New catalytic system for the synthesis of imidazo[1,2-*a*]pyridines by the Ugi reaction

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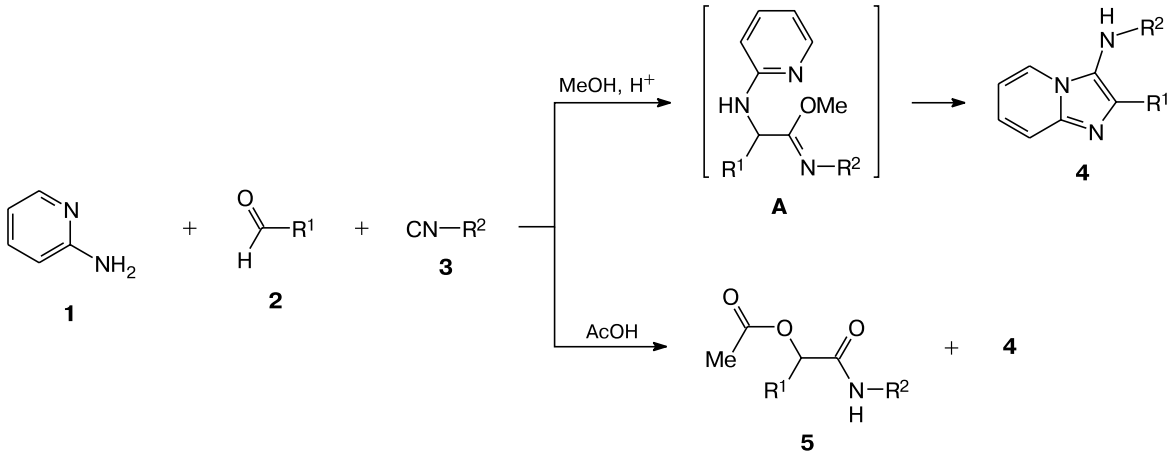
A combination of *N*-hydroxysuccinimide and *p*-toluenesulfonic acid is proposed as an efficient catalyst for the preparation of a great variety of imidazo[1,2-*a*]pyridine derivatives by three-component condensation of aromatic isocyanides, aldehydes, and 2-aminopyridine. The advantages of this procedure are high yields of the target products and the absence of side reactions.

Key words: Ugi reaction, isocyanides, imidazo[1,2-*a*]pyridine, catalysis, combinatorial synthesis.

Imidazo[1,2-*a*]pyridine derivatives have long attracted the attention of researchers engaged in medicinal chemistry, as these compounds possess a broad spectrum of biological activities. In particular, they act as cardiostimulators,[1] inhibit gastric secretion,[2] exhibit antibacterial[3] and fungicidal activities.[4] The permanent practical interest in imidazo[1,2-*a*]pyridines has stimulated the research aimed at the development of combinatorial methods for their synthesis, in particular, by multicomponent reactions. In 1998, three research groups published simultaneously a new version of the Ugi reaction in which 2-aminopyridine (**1**), aldehydes **2**, and isocyanides **3** react in the presence of an acid catalyst to give imidazo[1,2-*a*]pyridines **4** in one step (Scheme 1).[5—7] The possibility of varying several side groups in the target structure and lower cost of the synthesis markedly accelerated the search for new biologically active compounds of this series. As a result, compounds proposed for treating type 2 diabetes and fatty degeneration were found.[8] However, this synthesis suffers from considerable drawbacks, because acid catalysis stimulates a series of side transformations including polymerization of isocyanides and the Passerini reaction. In view of the crucial role of catalysts in attaining high yields of target imidazo[1,2-*a*]pyridines, the purpose of this study was to develop a more efficient catalytic system for the three-component reaction of 2-aminopyridine with isocyanides and aldehydes. A new catalyst should be highly active in the Ugi reaction and simultaneously have an exceptionally low activities in the Passerini reaction and polymerization of isocyanides. In addition, it should be easily separable from the product during purification and easily reusable.

