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ARTICLE

C-H Functionalization of azines. Anodic dehydroaromatization of 9-(hetero)aryl-9,10-dihydroacridines

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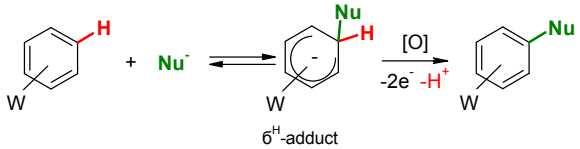
The data on anodic dehydroaromatization of 9,10-dihydroacridines, bearing aryl and heteroaryl fragments, are presented. Effects of both electron-donating and electron-withdrawing substituents on the current-voltage characteristics of these compounds have been established. The experimental data proved to be in a good agreement with quantum chemical calculations. A simple and convenient method for the electrochemical conversion of dihydroacridines into the corresponding 9-(hetero)aryl-N-methylacridinium salts has been advanced.

Introduction

Acridines belong to an important class of heteroaromatic compounds, which are widely used in photo-redox catalysis, molecular machines, sensors and transistors.[1] Arylacridines appear to be particularly attractive compounds due to their diverse biological activity.[2] Indeed, a whole number of acridines, exhibiting antitumor, antiviral, antimalarial, antiprion and analgesic properties have recently been revealed.[3] Importantly, that 9-aryl-substituted acridines are considered to be the most convenient models to study the hydride transfer reactions, proceeding with participation of the NAD^+ coenzyme.[4]

There are three main approaches to obtain 9-arylacridines. The first one suggests construction of the acridine tricyclic system, and it is based on condensation of the corresponding arylcarboxylic acid with diphenylamine in the presence of zinc chloride at temperatures 200-260 ^oC.[5] The second method, exploiting cross-coupling reactions, is associated with the necessity of incorporation of good leaving groups into acridines and use of metal catalysts.[6] Transition metal-catalyzed cross-coupling reactions are also used for the direct functionalization of C-H-bonds in acridines.[7] This method avoids use of halides; however, it does not eliminate all problems inherent for the metal-catalyzed reactions, including the formation of by-products with organometallic reagents, homo-coupling reactions and difficulties in removal of catalysts and auxiliary ligands from reaction mixtures.[8] All these features impose restrictions on use of such methods. At the same time, there are direct reactions of nucleophilic aromatic substitution of hydrogen (S_N^H Ar), that require neither metal complex catalysts, nor the presence of a halogen or other leaving groups.[9] The first step in the S_N^H reactions involves a nucleophilic attack at C-H carbon of an aromatic ring, thus leading to the intermediate 6^H-adduct. The next step is oxidative aromatization of this intermediate, accompanied by the loss of proton and a pair of electrons, formally of the hydride-ion (Scheme 1). It happens very often that the S_N^H reactions are carried out as three-component syntheses, i.e., an oxidant is injected into the reaction system together with the reaction partners. When considering susceptibility of reagents to oxidative process, the behavior of nucleophiles has first to be considered, although oxidative transformations of the starting aromatic substrates and S_N^H products are also possible. Therefore, choice of a suitable oxidant is the crucial factor to realize the S_N^H transformations. In spite of a considerable progress in studying of this type reactions, there are still no clear criteria for selection of an appropriate oxidant, and chemists have to settle themselves with experience, intuition and some empirical rules.[9,10]



W- electron withdrawing group

Scheme 1. Nucleophilic aromatic substitution of hydrogen

In this respect, use of electrochemical methods appears to be a very attractive approach.[11] Besides development of the atom-economical version of the oxidative reactions, electrochemical methods provide an opportunity to get insight into the reaction mechanism, thus making a choice of chemical oxidant to be a more rational one.[12,13] However, analysis of the

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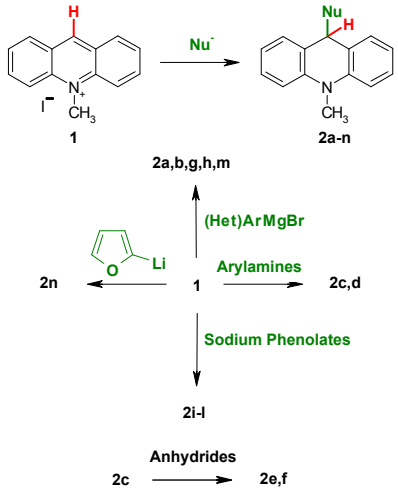
literature data shows that electrochemical methods have long been neglected, until a series of papers dedicated to electrochemical S_N^H reactions of nitroarenes with a variety of nucleophiles of different nature (C, N, O, P-centered) have been published.[13] As far as electrochemical conversions of heterocyclic σ^H-adducts are concerned, these examples are very rare, especially those arranged in the preparative mode.[14] As for dihydroacridines, the data on their preparative electrochemical dehydroaromatization have not so far been available in the literature.

