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Diversity-Oriented Synthesis of 1-Substituted 4-Aryl-6-oxo-1,6-dihydropyridine-3-carboxamides.

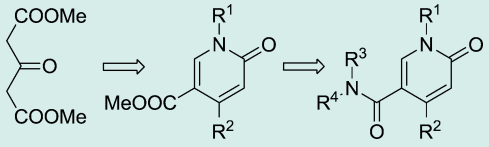
Jernej Baškovč,[†] Georg Dahmann,[‡] Amalija Golobič,[†] Uroš Grošelj,[†] Drago Kočar,[†] Branko Stanovnik,[†] and Jurij Svete*[,†]

[†]Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, P.O. Box 537, 1000 Ljubljana, Slovenia

[‡]Boehringer Ingelheim Pharma GmbH & Co. KG, Medicinal Chemistry, 88397 Biberach, Germany.

Supporting Information

ABSTRACT: A simple five-step diversity-oriented synthesis of 1-substituted 4-aryl-6-oxo-1,6-dihydropyridine-3-carboxamides was developed. Treatment of dimethyl 2-((dimethylamino)methylidene)-3-oxopentanedioate with twenty primary amines gave 1-substituted methyl 4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylates. Transformation into the corresponding 4-tosyloxy and 4-chloro derivatives, followed by Suzuki–Miyaura arylations gave a series of eleven N-substituted methyl 4-aryl-6-oxo-1,6-dihydropyridine-3-carboxylates. Combinatorial screening was employed to establish suitable reaction conditions for Suzuki–Miyaura arylation of N-alkylpyridones. Hydrolysis of the esters followed by parallel solution-phase amidation of the corresponding carboxylic acids with primary and secondary amines furnished a library of seventeen final products.



KEYWORDS: *parallel synthesis, cyclization, pyridones, Suzuki–Miyaura arylation, amidation*

INTRODUCTION

Heterocyclic compounds are important scaffolds for the preparation of compound libraries for medicinal and pharmaceutical applications.[1−4] Within this context, the 2-pyridone system is a useful core for derivatization and, hence, preparation of biologically active compounds. For example, 2-pyridone containing compounds have recently been prepared as MCH1R antagonists,[5] 11β-hydroxysteroid dehydrogenase 1 inhibitors,[6] P2X7 purinoceptor modulators,[7] inhibitors of cyclooxygenases and 5-lipoxygenase,[8] dopamine D3 receptor antagonists,[9] and antibiotics.[10] Therefore, synthesis of libraries of novel 2-pyridone derivatives and their fused analogues is of particular interest.

Nicotinamide (vitamin B_3) is an important pyridine derivative and a large number of its derivatives and analogues have been prepared, so far. However, 1,4-disubstituted 6-oxo-1,6-dihydropyridine-3-carboxamides that are unsubstituted at positions 2 and 5 are almost unexplored group of nicotinamide derivatives. To the best of our knowledge, only two compounds of this particular type are known.[11,12] The first one is N′-functionalized 2-(5-carbamoyl-2-oxo-4-(trifluoromethyl)-pyridin-1(2*H*)-yl)acetic acid, that has been prepared as chemokine modulator quite routinely by a three step derivatization of commercially available 6-hydroxy-4-trifluoromethylnicotinic acid.[11] The second one, N′-substituted 4-(3-chlorophenyl)-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide, has been prepared as farnesyltransferase inhibitor in five-step synthesis including pyridone ring formation. The synthesis comprises Heck-type arylation of diethyl glutaconate, formylation, cyclization with methylamine, hyrolysis of the ester, and amidation.[12a]

Within our long-term studies on enaminones as versatile reagents in heterocyclic synthesis,[13] a part of our research has been focused on the synthesis of fused pyridones[14] from pyridineacetic acid derivatives[13,15] and on the synthesis of 1,4-dihydropyridines[16] by cyclocondensations of bis-enaminones with primary amines[13,17] including parallel solution-phase approach.[15,18] For the synthesis of dihydropyridine derivatives, dimethyl acetone-1,3-dicarboxylate (**1**)[19] has been found as particularly useful starting material.[17a,b,d,18] Recently, we reported a simple one-pot transformation of **1** with ammonia and aliphatic primary amines into methyl 1-alkyl-4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylates.[20] In extension, we focused our attention on parallel preparation and transformations of 6-oxo-1,6-dihydropyridine derivatives with 4-aryl-6-oxo-1,6-dihydropyridine-3-carboxamides **11** as target compounds. Herein, we report a novel five-step synthesis of **11** (Scheme 1) comprising a enaminone-based preparation of methyl 4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylates **4** from primary amines **3**{*1*−*20*} (Figure 1), transformations into the corresponding tosylates **5** and chloro analogues **6**, Suzuki–Miyaura arylation of **5** and **6** with arylboronic acids **7**{*1*−*4*} (Figure 2), followed by hydrolysis of methyl 4-aryl-6-oxo-1,6-dihydropyridine-3-carboxylates **8**, and parallel amidations of the so-formed carboxylic acids **9** with aliphatic amines **3**{*20*−*27*} (Figure 1) to furnish title carboxamides **11** (Scheme 1).

