, M. Green, W. Gao, M. M. Herman, M. Ichise, R. B. Innis, *J. Med. Chem.* **2004**, *47*, 2208–2218; d) Z. P. Zhuang, M. P. Kung, A. Wilson, C. W. Lee, K. Plossl, C. Hou, D. M. Holtzman, H. F. Kung, *J. Med. Chem.* **2003**, *46*, 237–243; e) L. Cai, J. Cuevas, S. Temme, M. M. Herman, C. Dagostin, D. A. Widdowson, R. B. Innis, V. W. Pike, *J. Med. Chem.* **2007**, *50*, 4746–4758; f) C. J. R. Fookes, T. Q. Pham, F. Mattner, I. Greguric, C. Loc'h, X. Liu, P. Berghofer, R. Shepherd, M. C. Gregoire, A. Katsifis, *J. Med. Chem.* **2008**, *51*, 3700–3712.

[11] a) M. Aginagalde, Y. Vara, A. Arrieta, R. Zangi, V. L. Cebolla, A. Delgado-Camon, F. P. Cossio, *J. Org. Chem.* **2010**, *75*, 2776–2784; b) S. Takizawa, J. Nishida, Y. Yamashita, *J. Photopolym. Sci. Technol.* **2008**, *21*, 355–356.

[12] M. Hoffmann, A. Plutecka, U. Rychlewska, Z. Kucybala, J. Paczkowski, I. Pyszka, *J. Phys. Chem. A* **2005**, *109*, 4568–4574.

[13] a) S. Sharma, B. Saha, D. Sawant, B. Kundu, *J. Comb. Chem.* **2007**, *9*, 783–792; b) J. M. Chezal, E. Moreau, G. Delmas, A. Gueiffier, Y. Blache, G. Grassy, C. Lartigue, O. Chavignon, J. C. Teulade, *J. Org. Chem.* **2001**, *66*, 6576–6584.

[14] a) M. A. Metwally, E. Abdel-Latifl, *J. Sulfur Chem.* **2004**, *25*, 359–379; b) V. M. Muzalevskiy, V. G. Nenajdenko, A. V. Shastin, E. S. Balenkova, G. Haufe, *Synthesis* **2009**, 2249–2259; c) K. M. Dawood, H. A. Mohamed, B. F. Abdel-Wahab, *Chem. Heterocycl. Compd.* **2010**, *46*, 131–139; d) K. C. Chunavala, G. Joshi, E. Suresh, S. Adimurthy, *Synthesis* **2011**, 635–641; e) A. R. Harris, D. M. Nason, E. M. Collantes, W. Xu, Y. Chi, Z. Wang, B. Zhang, Q. Zhang, D. L. Gray, J. E. Davoren, *Tetrahedron* **2011**, *67*, 9063–9066.

[15] a) A. Basilio-Lopes, T. Mendonça de Aquino, A. Mongeot, J.-J. Bourguignon, M. Schmitt, *Tetrahedron Lett.* **2012**, *53*, 2583–2587; b) O. Kim, Y. Jeong, H. Lee, S.-S. Hong, S. Hong, *J. Med. Chem.* **2011**, *54*, 2455–2466.

[16] a) E. F. DiMauro, J. M. Kennedy, *J. Org. Chem.* **2007**, *72*, 1013–1016; b) K. Groebke, L. Weber, F. Mehlin, *Synlett* **1998**, 661–663; c) H. Bienayme, K. Bouzid, *Angew. Chem.* **1998**, *110*, 2349–2352; *Angew. Chem. Int. Ed.* **1998**, *37*, 2234–2237; d) C. Blackburn, B. Guan, P. Fleming, K. Shiosaki, S. Tsai, *Tetrahedron Lett.* **1998**, *39*, 3635–3638; e) A. L. Rousseau, P. Matlaba, C. J. Parkinson, *Tetrahedron Lett.* **2007**, *48*, 4079–4082; f) M. Adib, M. Mahdavi, M. A. Noghania, P. Mirzaei, *Tetrahedron Lett.* **2007**, *48*, 7263–7265; g) M. Adib, E. Sheibani, L.-G. Zhu, P. Mirzaei, *Tetrahedron Lett.* **2008**, *49*, 5108–5110; h) N. Chernyak, V. Gevorgyan, *Angew. Chem.* **2010**, *122*, 2803–2806; *Angew. Chem. Int. Ed.* **2010**, *49*, 2743–2746; i) S. Mishra, R. Ghosh, *Synthesis* **2011**, *21*, 3463–3470; j) R. Akbarzadeh, G. I. Shakibaei, A. Bazgir, *Monatsh. Chem.* **2010**, *141*, 1077–1081; k) E. Kianmehr, M. Ghanbari, M. N. Niri, R. Faramarzi, *J. Comb. Chem.* **2010**, *12*, 41–44; l) B. V. S. Reddy, P. S. Reddy, Y. J. Reddy, J. S. Yadav, *Tetrahedron Lett.* **2011**, *52*, 5789–5793.