In this communication we wish to report the synthesis of the series of 9-(hetero)aryl-9,10-dihydroacridines, to describe electrochemical method of their aromatization, and finally, to discuss correlations between DFT calculations and current-voltage characteristics.

Results and discussion

In order to obtain quantitative data on dehydroaromatization of azines, and to estimate effects of both electronic and steric factors on oxidation of these compounds, a series of 10-methyl-9-aryl substituted dihydroacridines have been synthesized (**2a-q**) (Table 1).

Dihydroacridines **2a**,**b**,**g**,**h**,**m** have been prepared through the reaction of 10-methylacridinium iodide with the corresponding magnesium aryl bromides. Compounds **2i-l** are derived from the reaction of the 10-methylacridinium ion with sodium phenolates in diethyl ether at room temperature. Arylamines proved to react directly in DMSO with the acridinium cation to form aminocompounds **2c** and **2d**.[15] Carbamoyl derivatives **2e** and **2f** were obtained by treatment of the amino compound **2c** with the corresponding anhydrides. Compound **2n** was prepared by reacting the lithium derivative of furan with acridine **1** (Scheme 2).



Scheme 2. Synthesis of dihydroacridines **2a-n**

Dihydroacridines **2o-q**, bearing electron-withdrawing substituents, which cannot be obtained by the methods described above, were prepared through the Pd-catalyzed cross-coupling reaction of 9-chloroacridine **4** with boronic acids **5o-q**, followed by quaternization, and reduction with $NaBH_4$ (Scheme 3). The cross-coupling products **6o-q** have been prepared by reacting chloroacridine **4** with boronic acids in the presence of 5% $Pd(PPh_3)_4$ and 2.5 equiv. of K_2CO_3 in dioxane - water (1:4) solution at 165 °C under microwave irradiation. Quaternization of **6o**,**p** has been performed with an excess of methyl iodide in diethyl ether at room temperature. In case of **6q** quaternization was carried out in refluxing dimethyl sulfate. The precipitates obtained were treated with $NaBH_4$ in boiling ethanol to give the corresponding dihydroacridines **2o-q**.

The behavior of σ^H-adducts **2a-q** was studied by cyclic voltammetry in anhydrous acetonitrile under argon (in the presence of NH_4BF_4) with a scan rate of 100 mV/s. All compounds proved to be characterized by well-defined peaks of irreversible two-electron oxidations (Figure 1). Values of oxidation potentials are given in Table 1.

The data of voltammetry studies show that oxidative potentials of compounds tested are quite sensitive to electronic effects of aryl substituents at C-9 of 9,10-dihydroacridines. As expected, introduction of a strong electron-donating substituent, such as 4-NH_2 (compound **2c**), decreases oxidation potential of 100 mV relative to unsubstituted analogue **2a**; also 4-$N(Et)_2$ group in **2d** proved to reduce the potential by 200 mV. In contrast, the transfer from compound **2d** to **2g**, bearing para-F substituent, enhances the oxidation potential of the latter up to 330 mV (130 mV relative to dihydroacridine **2a**).

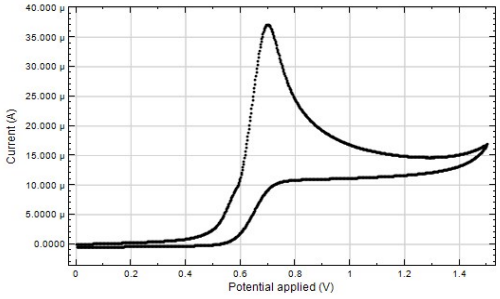


Figure 1. Cyclic voltammogram of **2m**, 10^{-3} M in CH_3CN, using a platinum disk electrode (2 mm diameter), supporting electrolyte NH_4BF_4 10^{-1}M; scan rate 100 mV/s; reference electrode $Ag/AgNO_3$

It could be anticipated that introduction of electron-withdrawing substituents, such as CN and CF_3 (compounds **2o** and **2p**), would increase significantly their oxidation potentials. However, the results of voltammetry measurements of these compounds have shown that oxidative potentials are practically unchanged, being at the level of unsubstituted compound **2a**. The presence of para-NO_2 group in compound **2q** enhances the oxidative potential by only 60 mV. This surprising fact can possibly be explained by the difference in geometrical configurations of compounds, bearing electron-donating (**2c**) and electron-withdrawing (**2p**) substituents.