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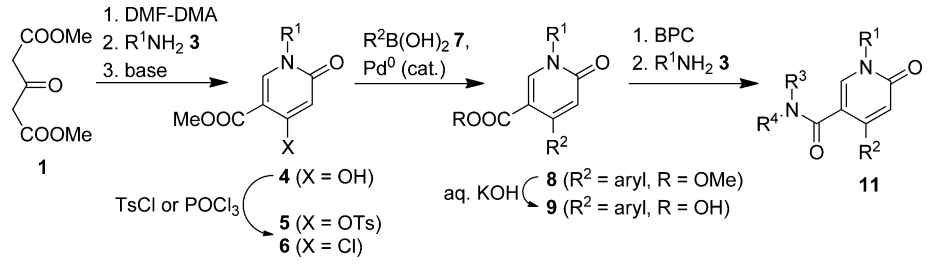
Scheme 1. General Synthetic Route



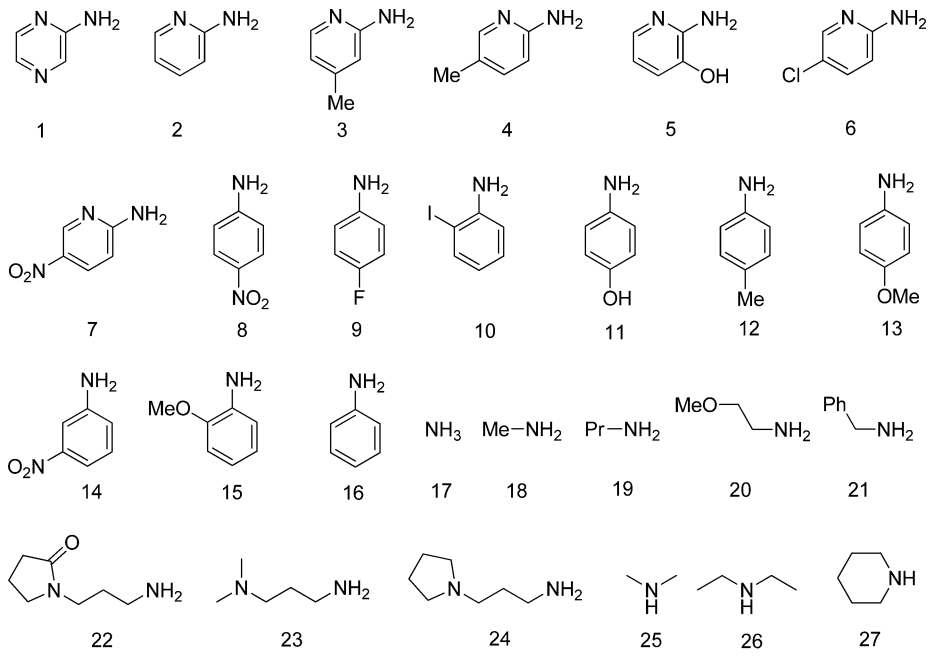


Figure 1. Diversity reagents 3{*1*−*20*} used for cyclization of enaminone **2** and diversity reagents 3{*20*−*27*} used for amidation of carboxylic acids **9**.

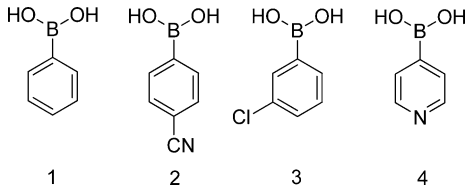


Figure 2. Diversity reagents 7{*1*−*4*} used for Suzuki−Miyaura arylations.