Scheme 1



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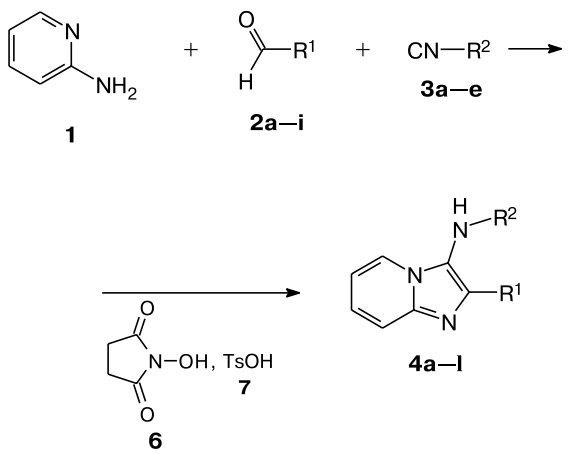
Results and Discussion

Theoretically, there are two methods of searching for an optimal catalyst for a new reaction: analytical method based on investigation of the reaction mechanism and combinatorial method, which implies item-by-item examination of many versions. All previous studies were based on the combinatorial approach; even the reaction giving imidazo[1,2-*a*]pyridines was discovered due to examination of a large array of data from libraries of compounds based on the four-component Ugi condensation.[9] The optimal catalysts for this reaction were also found by testing various carboxylic (R = Me, Et, Ph) and mineral acids[10] and also Lewis acids. It should be mentioned that all the proposed catalysts suffer from some drawbacks. For example, the use of acetic acid may result in Passerini reaction products **5**, while the use of scandium triflate leads to partial polymerization of isocyanides.[7] Rational design of a catalytic system was prevented by the lack of data on the reaction mechanism. Multicomponent reactions are characterized by the presence of numerous intermediate steps and pronounced dependence of the mechanism on the starting reactants and the catalysts chosen. Therefore, despite many years of research, the question of detailed mechanism of most multicomponent reactions, including the Ugi and Passerini condensations, remains open. When choosing the catalyst, one should take into account the fact that it can have opposite effects on different steps of a complex set of reactions such as the four-component Ugi condensation.

Convincing data published in recent years[11] indicate that imidates **A** are involved in the equilibrium intermediate steps of the Ugi reaction. Imidates play a key role in two new variants of the Ugi reaction;[11,12] in addition, their intermediate existence accounts for the formation of a series of by-products in the classical four-component condensation. The formation of imidazo[1,2-*a*]pyridines **4** with 2-aminopyridine used as the amino component in the Ugi reaction can also be attributed to acid-catalyzed intramolecular cyclization of unstable imidate **A** (see Scheme 1). This is confirmed by the fact that the reaction proceeds only when methanol is used as the solvent; in other solvents, by-products are formed. Even if another solvent is used, methanol is added as an activating component.[7] In view of this fact, a rational design of a catalytic system for this reaction should be based on searching for compounds promoting the formation of imidates **A**.

Previously, we showed[13] that nucleophilic additives used in the peptide chemistry (*N*-hydroxysuccinimide, *N*-hydroxybenzotriazole, 4-nitrophenol) are excellent catalysts for a series of multicomponent reactions of isocyanides. We suggest that imidates participate in these reactions as key intermediates, which ensure selectivity for the whole sequence of intermediate steps to give the only product. On the basis of these data, we attempted to use *N*-hydroxysuccinimide (**6**) as the catalyst for the three-component reaction of 2-aminopyridine with isocyanides and aldehydes (Scheme 2). Previously, we successfully used this compound as the catalyst for the Passerini reaction.[13] All experiments on the search for the optimal catalyst were carried out for the 2-aminopyridine (**1**)—4-nitrobenzaldehyde (**2a**)—4-methoxyphenyl isocyanide (**3a**) system. For reference samples, we chose the conditions proposed previously[5,10] (concentrated solutions of all reactants in methanol with acetic and toluenesulfonic (**7**) acids as catalysts). The reactions with *N*-hydroxysuccinumide (**6**) were carried out in an aprotic solvent, acetonitrile, in order to rule out the competing process giving rise to imidates **A**. Apart from pure catalysts, catalytic systems containing mixtures of catalysts were used. The procedure for isolation of product **4a** was selected in such a way as to maximize the accuracy of these experiments: the reaction mixture was concentrated to dryness, the product was extracted with 1 *M* HCl and precipitated with NH_4OH. No traces of the product were detected in the residue, as it was almost insoluble in water, while its hydrochloride was readily soluble.