To test this hypothesis, X-ray diffraction studies of single crystals of compounds **2a**, **2c**, **2p** have been carried out. A general view of these molecules and adopted numbering of atoms are given in Figure 2. According to the X-ray structural analysis (XRS) data, all compounds studied are crystallized in the cen-

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trosymmetric groups of the space symmetry. The molecular packing of these compounds is nonspecific, no significant truncation of contacts has been observed. Conformation of the central dihydropyridine ring in these compounds may be characterised as the pseudo-boat with the emerging plane of C(7) and N(1), and the axially extending substituent. In the test experiment the dihydropyridine fragment exhibits a flexion along the axis N(1)-C(7) in such a way, that the dihedral angle between the benzene rings achieves a substantial value (37.13° for compound **2p**, 35.24° for **2a**, 23.42° – **2c**). Bond lengths are in a good agreement with the standard values; length deviations are not exceeding 0.01 Å relative to the mean value. The nitrogen configuration in the pyridine ring is approximately planar: sums of CNC angles are equal to 358.0(3)° for **2c,** 355.2(3)° – for **2a**, and 355.8(3)° – for **2p**. Therefore, in all cases N-atoms appear to have the sp^2-configuration, and are strongly conjugated with the benzene rings. In spite of a low-temperature used in the x-ray experiment for **2p**, CF_3-groups of the Ph-substituent show a strong disordering. No shortened intermolecular contacts in this packing have been observed. Thus, the x-ray data demonstrate a close similarity in geometry of the tested compounds, and no significant differences between their structures have been observed.

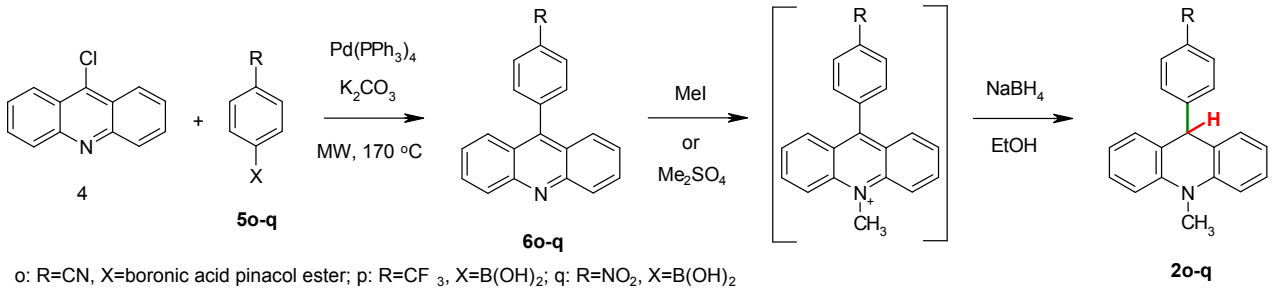
The DFT calculations of HOMO orbitals, directly involved in the oxidation process, have been performed. Analysis of the calculated HOMO energies (Table 1) and the experimentally obtained oxidation potentials has revealed the following general trend: the lower values of E_{pa}, the higher values of E_{HOMO}.

The visual representation of HOMO for dihydroacridines demonstrates clearly the electronic effects of substituents. For all compounds bearing electron-withdrawing substituents, the HOMO orbitals are localized on the acridine fragment of the molecules. This explains a low impact of electron-withdrawing substituents. As for dihydroacridines, bearing electron-donating groups (compounds **2c** and **2d**), the latter are also involved in the HOMO electron density distribution, thus explaining a decrease in oxidation potentials for these structures (Figure 3).

It should be noted that the observed values E_{pa} are in good agreement with constants $б_R$, which reflect resonance effects of substituents,[16] expressed in $б_R$ values:

R	NEt_2	NH_2	OMe	Me	F	CN	CF_3	NO_2
$б_R$	-0.57	-0.51	-0.43	-0.08	-0.48	0.08	0.08	0.15

These data show that oxidation potentials are depending mainly on substituents with a positive mesomeric effect (+M). Indeed, the compound **2g**, bearing para-F substituent (+M; -I) has a higher oxidation potential. Introduction of electron-withdrawing substituents, such as CN, CF_3 and NO_2 (-M; -I), has practically no effect on their oxidation potentials.



o: R=CN, X=boronic acid pinacol ester; p: R=CF_3, X=$B(OH)_2$; q: R=NO_2, X=$B(OH)_2$