RESULTS AND DISCUSSION

Following modified literature procedures,[18,20] commercially available dimethyl acetone-1,3-dicarboxylate (**1**) was first transformed with *N*,*N*-dimethylformamide dimethylacetal (DMF-DMA) into the enaminone **2**. Acid-catalyzed parallel treatment of **2** with primary amines 3{*1*−*20*} gave the intermediates **2**′{*1*−*20*},[18] which were directly (without isolation) cyclized into **4** by treatment with methanolic potassium hydroxide. Acidification and evaporation of the reaction mixtures followed by extraction of the products **4** from the solid residues with a 2:5 mixture of methanol and ethyl acetate, filtration, and evaporation furnished analytically pure methyl 1-aryl-4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylates **4**{*1*−*20*} in 40−80% yield. Further parallel treatment of 4-hydroxypyridones **4**{*1,3,8,9,13,16,18*−*20*} with tosyl chloride in DMF in the presence of triethylamine and 4-dimethylaminopyridine (DMAP) at 95 °C furnished the corresponding tosylates **5**{*1,3,8,9,13,16,18*−*20*} in 18−87% yield. Similarly, parallel chlorination of the pyridones **4**{*18*−*20*} in refluxing phosphorus oxychloride afforded the chloro analogues **6**{*18*−*20*} in 60−57% yield (Scheme 2, Table 1). It is noteworthy, that triflates and bromides should be better coupling partners in subsequent Suzuki−Miyaura reactions than the corresponding tosylates **5** and chlorides **6**. Unfortunatelly, attempts to obtain the corresponding triflate and bromide from pyridone **4**{*18*} failed. [Simplicity and cost-effectiveness of the cross-coupling method were also important to us. Preparation of triflates and bromides was not studied further for the following reasons: (a) the reagents, Tf_2O and $POBr_3$, are approximately ten times more expensive than TsCl and $POCl_3$; (b) the solid TsCl is much easier to handle than Tf_2O, which is a moisture-sensitive liquid; (c) excess $POCl_3$ (bp 106 °C) is easily removable by evaporation using a diaphragm pump, while $POBr_3$ (bp 192 °C) is not; (d) tosylates are more convenient to use, since they are usually crystalline and hydrolytically more stabile than triflates.]

Suzuki−Miyaura cross-coupling of the corresponding tosylates **5** with arylboronic acids **7** (Figure 2) was then studied. Reaction conditions were first optimized for the reaction of 1-phenyltosylate **5**{*16*} with phenylboronic acid **7**{*1*} and $Pd(PPh_3)_4$ as catalyst. Reaction in refluxing *tert*-butanol in the presence of potassium phosphate afforded the corresponding cross-coupling product **8**{*16/1*} in 10% yield.

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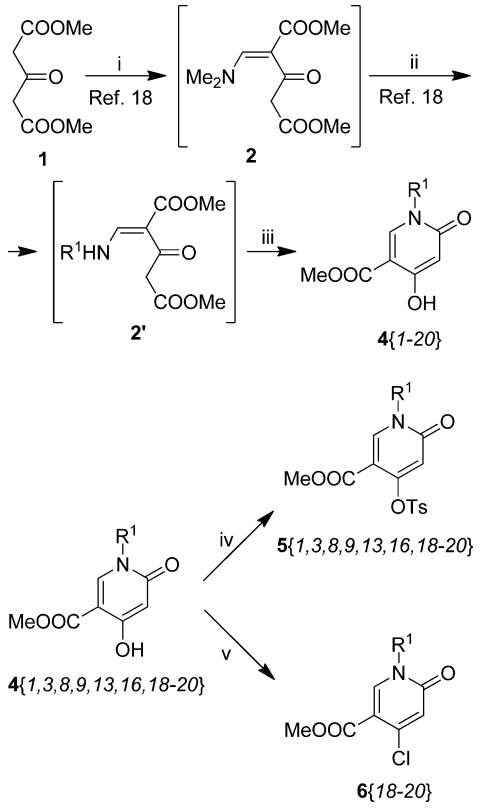
Scheme 2. Synthesis of Compounds 4–6[a]



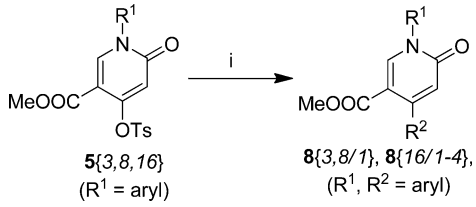
[a]Reaction conditions: (i) DMF-DMA, MeOH, r.t. (ref 18); (ii) R^1NH_2 **3**{*1–20*}, MeOH, 37% HCl (1 equiv.), r.t. (ref 18); (iii) KOH, MeOH, reflux; (iv) TsCl, DMF, Et_3N, DMAP (cat.), 95 °C; (v) $POCl_3$, reflux.

