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Synthesis and properties of imidazo[1,2-*a*]pyridinium-3-olate. Some revised structures

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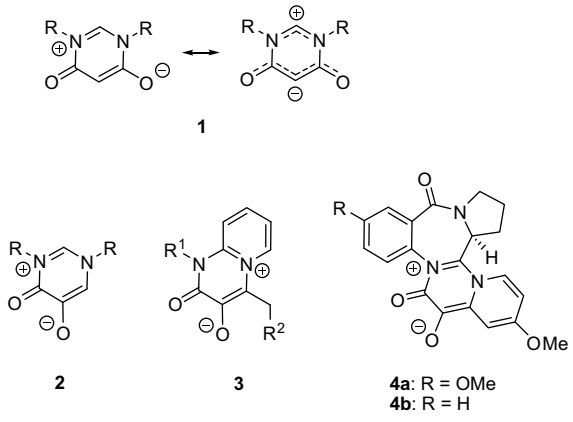
ABSTRACT

Reaction of 2-anilinopyridine with chloroacetyl chloride in the presence of *N*,*N*-dimethylacetamide resulted in the formation of the mesoion imidazo[1,2-*a*]pyridinium-3-olate instead of the reported 4-oxopyrimidinium-5-olate. We performed some functionalizations and present two single crystal X-ray analyses.

1. Introduction

Heterocyclic mesomeric betaines[1] are not only interesting starting materials for heterocyclic as well as natural product synthesis,[2] but also form a class of natural products by themselves.[3] More than thirty different structural types of mesomeric betaines were isolated from natural sources, among them conjugated, cross-conjugated as well as pseudo-cross-conjugated heterocyclic mesomeric betaines.[3] 4-Oxopyrimidinium-6-olate **1**[4] belongs to the class of cross-conjugated heterocyclic mesomeric betaines (CCMB). As evidenced by a single crystal X-ray analysis, the central pyrimidine ring of its tetraphenyl derivative is planar with C_s symmetry.[5] The charges are delocalized in separated parts of the common π-electron system, as the bonds N1–C6 and N3–C4 are essentially single bonds which are not involved in delocalisation.[1,5] Interest has been focussed on this molecule from the viewpoints of structural and synthetic organic chemistry[6] as well as of materials chemistry. This betaine has been used as partial structure of photosensitive films[7] and polymers.[8] Very recently, *N*-heterocyclic carbenes of this mesomeric betaine have been described (Scheme 1).[9]

The isomer of 4-oxopyrimidinium-6-olate **1**, the 4-oxopyrimidinium-5-olate **2**, has been described as pyrido[1,2-*a*]pyrimidinium-3-olates **3** in the literature.[10] In addition, it has been proposed as unusual partial structure of the alkaloids Circumdatin A and B (**4a** and **4b**, resp.) which were isolated from the fungus *Aspergillus ochraceus*.[11]



Scheme 1. Pyrimidiniumolates **1**–**3** and the Circumdatins A **4a** and B **4b**.

In continuation of our interest in heterocyclic mesomeric betaines,[12] *N*-heterocyclic carbenes,[13] and molecules which are related to the proposed structures **4** and **5**,[14] we reinvestigated the chemistry of the literature-known betaines **3** and found that these structures must be revised.

2. Results and discussion

Reaction of 2-anilinopyridine **5** with chloroacetyl chloride in the presence of *N*,*N*-dimethylacetamide at 50 °C yielded the title compound **6** instead of the previously reported[10] pyrido[1,2-*a*]-pyrimidinium-3-olate **3** (Scheme 2).

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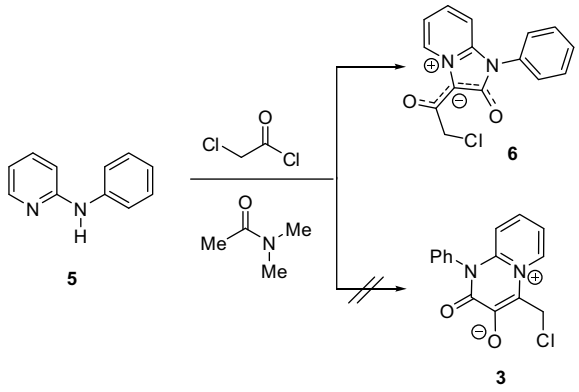


Scheme 2. Reaction of 2-anilinopyridine with chloroacetyl chloride.