Scheme 3. Synthesis of dihydroacridines **2o-q**

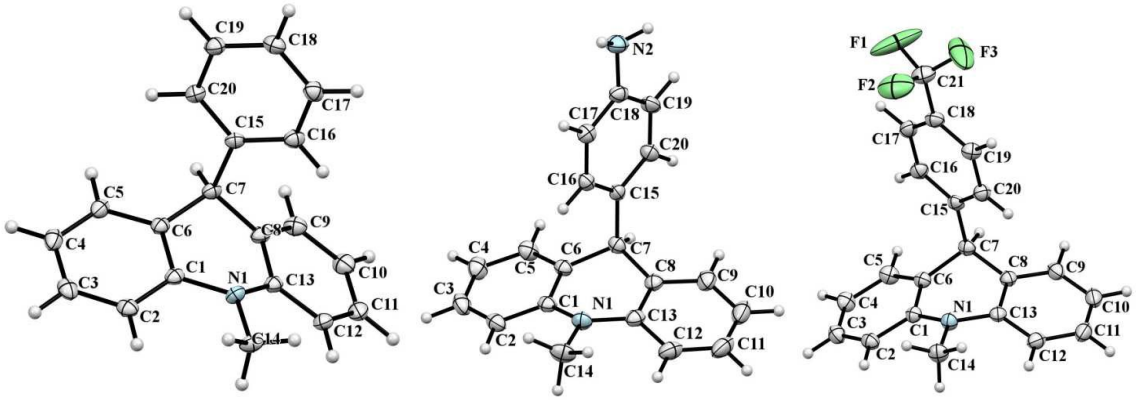


Figure 2. X-ray structures of **2a**, **2c**, **2p**.

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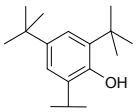
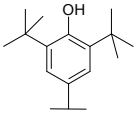
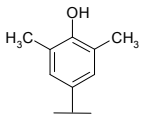
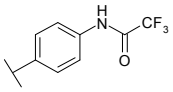
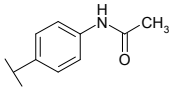
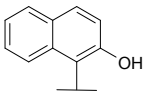
Table 1. Results of electrochemical studies and quantum chemical calculations obtained in the approximation of B3LYP/6-311+G (3df, 2p)

Compound **2**	Nu	E_{pa} (V) δ^H-adducts **2**	E_{HOMO} (eV)	Yields of the S_N^H products **3** (%)	Compound **2**	Nu	E_{pa} (V) δ^H-adducts **2**	E_{HOMO} (eV)	Yields of the S_N^H products **3** (%)
a	-Ph	0,68	-5,476	88					
b	-C_6H_4-CH_3-*p*	0,70	-5,451	92	**j**		0,64	-5,231	87
c	-C_6H_4-NH_2-*p*	0,58	-5,389	91	**k**		0,68	-5,418	87
d	-C_6H_4-NEt_2-*p*	0,48	-5,110	85	**l**		0,65	-5,330	90
e		0,69	-5,680	85	**m**		0,70	-5,498	95
f		0,66	-5,625	86	**n**		0,70	-5,446	91
g	-C_6H_4-F-*p*	0,81	-5,573	97	**o**	-C_6H_4-CN-*p*	0,68	-5,766	89
h	-C_6H_4-OCH_3-*p*	0,68	-5,349	91	**p**	-C_6H_4-CF_3-*p*	0,70	-5,590	92
i		0,57	-5,232	92	**q**	-C_6H_4-NO_2-*p*	0,74	-5,664	94

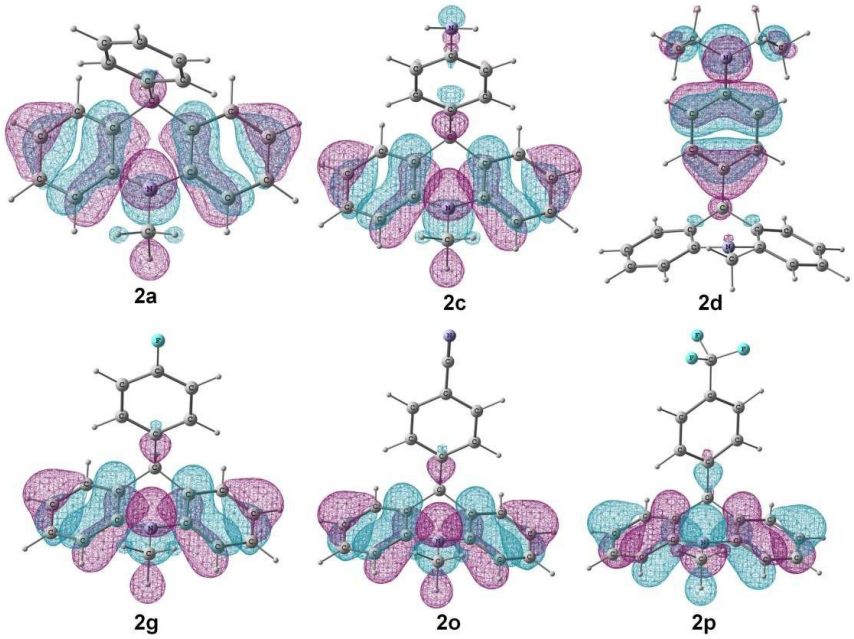


Figure 3. Visual representation of the HOMO obtained in the approximation of B3LYP/6-311+G (3df, 2p) for compounds **2a**, **2c**, **2d**, **2g**, **2o**, **2p**