Table 1. Experimental Data on Compounds 4–6[a]

			yield (%)		
entry	compound	R^1	**4**	**5**	**6**
1	**4**{*1*}, **5**{*1*}	pyrazinyl	58[b]	47[b]	
2	**4**{*2*}	pyridin-2-yl	63[b]		
3	**4**{*3*}, **5**{*3*}	4-methylpyridin-2-yl	65[b]	52[b]	
4	**4**{*4*}	5-methylpyridin-2-yl	60[b]		
5	**4**{*5*}	3-hydroxypyridin-2-yl	54[b]		
6	**4**{*6*}	5-chloropyridin-2-yl	80[b]		
7	**4**{*7*}	5-nitropyridin-2-yl	50[b]		
8	**4**{*8*}, **5**{*8*}	4-nitrophenyl	50[b]	87[b]	
9	**4**{*9*}, **5**{*9*}	4-fluorophenyl	46[b]	18[b]	
10	**4**{*10*}	2-iodophenyl	45[b]		
11	**4**{*11*}	4-hydroxyphenyl	45[b]		
12	**4**{*12*}	4-methylphenyl	45[b]		
13	**4**{*13*}, **5**{*13*}	4-methoxyphenyl	60[b]	36[b]	
14	**4**{*14*}	3-nitrophenyl	48[b]		
15	**4**{*15*}	2-methoxyphenyl	63[b]		
16	**4**{*16*}, **5**{*16*}	Ph	54[b]	75[b]	
17	**4**{*17*}	H	40[b]		
18	**4**{*18*}–**6**{*18*}	Me	60[b]	45[b]	62[b]
19	**4**{*19*}–**6**{*19*}	1-propyl	57[b]	29[b]	75
20	**4**{*20*}–**6**{*20*}	2-methoxyethyl	46[b]	35[b]	60

[a]All compounds were obtained in ≥80% purity (determined by LC-MS and ^{1}H NMR). [b]Analytical purity was determined by elemental analysis. The found values for C, H, and N were within ±0.4% range with respect to the theoretical values.

Scheme 3. Synthesis of 1,4-Diarylpyridones 8 (Method A)[a]



[a]Reaction conditions: (i) $R^2B(OH)_2$ **7** (chemset **7**), $Pd(PPh_3)_4$ (cat.), Cs_2CO_3, DMF–H_2O, 90 °C.

Table 2. Experimental Data on 1,4-Diarylpyridones 8[a]

entry	compound	R^1	R^2	yield (%)
1	**8**{*3/1*}	4-methylpyridin-2-yl	Ph	63
2	**8**{*8/1*}	4-nitrophenyl	Ph	82[b]
3	**8**{*16/1*}	Ph	Ph	72[b]
4	**8**{*16/2*}	Ph	4-cyanophenyl	67[b]
5	**8**{*16/3*}	Ph	3-chlorophenyl	58[b]
6	**8**{*16/4*}	Ph	pyridin-4-yl	50[b]

[a]All compounds were obtained in ≥80% purity (determined by LC-MS and ^{1}H NMR). [b]Analytical purity was determined by elemental analysis. The found values for C, H, and N were within ±0.4% range with respect to the theoretical values.

Next, reaction in aqueous DMF in the presence of cesium carbonate at 65 °C gave **8**{*16/1*} in 47% yield, while at 90 °C **8**{*16/1*} was obtained in 72% yield. Under microwave-irradiation at 90 °C, the yield was almost identical (71%). Next, parallel cross-coupling of the representative 1-phenyl-tosylate **5**{*16*} with arylboronic acids **7**{*1–4*} and reactions of **5**{*3*} and **5**{*8*} with phenylboronic acid **7**{*1*} was performed. Reactions were carried out in aqueous DMF, $Pd(PPh_3)_4$ as catalyst, and cesium carbonate at 90 °C followed by extraction and purification of the crude products by filtration through a short plug of silica gel to give 1,4-diarylpyridones **8** in 50–82% yield. Out of six pyridones **8**, five were analytically pure, while compound **8**{*3,1*} was also >80% pure according to ^{1}H NMR and LC-MS (Method A, Scheme 3, Table 2).