Scheme 2



4	R^1	R^2
a	4-$NO_2C_6H_4$	4-$MeOC_6H_4$
b	Me	2,6-$Me_2C_6H_3$
c	Pr^i	4-$Me_2NC_6H_4$
d	Cyclohexyl	4-$MeOC_6H_4$
e	4-FC_6H_4	2,6-$Me_2C_6H_3$
f	3,4-$(MeO)_2C_6H_3$	3,4-$CH_2O_2C_6H_3$
g	3,4-$(MeO)_2C_6H_3$	4-$Me_2NC_6H_4$
h	4-$Pr^iC_6H_4$	4-Morpholinophenyl
i	3,4,5-$(MeO)_3C_6H_2$	3,4-$CH_2O_2C_6H_3$
j	3,4,5-$(MeO)_3C_6H_2$	4-Morpholinophenyl
k	2-Thienyl	3,4-$CH_2O_2C_6H_3$
l	2-Thienyl	4-Morpholinophenyl

It can be seen from the data presented in Table 1 that no target product **4a** is formed in an aprotic solvent (aceto-

Table 1. Yields of product **4a** depending on the solvent and the catalyst used

Catalyst	Number of equiv.	Solvent	*t**/h	Yield (%)
—	—	MeCN	240	0
—	—	Benzene	240	0
—	—	MeOH	240	46
N-Hydroxysuccinimide	1	MeCN	240	42
AcOH	1	MeOH	20	68
AcOH	1	MeCN	20	23
TsOH	0.2	MeCN	20	14
TsOH	0.2	MeOH	20	50
Hydrochloric acid	0.2	MeOH	20	37
N-Hydroxysuccinimide—TsOH	1 : 0.1	MeCN	20	91

* Reaction time.

nitrile, benzene) without a catalyst. However, in methanol or acetonitrile in the presence of reagent **6**, the reaction proceeds successfully although at a low rate. On addition of an acid, the reaction time is considerably shortened, while the product yields increase only if the reaction mixture contains a hydroxyl-containing compound. Our data also indicate that the use of acid catalysts in aprotic solvents results in substantial amounts of by-products due to competing reactions (Passerini and polymerization reactions). Thus, the combination of a hydroxyl-containing compound (MeOH or **6**) and an acid gives better results than a single catalyst. Note that the yields of the target product increase on passing from methanol to solutions of *N*-hydroxysuccinimide, and the best results were attained for the *N*-hydroxysuccinimide—*p*-toluenesulfonic acid system. In this case, the formation of Passerini reaction product **5**, which is always detected when carboxylic acids are used, was completely avoided. In addition, this catalytic system does not promote polymerization of even a sensitive isocyanide such as **3a**, which opens up broad opportunities for involvement of diverse isocyanides into the reaction.