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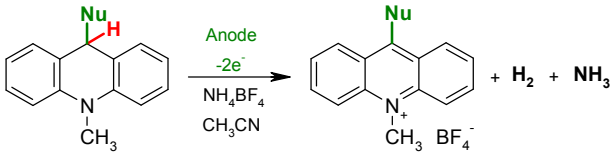
In summary, oxidation potentials of dihydroacridines **2a-q** are in the range of 0,48-0,81 V. However, most of compounds have the potentials close to 0,70 V, while introduction of electron-withdrawing substituents have no effect on values of oxidation potentials. Only the presence of electron-donating substituents leads to lower values of oxidation potentials. Obtained data can serve as a guide in the selection of the chemical oxidizing agent in S_N^H reactions at least in the series of acridines.

Taking into account the data, obtained by cyclic voltammetry, the 6^H-adducts have been subjected to preparative electrooxidation (Scheme 4).



2 a-q **3 a-q**

Scheme 4. Synthesis of acridinium tetrafluoroborates **3a-q**

Electrolysis was carried out under argon, using 0.1M solution NH_4BF_4 in CH_3CN-CH_3OH (5:1), as the supporting electrolyte. The electrolyte, containing 2 mmol of 6^H-adduct, was placed in an anode compartment of the cell, the electrodes of which were separated by a membrane of tracing paper. Electrolysis at the controlled potential (the reference electrode $Ag/AgNO_3$; 2.1 F/mol) leads to the loss of two electrons and a proton, thus resulting in the formation of aromatic S_N^H products **3a-q** (Table 1).

The reaction proceeds selectively, without any by-products, thus providing high yields of the target compounds (from 85 to 95%). Selection of NH_4BF_4 as electrolyte was due to its sufficient stability in the range of studied potentials and good results of the electrolysis. In fact, oxidation in $NaClO_4$ or $NaBF_4$ media failed, (yields were not exceeding 25%), while the presence of tetraalkylammonium salts proved to complicate significantly isolation of the target products.

Experimental

General Information

All starting reagents and solvents were obtained from commercial sources and dried by standard procedures before use. 10-Methylacridinium iodide was synthesized according to the known procedure.[17]

Cyclic voltammograms were recorded by an Autolab PGSTAT128N instrument. The experiments were carried out under argon in anhydrous acetonitrile with the additives of supporting electrolyte NH_4BF_4 (0.1 mol/L) at 17-18 °C in a three-electrode system. A platinum disk electrode (d=2 mm) used as a working electrode, a glass graphite rod as an auxiliary electrode, $Ag/AgNO_3$ was a reference electrode. The scanning rate was set 100 mV/s. The concentration of the samples was arbitrary.

Preparative electrolyses were carried out using Autolab PGSTAT128N in 50-mL three-electrode cell. The working surface of the platinum wire anode used as a working electrode was 15.0 cm^2. A tracing-paper was used as a membrane. A platinum wire served as a cathode, and the catholyte was a saturated solution of the background used in the catholyte in the corresponding solvent.

^1H and ^{13}C NMR spectra were recorded on a AVANCE-500 instruments using Me_4Si as an internal standard. Elemental analysis was carried on a Eurovector EA 3000 automated analyzer. Melting points were determined on Boetius combined heating stages and were not corrected.

The GC-MS analysis of all samples was carried out using an Agilent GC 7890A MS 5975C Inert XL EI/CI GC-MS spectrometer with a quadrupole mass-spectrometric detector with electron ionization (70 eV) and scan over the total ionic current in the range m/z 20–1000 and a quartz capillary column HP-5MS (30 m × 0.25 mm, film thickness 0.25 mm). Helium served as a carrier gas, the split ratio of the flow 1:50, and consumption through the column 1.0 mL min^{-1}; the initial temperature of the column 40 °C (storage 3 min), programming rate 10 °C min^{-1} to 290 °C (storage 20 min), the temperature of the evaporator 250 °C, the temperature of the source 230 °C, the temperature of the quadrupole 150 °C, and the temperature of the transition chamber 280 °C. Solutions of samples with concentration of 3–4 mg mL^{-1} were prepared in toluene. Samples of 1 mL of the obtained solutions were analyzed.

Microwave experiments were carried out in a Discover unimodal microwave system (CEM, USA) with a working frequency of 2.45 GHz and the power of microwave radiation ranged from 0 to 300 W. The reactions were carried out in a 10 mL reaction tube with hermetic Teflon cork. The temperature of the reaction was monitored using an inserted IR sensor for the external surface of the reaction vessel.