To our surprise, neither the 1-alkyl tosylates **5**{*18–20*}, nor the chloropyridones **6**{*18–20*}, underwent cross-coupling with phenylboronic acid **7**{*1*}. Several attempts to carry out these reactions by variation of reaction conditions (substrate, solvent, base, and catalyst) were futile as well. To prepare the 1-alkyl substituted pyridones **8**, extensive combinatorial screening for suitable reaction conditions with respect to the substrate, solvent, base, and catalyst was performed. A series of 320 Suzuki–Miyaura cross-coupling reactions were carried out, comprising combinations of one reagent **7**{*1*}, two substrates **5**{*18*} and **6**{*18*}, five solvents 1–5, four bases I–IV, and eight catalysts A–H. Parallel screening reactions were carried out at 60 °C on a 12 × 0.1 mmol scale in 2 mL glass vials using a standard magnetic stirrer/heater equipped with aluminum block with 12 positions and temperature controller. The reactions were monitored by TLC and by change of color. In the two successful cross-couplings, progress of the reaction was detected when the initially orange-brown reaction mixture turned dark green with precipitation of colloidal palladium black (Scheme 4).

Out of 320 reactions, just two of them gave the desired cross-coupling product **8**{*18/1*}: (a) reaction of the chloride **6**{*18*} in DMF, with KOH–MeOH as base, and $PdCl_2$/P(*p*-tolyl)$_3$ as

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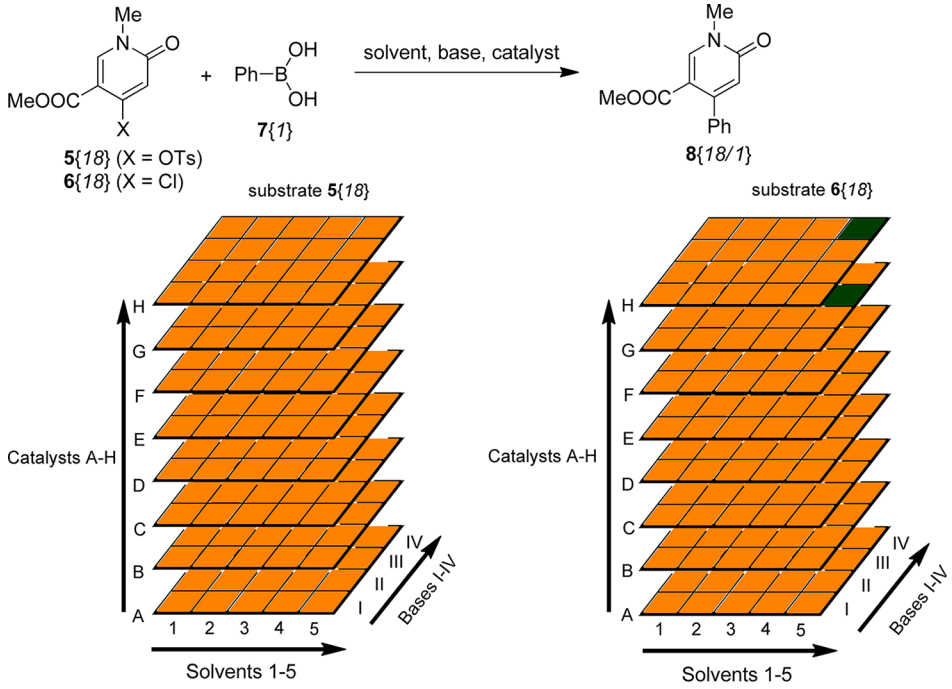
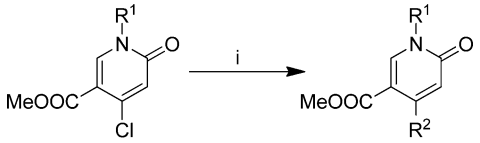
Scheme 4. Screening for Reaction Conditions for Arylation of 1-Alkylpyridones 5 and 6



