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TWO-STAGE ONE-POT INTERACTION OF ACYCLIC β-KETOESTERS, DMFDMA AND 2-CYANOMETHYLBENZIMIDAZOLE

M.A. Vodolazhenko[*†], A.E. Mykhailenko[*], N.Yu. Gorobets[*‡], S.M. Desenko[*‡]

A one-pot two-stage interaction of acyclic β-ketoesters, dimethylformamide dimethylacetal (DMFDMA) and 2-cyanomethylbenzimidazole was studied. Carried out under microwave irradiation in 2-propanol in the presence of piperidine, this transformation leads to the formation of 4-cyanobenzo[4,5]imidazo [1,2-α]pyridine-2-carboxylates, whereas at room temperature in methanol in the presence of sodium methylate 1-hydroxybenzo[4,5]imidazo[1,2-α]pyridine-4-carbonitriles are formed. Intermediate enamines initially formed from β-ketoesters and DMFDMA attack methylene group of 2-cyanomethylbenzimidazole followed by heterocyclizaton. In the presence of piperidine the benzimidazole nitrogen atom attacks the keto group of the β-ketoester fragment, whereas in the strong basic conditions cyclization occurs by the ester group.

Keywords: β-ketoester, 2-cyanomethylbenzimidazole, one-pot heterocyclization, DMFDMA, microwave irradiation.

Introduction

Multicomponent and one-pot multistage heterocyclzations are powerful tools to create a chemical complexity and increase molecular diversity of small drug-like molecules [1-4]. An accelerated research in this field has been driven by the fast development of the high-throughput biological screening and combinatorial chemistry. Since the simple variations of the widely known multicomponent reactions are largely investigated the more and more complex and polyfunctional starting building-blocks are involved in the studies of such processes [5-7]. A special attention here should be paid to the problem of selectivity and efficiency of such transformations, since the presence of several reaction centers in one building block often leads to an ambiguous reaction outcome.

Working in this field we studied previously several variations of a one-pot reaction between α-CH_2-carbonyl compounds, dimethylformamide dimethylacetal (DMFDMA) and active methylene nitriles giving a great diversity of heterocyclic compounds of different classes [8-13]. Selectivity and pathways of such transformations depend on both the reaction conditions and the structure of initial compounds. Nature of substituents in α-carbonyl CH-acids and methylene components also makes contribution into the determination of the reaction pathway in this process. All these factors can be used for the selectivity control in such reactions. In most of the above cited publications cyanoacetic acid amides and related acyclic derivatives of this acid were used as the active methylene nitriles [14]. However, heteroaryl substituted acetonitriles also have significant potential for the construction of complex heterocyclic systems in this approach [15]. One of the most commonly used reagent of this type, 2-(1*H*-benzo[*d*]imidazol-2-yl)acetonitrile (**4**), applied widely for construction of benzimidazole derivatives fused with various heterocycles [16,17]. Recently we used its reactivity within the discussed above synthetic approach using cyclic 1,3-dicarbonyl compounds of type **1** as the starting α-CH_2-carbonyls (Scheme 1). This condensation was found to be a highly selective process leading to 4-oxo-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-*a*]quinolin-6-yl cyanides (**5**) [18].

In this work we aimed to apply acyclic β-ketoesters in one-pot reaction with DMFDMA (**2**) and 2-cyanomethylbenzimidazole **4**.

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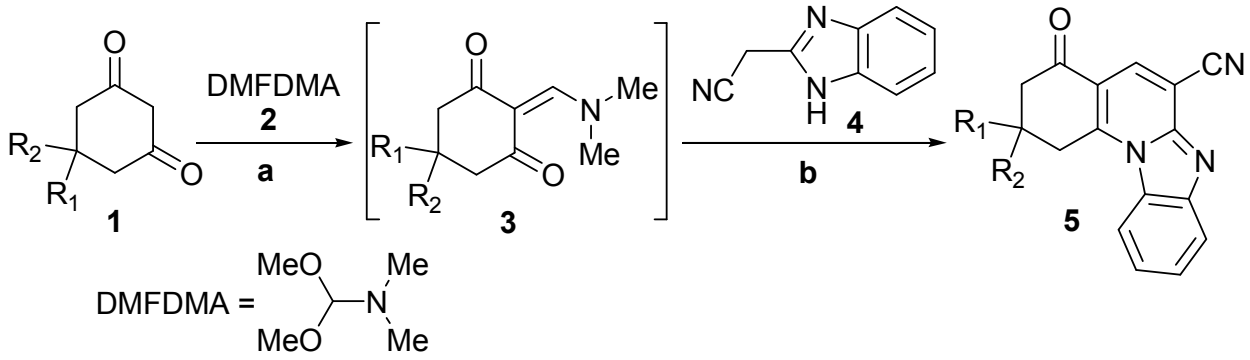


Scheme 1. Reaction conditions: ***a***: solvent-free, rt, 5 min or 1 h; ***b***: H_2O, rt 1 h or H_2O, MW, 120°C/5 min or *i*-PrOH, 120°C, 5 min.

Results and Discussion

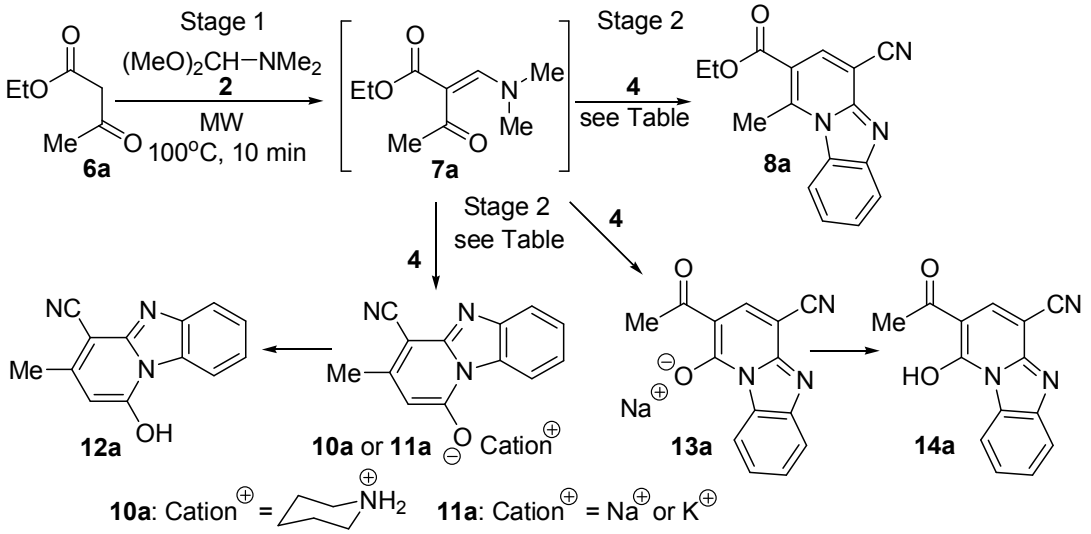
Search for optimal reaction conditions

Since the interaction between 1,3-cyclohexanediones **1**, DMFDMA (**2**) and 2-cyanomethylbenzimidazole **4** is a highly selective process, an analogous reaction applying acyclic β-ketoesters **6** as representatives of 1,3-diketocompounds was also expected to give the corresponding benzo[4,5]imidazo[1,2-*a*]pyridine-4-carbonitrile derivatives. For our initial experiments we chose ethyl acetoacetate (**6a**) as the simplest representative of acyclic β-ketoesters that on the first stage reacted with DMFDMA **2** (2.5 mmol of each reagent) to give enamine **7a** (Table 1) according to the known method [8] with the reaction time prolonged up to 10 min to increase the conversion extent (reaction monitored by GC-MS). On the second reaction stage an equivalent amount of nitrile **4** was added and the reaction conditions for this interaction were further screened. Generally, the reaction product was isolated as precipitate and analyzed by ^{1}H NMR to make a fast conclusion of the reaction outcome. The analysis of filtrates were performed for selected cases and discussed below.

The second stage in aqueous media carried out by analogy to Scheme 1 at room temperature or under microwave heating gave negative results: the starting nitrile **4** or its mixtures with by-product **12** were isolated (Table 1, Entries 1-3). Application of *i*-PrOH instead of water allowed us to detect the expected formation of **8a** in admixture with the starting nitrile **4** in low yield (Entries 4-8). The use of piperidine as catalyst in *i*-PrOH under microwave irradiation at 100 ºC during 5 min [8] resulted in formation of pure expected product **8a**, but the isolated yield was again very low (12%, Entry 9). Further experiments with catalytic amounts of piperidine, its stoichiometric quantities and excess at higher temperatures (Entries 10-14) showed that under such conditions increasing amounts of the undesired by-product **10a** appeared in the isolated material. The reaction carried out at 160 °C during 20 min under microwave irradiation gave the pure by-product (**10a**, Entry 15). Its identification will be discussed later, and its formation can be rationalized as a result of enamine **7a** decomposition in the reaction mixture at higher temperatures returning the initial ester **6a** followed by its reaction with **4**. Further optimization steps at room temperature during 48 h or at lower temperatures under microwave irradiation with longer reaction times (Entries 16-26) led to elucidation of optimal conditions, resulted in the pure product (**8a**) formation in a moderate yield (37 %, Entries 18 and 24). At the same time, attempts to carry out the reaction under reflux conditions or with ultrasonic activation (exampled by Entries 27 and 28) did not give better results.