XRD experiments were carried out on an automated diffractometer "Xcalibur S" with CCD detector on standard procedure (graphite monochromated Mo-K_α radiation with λ = 0.71069 Å, ω-scanning with step 1°). The unit cell parameters were refined using all collected spots after the integration process. The data were not corrected for absorption.

The structure **3n** was solved by direct methods with SHELX97 program package.[18] The structures **2a**, **2c** and **2p** were solved using Olex2[19] with the Superflip[20] structure solution program by Charge Flipping. All the structures were refined by full-matrix least squares on F2 using ShelXL97. All the non-hydrogen atoms were refined with anisotropic temperature factors. The H-atoms at the $C(sp^3)$-atoms in the dihydroazine rings were solved and refined independently in isotropic approximation. All other H-atoms were calculated with AFIX and were included in the refinement at "riding" model with a common isotropic temperature factor. Deposition numbers CCDC 1479455 for **3n**, CCDC 1479454 for **2a**, CCDC 1479456 for **2c**, CCDC 1479453 for **2p** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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IR spectra of samples (solid powders) were recorded on a Spectrum One Fourier transform IR spectrometer (Perkin Elmer) equipped with a diffuse reflectance attachment (DRA). Spectrum processing and band intensity determination were carried out using the special software supplied with the spectrometer.

Synthesis of 9,10-dihydroacridines

General procedure for the Synthesis of 2a,[21] 2b, 2g, 2h,[22] 2m. These compounds were prepared through the addition of the Grignard reagents to 10-methylacridinium iodide. Aryl Grignard reagents were prepared from the corresponding aryl bromides (3,74 mmol) and magnesium (89,8 mg, 3,74 mmol) in 20 mL of anhydrous ether. An ether solution of the Grignard reagent was transferred to flask containing a stirred suspension of 10-methylacridinium iodide (1.0 g, 3.12 mmol) in 20 mL of anhydrous ether. The stirring was continued until the red, ether-insoluble acridinium iodide was entirely consumed. 5 ML of methanol was added to destroy unreacted Grignard reagent. A white precipitate of magnesium salts was removed by filtration, and the solvent was evaporated under reduced pressure to give solid materials which were recrystallized from ethanol.

General procedure for the Synthesis of 2i-l. These compounds were prepared by addition of the corresponding phenolates to 10-methylacridinium iodide. Phenolates were prepared from phenols (3,74 mmol) and sodium (85.98 mg, 3,74 mmol) in 20 mL of anhydrous ether. An ether solution of the corresponding phenolate was transferred to a flask, containing a stirred suspension of 10-methylacridinium iodide (1.0 g, 3.12 mmol) in 20 mL of anhydrous ether. The stirring was continued until the red, ether - insoluble acridinium iodide was entirely consumed. The solvent was removed by evaporation under reduced pressure to give a pale yellow solid, which was recrystallized from ethanol.

Synthesis of 2c, 2d. These compounds were synthesized according to the published procedures.[15]

Synthesis of 2e, 2f. To a solution of 10-methyl-9-(4-aminophenyl)-9,10-dihydroacridine **2c** (286 mg, 1mmol) in 5 mL acetonitrile 1,05 mmol the corresponding anhydride was added. After 10 minutes solvent was distilled off under a reduced pressure, and the residue was recrystallized from ethanol.

General procedure for the microwave-assisted palladium catalyzed cross-coupling reactions for synthesis 6o-q. 9-Chloroacridine **4** (100 mg, 0.47 mmol), the corresponding phenylboronic acid (**5o-q**) (0.564 mmol), $Pd(PPh_3)_4$ (27 mg, 0.023 mmol) and K_2CO_3 (162 mg, 1.17 mmol) were dissolved in 4 mL dioxane and 1 mL water. The resulting mixture was deaerated by bubbling argon and irradiated in a microwave apparatus at 165 °C (250 W) for 15 min. After that solvent was distilled off under a reduced pressure, and the residue was washed with 30 mL methylene chloride. The organic solvent was distilled off under reduced pressure, the residue was recrystallized from ethanol.

Synthesis of 2o-q. To a solution of compound **6o** or **6p** (1 mmol) in 10 mL of diethyl ether 0.3 mL of methyl iodide was added. After 24 hours the precipitate was filtered and dissolved in 10 mL of hot ethanol. To the stirred solution was added 37.83 mg (1 mmol) $NaBH_4$. The solid was filtered off after cooling. Nitrophenyl acridine **6q** (1 mmol) was suspended in 3 mL of dimethyl sulfate and heated for 6 hours, after that it was cooled and poured into 30 mL of ether. The solid was filtered, dissolved in 10 mL of hot ethanol and treated with $NaBH_4$.

