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Oxidative S_NH amidation of acridine and tautomerism of *N*-(acridin-9-yl)benzamides

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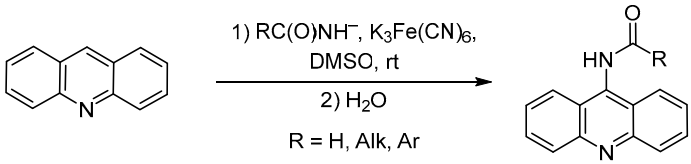


Direct oxidative nucleophilic substitution of hydrogen atom in acridine molecule was used to synthesize 9-acylaminoacridines. The prototropic amine-imine tautomerism of these compounds was studied.

Keywords: acridine, nucleophilic substitution of hydrogen, oxidative amidation, tautomerism.

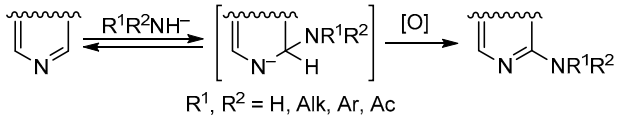
The development of selective C–N bond formation reactions is an important direction in contemporary organic synthesis, because compounds containing amino groups or their derivatives show various biological activity, are used in medicinal chemistry, as well as in chemical technology and biotechnology.[1] The most general method for the preparation of such compounds is nucleophilic substitution of halogens or other nucleofugic groups either in the absence of catalyst[2] or under catalytic conditions.[3] Direct methods for the introduction of amine and amide functionality in electron-rich heterocycles by activation of C–H bonds with transition metal complexes have been actively developed in recent years.[4]

In the case of electron-deficient substrates, such as azines and nitroarenes, an attractive alternative to the aforementioned methods is nucleophilic aromatic substitution of hydrogen atom (S_NH),[5] including the oxidative[6] and vicarious[7] versions of this reaction. The methodology of oxidative nucleophilic substitution of hydrogen atom does not require preliminary introduction of classical leaving groups in the molecule of aromatic substrate or reagent and the use of costly catalysts and ligands.

The mechanism of S_NH reaction includes the formation of σ^H-adduct, followed by its aromatization (Scheme 1).

The second step is always rate limiting for the whole process, because the formally eliminated hydride anion is a very poor nucleofuge. The elimination step occurs as a redox process that includes a sequence of electron transfer, proton transfer, and another electron transfer from σ^H-adduct to the oxidant (EPE mechanism).[8] The external oxidant can be either inorganic (air oxygen, halogens, sulfur, metal cations etc.) or organic reagents (quinones, carbocations, nitro compounds, etc.). In the absence of external oxidant, the starting π-electron-deficient substrate may also act as an oxidant.

Scheme 1



Compared to the well known achievements in the field of oxidative amination and alkylamination[6] of azines, the S_NH amidation reaction remains little studied. The first example of this reaction was reported in early 1990s, using nitrobenzene.[9] Subsequently, benzamidation of 1,3-dinitrobenzene under anaerobic conditions was used to synthesize *N*-(2,4-dinitrophenyl)benzamide in 12% yield.[10]

Our research group recently performed the first S_NH amidation of a heteroaromatic compound, namely, 1,3,7-triazapyrene.[11] The reaction between the heterocycle and N-anion of the respective amide proceeded in anhydrous DMSO at room temperature, with air oxygen acting as the oxidant.

The aim of this work was to study the possibilities for introducing *N*-amide functionality in the ring of acridine (**1**) by direct substitution of hydrogen atom under the aforementioned conditions. Regioselective S_NH reactions at position 9 of acridine system are well known,[12] but in the case of N-nucleophiles always occur with difficulty and

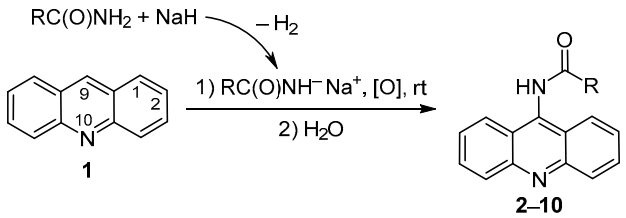
produce unreliable results. For example, acridine underwent Chichibabin reaction with sodium amide only at 180°C in *N*,*N*-dimethylaniline[13a] or upon fusion with $NaNH_2$.[13b] However, the yield of 9-aminoacridine in both cases was only 31%; also significant amounts of the starting material and 9,9'-biacridane were isolated.

We should note that derivatives of acridine, and especially those of 9-aminoacridine, have a wide range of applications as fluorescent biochemical markers,[14] as well as antitumor,[15] antibacterial,[16] antiHIV,[17] and antimalarial drugs.[18]

Before optimizing the reaction conditions for the introduction of *N*-amide group, we first studied the benzamidation of acridine (**1**). At first, the benzamide anion was obtained by treatment with sodium hydride in anhydrous DMSO, under the conditions that are known to enhance the nucleophilicity of anions due to the absence of solvate shell. It was found that the interaction of acridine (**1**) with a 6-fold molar excess of benzamide N-anion in DMSO occurred quite slowly at room temperature. Thus, 48% of 9-benzoylaminoacridine (**2**) along with 50% of the starting acridine were isolated from the reaction mixture after 54 h (Scheme 2, Table 1, experiment 1). Remarkably, increasing the temperature to 65–70°C practically did not accelerate the benzamidation reaction, but led to the appearance of by-products and decreased the yield of product **2** (Table 1, experiment 2).