In our further attempts to find more efficient reaction conditions we used different basic catalysts. Application of triethylamine and K_2CO_3 led to formation of **8a** (Entries 29-31) but in lower yields than for the cases with piperidine or with large amounts of admixtures. Interestingly, the use of stronger bases (NaOH, *t*-BuOK, MeONa) resulted in formation of a product **13a** in a new alternative reaction (Entries 32-35) and the use of MeONa at room temperature allowed the isolation of **13a** in 44% yield (Entry 34).

Table 1. Optimization of the reaction conditions towards products **8a** and **13a**.



Entry	Conditions for Stage 2	Crude product yield[a]	Admixtures in the crude product[b]
1	H_2O (7.0 mL), r.t., 24 h	–	**4**
2	H_2O (4.0 mL), MW: 80-100°C/60 min	–	**4**+**12a** (10-20%)
3	H_2O (4.0 mL), MW: 120-140°C/60 min	–	**4**
4	*i*-PrOH (5.0 mL), r.t., 24 h	traces of **8a**	**4**
5	*i*-PrOH (5.0 mL), MW: 120°C/10 min	**8a**, 12%	15% of **4**
6	*i*-PrOH (5.0 mL), MW: 130°C/60 min	**8a**, 14%	10% of **4**
7	*i*-PrOH (5.0 mL), MW: 140°C/60 min	**8a**, 11%	15% of **4**
8	*i*-PrOH (1.5 mL), MW: 140°C/25 min	**8a**, 28%	35% of **4**
9	piperidine (cat.), *i*-PrOH (2.0 mL), MW: 100°C/5 min	**8a**, 12%	–
10	piperidine (cat.), *i*-PrOH (1.5 mL), MW: 120°C/10 min	**8a**, 27%	50% of **4**
11	piperidine (cat.), *i*-PrOH (1.5 mL), MW: 140°C/15-25 min	**8a**, 20-25%	35-45% of **4** and unidentified admixtures
12	piperidine (cat.), *i*-PrOH (1.5 mL), MW: 160°C/10 min	**8a**, 26%	25% of **4** and unidentified admixtures
13	piperidine (1.0 equiv), *i*-PrOH (1.5 mL), MW: 140°C/10 min	**8a**, 12%	10% of **10a** and unidentified admixtures
14	piperidine (2.0 equiv), *i*-PrOH (1.5 mL), MW: 140°C/10 min	**8a**, 10%	10% of **10a** and unidentified admixtures
15	**piperidine (2.0 equiv), *i*-PrOH (0.8 mL), MW: 160°C/20 min**	**10a**, 20%	–
16	piperidine (5.0 equiv), *i*-PrOH (3 mL), r.t., 48h	**8a**, 37%	10% of **4**
17	piperidine (6.0 equiv), *i*-PrOH (3 mL), r.t., 48h	**8a**, 37%	10% of **4**
18	**piperidine (7.0 equiv), *i*-PrOH (3 mL), r.t., 48h**	**8a**, 37%	–
19	piperidine (10.0 equiv), *i*-PrOH (3 mL), r.t., 48h	**8a**, 30%	–
20	piperidine (15.0 equiv), *i*-PrOH (3 mL), r.t., 48h	**8a**, 26%	–
21	piperidine (3.0 equiv), *i*-PrOH (2 mL), MW: 100°C/20 min	**8a**, 19%	–
22	piperidine (1.0 equiv), *i*-PrOH (2 mL), MW: 100°C/40 min	**8a**, 28%	–
23	piperidine (1.0 equiv), *i*-PrOH (2 mL), MW: 90°C/60 min	**8a**, 31%	–

Continuation of table 1.

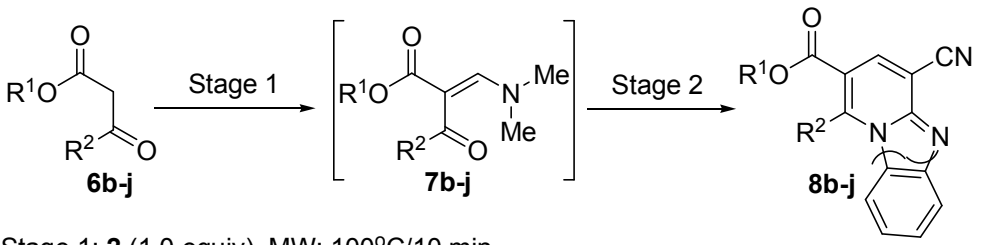
Entry	Conditions for Stage 2	Crude product yield[a]	Admixtures in the crude product[b]
24	**piperidine (1.0 equiv), *i*-PrOH (2 mL), MW: 80°C/70 min**	**8a**, 37%	–
25	piperidine (1.0 equiv), *i*-PrOH (2 mL), MW: 70°C/85 min	**8a**, 36%	10% of **4**
26	piperidine (1.0 equiv), *i*-PrOH (2 mL), MW: 60°C/110 min	**8a**, 34%	–
27	piperidine (0.5 equiv), *i*-PrOH (7.5 mL), Δ, 9h	**8a**, 27%	5% of **4**, 5% of **10a**
28	piperidine (7.0 equiv), *i*-PrOH (4.0 mL), US, 30 ºC, 60 min	**8a**, 26%	20% of unidentified admixtures
29	NEt_3 (1.0 equiv), *i*-PrOH (2 mL), MW: 80°C/70 min	**8a**, 20%	–
30	NEt_3 (7.0 equiv), *i*-PrOH (2 mL), r.t., 48h	**8a**, 24%	–
31	K_2CO_3 (2.0 equiv), DMF (3.5 mL), r.t., 6 days	**8a**, 74%	50% of unidentified admixture
32	NaOH (2.0 equiv), H_2O (3.0 mL), r.t., 48h	**13a**, 17%	50% of **11a**
33	*t*-ButOK (2.0 equiv), *i*-PrOH (4.0 mL), r.t., 4.5h	**13a**, 42%	25% of **8a**, 5% of **11a**, unidentified admixtures
34	**MeONa (2.0 equiv), MeOH (3 mL), r.t., 3.5h**	**13a**, 44%	–
35	MeONa (2.0 equiv), MeOH (3 mL), MW: 100°C/25 min	**13a**, 34%	–

[a]The yield of the crude product accounted for the expected product specified in the table.
[b]The admixture content defined by ^{1}H NMR of the crude product.

Reactions involving various β-ketoesters

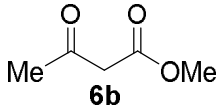
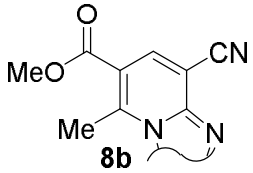
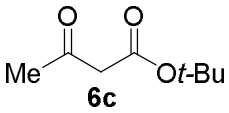
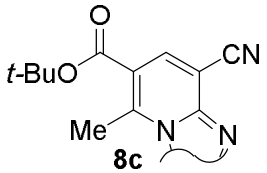
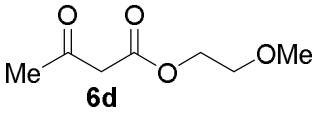
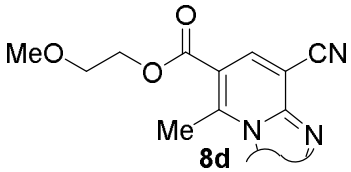
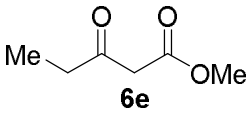
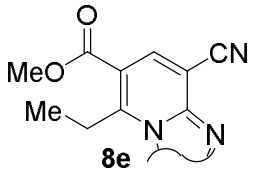
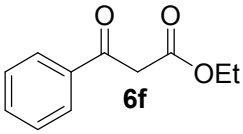
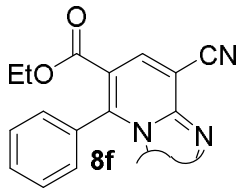
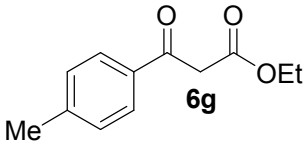
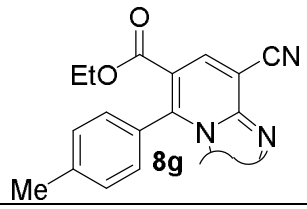
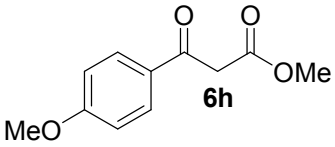
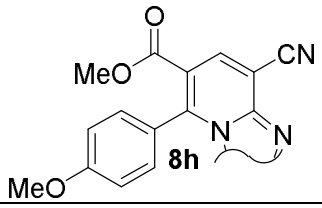
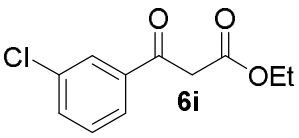
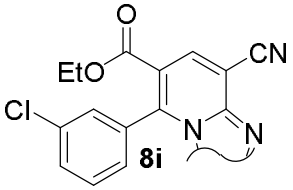
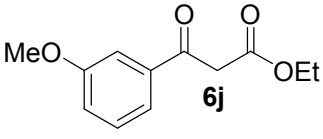
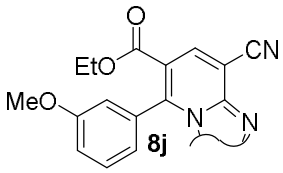
Based on our results obtained with ethyl acetoacetate **6a**, we further used different other β-ketoesters **6b-j** in similar one-pot transformations. From the initial experiments on this research stage it became clear that the reaction outcome strongly depends on the nature of the starting β-ketoester and requires additional optimization steps to obtain an individual product with a reasonable yield. Thus, the progress of reactions was monitored by TLC, and the reaction times and temperatures under microwave heating were tuned to ensure the disappearance of the initial nitrile **4** (Table 2). The isolated yields over two reaction steps were generally moderate, a good yield (51%, Entry 8) was achieved only in the case of ethyl 3-(3-chlorophenyl)-3-oxopropanoate (**6i**). At the same time the yields for other aromatic β-ketoesters were lower, especially for those ones containing electron donating substituents in aromatic ring (**6g**, **6h**, and **6j**, Entries 6, 7 and 9). Such influence of the donating substituents can be racionalized as increasing the electron density on the ketone carbon atom that should decrease the electrophilic properties of the carbonyl group. An attempt was made to carry out the reaction between enamine **7f** and nitrile **4** in glacial acetic acid [19] under reflux conditions. After 1.5 h the reaction was complete (TLC-control) resulting in the same product **8f** isolated in lower yield (21%, compare with Entry 5).