Solvents 1-5: MeOH (1), *n*-PrOH (2), *t*-BuOH (3), MeCN (4), DMF (5)
Bases I-IV: K_3PO_4 (I), NaOH (II), KOH (III), Cs_2CO_3 (IV)
Catalysts A-H: $Pd(OAc)_2$-PPh_3 (Catalyst A), $PdCl_2$-PPh_3 (Catalyst B), $Pd(OAc)_2$-P(naphthyl)$_3$ (Catalyst C), $PdCl_2$-P(naphthyl)$_3$ (Catalyst D), $Pd(OAc)_2$-(dicyclohexyl)(*N*-(2'-tolyl)indol-2-yl)phosphine (Catalyst E), $Pd(OAc)_2$/(dicyclohexyl)(*N*-(2'-tolyl)indol-2-yl)phosphine (Catalyst F), $PdCl_2$/P(*p*-tolyl)$_3$ (Catalyst G), $Pd(PPh_3)_4$-$[PdCl(allyl)]_2$ (Catalyst H).

Scheme 5. Synthesis of 1-Alkyl-4-arylpyridones 8 (Method B)[a]



[a]Reaction conditions: (i) $R^2B(OH)_2$ **7**, Cs_2CO_3, DMF–H_2O, $Pd(PPh_3)_4$–$[PdCl(allyl)]_2$ (cat.), 55–65 °C.

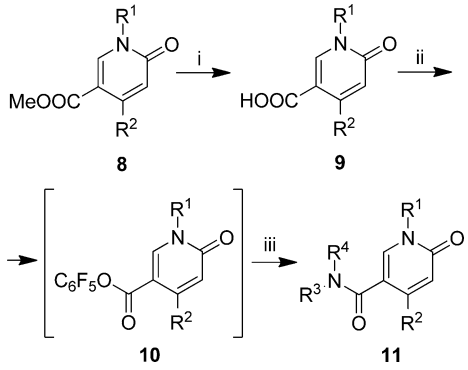
Table 3. Experimental Data on 1-Alkyl-4-arylpyridones 8[a]

entry	compound	R^1	R^2	yield (%)
1	**8**{*18/1*}	Me	Ph	73[b]
2	**8**{*18/3*}	Me	3-chlorophenyl	49
3	**8**{*19/1*}	1-propyl	Ph	61
4	**8**{*20/3*}	2-methoxyethyl	3-chlorophenyl	45

[a]All compounds were obtained in ≥80% purity (determined by LC-MS and ^{1}H NMR). [b]Analytical purity was determined by elemental analysis. The found values for C, H, and N were within ±0.4% range with respect to the theoretical values.

catalyst and (b) reaction of the chloride **6**{*18*} in DMF, Cs_2CO_3 as base, and combination of $Pd(PPh_3)_4$ and $[PdCl(allyl)]_2$ as the catalyst (Scheme 3). However, only the latter reaction was reproducible and, consequently, these conditions were finally employed for the preparation of five 1-alkyl-4-aryl pyridones **8**. In this manner, compounds **8**{*18/1,3*}, **8**{*19/1*}, and **8**{*20/3*} were obtained in 45–73% yield and in >80% purity (determined by LC-MS and ^{1}H NMR)(Method B, Scheme 5, Table 3).

Scheme 6. Synthesis of Compounds 9 and 11[a]



[a]Reaction conditions: (i) 1 M KOH–MeOH, reflux; (ii) Et_3N, BPC, MeCN, r.t.; (iii) R^3R^4NH **3**{*20–27*}, Et_3N, MeCN, r.t.

Although our primary goal was to obtain the 4-arylpyridones **8**, several attempts were also made to prepare the 4-alkyl and the 4-alkyenyl substituted compounds **8** by cross-coupling of **5**{*16*} and **6**{*18*} with butyl-, isobutyl-, cyclopentyl-, and *trans*-styrylboronic acid, yet without success. Even under microwave irradiation formation of the corresponding cross-coupling products was not observed.

Finally, transformation of the esters **8** into the corresponding carboxamides **11** was performed (Scheme 6). Hydrolysis of the esters **8** was carried out in parallel with 1 M KOH in methanol

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Table 4. Experimental Data on Compounds 9[a]

entry	compound	R^1	R^2	yield (%)
1	**9**{*8/1*}	4-nitrophenyl	Ph	95
2	**9**{*16/1*}	Ph	Ph	80
3	**9**{*16/2*}	Ph	4-cyanophenyl	83[b]
4	**9**{*16/3*}	Ph	3-chlorophenyl	83[b]
5	**9**{*16/4*}	Ph	pyridin-2-yl	65[b]
6	**9**{*18/1*}	Me	Ph	98[b]
7	**9**{*18/3*}	Me	3-chlorophenyl	94[b]
8	**9**{*19/1*}	*n*-Pr	Ph	74[b]
9	**9**{*20/3*}	$MeO(CH_2)_2$–	3-chlorophenyl	82[b]

[a]All products were obtained in ≥80% purity (determined by LC-MS and ^{1}H NMR). [b]Analytical purity was confirmed by elemental analysis. The found values for C, H, and N were within ±0.4% range with respect to the theoretical values.