Synthesis of 2n. To a Schlenk flask with 0.27 mL (3.75 mmol) furan 10 mL of ether were added. The solution was cooled down to -78°C for 15 min and hexane solution of n-butyl lithium (1.6M, 2.34 mL, 3.75 mmol) were added. The solution was allowed to warm up to 0°C for 30 min, resulting in the formation of the furyllithium. The ether solution of lithium intermediate was transferred to flask containing a stirred suspension of 10-methylacridinium iodide (1.0 g, 3.12 mmol) in 20 mL of anhydrous ether. The stirring was continued until the red, ether - insoluble acridinium iodide was entirely consumed. 5 ML of methanol was added to destroy unreacted lithium reagent, and the solvent was removed by evaporation under reduced pressure, to give a pale yellow solid, which was recrystallized from ethanol.

General Procedure for the electrochemical oxidation of 6^H-adducts 2a-q. Electrolysis was carried out in a stream of argon using a 0.1 M NH_4BF_4 solution in a CH_3CN–CH_3OH (5:1) mixture as the supporting electrolyte, in a temperature-controlled (20 °C). The supporting electrolyte (50 mL) containing 2 mmol 6^H-adduct **2a-q** of was placed in the anode cell compartment and the supporting electrolyte (10 mL) was placed in the cathode compartment. Electrolysis was carried out at a controlled potential (reference electrode $Ag/AgNO_3$). Upon passing 2.1F of electricity (for a two-electron process), the electrolysis was stopped, the solvent was distilled off in vacuum from the anolyte, the residue was washed with ether. The residue was recrystallized from water and dried on air.

Conclusions

A convenient, simple and highly selective method for electrochemical conversion of dihydroacridines into the corresponding 9-arylacridines has been advanced. This method is based on using the electric energy, requires no external oxidant, provides high yields of the target products and corresponds to the principles of green chemistry.[23]

Experimental and calculation data concerning anodic dehydroaromatization of a variety of 9,10-dihydroacridines, bearing aryl and hetaryl fragments with electron-donating or electron-withdrawing substituents have been obtained. It has been demonstrated that introduction of electron-donating substituents results in a substantial decrease of oxidation potentials, while electron-withdrawing groups have a minimal effect.