Table 2. Synthesis of compounds **8b-j**.



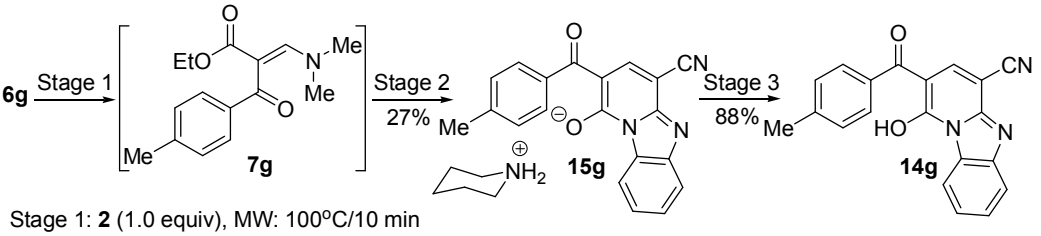
Stage 1: **2** (1.0 equiv), MW: 100°C/10 min
Stage 2: **4** (1.0 equiv), piperidine (1.0 equiv), *i*-PrOH (2.0 mL), MW: see Table 2

Continuation of table 2.

Entry	Initial β-ketoester	Stage 2, MW conditions	Product	Yield
1	 **6b**	100°C/45 min	 **8b**	21%
2	 **6c**	100°C/45 min	 **8c**	32%
3	 **6d**	100°C/45 min	 **8d**	22%
4	 **6e**	80°C/115 min	 **8e**	26%
5	 **6f**	100°C/50 min	 **8f**	30%
6	 **6g**	100°C/60 min	 **8g**	20%
7	 **6h**	80°C/120 min[a]	 **8h**	10%
8	 **6i**	100°C/40 min	 **8i**	51%
9	 **6j**	100°C/70 min	 **8j**	19%

[a]Conditions for Stage 1: MW: 100 ºC/20 min

Interestingly, in contrast to ethyl acetoacetate (Table 1, Entry 18) in the case of β-ketoester **6g** a room temperature transformation catalyzed by piperidine excess resulted in formation of piperidinum salts **15g** (Scheme 2). In the case of ethyl acetoacetate such heterocyclization involving the ester group was accomplished in the presence of MeONa as much stronger base than piperidine (**6a** → **13a**, Table 1, Entry 34). It can be presumed that the decreased reactivity of the carbonyl group in **7g** is due to the influence of electron donating methyl substituent in the aromatic ring (see above) that may result in the manifestation of the competing cyclization process involving the ester group. However, we could not isolate or even detect formation of such salts or any other product in similar reaction of **6h** (with electron donating substituent, OMe) proceeded for 15 days. Thus, the reasons for the increased stability of salt **15g** are not obvious.

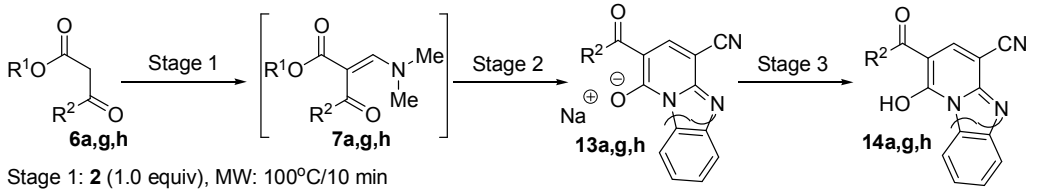


Stage 1: **2** (1.0 equiv), MW: 100°C/10 min
Stage 2: **4** (1.0 equiv), piperidine (7.0 equiv), *i*-PrOH (3.0 mL), rt, 6 days
Stage 3: AcOH:*i*-PrOH (1:1), r.t.

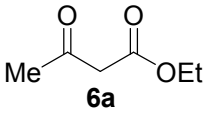
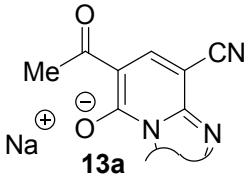
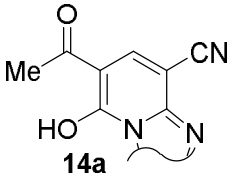
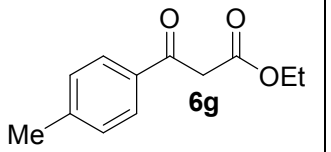
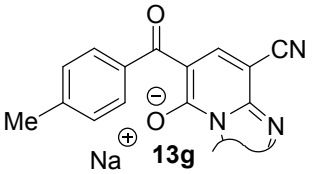
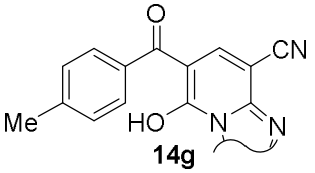
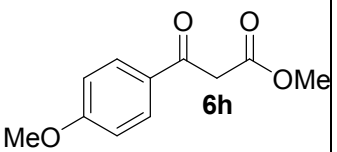
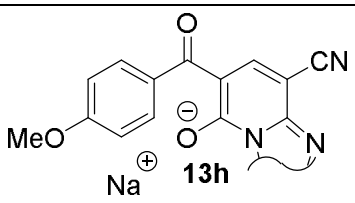
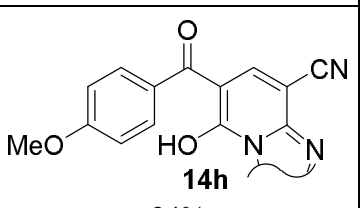
Scheme 2.

The products of the alternative heterocyclization were obtained for the selected representatives of β-ketoesters **6a,g,h** at room temperature in the presence of sodium methylate as it is shown in Table 3. The resulting sodium salts **13a,g,h** precipitated from the reaction mixtures. Their neutralization by acetic acid resulted in formation of novel compounds **14a,g,h**.

Table 3. Synthesis of compounds **13a,g,h** and **14a,g,h**

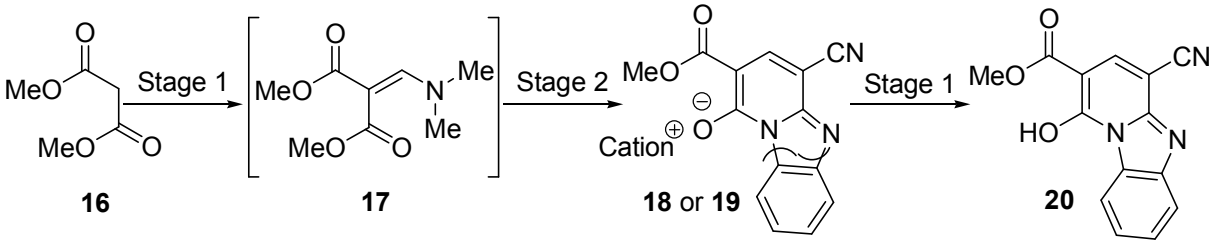


Stage 1: **2** (1.0 equiv), MW: 100°C/10 min
Stage 2: **4** (1.0 equiv), MeONa (2.0 equiv), MeOH (3.0 mL), r.t.: see Table 3
Stage 3: AcOH:*i*-PrOH (1:1), r.t.

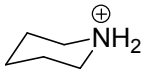
Entry	Initial β-ketoester	Stage 2	Stage 2: Product and Yield	Stage 3: Product and Yield
1	 **6a**	3.5h	 **13a** 44%	 **14a** 75%
2	 **6g**	6 days	 **13g** 37%	 **14g** 60%
3	 **6h**	8 days	 **13h** 75%	 **14h** 24%

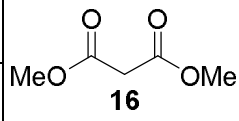
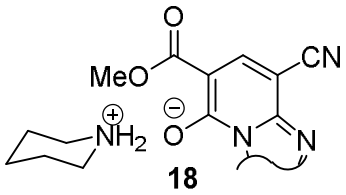
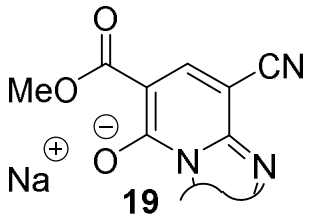
In the case of dimethyl malonate **16** the second stage was carried out at room temperature in the presence of piperidine or MeONa catalysts, and for both conditions the corresponding salts **18** and **19** were obtained in moderate yields (Table 4). Their acidification with AcOH in *i*-PrOH gave the neutral product **20**.