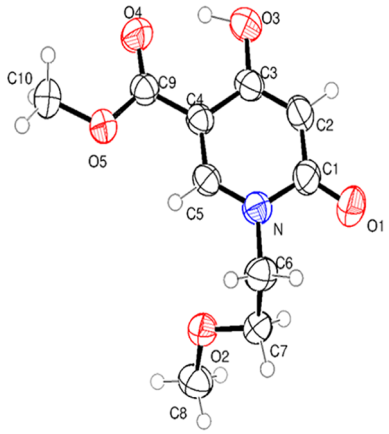
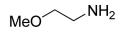
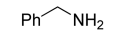
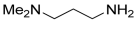
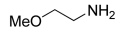
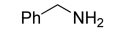
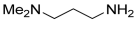
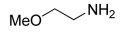
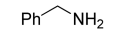
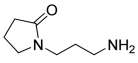
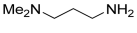
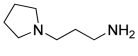
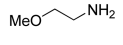
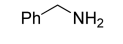
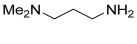


Figure 3. Molecular structure of compound **4**{*20*}.

under reflux to afford analytically pure carboxylic acids **9** in 76–98% yield upon simple filtration workup (Scheme 6, Table 4).

Carboxylic acids **9**{*16/1,3*} and **9**{*18/1,3*} and amines **3**{*20,21,23*} were chosen as model substrates for parallel amidation. In addition, five other amidations of the acids **9**{*16,18/1*} and **9**{*20/3*} with amines **3**{*22,24–27*} were performed as well. The acids **9** were activated with bis(pentafluorophenyl) carbonate (BPC) to give the pentafluorophenyl esters **10**, followed by treatment with aliphatic amines **3**{*20–27*} (Figure 1) to furnish title compounds **11** in 48–98% yield. Since BPC-mediated amidation affords only volatile byproduct, it allows simple evaporative workup. Thus, all seventeen title compounds **11** were primarily isolated just by filtration of the reaction mixtures (to remove the precipitated ammonium salts) followed by thorough evaporation of the filtrates at 100 °C/0.01 Torr (Workup A). Ten products, compounds **11**{*16/1/20,23*}, **11**{*16/3/20,21,23*}, **11**{*18/1/*

Table 5. Experimental Data on Compounds 11[a]

Entry	Compound	R^1	R^2	R^3R^4NH (**3**)	Workup	Yield (%)
1	**11**{*16/1/20*}	Ph	Ph		A	96
2	**11**{*16/1/21*}	Ph	Ph		B	78[b]
3	**11**{*16/1/23*}	Ph	Ph		A	98
4	**11**{*16/1/26*}	Ph	Ph		B	48
5	**11**{*16/3/20*}	Ph	3-chlorophenyl		A	91
6	**11**{*16/3/21*}	Ph	3-chlorophenyl		A	85[b]
7	**11**{*16/3/23*}	Ph	3-chlorophenyl		A	98
8	**11**{*18/1/20*}	Me	Ph		A	87[b]
9	**11**{*18/1/21*}	Me	Ph		A	84[b]
10	**11**{*18/1/22*}	Me	Ph		B	57
11	**11**{*18/1/23*}	Me	Ph		B	91[b]
12	**11**{*18/1/24*}	Me	Ph		B	54[b]
13	**11**{*18/1/25*}	Me	Ph		B	62[b]
14	**11**{*18/3/20*}	Me	3-chlorophenyl		A	83[b]
15	**11**{*18/3/21*}	Me	3-chlorophenyl		A	80
16	**11**{*18/3/23*}	Me	3-chlorophenyl		A	97
17	**11**{*20/3/27*}	$MeO(CH_2)_2$-	3-chlorophenyl		B	92

[a]All products were obtained in ≥80% purity (determined by LC-MS and ^{1}H NMR). [b]Analytical purity was confirmed by elemental analysis. The found values for C, H, and N were within ±0.4% range with respect to the theoretical values.