The spectroscopic data such as ^{1}H NMR spectra we measured are identical to those reported. In addition, we performed HMBC, HSQC, HH-COSY and ^{15}N HMBC measurements. In accordance with structure **6** and in disagreement to structure **3** a strong coupling between the methylene group and one of the keto functionalities was observed by HMBC-NMR measurements, and only a weak coupling between this CH_2-group and the enolate carbon atom. The nitrogen atoms appear at δ=−184.5 and −218.9 ppm in ^{15}N NMR spectroscopy. The structure **6** was also confirmed by an X-ray single crystal analysis, the result of which is shown in Figure 1. Single crystals were obtained by slow evaporation of **6** in ethanol.

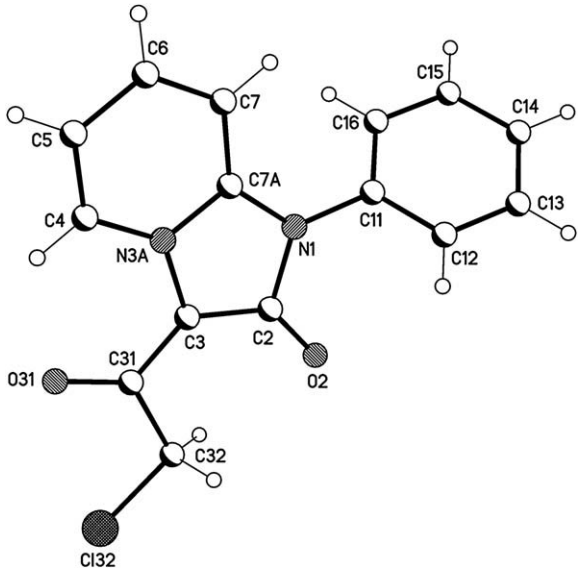


Figure 1. Molecular drawing of mesoion **6**.

The phenyl substituent is twisted out of the plane of the pyridinium ring. Thus, the dihedral angles of C7A–N1–C11–C16 (crystallographic numberings) and C2–N1–C11–C12 are −53.4(6)° and −50.7(6)°, respectively. In addition, neither the propenone-3-olate partial structure delocalizing the negative charge nor the imidazopyridinium ring system are planar: As examples, dihedral angles of −6.1(8)° [O2–C2–C3–C31] and 9.1(6)° [C31–C3–N3A–C4] were determined. The bond distances of C2–C3 and C3–C31 are 141.4(6) pm and 142.4(6) pm, respectively, and possess values between single and double bonds [148 pm and 132 pm, respectively]. The bond distances of C2–O2 and C31–O31 are almost identical [123.5(5) pm and 122.5(5) pm, respectively] and correspond to values between C–O single- and C=O double-bonds. In accordance with the delocalized negative charge no C=O absorption at 1700 cm^{-1} was detectable by IR spectroscopy. In NMR spectroscopy, these two CO groups differ considerably, as they are detectable at δ=179 ppm and 158.3 ppm, respectively.

The first synthesis of this compound was reported as early as 1971.[15] Some imidazolium-4-olates annelated to other rings such as Besthorn's red[16] are of historical interest, other ring annelations such as imidazolo[2,3-*b*]thiazinylium-2-olates,[17] imidazo[1,2-*c*]pyrimidin-3-olate,[18] imidazo[1,2-*a*]pyridinium-2-olate,[19] 5,6-dihydrobenzo[*h*]-imidazo[1,2-*c*]quinazolinium-1-olate[20] or substitution patterns[21] have also been prepared. Pharmacological interest has been focussed on 5-aryloxyimidazoles which were synthesized as potential inhibitor of HIV reverse transcriptase.[22]