Table 4. Synthesis of compounds **18**, **19** and **20**.



Stage 1: **2** (1.0 equiv), MW: 100°C/10 min
Stage 2: **4** (1.0 equiv), see Table 4
Stage 3: AcOH:*i*-PrOH (1:1), r.t.

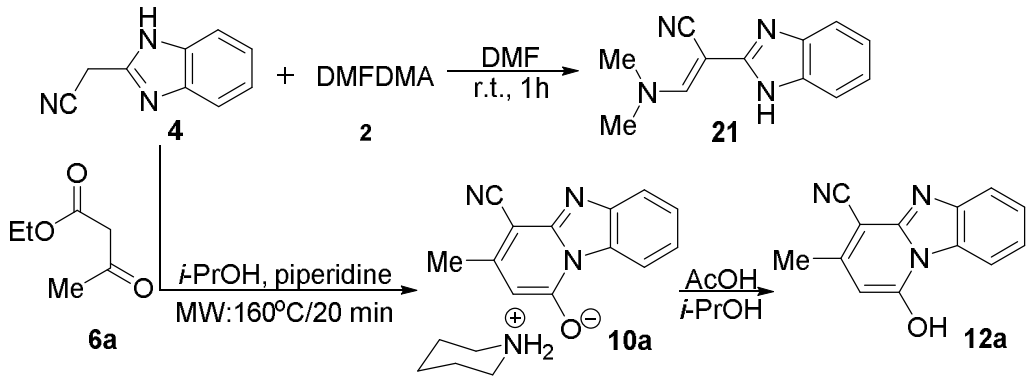
18: Cation$^{\oplus}$ =  **19**: Cation$^{\oplus}$ = Na$^{\oplus}$

Entry	Initial diester	Stage 2	Stage 2: Product and Yield	Stage 3: Yield
1.	 **16**	piperidine (7.0 equiv), *i*-PrOH (3.0 mL), r.t., 6 days	 **18** 24%	27%
2.		MeONa (2.0 equiv), MeOH (3.0 mL), r.t., 13 days	 **19** 44%	15%

Thus, the studied two-stage one-pot interaction allowed synthesis of individual products of different types in one-pot format. All products were obtained as precipitates with fast and facile isolation in moderate yields. Analysis of the filtrates by means of ^{1}H NMR method for the selected reaction mixtures in the case of ethyl acetoacetate **6a** showed that the formation of the by-product **12a** due to decomposition of enamine **7a** is the main competing process. This transformation prevailed at elevated temperatures (Table 1, Entries 23, 24), whereas at lower temperatures formation of unidentified admixtures was also observed (Table 1, Entries 25, 26). The filtrate analysis for the reactions of other β-ketoesters showed similar situation. In the case of starting β-ketoesters **6c** and **6b** the salt **10a** was detected, whereas in case **6e** the formation of corresponding pure by-product **12e** was observed (Table 2, Entries 1, 2, 4).

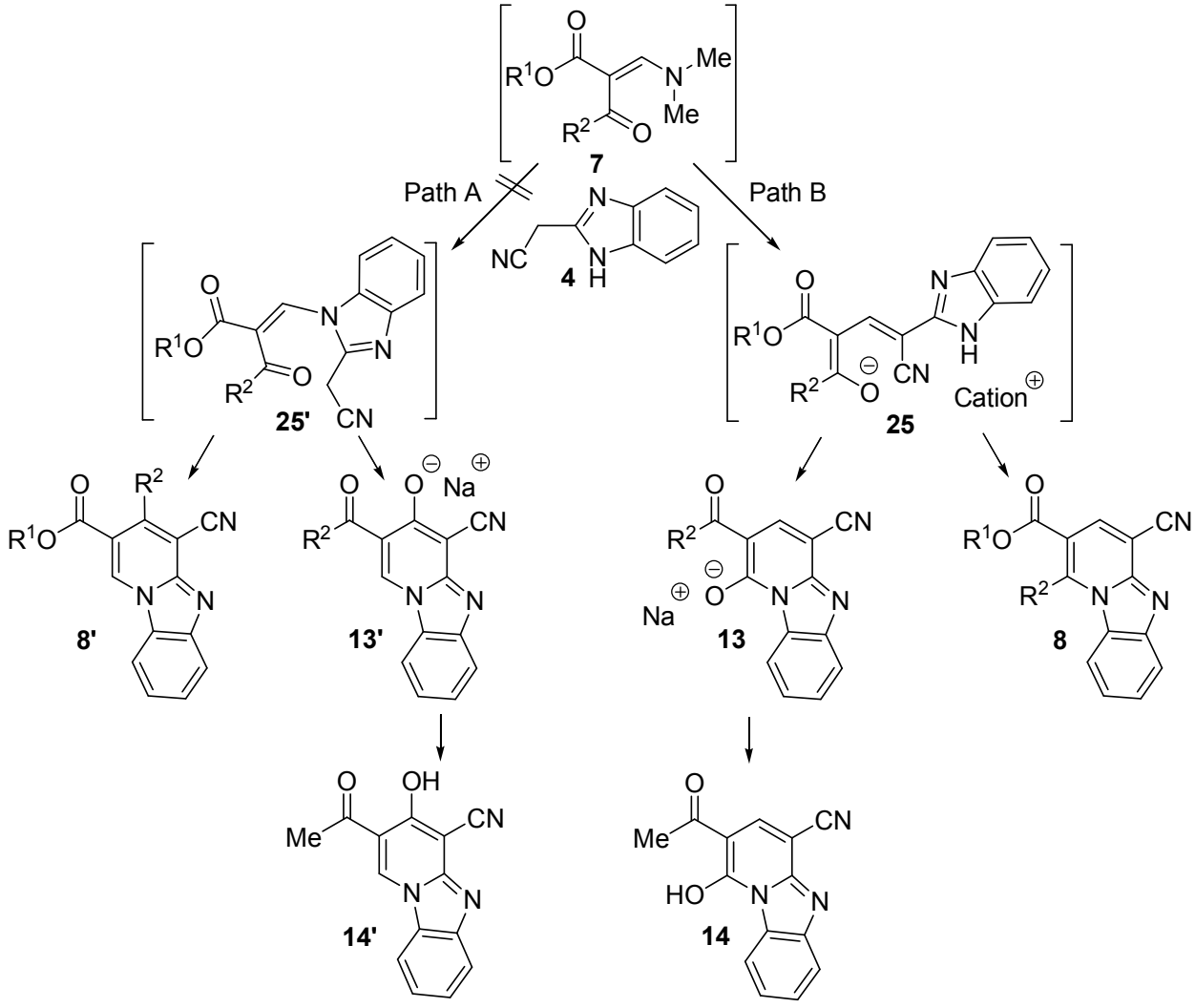
Determination of the product structure

To determine the origin of the main admixture two possible by-products **21** and **12a** were synthesized in two-component reactions of the starting reagents **4** and **6a** (Scheme 3). From the comparison of ^{1}H NMR spectra of the obtained samples with spectra of the studied reaction product obtained at 160°C (Entry 15, Table 1) we assumed that compound **10a** often accompanied the formation of the main product **8a**, but the formation of the possible by-product **21** has never been detected in the studied reaction mixtures.



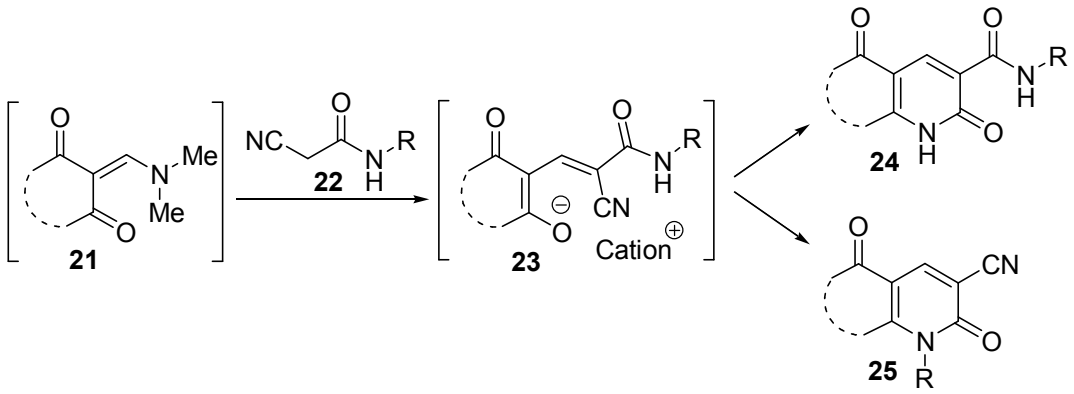
Scheme 3.

However, the formation of two different structures in the course of the above described reactions is possible following two alternative reaction mechanisms (Paths A and B, Scheme 4).



Scheme 4.

In the earlier papers of our group [8, 10] enamines **21** were shown to react with N-substituted cyanoacetamides **22** *via* intermediate formation of resonance-stabilized enolates **23** (Scheme 5) similarly to Path B (Scheme 4). The intermediates **23** were isolated as precipitates and their structure was defined in X-ray diffraction study [9].



Scheme 5.

In addition the condensation of cyclic 1,3-dicarbonyl compounds of type **1** with DMFDMA **2** and 2-(1*H*-benzo[*d*]imidazol-2-yl)acetonitrile **4** (Scheme 1) resulted in selective formation of cyanides **5** and our attempts to isolate other types of reaction products by variation of reaction conditions were unsuccessful [18]**.** Based on these considerations we assume that the main product obtained in the presence of piperidine (Tables 1,2) is formed by Path B (Scheme 4) and formulated as **8**.