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Notes and references

1 a) A. J. Perkowski, D. A. Nicewicz, *J. Am. Chem. Soc.*, 2013, **135**, 10334-10337; b) A. Raskosova, R. Stober, W. Abraham, *Chem. Commun.*, 2013, **49**, 3964-3966; c) H. Kotani, K. Ohkubo, M. J. Crossley, S. Fukuzumi, *J. Am. Chem. Soc.*, 2011, **133**, 11092-11095; d) H. Sakai, K. Konno, H. Murata, *Appl. Phys. Lett.*, 2009, **94**, 073304.
2 Singh, H. Singh, S. Sharma, P. M. Singh Bedi, *Heterocycles,* 2015, **91**, 2043-2085.
3 a) O. Sedlacek, M. Hruby, M. Studenovsky, D. Vetvicka, J. Svoboda, D. Kankova, J. Kovar, K. Ulbrich, *Bioorg. Med. Chem.*, 2012, **20**, 4056-4063; b) N. Desbois, M. Gardette, J. Papon, P. Labarre, A. Maisonial, P. Auzeloux, C. Lartigue, B. Bouchon, E. Debiton, Y. Blache, O. Chavignon, J.-C. Teulade, J. Maublant, J.-C. Madelmont, N. Moins, J.-M. Chezal, *Bioorg. Med. Chem.*, 2008, **16**, 7671-7690; c) M. Tonelli, G. Vettoretti, B. Tasso, F. Novelli, V. Boido, F. Sparatore, B. Busonera, A. Ouhtit, P. Farci, S. Blois, G. Giliberti, P. La Colla, *Antiviral Research*, 2011, **91**, 133-141; d) A. Kumar, K. Srivastava, S. R. Kumar, S. K. Puri, P. M. S. Chauhan, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 6996-6999; e) T. Nguyen, Y. Sakasegawa, K. Dohura, Mei-Lin Go, *Eur. J. Med. Chem.*, 2011, **46**, 2917-2929; f) S. M. Sondhi, N. Singh, A. M. Lahoti, K. Bajaj, A. Kumar, O. Lozach, L. Meijer, *Bioorg. Med. Chem.*, 2005, **13**, 4291-4299.
4 a) S. Fukuzumi, K. Ohkubo, T. Suenobu, K. Kato, M. Fujitsuka, O. Ito, *J. Am. Chem. Soc.,* 2001, **123**, 8459-8467; b) Xiao-Qing Zhu, Fei-Huang Deng, Jin-Dong Yang, Xiu-Tao Li, Qiang Chen, Nan-Ping Lei, Fan-Kun Meng, Xiao-Peng Zhao, Su-Hui Han, Er-Jun Hao, Yuan-Yuan Mu, *Org. Biomol. Chem.*, 2013, **11**, 6071-6089; c) In-Sook Han Lee, Hyun Joo Kil, Young Ran Ji, *J. Phys. Org. Chem.*, 2007, **20**, 484-490.
5 a) P. Audebert, P. Hapiot, *J. Electroanal. Chem*., 1993, **361**, 177-183; b) A. Bernthsen, *Ann*.,1884, **224**, 1-56.
6 Z. Liu, N. Dong, M.Xu, Z. Sun, T. Tu, *J. Org. Chem.*, 2013, **78**, 7436-7444.
7 I. Hyodo, M. Tobisu, N. Chatani. Chem. Commun., 2012, 48, 308- 310.
8 G. Dyker, ed., *Handbook of C-H transformations: Applications in organic synthesis,* Wiley–VCH: Weinheim, Germany, 2005.
9 a) O. N. Chupakhin, V. N. Charushin, *Tetrahedron Lett*., 2016, **57**, 2665-2672; b) M, Makosza, K. Wojciechowski, *Chem. Rev*., 2004, **104**, 2631-2666; c) F. Terrier, *Modern Nucleophilic Aromatic Substitution*, Wiley-VCH, Weinheim, 2013, 488 p.
10 M. Mąkosza, *Chem. Soc. Rev.*, 2010, **39**, 2855-2868.
11 a) A. V. Shchepochkin, O. N. Chupakhin, V. N. Charushin, V. A. Petrosyan, *Russ. Chem. Rev.*, 2013, **82** (8), 747-771; b) V. A. Petrosyan, *Mendeleev Commun.*, 2011, **21**, 115-121.
12 J.-i. Yoshida, K. Kataoka, R. Horcajada, A. Nagaki, *Chem. Rev.*, 2008, **108**, 2265-2299.
13 I. Gallardo, G. Guirado, *Metal Free C-H Functionalization of Aromatics. Nucleophilic Displacement of Hydrogen*, ed. V. N. Charushin, O. N. Chupakhin, in *Topics in Heterocyclic Chemistry*, vol. 37, ed. B .U. W. Maes, J. Cossy, S. Poland, Springer, 2014, 241-276.
14 a) B. Turovska, J. Stradins, I. Turovskis, A. Plotniece, A. Shmidlers, G. Duburs, *Chem. Heterocycl. Comp.*, 2004, **40**, 753-758; b) D. L. Comins, M. 0. Killpack, *Heterocycles*, 1990, **31**, 2025-2028.
15 V. N. Charushin, O. N. Chupakhin, E. O. Sidorov, Yu. I. Beilis, I. A. Terent´eva, *Zh. Org. Khim.*, 1978, **14**, 140-146 (in English Russ. *J. Org. Chem.*).
16 R. T. C. Brownlee, R. E. J. Hutchinson, A. R. Katritzky, T. T. Tidwell, R. D. Topsom, *J. Am. Chem. Soc.*, 1968, **90**, 1757-1767.
17 O. N. Chupakhin, V. L. Rusinov, *Chem. Heterocycl. Compd.*, 1976, **12**, 1015-1019.
18 SHELXTL, G.M. Sheldrick, *Acta Cryst.*, 2008, **A64**, 112-122.
19 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339-341.
20 L. Palatinus, G. Chapuis, *J. Appl. Cryst.*, 2007, **40**, 786-790.
21 a) S. Fukuzumi, Y. Tokuda, T. Kitano, T. Okamoto, J. Otera, *J. Am. Chem. Soc.*, 1993, **115**, 8960-8968; b) X. Yang, J. Walpita, D. Zhou, H. L. Luk, S. Vyas, R. S. Khnayzer, S. C. Tiwari, K. Diri, C. M. Hadad, F. N. Castellano, A. I. Krylov, K. D. Glusac, *J. Phys. Chem. B*, 2013, **117**, 15290–15296.
22 In-Sook Han Lee, Kim-Hung Chow, M. M. Kreevoy, *J. Am. Chem. Soc.*, 2002, **124**, 7755–7761.
23 D. J. C. Constable, P. J. Dunn, J. D. Hayler, G. R. Humphrey, J. L. Leazer, Jr., R. J. Linderman, K. Lorenz, J. Manley, B. A. Pearlman, A. Wells, A. Zaks and T. Y. Zhang, *Green Chem.*, 2007, **9**, 411-420.

A simple and efficient electrochemical method for the oxidative conversion of dihydroacridines into the corresponding 9-(hetero)aryl-N-methylacridinium salts has been developed. Current-voltage characteristic of dihydroacridines are given.

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