We assumed that a possible reason for the slow reaction progress at room temperature was the low efficiency of air oxygen as oxidant during the aromatization of σ^H-adduct.

Scheme 2



During our earlier studies of such S_NH reactions of 1,3,7-triazapyrene as hydroxylation,[19a] alkoxylation,[19b,c] amination,[19a] and alkylamination,[19d] we successfully used the common one-electron oxidant $K_3Fe(CN)_6$. Applying it to the benzamidation of acridine shortened the reaction duration to 8 h and increased the product yield to 78% (Table 1, experiment 3). The same system of reagents was successfully used at room temperature to interact acridine with other primary aromatic amides both with electron-donating and electron-withdrawing substituents in the benzene ring (Table 1, experiments 4–7).

Contrary to the case of 1,3,7-triazapyrene,[11] the reaction of acridine with amides of aliphatic carboxylic acids (formic, acetic, propionic, and isobutyric acids) proceeded smoothly under the conditions described above, forming high yields of the respective 9-acylaminoacridines (Table 1, experiments 8–11).

It should be noted that, while ^{1}H NMR spectra (DMSO-d_6) of compounds **7–10** obtained from aliphatic amides fully corresponded to the structure of 9-acylaminoacridine, the spectra of their aromatic analogs **2**–**6** featured significantly broadened proton signals, preventing accurate assignment of these signals (Fig. 1*a*). Apparently, the averaging of spectra was caused by the non-degenerate prototropic aminoacridine-acridanimine tautomerism known in compounds of acridine series.[20] In our case, this tautomerism occurred between the acylamine form **A** and acylimine form **B** of compounds **2**–**6** (Scheme 3).

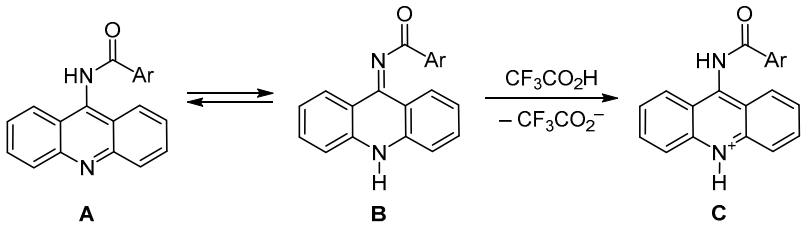
The rates of tautomeric transformations in DMSO solution were quite different for compounds **2**–**6**. For example, besides the proton multiplets of one tautomer, the spectrum of 9-benzoylaminoacridine (**2**) also contained a set of significantly broadened singlets from the other tautomer at ~7.2, 7.5, 8.0, and 11.8 ppm. The ratio of tautomers was ~ 9:1 according to the integrated intensity of signals. Therefore, in the case of amide **2**, the prototropic transformations became slow on NMR timescale, and distinct signals of both tautomers were simultaneously observed, uncharacteristically for such a polar solvent.[21a]

Table 1. The synthesis conditions and yields 9-acylaminoacridines **2**–**10**

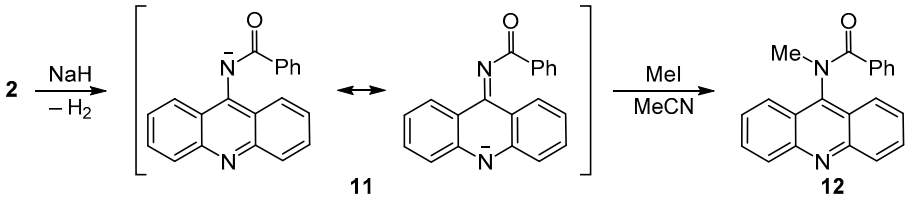
Experiment	R	Reaction product	Temperature, °C	Oxidant	Reaction time, h	Yield, %
1	Ph	**2**	Room	O_2 (air)	54	48*
2	Ph	**2**	65–70	O_2 (air)	54	24**
3	Ph	**2**	Room	$K_3Fe(CN)_6$	8	78
4	4-MeC_6H_4	**3**	Room	$K_3Fe(CN)_6$	8	92
5	4-$MeOC_6H_4$	**4**	Room	$K_3Fe(CN)_6$	8	96
6	4-$O_2NC_6H_4$	**5**	Room	$K_3Fe(CN)_6$	12	78
7	2-$O_2NC_6H_4$	**6**	Room	$K_3Fe(CN)_6$	12	75
8	H	**7**	Room	$K_3Fe(CN)_6$	10	71
9	Me	**8**	Room	$K_3Fe(CN)_6$	10	73
10	Et	**9**	Room	$K_3Fe(CN)_6$	8	67
11	2-Pr	**10**	Room	$K_3Fe(CN)_6$	8	66

* Isolated 50% of the starting compounds.
** Isolated 20% of the starting compounds.

Scheme 3



Scheme 4



The addition a small amount of trifluoroacetic acid to the solution of amide **2** in DMSO-d_6 resulted, as expected, in a simpler spectrum, since both tautomers were protonated to the same cation, in which the positive charge was delocalized between two nitrogen atoms (Scheme 3 and Fig. 1*b*). However, the signals of second tautomer were not identified in the spectra of amides **3**–**6**, indicating a higher rate of tautomeric transformations. Taking this into account, ^{1}H and ^{13}C NMR spectra are further reported for the protonated forms of compounds **2**–**6** (Experimental).