Routine spectral data can not allow the unambiguous structural assignment for the by-product, and the products of the alternative reaction, and structural pairs: **8** and **8'**, **13** and **13'**, **14** and **14'** have to de distinguished using the additional spectral study.

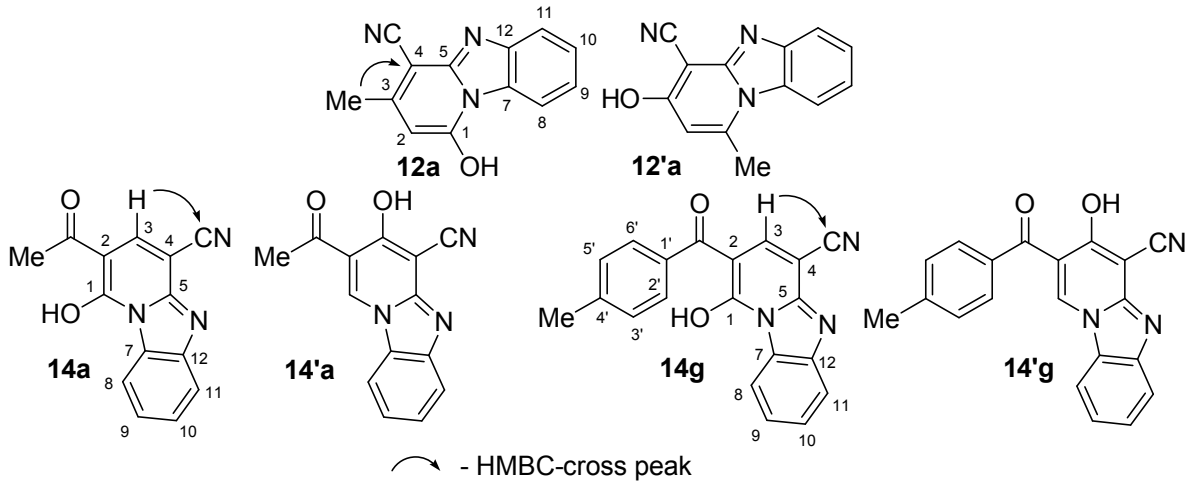


Figure 1. Distinction of the regioisomers of the obtained products

To resolve this structural issue for the main by-product (**12** or **12'**) and the product of alternative direction (**14** or **14'**) we used APT, HSQC and HMBC methods for representatives **12a, 14a** and **14g**. In HMBC spectrum of the main by-product (Figure 2) the expected correlations for **12a** between the signals of the methyl group protons and the quaternary 4-C carbon signal was observed that proves the close disposition of the methyl group and pyridine carbon in position 4, which is impossible for **12'a**. For **14a** and **14g**, (Figures 3 and 4) HMBC correlation between the 4-CH proton signal and the carbon signal of the CN group, clearly showed the close disposition of the nitrile group with the mentioned proton strongly supporting the suggested structures **14a** and **14g**.

Conclusion

The studied one-pot two-stage interaction of acyclic β-ketoesters, DMFDMA and 2-cyanomethylbenzimidazole **4** was found to have low regioselectivity and give unambiguous results. The piperidine catalized process results in formation of esters **8** due to heterocycle ring closure with participation of β-ketoester keto group and the benzimidazole amino function. In the presence of a stronger base, MeONa, the ring closure involves the ester group of **6** and benzimidazole nitrogen

atom. Both reactions follow Path B (Scheme 4), and in our opinion, after the formation of intermediate **25** in the presence of piperidine (for the most cases) the benzimidazole nitrogen atom attacks the keto group of the β-ketoester fragment as a relatively softer electrophilic center compared to the competing ester function to form compounds **8**. The change of the reaction detraction in the presence of an excess of the strong base (MeONa) can be rationalized by the effect of two unidirectional factors. In this medium deprotonation or even double deprotonation of the intermediate **25** is probably possible, and the enolate formation is worsen significantly the hydroxyl group properties as a leaving group. More over, in accordance with HSAB theory, the formed much harder nucleophile (benzimidazole N^-) would attack the harder electrophilic center, the ester group to form compounds **14**. The side products of a type **12** are formed due to decomposition of the intermediate enamine **7** at the reaction conditions returning the initial ester **6a** with its consequent reaction with **4**.

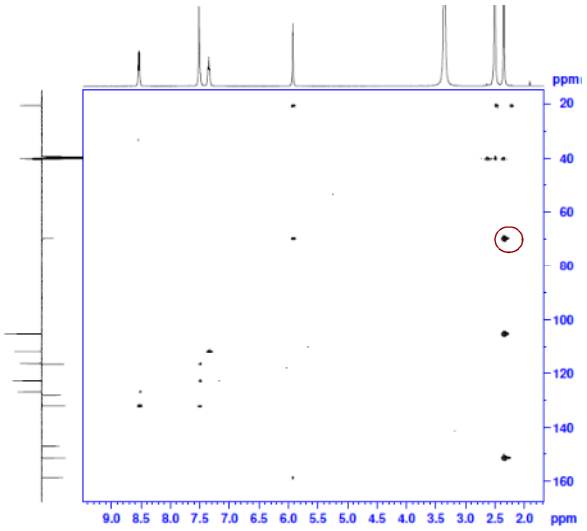


Figure 2. HMBC spectrum fragment for compound **12a** (APT and ^{1}H NMR spectra were laid out on the vertical and horizontal axis, correspondingly).

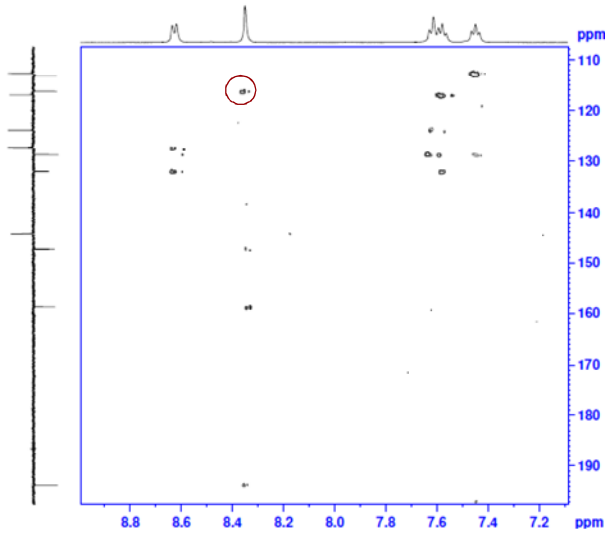


Figure 3. HMBC spectrum fragment for compound **14a** (APT and ^{1}H NMR spectra were laid out on the vertical and horizontal axis, correspondingly).

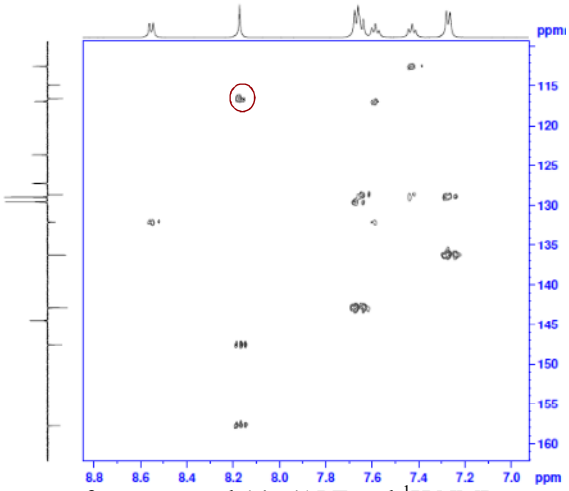


Figure 4. HMBC spectrum fragment for compound **14g** (APT and ^{1}H NMR spectra were laid out on the vertical and horizontal axis, correspondingly).

Experimental section

General information

The structure of all the obtained compounds was confirmed using ^{1}H NMR spectroscopy. Selected representatives were analyzed by means of IR spectroscopy, mass-spectrometry, LC-MS and elemental analysis, ^{13}C NMR, APT NMR as well as HSQC and HMBC correlation NMR spectroscopy. NMR spectra were recorded on a *Bruker Avance drx 500MHz* (126MHz for ^{13}C NMR; Bruker Spectrospin

Ltd., Coventry, United Kingdom), *Varian MR 400MHz* spectrometer (100MHz for ^{13}C NMR), and *Varian Mercury VX 200MHz* (Varian Inc., Palo Alto, CA) using DMSO-d_6 as a solvent and residual solvent signal as the reference (TMS scale). IR spectra were recorded on a *Perkin Elmer Spectrum One* FTIR spectrometer (PerkinElmer, Inc., Shelton, CT) (in KBr pellets). Mass spectra were recorded on a *Varian 1200L GC-MS* instrument with the use of direct exposure probe method with 70 eV EI ionization. LC-MS analyses were carried out with the use of chromatographic/mass-spectrometric system, which consist of HPLC chromatograph equipped with diode matrix and mass-selective detector, in the atmospheric pressure chemical ionization (negative or positive APCI) mode, simultaneous scanning of positive ions in mass diapason 80–1,000 m/z. Elemental analysis was performed on a *EuroVector EA-3000* instrument. Melting points were measured in open capillary tubes and are uncorrected. Microwave experiments were carried out using the *EmrysTM Creator EXP* from Biotage (Uppsala, Sweden) in sealed microwave process vials (for maximum 2.5mL of the reaction mixture) utilizing the "High" absorbance level (150W maximum power) and a monomode *Anton Paar Monowave 300* microwave reactor (2.45 GHz) in G4 (for maximum 2.5 mL of the reaction mixture) microwave process vials. Reaction times under microwave conditions correspond to the time of reaction mixture was kept at the designated temperature. After completion of the reaction, the vial was cooled to 50°C by air jet cooling. Reaction temperatures were monitored by an IR sensor. All reagents including β-ketoesters **6a-j**, dimethyl malonate **16** and 2-cyanomethylbenzimidazole **4** and solvents were purchased from commercial suppliers and used without further purification.