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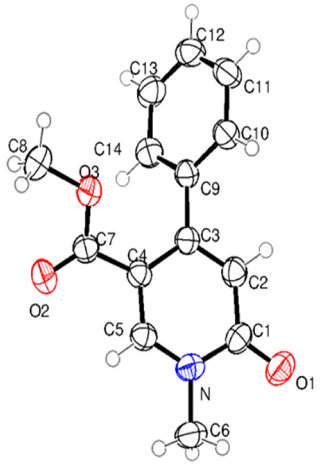

Figure 4. Molecular structure of compound **8**{*18/1*}.

20,21}, and **11**{*18/3/20,21,23*} were obtained in this way in 83−98% yield and in 80−98% purity. The purity of seven other products, **11**{*16/1/21,26*}, **11**{*18/1/22−25*}, and **11**{*20/3/27*} was not satisfactory upon Workup A. These crude products were further purified by trituration with 1 M hydrochloric acid followed by extraction with ethyl acetate (Workup B) to give the corresponding purified products **11** in 48−92% yield and in 87−100% purity. Of the seventeen final library members **11**, seven were ≥95% pure as confirmed also by elemental analyses for C, H, and N (Scheme 6, Table 5).

The structures and purities of novel compounds in chemsets **4**−**6**, **8**, **9**, and **11** were determined by spectroscopic methods (IR, NMR, MS, HRMS), by LC-MS, and by elemental analyses for C, H, and N. Physical and spectral data for known compounds **4**{*17*} and **4**{*18*} were in agreement with the literature data.[18] Characterization data for all compounds of chemsets **4**−**6**, **8**, **9**, and **11** are given in the Supporting Information.

The structures of compounds **4**{*20*} and **8**{*18/1*} were determined by X-ray diffraction (Figures 3 and 4, see also the Supporting Information).

CONCLUSION

A five-step parallel solution-phase synthesis of 1-substituted 4-aryl-6-oxo-1,6-dihydropyridine-3-carboxamides **11** from dimethyl 3-oxopentanedioate (**1**) was developed. The synthesis starts with one-pot preparation of methyl 4-hydroxy-6-oxo-1,6-dihydropyridine-3-carboxylates **4**. O-tosylation or nucleophilic chlorination of 4-hydroxypyridines **4**, followed by Suzuki−Miyaura cross-coupling of the corresponding tosyloxy- **5** or chloro derivatives **6** with arylboronic acids **7** gave 4-aryl-6-oxo-1,6-dihydropyridine-3-carboxylates **8** as the key-intermediates. Combinatorial screening was crucial for determining of the optimal reaction conditions for the synthesis of 1-alkyl-4-arylpyridones **8**. Hydrolysis of the esters **8** followed by BPC-mediated parallel solution-phase amidation of the acids **9** gave the title compounds **11** in good yields and purities. Typical overall yield of the final carboxamides **11** obtained from the representative amines **3**{*20,21,23*} and 1-arylcarboxylic acids **9**{*16/1,3*} (∼20%, R^1 = Ph, R^2 = Ar) and **8**{*18/1,3*} (∼15%, R^1 = Me, R^2 = Ar) shows that the method is somewhat more efficient for the preparation of the 1-aryl- that for the 1-alkyl substituted compounds. In summary, this method allows introduction of diverse substituents at three different positions: N(1), C(4), and the carboxy group in the 6-oxo-1,6-dihydropyridine-3-carboxylic acid core. Hence, it offers an easy access to 1-substituted 4-aryl-6-oxo-1,6-dihydropyridine-3-carboxamides **11** and could also serve as a useful tool for the preparation of novel compound libraries for pharmaceutical and other practical applications.

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures, characterization data, and the representative spectra for chemsets **4**−**6**, **8**, **9**, and **11**. This information is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*Tel.: +386 1 2419 100. Fax: +386 1 2419 220. E-mail: jurij.svete@fkkt.uni-lj.si.

Author Contributions

The manuscript was written with contributions from all authors. All authors have given approval to the final version of the manuscript.

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Notes

The authors declare no competing financial interest.

ABBREVIATIONS

BPC, bis(pentafluorophenyl) carbonate; DMAP, 4-dimethylaminopyridine; DMF, *N*,*N*-dimethylformamide; DMF-DMA, *N*,*N*-dimethylformamide dimethylacetal; TLC, thin layer chromatography

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