During this work, we carried out a special study to determine the optimal ratio of catalysts **6** and **7** and the most appropriate solvent. It was shown that acid **7** should be used in catalytic amounts (0.05—0.1 mol equiv.), as its high concentration promotes polymerization of isocyanide **3a**. Meanwhile, *N*-hydroxysuccinimide (**6**) has a favorable effect on the yields of the target product and the reaction time over a broad concentration range. However, the best results were obtained at an equimolar ratio of the reactants and hydroxyl-containing compound **6**; in this case, the side reactions observed in the presence of only acid **7** were suppressed most efficiently. It should be emphasized that the use of an excess of hydroxyl-containing compound **6** does not give any advantage. Note that *N*-hydroxysuccinimide (**6**) remains unchanged upon the reaction and can be recovered for reuse. Therefore, depending on the concentration used, this compound can be regarded as either a catalyst or a catalytic additive. Besides acetonitrile, we tested other solvents, in particular, benzene, ethyl acetate, methanol, and water; however, in none of these solvents, were the results obtained in acetonitrile surpassed; therefore, subsequently we used acetonitrile as the main solvent.

For testing this procedure, we prepared a series of imidazo[1,2-*a*]pyridines **4a—l** based on polymerization-sensitive isocyanides **3a—e** (see Scheme 2). Depending on the structure and stability, each particular imidazo[1,2-*a*]pyridine **4** was isolated as either the hydrochloride or the free base. In all cases, we attained high yields of the target products with minimum time required for isolation and purification. The use of evaporation of the reaction mixture and extraction of the solid residue with 1 *M* hydrochloric acid showed high efficiency; this procedure can be used in the synthesis of large libraries of imidazo[1,2-*a*]pyridines **4** for biological screening. The proof of the structures of the obtained compounds did not cause difficulty, because it relied on many analogies.[5—7,10] The mass spectra of imidazo[1,2-*a*]pyridines **4a—l** exhibit intensive molecular ion peaks (in most cases, 100%), which correspond to their calculated mass. The ^{1}H NMR spectra of compounds **4a—l** exhibit characteristic signals for the imidazopyridine ring: a doublet for the H(8) proton at δ 7.9—8.7 (J = 6.7—7.0 Hz) and a doublet for the H(5) proton at δ 7.4—8.1 (J = 8.6—9.2 Hz). The ^{1}H NMR spectra of imidazo[1,2-*a*]pyridine derivatives differ from one another by the sets of signals for the side groups and by the multiplicity of the H(6) and H(7) proton signals of the imidazopyrimidine ring. The spectral data of the synthesized compounds are presented in Table 2. It is noteworthy that all the described compounds were synthesized for the first time.

In our opinion, the mechanism of action of the catalytic system we propose is based on the intermediate formation of imidates similar to compounds **A**. Fast cyclization of these compounds results in products **4**, which, in turn, is the main obstacle to the isolation and investigation of the imidates containing a 2-aminopyridine fragment. Note that imidates with similar structure formed as intermediate products in the Ugi reaction were isolated and characterized by a number of researchers.[9,11,12]

Thus, our study demonstrated that a combination of *N*-hydroxysuccinimide and *p*-toluenesulfonic acid surpasses in efficiency the catalysts known previously for the three-component reaction of 2-aminopyridine with aldehydes and isocyanides, resulting in imidazo[1,2-*a*]pyridine derivatives. The use of this system allows one to avoid the side formation of undesirable products of the Passerini reaction and polymerization of unstable isocyanides.