In order to determine the major tautomer in the equilibrium mixture of 9-benzoylaminoacridine (**2**), it was necessary to obtain model compounds of tautomers **A** and **B**, which usually has been achieved in the form of their fixed (*N*-methylated) derivatives.[21b] Methylation of the ambident anion **11** of compound **2** with methyl iodide at room temperature in anhydrous acetonitrile (Scheme 4) gave a mixture of compounds. An fixed analog of tautomer **A**, *N*-(acridin-9-yl)-*N*-methylbenzamide (**12**) was isolated from this mixture, resulting from methylation at the exocyclic nitrogen atom.

The analog of tautomer **B** was *N*-(10-methyl-10*H*-acridin-9-ylidene)benzamide (**14**), which could be isolated in merely 6% yield from attempted oxidative benzamidation of *N*-methylacridinium methyl sulfate (**13**) (Scheme 5). The main product from this reaction was *N*-methylacridone **15**.

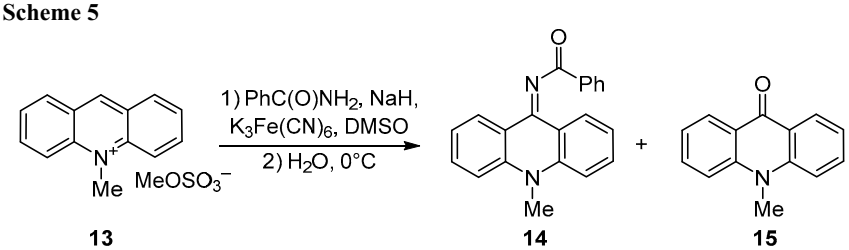
The acridone **15** was likely formed during the hydrolysis of oxidative benzamidation product **14**. Such hydrolysis may occur not only at the isolation step, but also in the reaction mixture due to the presence of water formed during oxidation of the σ-adduct.

The structures of model compounds **12** and **14** were proved conclusively by homonuclear and heteronuclear 2D NMR experiments. A key spectral feature for establishing the methyl group position in compound **12** was the coupling of methyl group protons in ^{1}H–^{13}C HSQC and HMBC spectra with the carbon atom of carbonyl group (170.8 ppm) and C-9 atom (145.5 ppm) of the acridine fragment. In the case of compound **14**, the protons of NCH_3 group were coupled to the C-4a(10a) atom (141.4 ppm) and C-4(5) atom (116.2 ppm). In this study we assigned all ^{1}H and ^{13}C NMR signals of compounds **12** and **14** and also identified the missing C-9 signal in one-dimensional ^{13}C NMR spectrum of compound **4** (150.7 ppm) (see the Experimental and the Supplementary information file).

The comparison of ^{1}H NMR spectrum of 9-benzoylaminoacridine (**2**) (Fig. 1*a*) with the spectra of model compounds **12** and **14** (Fig. 1*c* and 1*d*, respectively) indicated that the benzoylamine form **A** was the major component at equilibrium (the content of benzoylimine form **B** did not exceed 10%). Certainly, the absence of signal broadening in NMR spectra of compounds **7**–**10** did not rule out the presence of an equilibrium: the equilibrium was merely strongly shifted towards the acylamine tautomer.

Thus, acridine readily underwent direct oxidative substitution of hydrogen atom with an *N*-amide group. The amidation with separately prepared N-anion of aliphatic or aromatic amide in anhydrous DMSO occurred at room temperature in the presence of $K_3Fe(CN)_6$, enabling the synthesis of 9-acylaminoacridines in a single step and in high yields. The obtained amides showed prototropic tautomerism.