General procedure for preparation of 4-cyanobenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylates (8a-j). Enamines **7a-j** were obtained by reaction of neat β-ketoesters **6a-j** (2.5 mmol) with DMFDMA (297 mg, 2.5 mmol) heated under microwave irradiation at 100°C during 10 min (20 min for enamine **7h**). Than 2-cyanomethylbenzimidazole **4** (393 mg, 2.5 mmol), piperidine (1.0 equiv, 2.5 mmol, 213 mg) and 2.0 mL of *i*-PrOH were added to the obtained mixture. The vial was encapsulated and heated again under microwave irradiation (Table 2). After cooling, the precipitate obtained was filtered off and washed with Et_2O or *t*-BuOMe, then dried on air. For **8h** the product was isolated from the filtrate that was evaporated in vacuum, and than diluted with 10.0 mL of cold *i*-PrOH, the precipitate obtained was filtered off, washed with *i*-PrOH, then dried on air.

Procedure for preparation of piperidin-1-ium 4-cyano-2-(4-methylbenzoyl)benzo[4,5]imidazo[1,2-*a*]pyridin-1-olate (15g) and piperidin-1-ium 4-cyano-2-(methoxycarbonyl)benzo[4,5]imidazo[1,2-*a*]pyridin-1-olate (18). Enamines **7g** and **17** were obtained by reaction of neat β-ketoesters **6g** or dimethyl malonate **16** (2.5 mmol) with DMFDMA (297 mg, 2.5 mmol) under microwave heating to 100°C during 10 min. Than 2-cyanomethylbenzimidazole **4** (393 mg, 2.5 mmol), piperidine (7.0 equiv, 17.5 mmol, 1.488 g) and 3.0 mL of *i*-PrOH were added to the obtained mixture, which further was stirred at room temperature during 6 days. The precipitate obtained was filtered off and washed with Et_2O or *t*-BuOMe, then dried on air.

General procedure for preparation of sodium 4-cyanobenzo[4,5]imidazo[1,2-*a*]pyridin-1-olates (13a,g,h) and sodium 4-cyano-2-(methoxycarbonyl)benzo[4,5]imidazo[1,2-*a*]pyridin-1-olate (19). Enamines **7a,g,h** were obtained by a reaction of neat β-ketoester **6a,g,h** (2.5 mmol) with DMFDMA (297 mg, 2.5 mmol) under microwave heating at 100°C during 10 min. Then 2-cyanomethylbenzimidazole **4** (393 mg, 2.5 mmol) and freshly prepared solution of MeONa (2.0 equiv) in 3.0 mL of MeOH (solution of 0.115g of Na in 3.0 mL of MeOH) were added to the obtained mixture, which further was stirred at room temperature (time for each case is given in Tables 3 and 4). The precipitate obtained was filtered off, washed with corresponding solvent (**13a** with MeOH, **13h** with *t*-BuOMe, **13g** and **19** with CH_3CN) and dried on air.

General procedure for preparation of 1-hydroxybenzo[4,5]imidazo[1,2-*a*]pyridine-4-carbonitriles (14a,g,h) and methyl 4-cyano-1-hydroxybenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (20). 1.0 mL of *i*-PrOH and 1.0 mL of glacial acetic acid were added to isolated products **13a,g,h**, **15g**, **19** (100 mg), than stirred at room temperature for 1h, precipitated solid was filtered off, washed with water, dried on air.

Procedure for preparation of piperidin-1-ium 4-cyano-3-methylbenzo[4,5]imidazo [1,2-*a*]pyridin-1-olate (10a). Ethyl acetoacetate **6a** (325 mg, 2.5 mmol), 2-cyanomethylbenzimidazole **4** (393 mg, 2.5 mmol) and 0.8 mL of *i*-PrOH were mixed. The vial was encapsulated, and the reaction mixture was heated under microwave irradiation at 160°C during 20 min. After cooling under stirring,

the product was upsetted with water; precipitate obtained was filtered off and washed with water, then dried on air. Yield 42% (323 mg).

Procedure for preparation of 1-hydroxy-3-methylbenzo[4,5]imidazo[1,2-*a*]pyridine-4-carbonitrile (12a). Isolated product **10a** (100 mg), 1.0 mL of *i*-PrOH and 1.0 mL of glacial acetic acid were mixed, the reaction mixture was stirred at room temperature for 1 h, precipitated solid was filtered off, washed with water, dried on air. Yield 81% (58 mg).

Procedure for preparation of 2-(1*H*-benzo[*d*]imidazol-2-yl)-3-(dimethylamino)acrylonitrile (21). 2-Cyanomethylbenzimidazole **4** (393 mg, 2.5 mmol), DMFDMA (297 mg, 2.5 mmol) and 1.0 mL of DMF were mixed and stirred at room temperature for 12 h, precipitated solid was filtered off, washed with *i*-PrOH, dried on air. Yield 71% (375 mg).

Ethyl 4-cyano-1-methylbenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8a). Pale yellow solid. Yield 37%. Mp 221°C. Anal. calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.91; H, 4.72; N, 15.08; ^{1}H NMR (200 MHz, DMSO-d_6) δ 1.36 (t, J = 7.1 Hz, 3H), 3.39 (s, 3H), 4.35 (q, J = 7.0 Hz, 2H), 7.40-7.54 (m, 1H), 7.57-7.72 (m, 1H), 7.88-7.02 (m, 1H), 8.33-8.47 (m, 1H), 8.51 (s, 1H); ^{13}C NMR, APT, HSQC (125 MHz, DMSO-d_6) δ 14.5 ($\underline{CH_3}CH_2O$), 19.3 (CH_3), 62.2 ($CH_3\underline{CH_2}O$), 98.8 (C-4), 113.1 (CN), 113.4 (C-7), 117.8 (C-2), 119.3 (CH, C-8), 120.2 (CH, C-11), 121.3 (CH, C-9), 127.2 (CH, C-10), 131.0 (C-5), 138.3 (C-3), 141.2 (C-12), 164.9 (C-1), 191.0 (C=O); MS: (70eV, electron impact) *m/z* 279 (M^+); LC-MS: purity 100%, m/z (APCI, pos.) 280 ($M+H^+$); IR (KBr), ν: 3420, 2981, 2230, 1716, 1625, 1592, 1366, 1235, 1067, 1031, 754 cm^{-1}.

Methyl 4-cyano-1-methylbenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8b). Pale beige-yellow solid. Yield 21%. Mp 200-205°C (decomp.). Anal. calcd for $C_{18}H_{17}N_3O_2$: C, 67.92; H, 4.18; N, 15.84. Found: C, 68.06; H, 4.15; N, 15.89; ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.39 (s, 1H), 3.89 (s, 1H), 7.41-7.54 (m, 1H), 7,59-7,7 (m, 1H), 7.9-7.99 (m, 1H), 8.8-8.47 (m, 1H), 8.5 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 19.3, 53.3, 97.88, 97.90, 113.1, 115.6, 117.8, 120.18, 120.22, 120.23, 123.1, 127.3, 131.0, 138.3, 165.3; LC-MS: purity 96.7%, m/z (APCI, pos.) 266 ($M+H^+$); IR (KBr), ν: 3432, 3086, 2925, 2227, 1723, 1435, 1363, 1241, 1203, 1066, 752, 735 cm^{-1}.

Tert-butyl 4-cyano-1-methylbenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8c). Pale yellow solid. Yield 36%. Mp 287°C. Anal. calcd for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.42; H, 5.55; N, 13.69; ^{1}H NMR (200 MHz, DMSO-d_6) δ 1.59 (s, 9H), 3,36 (s, 3H), 7.38-7.53 (m, 1H), 7.55-7.72 (m, 1H), 8.30-8.44 (m, 1H), 8.45 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 19.2, 28.23, 28.25, 28.3, 92.4, 120.20, 120.23, 123.0, 123.3, 125.3, 127.2, 143.46, 143.47, 143.7, 148.8, 151.6, 187.2; MS: (70eV, electron impact) *m/z* 307 (M^+); LC-MS: purity 97.17%, m/z (APCI, pos.) 308 ($M+H^+$); IR (KBr), ν: 3421, 2976, 2932, 2231, 1954, 1819, 1717, 1627, 1593, 1369, 1247, 1168, 1154 cm^{-1}.