Table 2. ^{1}H NMR and mass spectrometry data for products **4a—l**

Compound	^{1}H NMR (DMSO-d_6), δ (*J*/Hz)	Mass spectrum, *m*/*z* (I_{rel} (%))
4a	8.19, 8.32 (both d, 2 H each, Ar, *J* = 9.2); 7.95 (d, 1 H, H(8), *J* = 6.7); 7.91 (s, 1 H, NH); 7.56 (d, 1 H, H(5), *J* = 9.1); 7.25—7.30 (m, 1 H, H(6)); 6.85—6.89 (m, 1 H, H(7)); 6.47, 6.68 (both d, 2 H each, Ar, *J* = 8.9); 3.65 (s, 3 H, OMe)	360 $[M]^+$ (100), 345 (7), 330 (7), 226 (11), 180 (8), 78 (57)
4b	8.70 (d, 1 H, H(8), *J* = 6.7); 7.91 (d, 1 H, H(5), *J* = 8.9); 7.81—7.86 (m, 1 H, H(6)); 7.59 (s, 1 H, NH); 7.42—7.46 (m, 1 H, H(7)); 7.01 (d, 2 H, Ar, *J* = 8.2); 6.89 (dd, 1 H, Ar, $J_1 = J_2$ = 8.2); 2.04 (s, 6 H, 2 Me); 1.92 (s, 3 H, Me)	251 $[M]^+$ (100), 236 (7), 158 (22), 132 (59), 119 (35), 78 (59)
4c	8.80 (s, 1 H, NH); 8.18 (d, 1 H, H(8), *J* = 6.7); 7.95 (d, 1 H, H(5), *J* = 8.6); 7.74—7.78 (m, 1 H, H(6)); 7.28—7.31 (m, 1 H, H(7)); 6.74, 6.51 (both d, 2 H each, Ar, *J* = 8.5); 3.17—3.25 (m, 1 H, CH); 2.82 (s, 6 H, NMe_2); 1.36 (d, 6 H, 2 Me, *J* = 6.6)	294 $[M]^+$ (100), 279 (14), 148 (23), 147 (21), 139 (8), 105 (7), 78 (28)
4d	8.25 (d, 1 H, H(8), *J* = 7.0); 8.12 (s, 1 H, NH); 8.04 (d, 1 H, H(5), *J* = 9.2); 7.88—7.91 (m, 1 H, H(6)); 7.38—7.41 (m, 1 H, H(7)); 6.72, 6.55 (both d, 2 H each, Ar, *J* = 8.9); 3.68 (s, 3 H, OMe); 3.08—3.17 (m, 1 H, CH); 1.98—2.30 (m, 10 H, 5 CH_2)	319 $[M]^+$ (100), 318 (7), 304 (9), 250 (14), 185 (9), 132 (8), 105 (13), 78 (36)
4e	8.52 (d, 1 H, H(8), *J* = 7.0); 8.07 (d, 1 H, H(5), *J* = 9.2); 7.96 (s, 1 H, NH); 7.90—7.93 (m, 1 H, H(6)); 7.81 (dd, 2 H, Ar, *J* = 8.6, *J* = 5.5); 7.43—7.47 (m, 1 H, H(7)); 7.09 (d, 2 H, Ar, *J* = 8.6); 6.87 (d, 2 H, Ar, *J* = 8.2); 6.74 (dd, 1 H, Ar, $J_1 = J_2$ = 8.2); 1.97 (s, 6 H, 2 Me)	331 $[M]^+$ (100), 238 (14), 212 (67), 199 (26), 165 (8), 132 (8), 78 (74)
4f	8.56 (s, 1 H, NH); 8.43 (d, 1 H, H(8), *J* = 6.7); 8.05 (d, 1 H, H(5), *J* = 8.8); 7.90—7.94 (m, 1 H, H(6)); 7.68 (d, 1 H, $H(2)_{Ar}$, *J* = 1.8); 7.62 (dd, 1 H, $H(6)_{Ar}$, *J* = 8.5, *J* = 1.8); 7.44—7.46 (m, 1 H, H(7)); 7.24 (d, 1 H, $H(5)_{Ar}$, *J* = 8.5); 6.71 (d, 1 H, $H(5)_{Ar}$, *J* = 8.6); 6.46 (d, 1 H, $H(2)_{Ar}$, *J* = 2.4); 6.17 (dd, 1 H, $H(6)_{Ar}$, *J* = 8.6, *J* = 2.4); 5.88 (s, 2 H, O_2CH_2); 3.80, 3.75 (both s, 3 H each, OMe)	389 $[M]^+$ (100), 388 (6), 241 (16), 211 (6), 194 (6), 122 (5), 78 (38)