Scheme 5



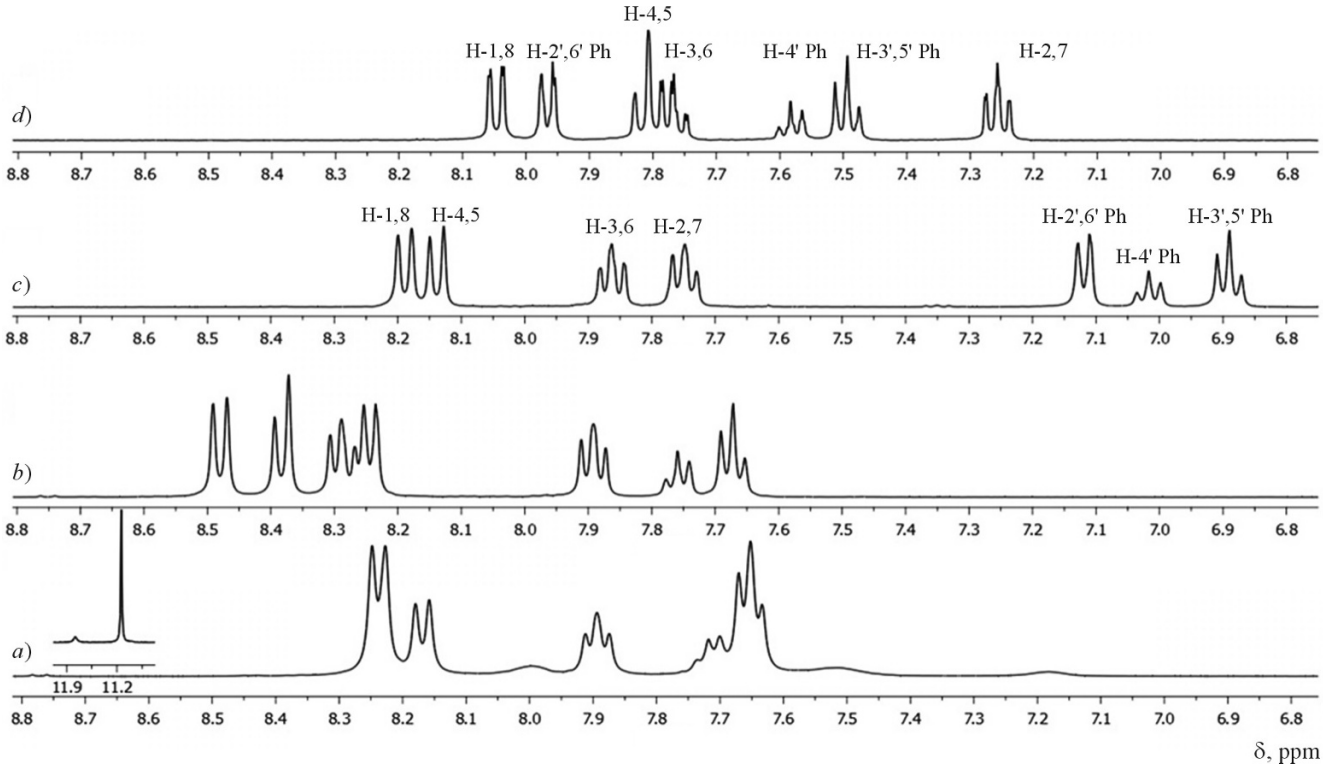


Figure 1. ^{1}H NMR spectra: *a*) 9-benzoylaminoacridine (**2**) in DMSO-d_6, *b*) 9-benzoylaminoacridine (**2**) in DMSO-d_6 + CF_3COOH, *c*) *N*-(acridin-9-yl)-*N*-methylbenzamide (**12**) in DMSO-d_6, *d*) *N*-(10-methyl-10*H*-acridin-9-ylidene)benzamide (**14**) in DMSO-d_6.

Experimental

^{1}H and ^{13}C NMR spectra were acquired on a Bruker Avance HD 400 instrument (400 and 100 MHz, respectively); the solvent signals of DMSO-d_6 were used as internal standard[22] (2.50 ppm for ^{1}H nuclei, 40.45 ppm for ^{13}C nuclei). ^{1}H–^{13}C HSQC and HMBC spectra were acquired on the same instrument. Mass spectral analysis was performed on a Bruker UHR-TOF maXis Impact instrument (electrospray ionization). Melting points were determined with a PTP-1 apparatus. The reaction progress and purity of the obtained compounds were controlled by TLC on Silufol UV-254 plates.

Sodium hydride (60% suspension in paraffin oil) was purchased from Merck. 10-Methylacridinium methyl sulfate (**13**) was obtained according to a published procedure.[23] The commercially available reagents were used without additional purification.

Synthesis of *N*-(acridin-9-yl)acylamides 2–10 (General method). The reaction was performed in a vessel protected from air moisture. Sodium hydride (60% suspension in oil, 120 mg, 3 mmol) was added with stirring to a solution of the appropriate amide (3 mmol) in anhydrous DMSO (4 ml). After the evolution of hydrogen ceased (~0.5 h), the reaction mixture was treated with acridine (**1**) (89.5 mg, 0.5 mmol), $K_3Fe(CN)_6$ (1 g, 3 mmol) and vigorously stirred at room temperature for the duration indicated in Table 1. Then the mixture was poured into cold water (50 ml) and acidified with dilute HCl solution to pH ~7. The precipitate was filtered off, washed with water, dried (when isolating the amide **5**, the precipitate on filter was washed at first with 100 ml of hot water (~90°C) to remove the exess of 4-nitrobenzamide). The products were further purified by recrystallization from the appropriate solvents.

***N*-(Acridin-9-yl)benzamide (2)**. Yield 116 mg (78%), yellow crystals, mp 235–236°C (EtOAc) (mp 166–169°C[24]). ^{1}H NMR spectrum (DMSO-d_6 + CF_3COOH)*, δ, ppm (*J*, Hz): 7.66 (2H, dd, *J* = 7.3, *J* = 7.6, H-3',5' Ph); 7.75 (1H, t, *J* = 7.3, H-4' Ph); 7.88 (2H, dd, *J* = 7.6, *J* = 8.7, H-2,7); 8.24 (2H, d, *J* = 7.6, H-2',6' Ph); 8.28 (2H, dd, *J* = 7.6, *J* = 8.6, H-3,6); 8.38 (2H, d, *J* = 8.6, H-4,5); 8.48 (2H, d, *J* = 8.7, H-1,8). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 123.1; 124.4; 126.2; 128.1; 128.7; 129.3; 130.5; 132.2; 133.6; 140.6; 149.0; 166.6. Found, *m*/*z*: 299.1184 $[M+H]^+$. $C_{20}H_{15}N_2O$. Calculated, *m*/*z*: 299.1179.