2-Methoxyethyl 4-cyano-1-methylbenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8d). Yellow solid. Yield 21%. Mp 152-153°C Anal. calcd for $C_{18}H_{17}N_3O_2$: C, 66.01; H, 4.89; N, 13.58. Found: C, 66.14; H, 4.81; N, 13.59; ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.32 (s, 3H), 3.39 (s, 3H), 3.63-3.73 (m, 2H), 4.36-4.51 (m, 2H), 7.39-7.52 (m, 1H), 7.57-7.69 (m, 1H), 7.88-7.97 (m, 1H), 8.34-8.50 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 19.3, 58.6, 65.0, 70.1, 97.9, 113.1, 115.6, 117.8, 120.2, 123.1, 127.2, 130.9, 138.2, 145.3, 146.0, 152.1, 164.9; LC-MS: purity 97.42%, m/z (APCI, pos.) 310 ($M+H^+$); IR (KBr), ν: 3436, 2926, 2230, 1717, 1624, 1591, 1363, 1235, 1066, 1035, 754 cm^{-1}.

Methyl 4-cyano-1-ethylbenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8e). Beige-yellow solid. Yield 26%. Mp 224-225°C (decomp.). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.44 (t, J = 7.3 Hz, 3H), 3.79 (q, J = 7.6 Hz, 2H), 3.9 (s, 3H), 7.47-7.58 (m, 1H), 7.61-7.72 (m, 1H), 7.93-8.04 (m, 1H), 8.23-8.36 (m, 1H), 8.52 (s, 1H).

Ethyl 4-cyano-1-phenylbenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8f). Yellow solid. Yield 30%. Mp 273 °C (decomp.). ^{1}H NMR (200 MHz, DMSO-d_6) δ 0.98 (t, J = 7.5 Hz, 3H), 4.05 (d, J = 6.6 Hz, 2H), 5.89-6.07 (m, 1H), 6.92-7.14 (m, 1H), 7.41-7.54 (m, 1H), 7.54-7.82 (m, 5H), 7.83-7.95 (m, 1H), 8.53(s, 1H).

Eethyl 4-cyano-1-(p-tolyl)benzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8g). Pale yellow solid. Yield 20%. Mp 248°C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 0.96 (t, J = 7.0 Hz, 3H), 4.02 (q, J = 6.9 Hz, 2H), 5.91-6.06 (m, 1H), 6.97-7.14 (m, 1H), 7.38-7.59 (m, 5H), 7.83-7.98 (m, 1H), 8.61 (s, 1H).

Methyl 4-cyano-1-(4-methoxyphenyl)benzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8h). Pale green-yellow solid. Yield 10%. Mp 269°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.61(s, 1H), 3.91 (s, 1H), 5.91-6.11 (m, 1H), 7.01-7.16 (m, 1H), 7.16-7.96 (m, 2H), 7.44-7.55 (m, 3H), 7.88-7.96 (m, 1H) 8.64 (s, 1H).

Ethyl 1-(3-chlorophenyl)-4-cyanobenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (8i). Yellow solid. Yield 51%. Mp 272°C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 0.97 (t, J = 7.2 Hz, 3H), 4.04 (d, J = 6.6 Hz, 2H), 5.81-6.04 (m, 1H), 7.05-7.23 (m, 1H), 7.46-7.65 (m, 2H), 7.66-7.88 (m, 3H), 7.90-8.00 (m, 1H), 8.69 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.9, 61.8, 115.3, 120.6, 123.0, 127.3, 127.7, 128.9, 130.5, 131.0, 131.7, 134.9, 138.5, 145.4, 145.5, 145.6, 145.7, 146.4, 146.6, 163.7, 163.8; LC-MS: purity 100%, m/z (APCI, pos.) 376 ($M+H^+$); IR (KBr), ν: 3415, 3063, 2980, 2235, 1712, 1445, 1373, 1318, 1253, 1229, 1017, 759, 735 cm^{-1}.

Ethyl 4-cyano-1-(3-methoxyphenyl)benzo[4,5]imidazo[1,2-a]pyridine-2-carboxylate (8j). Yellow solid. Yield 21%. Mp 218°C (decomp.). ^{1}H NMR (200 MHz, DMSO-d_6) δ 0.95 (t, J = 7.2 Hz, 3H), 3.77 (s, 3H), 4.03 (q, J = 7.0 Hz, 2H), 5.87-6.05 (m, 1H), 7.02-7.34 (m, 4H), 7.44-7.65 (m, 2H), 7.85-7.96 (m, 1H), 8.63 (s, 1H).

Piperidin-1-ium 4-cyano-3-methylbenzo[4,5]imidazo[1,2-*a*]pyridin-1-olate (10a). Dark beige solid. Yield 42%. Mp 240-245 °C decomp. ^{1}H NMR (200 MHz, DMSO-d_6) δ 1.44-1.7 (m, 6H), 2.25 (s, 3H), 2.91-3.06 (m, 4H), 5.33 (s, 1H), 6.90-7.05 (m, 1H), 7.14-7.29 (m, 1H), 7.36-7.47 (m, 1H), 8.35-8.51 (m, 1H).

1-Hydroxy-3-methylbenzo[4,5]imidazo[1,2-*a*]pyridine-4-carbonitrile (12a). Pale beige solid. Yield 34%. Mp >270°C decomp. ^{1}H NMR (200 MHz, DMSO-d_6) δ 2.32 (s, 3H), 5.91 (s, 1H), 7.25-7.40 (m, 1H), 7.42-7.57 (m, 2H), 8.41-8.61 (m, 1H), 13.55 (br.s., 1H) ^{13}C NMR, APT, HSQC, HMBC (125 MHz, DMSO-d_6) δ 20.8 (CH_3), 69.9 (C-4), 105.4 (CH, C-2), 111.9 (CH, C-11), 116.7 (CH, C-8), 118.0 (CN), 123.1 (CH, C-9), 126.8 (CH, C-10), 128.2 (C-7), 132.0 (C-12), 146.9 (C-5), 151.4 (C-3), 158.7 (C-1).

Sodium 2-acetyl-4-cyanobenzo[4,5]imidazo[1,2-*a*]pyridin-1-olate (13a). Pale pink solid. Yield 44%. >300 °C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 2.53 (s, 3H), 7.08-7.25 (m, 1H), 7.26-7.42 (m, 1H), 7.53-7.49 (m, 1H), 8.20 (s, 1H), 8.47-8.64 (m, 1H).

Sodium 4-cyano-2-(4-methylbenzoyl)benzo[4,5]imidazo[1,2-*a*]pyridin-1-olate (13g). Beige-yellow solid. Yield 37%. Mp >305°C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 2.35 (s, 3H), 7.02-7.24 (m, 2H), 7.24-7.41 (m, 1H), 7.43-7.54 (m, 2H), 7.54-7.66 (m, 1H), 7.98 (s, 1H), 8.30-8.55 (m, 1H).

2-Acetyl-1-hydroxybenzo[4,5]imidazo[1,2-*a*]pyridine-4-carbonitrile (14a). Pale beige solid. Yield 33%. Mp 221°C. Anal. calcd for $C_{18}H_{17}N_3O_2$: C, 66.93; H, 3.61; N, 16.73. Found: C, 67.06; H, 3.59; N, 16.76; ^{1}H NMR (200 MHz, DMSO-d_6) δ 2.57 (s, 3H), 7.39-7.50 (m, 1H), 7.52-7.67 (m, 2H), 8.37 (s, 1H), 8.55-8.74 (m, 1H); ^{13}C NMR, APT, HSQC, HMBC (125 MHz, DMSO-d_6) δ 31.1 (CH_3), 72.3 (C-4), 112.8 (CH, C-11), 113.2 (C-2), 116.4 (CH, C-8), 117.1 (CN), 124.0 (CH, C-9), 127.4 (CH, C-10), 128.9 (C-7), 132.2 (C-5), 144.4 (CH, C-3), 147.4 (C-12), 158.9 (C-1), 193.8 (C=O); MS: (70eV, electron impact) *m/z* 251 (M^+); LC-MS: purity 100%, m/z (APCI, pos.) 252 ($M+H^+$); IR (KBr), ν: 3383, 3124, 3059, 2999, 2878, 2218, 1927, 1894, 1695, 1637, 1545, 1487, 1300 1251, 1237, 971, 775, 761 cm^{-1}.

1-Hydroxy-2-(4-methylbenzoyl)benzo[4,5]imidazo[1,2-a]pyridine-4-carbonitrile (14g). Wight solid. Yield 22%. Mp 310-312°C (decomp.). ^{1}H NMR (200 MHz, DMSO-d_6) δ 2.36 (s, 3H), 7.18-7.34 (m, 2H), 7.35-7.47 (m, 1H), 7.51-7.71 (m, 4H), 8.16 (s, 1H), 8.47-8.61 (m, 1H); ^{13}C NMR, APT, HSQC, HMBC (125 MHz, DMSO-d_6) δ 21.7 (CH_3), 71.0 (C-4), 112.6 (CH, C-11), 115.0 (C-2), 116.8 (CN), 117.0 (CH, C-8), 123.7 (CH, C-9), 127.4 (CH, C-10), 128.9 (C-1`),129.1 (2CH, C-3`, C-5`), 129.7 (2CH, C-2`, C-6`), 132.3 (C-7), 136.4 (C-5), 142.9 (C-4`), 144.5 (CH, C-3), 147.7 (C-12), 157.9 (C-1), 192.5 (C=O); LC-MS: purity 100%, m/z 328 (APCI, pos.) ($M+H^+$); IR (KBr), ν: 3430, 3131, 3069, 2997, 2951, 2871, 2810, 2743, 2345, 2226, 1923, 1869, 1803, 1687, 1634, 1548, 1487, 1256, 1236, 785, 761 cm^{-1}.