4g	7.92 (d, 1 H, H(8), *J* = 6.7); 7.64 (d, 1 H, $H(2)_{Ar}$, *J* = 1.8); 7.59 (dd, 1 H, $H(6)_{Ar}$, *J* = 8.2, *J* = 1.8); 7.50 (s, 1 H, NH); 7.48 (d, 1 H, H(5), *J* = 8.9); 7.18—7.21 (m, 1 H, H(6)); 6.86 (d, 1 H, $H(5)_{Ar}$, *J* = 8.2); 6.77—6.81 (m, 1 H, H(7)); 6.42, 6.58 (both d, 2 H each, Ar, *J* = 8.9); 3.70, 3.76 (both s, 3 H each, OMe); 2.74 (s, 6 H, NMe_2)	388 $[M]^+$ (100), 373 (7), 241 (14), 194 (18), 121 (11), 78 (37)
4h	7.94 (d, 2 H, Ar, *J* = 8.6); 7.89 (d, 1 H, H(8), *J* = 6.7); 7.66 (s, 1 H, NH); 7.56 (d, 1 H, H(5), *J* = 9.2); 7.26 (d, 2 H, Ar, *J* = 8.6); 7.19—7.23 (m, 1 H, H(6)); 6.80—6.85 (m, 1 H, H(7)); 6.45, 6.72 (both d, 2 H each, Ar, *J* = 8.5); 3.70 (t, 4 H, $O(CH_2)_2$, *J* = 4.9); 2.92 (t, 4 H, $N(CH_2)_2$, *J* = 4.9); 1.86—1.90 (m, 1 H, CH); 1.23 (d, 6 H, 2 Me, *J* = 7.3)	412 $[M]^+$ (100), 223 (12), 181 (11), 105 (12), 78 (24)
4i	7.98 (d, 1 H, H(8), *J* = 6.7); 7.86 (s, 1 H, NH); 7.51 (d, 1 H, H(5), *J* = 9.2); 7.35 (s, 2 H, Ar); 6.90—6.94 (m, 1 H, H(6)); 6.82—6.86 (m, 1 H, H(7)); 6.57 (d, 1 H, $H(5)_{Ar}$, *J* = 8.2); 6.15 (d, 1 H, $H(2)_{Ar}$, *J* = 2.1); 5.92 (dd, 1 H, $H(6)_{Ar}$, *J* = 8.2, *J* = 2.1); 5.82 (s, 2 H, O_2CH_2); 3.74 (s, 6 H, 2 OMe); 3.69 (s, 3 H, OMe)	419 $[M]^+$ (100), 404 (7), 271 (10), 241 (7), 194 (8), 125 (4), 105 (4), 78 (34)
4j	7.98 (d, 1 H, H(8), *J* = 6.7); 7.73 (s, 1 H, NH); 7.51 (d, 1 H, H(5), *J* = 8.9); 7.33 (s, 2 H, Ar); 7.19—7.23 (m, 1 H, H(6)); 6.80—6.85 (m, 1 H, H(7)); 6.71, 6.46 (both d, 2 H each, Ar, *J* = 8.9); 3.72 (t, 4 H, $O(CH_2)_2$, *J* = 4.9); 3.70 (s, 6 H, 2 OMe); 3.67 (s, 3 H, OMe); 2.90 (t, 4 H, $N(CH_2)_2$, *J* = 4.9)	460 $[M]^+$ (100), 445 (4), 271 (8), 230 (16), 82 (19), 78 (20)
4k	7.92 (d, 1 H, H(8), *J* = 6.7); 7.78 (s, 1 H, NH); 7.50 (d, 1 H, H(5), *J* = 8.9); 7.44 (dd, 1 H, thiophene H(3), *J* = 3.7, *J* = 1.2); 7.34 (dd, 1 H, thiophene H(5), *J* = 4.9, *J* = 1.2); 7.20—7.24 (m, 1 H, H(6)); 7.02 (dd, 1 H, thiophene H(4), *J* = 4.9, *J* = 3.7); 6.82—6.86 (m, 1 H, H(7)); 6.57 (d, 1 H, $H(5)_{Ar}$, *J* = 8.5); 6.18 (d, 1 H, $H(2)_{Ar}$, *J* = 2.1); 5.89 (dd, 1 H, $H(6)_{Ar}$, *J* = 8.5, *J* = 2.1); 5.83 (s, 2 H, O_2CH_2)	337 $[M + 2]^+$ (7), 335 $[M]^+$ (100), 262 (6), 214 (6), 187 (36), 122 (6), 84 (10), 78 (55)
4l	7.89 (d, 1 H, H(8), *J* = 6.7); 7.65 (s, 1 H, NH); 7.49 (d, 1 H, H(5), *J* = 9.2); 7.44 (dd, 1 H, thiophene H(3), *J* = 3.7, *J* = 1.2); 7.32 (dd, 1 H, thiophene H(5), *J* = 4.9, *J* = 1.2); 7.21—7.25 (m, 1 H, H(6)); 7.00 (dd, 1 H, thiophene H(4), *J* = 4.9, *J* = 3.7); 6.80—6.85 (m, 1 H, H(7)); 6.44, 6.70 (both d, 2 H each, Ar, *J* = 8.9); 3.69 (t, 4 H, $O(CH_2)_2$, *J* = 4.9); 2.91 (t, 4 H, $N(CH_2)_2$, *J* = 4.9)	378 $[M + 2]^+$ (8), 376 $[M]^+$ (100), 318 (10), 188 (14), 187 (23), 121 (12), 78 (30)