***N*-(Acridin-9-yl)-4-methylbenzamide (3)**. Yield 144 mg (92%), yellow crystals, mp 255–256°C (EtOH–EtOAc). ^{1}H NMR spectrum (DMSO-d_6 + CF_3COOH), δ, ppm (*J*, Hz): 2.46 (3H, s, CH_3); 7.47 (2H, d, *J* = 8.1, H-3',5' Ar); 7.82 (2H, br. t, *J* = 8.0, H-2,7); 8.13 (2H, d, *J* = 8.1, H-2',6'); 8.19 (2H, br. t, *J* = 8.0, H-3,6); 8.31 (2H, d, *J* = 8.7, H-4,5); 8.37 (2H, d, *J* = 8.7, H-1,8). ^{13}C NMR spectrum (DMSO-d_6 + CF_3COOH), δ, ppm: 21.2; 121.4; 122.1; 126.3; 127.3; 128.7; 129.3; 130.0; 136.4; 141.5; 143.3; 151.1; 167.2. Found, *m*/*z*: 313.1353 $[M+H]^+$. $C_{21}H_{17}N_2O$. Calculated, *m*/*z*: 313.1335.

***N*-(Acridin-9-yl)-4-methoxybenzamide (4)**. Yield 157 mg (96%), yellow crystals, mp 263–264°C (EtOH–EtOAc). ^{1}H NMR spectrum (DMSO-d_6 + CF_3COOH), δ, ppm (*J*, Hz): 3.91 (3H, s, CH_3O); 7.19 (2H, d, *J* = 8.8, H-3',5' Ar); 7.83

* Here and further the ^{1}H and ^{13}C NMR signals of trifluoroacetic acid are not listed. The atom numbering in phenyl group is indicated with apostrophes.

(2H, br. t, *J* = 7.5, H-2,7); 8.18–8.25 (4H, m, H-3,6,2',6' Ar); 8.31 (2H, d, *J* = 8.7, H-4,5); 8.39 (2H, d, *J* = 8.7, H-1,8). ^{13}C NMR spectrum (DMSO-d_6 + CF_3COOH), δ, ppm: 55.7 (CH_3); 114.0 (C-3',5' Ar); 122.0 (C-8a,9a); 122.2 (C-4,5); 125.0 (C-1' Ar); 126.1 (C-1,8); 126.9 (C-2,7); 130.7 (C-2',6' Ar); 135.5 (C-3,6); 142.3 (C-4a,10a); 150.7 (C-9); 163.0 (C-4' Ar); 166.8 (C=O). Found, *m*/*z*: 329.1292 $[M+H]^+$. $C_{21}H_{17}N_2O_2$. Calculated, *m*/*z*: 329.1285.

***N*-(Acridin-9-yl)-4-nitrobenzamide (5)**. Yield 134 mg (78%), orange crystals, mp 298–299°C (EtOH). ^{1}H NMR spectrum (DMSO-d_6 + CF_3COOH), δ, ppm (*J*, Hz): 7.80 (2H, br. t, *J* = 8.1, H-2,7); 8.17 (2H, br. t, *J* = 8.0, H-3,6); 8.30 (2H, d, *J* = 8.6, H-4,5); 8.40 (2H, d, *J* = 9.0, H-2',6'); 8.44 (2H, d, *J* = 9.1, H-1,8); 8.49 (2H, d, *J* = 9.0, H-3',5' Ar). ^{13}C NMR spectrum (DMSO-d_6 + CF_3COOH), δ, ppm: 121.9; 122.6; 123.8; 126.0; 127.0; 130.1; 135.3; 138.9; 142.7 (2C); 149.9; 166.1. Found, *m*/*z*: 344.1043 $[M+H]^+$. $C_{20}H_{14}N_3O_3$. Calculated, *m*/*z*: 344.1030.

***N*-(Acridin-9-yl)-2-nitrobenzamide (6)**. Yield 129 mg (75%), yellow crystals, mp 265–266°C (EtOH). ^{1}H NMR spectrum (DMSO-d_6 + CF_3COOH), δ, ppm (*J*, Hz): 7.88–7.95 (3H, m, H-2,7, H-4' Ar); 8.05 (1H, br. t, *J* = 7.6, H-5' Ar); 8.21–8.28 (3H, m, H-3,6, H-6' Ar); 8.32 (1H, d, *J* = 8.1, H-3' Ar); 8.35 (2H, d, *J* = 8.7, H-4,5); 8.57 (2H, d, *J* = 8.7, H-1,8). ^{13}C NMR spectrum (DMSO-d_6 + CF_3COOH), δ, ppm: 121,9; 122.5; 124.7; 125.8; 127.3; 129.9; 131.6; 131.9; 134.6; 135.7; 142.6 (2C); 146.4; 165.7. Found, *m*/*z*: 344.1042 $[M+H]^+$. $C_{20}H_{14}N_3O_3$. Calculated, *m*/*z*: 344.1030.