1-Hydroxy-2-(4-methoxybenzoyl)benzo[4,5]imidazo[1,2-*a*]pyridine-4-carbonitrile (14h). Wight solid. Yield 18%. Mp 289°C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.83 (s, 3H), 6.92-7.06 (m, 2H), 7.34-7.48 (m, 1H), 7.51-7.68 (m, 2H), 7.70-7.83 (m, 2H), 8.14 (s, 1H), 8.49-8.62 (m, 1H); LC-MS: purity 100%, m/z (APCI, pos.) 344 ($M+H^+$).

Piperidin-1-ium 4-cyano-2-(4-methylbenzoyl)benzo[4,5]imidazo[1,2-*a*]pyridin-1-olate (15g). Yield 34%. Mp 114-115°C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 1.41-1.75 (m, 6H), 2.35 (s, 3H), 2.91-3.06 (m, 4H), 7.04-7.14 (m, 1H), 7.14-7.24 (m, 2H), 7.25-7.37 (m, 1H), 7.44-7.54 (m, 1H), 7.54-7.64 (m, 1H), 7.99 (s, 1H), 8.2 (br. s., 2H), 8.34-8.44 (m, 1H).

Methyl 4-cyano-1-hydroxybenzo[4,5]imidazo[1,2-*a*]pyridine-2-carboxylate (20). Purple solid. Yield 7%. Mp 280-282°C decomp. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.74 (s, 1H), 7.38-7.70 (m, 3H), 8.44 (s, 1H), 8.57-8.72 (m, 1H).

2-(1*H*-Benzo[*d*]imidazol-2-yl)-3-(dimethylamino)acrylonitrile (21). Yield 71%. Mp 224-226°C. ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.34 (s, 3H), 6.94-7.09 (m, 2H), 7.27-7.41 (m, 2H), 7.94 (s, 1H), 11.91 (s, 1H).

References

1. J. E. Biggs-Houck, A. Younai, J. T. Shaw, Recent advances in multicomponent reactions for diversity-oriented synthesis, Curr. Opin. Chem. Biol. 14 (2010), 371-382.
2. E. Ruijter, R. Scheffelaar, R. V. A. Orru, Multicomponent reaction design in the quest for molecular complexity and diversity, Angew. Chem. Int. Ed. 50 (2011), 6234-6246.
3. A. Dömling, W. Wang, K. Wang, Chemistry and biology of multicomponent reactions, Chem. Rev. 112 (2012), 3083-3135.
4. G. van der Heijden, E. Ruijter, R. V. A. Orru, Efficiency, diversity, and complexity with multicomponent reactions, Synlett 24 (2013), 666-685.
5. V. A. Chebanov, K. A. Gura, S. M. Desenko, Aminoazoles as key reagents in multicomponent heterocyclizations, Top. Heterocycl. Chem. 23 (2010), 41-84.
6. Y. V. Sedash, N. Yu. Gorobets, V. A. Chebanov, I. S. Konovalova, O. V. Shishkin, S. M. Desenko, Dotting the i's in three-component Biginelli-like condensations using 3-amino-1,2,4-triazole as a 1,3-binucleophile, RSC Adv. 2 (2012), 6719-6728.
7. V. A. Chebanov, S. M. Desenko, Multicomponent heterocyclization reactions with controlled selectivity (review), Chem. Heterocycl. Comp. 48 (2012), 566-583.
8. N. Yu. Gorobets, B. H. Yousefi, F. Belaj, C. O. Kappe, Rapid microwave-assisted solution phase synthesis of substituted 2-pyridone libraries, Tetrahedron 60 (2004), 8633-8644.
9. S. A. Yermolayev, N. Yu. Gorobets, E. V. Lukinova, O. V. Shishkin, S. V. Shishkina, S. M. Desenko, An efficient synthesis of N1-substituted 2,5-dioxo-1,2,5,6,7,8-hexahydro-3-quinolinecarboxamide via enolate salts, Tetrahedron 64 (2008), 4649-4655.
10. S. A. Yermolayev, N. Yu. Gorobets, S. M. Desenko, Rapid three-step one-pot microwave-assisted synthesis of 2,5-dioxo-1,2,5,6,7,8-hexahydro-3-quinolinecarbonitrile Library, J. Comb. Chem. 11 (2009), 44-46.
11. S. A. Yermolayev, N. Yu. Gorobets, O. V. Shishkin, S. V. Shishkina, N. E. Leadbeater, Pathways for cyclizations of hydrazine-derived 2-(2-cyanovinyl)-3-oxo-cyclohex-1-ene enolates, Tetrahedron 67 (2011), 2934-2941.
12. M. A. Vodolazhenko, N. Yu. Gorobets, S. A. Yermolayev, V. V. Musatov, V. A. Chebanov, S. M. Desenko, Application of stable fused dienolates for diversity oriented synthesis of 2,5-dioxo-5,6,7,8-tetrahydro-2H-chromene-3-carboxamides, RSC Adv. 2 (2012), 1106-1111.
13. M. A. Vodolazhenko, N. Yu. Gorobets, O. A. Zhikol, S. M. Desenko, O. V. Shishkin, A quantum chemical approach towards understanding stability and tautomerism of 2-imino-2H-pyran derivatives, RSC Adv. 6 (2016), 52201-52211.
14. M. A. Vodolazhenko, N. Yu. Gorobets, Synthesis of highly substituted 2-pyridones (microreview), Chem. Heterocycl. Comp. 52 (2016), 894-896.
15. S. G. Dzhavakhishvili, N. Yu. Gorobets, V. N. Chernenko, V. I. Musatov, S. M. Desenko, Synthesis of novel 3-(1,3-thiazol-2-yl)-7,8-dihydroquinoline-2,5(1H,6H)-diones, Russ. Chem. Bull. 57 (2008), 422-427.
16. K. M. Dawood, B. F. Abdel-Wahabb, Synthetic routes to benzimidazole-based fused polyheterocycles, ARKIVOC 1 (2010), 333-389.
17. K. M. Dawood, N. M. Elwan, B. F. Abdel-Wahab, Recent advances on the synthesis of azoles, azines and azepines fused to benzimidazole, ARKIVOC 2011), 111-195.
18. M. A. Vodolazhenko, A. E. Mykhailenko, N. Yu. Gorobets, S. M. Desenko, One-pot synthesis of benzo[4,5]imidazo[1,2-a]pyridine derivatives in aqueous conditions, J. Heterocycl. Chem. 54 (2017), 753-757.

19. A. Z. A. Hassanien, M. H. Mohamed, S. A. S. Gohzlan, Aminomethylene ketones and enamines in heterocyclic synthesis: synthesis of functionally substituted pyridine, pyrazole, fused pyrimidine and fused [1,5]diazocine derivatives, J. Chem. Res. 2005 (2005), 440-445.

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М.А. Водолаженко, А.Е. Михайленко, Н.Ю. Горобец, С.М. Десенко. Двухстадийное однореакторное взаимодействие ациклических β-кетоэфиров, ДМФДМА и 2-цианометилбензимидазола

Изучено однореакторное двухстадийное взаимодействие ациклических β-кетоэфиров, диметилацеталя N,N-диметилформамида (ДМФДМА) и 2-(1H-бензо[d]имидазол-2-ил)ацетонитрила. Под действием микроволнового излучения в 2-пропаноле в присутствии пиперидина оно приводит к образованию 4-цианобензо[4,5]имидазо[1,2-a]пиридин-2-карбоксилатов, тогда как при комнатной температуре в метаноле в присутствии метилата натрия образуются 1-гидроксибензо[4,5]имидазо[1,2-a]пиридин-4-карбонитрилы. Промежуточные енамины, которые образуются на первой стадии из β-кетоэфиров и ДМФДМА, реагируют по метиленовой группе 2-цианометилбензимидазола с последующей гетероциклизацией. В присутствии пиперидина циклизация идет с участием атома азота бензимидазола и кетогруппы β-кетоэфирного фрагмента, тогда как в присутствии сильного основания циклизация происходит по сложноэфирной группе.

Ключевые слова: β-кетоэстер, 2-цианометилбензимидазол, однореакторная гетероциклизация, ДМФДМА, микроволновое излучение.

М.О. Водолаженко, А.Є. Михайленко, М.Ю. Горобець, С.М. Десенко. Двостадійна однореакторна взаємодія ациклічних β-кетоестерів, ДМФДМА та 2-ціанометилбензімідазолу.

Вивчено однореакторну двохстадійну взаємодію ациклічних β-кетоефірів, диметилацеталю N,N-диметилформаміду (ДМФДМА) та 2-(1H-бензо[d]імідазол-2-іл)ацетонітрила. Під дією мікрохвильового опромінення в 2-пропанолі в присутності піперидину вона призводить до 4-ціанобензо[4,5]імідазо[1,2-a]піридин-2-карбоксилатів, тоді як при кімнатній температурі в метанолі у присутності метилату натрію спостерігається утворення 1-гідроксибензо[4,5]імідазо[1,2-a]піридин-4-карбонітрилів. Проміжні єнаміни, які утворюються на першій стадії з β-кетоефірів та ДМФДМА, реагують за метиленовою групою 2-ціанометилбензімідазолу з наступною гетероциклізацією. У присутності піперидину циклізація іде з участю атому азоту бензімідазолу та кетогрупи β-кетоефірного фрагменту, тоді як у присутності сильної основи циклізація проходить за естерною групою.

Ключові слова: β-кетоестер, 2-ціанометилбензімідазол, однореакторна гетероциклізація, ДМФДМА, мікрохвильове опромінення.