The developed procedure for the preparation of imidazo[1,2-*a*]pyridines opens up the way to the synthesis of a broad range of derivatives for biological screening. Generally, this work demonstrates good prospects of hydroxyl-containing compounds as catalysts for multicomponent reactions of isocyanides.

Experimental

The reactions were monitored and the purity of the synthesized compounds was checked by TLC on Silufol-254 and Sorbfil-254 plates in the following systems: chloroform, chloroform—ethanol (9 : 1, 15 : 1, and 20 : 1). ^{1}H NMR spectra were

Table 3. Yields, melting points, and elemental analysis data for products **4a—l**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%) C	H	N	Molecular formula
4a	91	162—163	66.95 / 66.67	4.25 / 4.45	15.44 / 15.56	$C_{20}H_{16}N_4O_3$
4b	85	236—237	66.68 / 66.78	9.71 / 9.74	14.65 / 14.61	$C_{16}H_{27}N_3 \cdot HCl$
4c	89	204—205	65.58 / 65.36	6.97 / 6.96	16.92 / 16.95	$C_{18}H_{22}N_4 \cdot HCl$
4d	86	199—200	67.75 / 67.51	6.15 / 6.19	11.88 / 11.81	$C_{20}H_{21}N_3O \cdot HCl$
4e	81	205—206	68.46 / 68.57	5.29 / 5.17	11.38 / 11.43	$C_{21}H_{18}FN_3 \cdot HCl$
4f	84	186—187	62.12 / 62.05	4.75 / 4.70	9.86 / 9.87	$C_{22}H_{19}N_3O_4 \cdot HCl$
4g	90	195—196	70.98 / 71.13	6.16 / 6.19	14.30 / 14.43	$C_{23}H_{24}N_4O_2$
4h	92	236—237	75.64 / 75.73	6.68 / 6.80	13.53 / 13.59	$C_{26}H_{28}N_4O$
4i	98	203—204	65.78 / 65.87	5.09 / 5.02	10.13 / 10.03	$C_{23}H_{21}N_3O_5$
4j	98	217—218	68.01 / 67.83	5.99 / 6.09	12.15 / 12.17	$C_{26}H_{28}N_4O_4$
4k	87	213—214	64.67 / 64.48	3.73 / 3.88	12.60 / 12.54	$C_{18}H_{13}N_3O_2S$
4l	85	256—257	67.15 / 67.02	5.28 / 5.32	14.84 / 14.89	$C_{21}H_{20}N_4OS$