***N*-(Acridin-9-yl)formamide (7)**. Yield 79 mg (71%), pale-yellow crystals, subl. 220°C (EtOAc). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 7.66 (2H, br. t, *J* = 7.3, H-2,7); 7.88 (2H, br. t, *J* = 7.5, H-3,6); 8.16 (2H, d, *J* = 8.5, H-4,5); 8.18 (2H, d, *J* = 8.6, H-1,8); 8.70 (1H, s, CHO); 10.93 (1H, s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 122.0; 124.4; 126.0; 129.3; 130.5; 138.9; 148.9; 161.0. Found, *m*/*z*: 223.0866 $[M+H]^+$. $C_{14}H_{11}N_2O$. Calculated, *m*/*z*: 223.0866.

***N*-(Acridin-9-yl)acetamide (8)**. Yield 86 mg (73%), pale-yellow crystals, mp 274–275°C (EtOAc) (mp 277–279°C (acetone)[25]). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 2.36 (3H, s, CH_3); 7.62 (2H, br. t, *J* = 7.7, H-2,7); 7.86 (2H, br. t, *J* = 8.0, H-3,6); 8.14 (2H, d, *J* = 8.5, H-4,5); 8.17 (2H, d, *J* = 8.6, H-1,8); 10.66 (1H, s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 23.0; 122.5; 124.6; 125.8; 129.2; 130.4; 140.4; 148.9; 169.5. Found, *m*/*z*: 237.1028 $[M+H]^+$. $C_{15}H_{13}N_2O$. Calculated, *m*/*z*: 237.1022.

***N*-(Acridin-9-yl)propionamide (9)**. Yield 84 mg (67%), yellow crystals, subl. 220°C (EtOAc). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.26 (3H, t, *J* = 7.5, CH_3); 2.70 (2H, q, *J* = 7.5, CH_2); 7.63 (2H, br. t, *J* = 7.6, H-2,7); 7.86 (2H, br. t, *J* = 8.3, H-3,6); 8.12 (2H, d, *J* = 8.7, H-4,5); 8.17 (2H, d, *J* = 8.7, H-1,8); 8.70 (1H, s, C<u>H</u>O); 10.60 (1H, s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 9.9; 28.9; 122.6; 124.5; 125.8; 129.2; 130.4; 140.4; 148.9; 173.3. Found, *m*/*z*: 251.1186 $[M+H]^+$. $C_{16}H_{15}N_2O$. Calculated, *m*/*z*: 251.1179.

***N*-(Acridin-9-yl)isobutyramide (10)**. Yield 87 mg (66%), pale-yellow crystals, subl. 225°C (EtOAc). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.32 (6H, d, *J* = 6.9, $CH(C\underline{H}_3)_2$); 3.02 (1H, m, $C\underline{H}(CH_3)_2$); 7.64 (2H, br. t, *J* = 7.5, H-2,7); 7.86 (2H, br. t, *J* = 8.2, H-3,6); 8.07 (2H, d, *J* = 8.6, H-4,5); 8.17 (2H, d, *J* = 8.7, H-1,8); 10.59 (1H, s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 19.7; 34.6; 122.7; 124.3; 125.9; 129.3; 130.4; 140.3; 148.9; 176.4. Found, *m*/*z*: 265.1342 $[M+H]^+$. $C_{17}H_{17}N_2O$. Calculated, *m*/*z*: 265.1335.

***N*-(Acridin-9-yl)-*N*-methylbenzamide (12)**. The reaction was performed in a vessel protected from air moisture. Sodium hydride (60% suspension in oil, 40 mg, 1 mmol) was added with stirring to a solution of 9-benzoylaminoacridine (**2**) (149 mg, 0.5 mmol) in anhydrous acetonitrile (4 ml). After the evolution of hydrogen ceased (~0.5 h), the reaction mixture was treated with methyl iodide (142 mg, 1 mmol) and vigorously stirred for 2 h. Then the mixture was poured on ice (~50 g) and acidified with dilute HCl solution to pH ~7. The precipitate was filtered off, washed with water, dried, and crystallized from ethyl acetate. Yield 19 mg (12%), beige crystals, mp 209–210°C (EtOAc). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 3.57 (3H, s, CH_3); 6.88 (2H, br. t, *J* = 7.6, H-3',5' Ph); 7.00 (1H, br. t, *J* = 7.4, H-4' Ph); 7.11 (2H, d, *J* = 7.3, H-2',6' Ph); 7.74 (2H, br. t, *J* = 8.0, H-2,7); 7.86 (2H, br. t, *J* = 8.0, H-3,6); 8.13 (2H, d, *J* = 8.7, H-4,5); 8.18 (2H, d, *J* = 8.6, H-1,8). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 37.9 (CH_3); 122.8 (C-8a,9a); 123.2 (C-1,8); 126.5 (C-2',6' Ph); 127.5 (C-3',5' Ph); 127.7 (C-2,7); 129.7 (C-4,5); 130.0 (C-4' Ph); 130.7 (C-3,6); 135.7 (C-1' Ph); 145.5 (C-9); 149.1 (C-4a,10a); 170.8 (C=O). Found, *m*/*z*: 313.1348 $[M+H]^+$. $C_{21}H_{17}N_2O$. Calculated, *m*/*z*: 313.1335.