[17] Zh. Wu, Y. Pan, X. Zhou, *Synthesis* **2011**, *14*, 2255–2260.

[18] a) C. Enguehard, J. Renou, V. Collot, M. Hervet, S. Rault, A. Gueiffier, *J. Org. Chem.* **2000**, *65*, 6572–6575; b) J. Koubachi, S. E. Kazzouli, S. B. Raboin, A. Mouaddib, G. Guillaumet, *Synlett* **2006**, 3237–3242.

[19] a) A. R. Katritzky, Y. J. Xu, H. B. Tu, *J. Org. Chem.* **2003**, *68*, 4935–4937; b) A. R. Katritzky, G. Qiu, Q. Long, H. He, P. J. Steel, *J. Org. Chem.* **2000**, *65*, 9201–9205.

[20] A. Kiselyov, *Tetrahedron Lett.* **2005**, *46*, 4487–4490.

[21] J. S. Yadav, B. V. S. Reddy, Y. G. Rao, M. Srinivas, A. V. Narsaiah, *Tetrahedron Lett.* **2007**, *48*, 7717–7720.

[22] V. N. Britsun, A. N. Borisevich, V. B. Pirozhenko, M. O. Lozinskii, *Russ. J. Org. Chem.* **2007**, *43*, 276–279.

[23] T. Kondo, S. Kotachi, S.-I. Ogino, Y. Watanabe, *Chem. Lett.* **1993**, 1317–1320.

[24] V. B. Kurteva, L. A. Lubenov, D. V. Nedeltcheva, R. P. Nikolova, B. L. Shivachev, *ARKIVOC (Gainesville, FL, U.S.)* **2012**, *8*, 282–294.

[25] G. G. Levkovskaya, T. I. Drozdova, I. B. Rozentsveig, A. N. Mirskova, *Russ. Chem. Rev.* **1999**, *68*, 581–604.

[26] a) L. B. Krivdin, K. A. Chernyshev, G. N. Rosentsveig, I. V. Ushakova, I. B. Rosentsveig, G. G. Levkovskaya, *Magn. Reson. Chem.* **2007**, *45*, 980–984; b) I. B. Rozentsveig, G. N. Rozentsveig, A. N. Mirskova, K. A. Chernyshev, L. B. Krivdin, G. G. Levkovskaya, *Russ. J. Gen. Chem.* **2008**, *78*, 1371–1379.

[27] a) G. N. Rozentsveig, I. B. Rozentsveig, G. G. Levkovskaya, I. T. Evstaf′eva, A. N. Mirskova, *Russ. J. Org. Chem.* **2001**, *37*, 1297–1301; b) G. N. Rosentsveig, Yu. A. Aizina, I. B. Rosentsveig, G. G. Levkovskaya, G. I. Sarapulova, A. N. Mirskova, T. I. Drozdova, *Russ. J. Org. Chem.* **2003**, *39*, 554–558; c) I. B. Rozentsveig, I. V. Ushakova, E. V. Kondrashov, G. N. Rozentsveig, G. G. Levkovskaya, A. N. Mirskova, *Russ. J. Org. Chem.* **2005**, *41*, 1558–1560; d) E. V. Kondrashov, E. V. Rudyakova, I. B. Rozentsveig, I. V. Ushakova, G. N. Rozentsveig, V. A. Savosik, K. A. Chernyshev, L. B. Krivdin, G. G. Levkovskaya, *Russ. J. Org. Chem.* **2008**, *44*, 86–94; e) I. B. Rozentsveig, B. A. Shainyan, E. V. Kondrashov, E. V. Rudyakova, G. N. Rozentsveig, K. A. Chernyshev, G. G. Levkovskaya, *Russ. J. Org. Chem.* **2008**, *44*, 1332–1337; f) G. N. Rozentsveig, A. V. Popov, I. B. Rozentsveig, G. G. Levkovskaya, *Russ. J. Org. Chem.* **2008**, *44*, 1486–1489; g) E. V. Kondrashov, E. V. Rudyakova, G. N. Rozentsveig, I. B. Rozentsveig, K. A. Chernyshev, L. B. Krivdin, G. G. Levkovskaya, *Russ. J. Org. Chem.* **2009**, *45*, 1365–1374; h) I. B. Rozentsveig, G. N. Rozentsveig, V. Yu. Serykh, K. A. Chernyshev, G. G. Levkovskaya, *Eur. J. Org. Chem.* **2011**, 4415–4421.

Received: July 27, 2012
Published Online: November 12, 2012