recorded on a Bruker DRX-400 spectrometer (400 MHz) in DMSO-d_6 or DMSO-d_6 + CCl_4, Me_4Si as the internal standard; mass spectra were run on a Varian MAT 311A spectrometer (accelerating voltage 3 kV, electron ionization energy 70 eV, direct sample injection into the ion source). The melting points were not corrected.

***N*-(4-Methoxyphenyl)-2-(4-nitrophenyl)imidazo[1,2-*a*]pyridin-3-ylamine (4a).** 2-Aminopyridine (0.5 mmol) and 4-nitrobenzaldehyde (0.55 mmol) were added to a solution of 4-methoxyphenyl isocyanide (0.5 mmol) in the specified solvent (0.75 mL). The reaction mixture was stirred at ~20 °C and the specified catalyst was added. After keeping the mixture for 20 h at ~20 °C, it was concentrated to dryness. The residue was extracted with 1 *M* HCl (2×10 mL), the extract was neutralized with NH_4OH, and the resulting precipitate was filtered off and recrystallized from ethanol. The ^{1}H NMR and mass spectra of this compound are presented in Table 2; the yields, melting points, and elemental analysis data are in Table 3.

2-Acetoxy-*N*-(4-methoxyphenyl)-2-(4-nitrophenyl)acetamide (5) (Passerini reaction product). When acetic acid was used as the catalyst, the residue after extraction with hydrochloric acid represented a mixture of the Passerini reaction product, the starting compounds, and isocyanide-derived polymers. The Passerini reaction product was isolated by flash chromatography (silica gel 40/5μ, elution with chloroform—ethanol, 9 : 1). Yield 79 mg (23%), m.p. 217—218 °C. Found (%): C, 59.54; H, 4.57; N, 7.98. $C_{17}H_{16}N_2O_6$. Calculated (%): C, 59.30; H, 4.68; N, 8.14. ^{1}H NMR (DMSO-d_6), δ: 2.19 (s, 3 H, Me); 5.92 (s, 1 H, CH); 6.83, 7.32 (both d, 2 H each, C_6H_4OMe, J = 8.2 Hz); 8.11, 8.25 (both d, 2 H each, $C_6H_4NO_2$, J = 8.8 Hz); 9.62 (br.s, 1 H, NH).

***N*-Arylimidazo[1,2-*a*]pyridin-3-ylamines 4b—l** were prepared by the above procedure for the synthesis of compound **4a** using the *N*-hydroxysuccinimide (0.5 mmol)—*p*-toluenesulfonic acid (0.05 mmol) system as the catalyst. After storage for 20 h at ~20 °C, the reaction mixture was concentrated to dryness.

Preparation of the product as a free base. The residue was extracted with 1 *M* HCl (2×10 mL), the extract was neutralized by NH_4OH, and the resulting precipitate was filtered off and recrystallized from ethanol.

Preparation of the product as the hydrochloride. The residue was dissolved in toluene (5 mL) and washed with a 10% aqueous solution of sodium carbonate and water. The organic layer was dried with sodium sulfate, and several drops of a solution of HCl in ethanol were added. The precipitate was filtered off and dried.

The ^{1}H NMR and mass spectra of the obtained compounds are presented in Table 2; the yields, melting points, and elemental analysis data are in Table 3.

Recovery of *N*-hydroxysuccinimide. The aqueous extracts remaining after the isolation of the target product were concentrated and extracted with a 2 : 1 toluene—methyl ethyl ketone mixture. Concentrating and cooling of this solution gave *N*-hydroxysuccinimide, which can be used repeatedly. For further purification, this product was crystallized from ethyl acetate, m.p. 97—98 °C.

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