Benzamidation of *N*-methylacridinium methyl sulfate (13). The reaction was performed in a vessel protected from air moisture. Sodium hydride (60% suspension in oil, 120 mg, 3 mmol) was added with stirring to a solution of benzamide (363 mg, 3 mmol) in anhydrous DMSO (4 ml). After the evolution of hydrogen ceased (~0.5 h), *N*-methylacridinium methyl sulfate (**13**) (152.5 mg, 0.5 mmol) and $K_3Fe(CN)_6$ (1 g, 3 mmol) were added, and the reaction mixture was vigorously stirred for 3 h. The mixture was then poured on crushed ice (~50 g), allowed to warm to room temperature, and acidified with dilute HCl solution to pH ~7. The precipitate was filtered off, washed with water, and dried. The obtained mxture was separated by dry silica gel flash chromatography,[26] eluting the first fraction with benzene and the second fraction with ethyl acetate. The first colorless fraction after evaporation of solvent gave 83 mg (79%) of **10-methyl-10*H*-acridin-9-one** (**15**). Yellow crystals, mp 202–203°C (benzene) (mp 203°C (benzene)[27]). The second, pale-yellow fraction contained 19 mg (6%) of ***N*-(10-methyl-10*H*-acridin-9-ylidene)-benzamide** (**14**). Yellow crystals, mp 187–188°C (EtOAc). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 3.92 (3H, s, CH_3); 7.25 (2H, dd, *J* = 7.8, *J* = 8.2, H-2,7); 7.49 (2H, br. t, *J* = 7.5, H-3',5' Ph); 7.58 (1H, br. t, *J* = 7.3, H-4' Ph); 7.76 (2H, dd, *J* = 7.8, *J* = 8.2, H-3,6); 7.81 (2H, br. d, *J* = 8.2, H-4,5); 7.96 (2H, d, *J* = 7.8, H-2',6' Ph); 8.04 (2H, dd, *J* = 8.2, *J* = 1.2, H-1,8). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 34.4 (CH_3); 116.2 (C-4,5); 117.9 (C-8a,9a); 121.6 (C-2,7); 127.1 (C-1,8); 128.6 (C-2',6'); 128.7 (C-3',5');

132.3 (C-4'); 133.4 (C-3,6); 134.5 (C-1'); 141.4 (C-4a,10a); 152.7 (C-9); 176.0 (C=O). Found, *m/z*: 313.1349 $[M+H]^+$. $C_{21}H_{17}N_2O$. Calculated, *m/z*: 313.1335.

A Supplementary information file containing ^1H and ^{13}C NMR spectra of the synthesized compounds is available online at http://link.springer.com/journal/10593.

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References

1. (a) Corey, E. J.; Czakó, B.; Kürti, L. *Molecules and Medicine*; Wiley: Hoboken, 2007. (b) Travis, A. S. In *The Chemistry of Anilines*; Rappoport, Z., Ed.; Wiley: Chichester, 2007, p. 715. (c) *Amino Group Chemistry: From Synthesis to the Life Sciences*; Ricci A., Ed.; Wiley-VCH: Weinheim, 2008. (d) Gangopadhyay, P.; Radhakrishnan, T. P. *Chem. Mater.* **2000**, *12*, 3362. (e) Bag, B.; Bharadwaj, P. K. *J. Phys. Chem. B* **2005**, *109*, 4377.
2. Terrier, F. *Modern Nucleophilic Aromatic Substitution*: Wiley-VCH: Weinheim, 2013.
3. (a) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem*. **2000**, *65*, 1158. (b) Surry, D. S.; Buchwald, S. L. *Angew. Chem*., *Int. Ed.* **2008**, *47*, 6338. (c) Roiban, G.-D.; Mehler, G.; Reetz, M. T. *Eur. J. Org. Chem*. **2014**, 2070.
4. (a) Kim, J.; Kim, J.; Chang, S. *Chem. Eur. J*. **2013**, *19*, 7328 and references cited therein. (b) Ryu, J.; Shin, K.; Park, S. H.; Kim, J. Y.; Chang, S. *Angew. Chem.*, *Int. Ed.* **2012**, *51*, 9904. (d) Shi, J.; Zhou, B.; Yang, Y.; Li, Y. *Org. Biomol. Chem*. **2012**, *10*, 8953.
5. (a) Chupakhin, O. N.; Charushin, V. N.; van der Plas, H. C. *Nucleophilic Aromatic Substitution of Hydrogen*; Academic Press: San Diego, 1994. (b) Mąkosza, M.; Wojciechowski, K. *Chem. Rev*. **2004**, *104*, 2631.
6. (a) van der Plas, H. C. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Elsevier: New York, 2004, *86*, 1. (b) Gulevskaya, A. V.; Pozharskii, A. F. *Russ. Chem. Bull*. **2008**, *57*, 913 [*Izv. Akad. Nauk*, *Ser. Khim.* **2008**, 899.] (c) Charushin, V. N.; Chupakhin, O. N. *Top. Heterocycl. Chem.* **2014**, *37*, 1. (d) Gulevskaya, A. V.; Pozharskii, A. F. *Top. Heterocycl. Chem.* **2014**, *37*, 179. (e) Gulevskaya, A. V.; Maes, B. U. W.; Meyers, C.; Herrebout, W. A.; van der Veken, B. J. *Eur. J. Org. Chem*. **2006**, 5305.
7. (a) Makosza, M.; Wojciechowski, K. *Top. Heterocycl. Chem*. **2014**, *37*, 51. (b) Makosza, M. *Russ. Chem. Bull*. **1996**, 45, 491. [*Izv. Akad. Nauk*, *Ser. Khim.* **1996**, 531.] (c) Bakke, J. M.; Svensen, H.; Trevisan, R. *J. Chem. Soc*., *Perkin Trans. 1* **2001**, 376. (d) Makosza, M.; Białecki, M. *J. Org. Chem*. **1998**, *63*, 4878.
8. Matern, A. I.; Charushin, V. N.; Chupakhin, O. N. *Russ. Chem. Rev*. **2007**, *76*, 23. [*Usp. Khim.* **2007**, *76*, 27.]
9. Stern, M. K.; Cheng, B. K. *J. Org. Chem*. **1993**, *58*, 6883.
10. Gulevskaya, A. V.; Tyaglivaya, I. N.; Verbeeck, S.; Maes, U. W.; Tkachuk, A. V. *ARKIVOC* **2011**, (ix), 238.
11. Borovlev, I. V.; Demidov, O. P.; Kurnosova, N. A.; Amangasieva, G. A.; Avakyan, E. K. *Chem. Heterocycl. Compd.* **2015**, *51*, 170. [*Khim. Geterotsikl. Soedin.* **2015**, *51*,170.]
12. (a) Chiron, J.; Galy, J-P. *Synthesis* **2004**, 313. (b) Skonieczny, S. *Heterocycles* **1977**, *6*, 987.
13. a) Pozharskii, A. F.; Konstantinchenko, A. A. *Chem. Heterocycl. Compd*. **1972**, *8*, 1518. [*Khim. Geterotsikl. Soedin.* **1972**, 1657.] (b) Kitahara, T.; Ishihara, Y.; Takano, J. *Nippon Kagaku Kaishi* **1997**, *12*, 876; *Chem. Abstr*. **1997**, *128*, 22802.
14. *Fluorescent and Luminescent Probes*; Mason, W. T., Ed.; 2nd ed.; Academic Press: London, 1999.
15. Denny, W. A. *Curr. Med. Chem*. **2002**, *9*, 1655.
16. Wainwright, M. J. *Antimicrob. Chemother*. **2001**, *47*, 1.
17. Hamy, F.; Brondani, V.; Flörsheimer, A.; Stark, W.; Blommers, M. J. J.; Klimkait, T. *Biochemistry* **1998**, *37*, 5086.
18. Greenwood, D. J. *Antimicrob. Chemother*. **1995**, *36*, 857.
19. (a) Demidov, O. P.; Borovlev, I. V.; Saigakova, N. A.; Nemykina, O. A.; Demidova, N. V.; Pisarenko, S. V. *Chem. Heterocycl. Compd*. **2011**, *47*, 114. [*Khim. Geterotsikl. Soedin.* **2011**, 142.] (b) Demidov, O. P.; Borovlev, I. V.; Pisarenko, S. V.; Nemykina, O. A.; Saigakova, N. A. *Chem. Heterocycl. Compd*. **2010**, *46*, 636. [*Khim. Geterotsikl. Soedin.* **2010**, 791.] (c) Borovlev, I. V.; Demidov, O. P.; Saigakova, N. A. *Russ. Chem. Bull*. **2011**, *60*, 1784. [*Izv. Akad. Nauk*, *Ser. Khim.* **2011**, 1755.] (d) Borovlev, I. V.; Demidov, O. P.; Saigakova, N. A.; Pisarenko, S. V.; Nemykina, O. A. *J. Heterocycl. Chem*. **2011**, *48*, 1206.
20. (a) Stezowski, J. J.; Kollat, P.; Bogucka-Ledochowska, M.; Glusker, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 2067. (b) Rak, J.; Blazejowski, J.; Zauhar R. J. *J. Org. Chem.* **1992**, *57*, 3720. (c) Boyd, M.; Denny, W. A. *J. Med. Chem*. **1990**, *33*, 2656.
21. (a) Filatova, E. A.; Borovlev, I. V.; Pozharskii, A. F.; Starikova, Z. A.; Vistorobskii, N. V. *Mendeleev Commun*. **2000**, 178. (b) Wofford, D. S.; Forkey, D. M.; Russell, J. G. *J. Org. Chem.* **1982**, *47*, 5132.
22. Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem*. **1997**, *62*, 7512.
23. Storoniak, P.; Krzyminski, K.; Dokurno, P.; Konitz, A.; Blazejowski, J. *Aust. J. Chem*. **2000**, *53*, 627.
24. Lang, X.; Li, L.; Chen, Y.; Sun, Q.; Wua, Q.; Liu, F.; Tan, C.; Liu, H.; Gao, C.; Jiang, Y. *Bioorg. Med. Chem.* **2013**, *21,* 4170.
25. Shields, C. J.; Falvey, D. E.; Schuster, G. B.; Buchardt, J. O.; Nielsen, P. E. *J. Org. Chem.* **1988**,*53*, 3501.
26. Sharp, J. T.; Gosney, I.; Rowley, A. G. *Practical Organic Chemistry*; Springer: London, New York, 1989.
26. Storoniak, P.; Krzymicski, K.; Bouïyk, A.; Koval'chuk, E. P.; Blaïejowski, J. *J. Therm. Anal. Calorim*. **2003**, *74*, 443.