The mesomeric betaine **6** belongs to the class of mesoions, i.e. to the conjugated heterocyclic mesomeric betaines. Characteristic for that class of compounds are common atoms for the positive as well as the negative charge in the resonance structures (Fig. 2). Mesoion **6** is isoconjugated with the even, non-alternant hydrocarbon dianion depicted in Figure 2, so that this betaine belongs to class no. 4 according to the comprehensive classification system proposed by Ollis, Stanforth, and Ramsden in 1985.[1] Nevertheless, the X-ray data show that the negative charge is not delocalized in the entire π-conjugated system, but that it is separated from the cationic partial structure by single bonds. Thus, the bond lengths C3–N3A and N1–C7A (crystallographic numbering, cf. Fig. 1) were determined to be 142.4(5) pm and 137.1(5) pm, respectively.

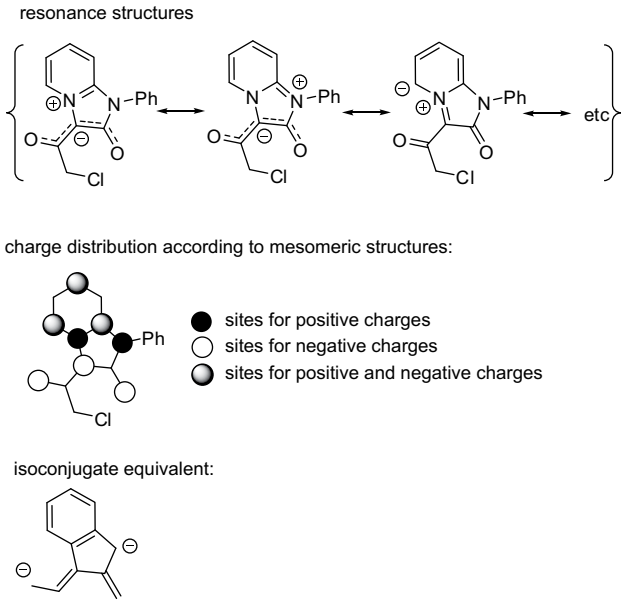
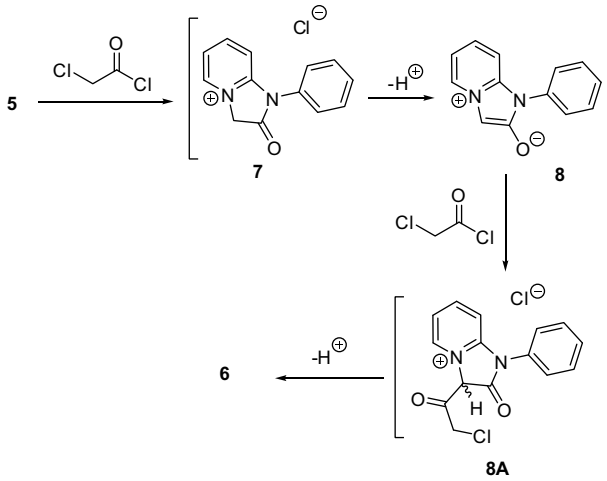


Figure 2. Classification of mesoion **6**.

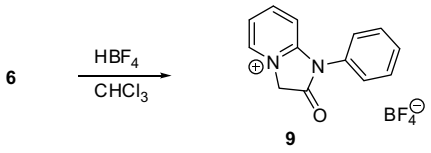
The formation of **6** obviously proceeds by reaction of chloroacetyl chloride with the bisnucleophile **5** via pyridinium salt **7** and mesoion **8** which is formed on deprotonation of **7** under the reaction conditions. The resulting mesoion **8** then attacks a second molecule of chloroacetyl chloride to give **6** via cation **8A** (Scheme 3).

In a reverse process, the mesomeric betaine **6** forms the stable salt **9** in quantitative yields on treatment with aqueous HBF_4 in chloroform (Scheme 4). In accordance to this structure, the resonance frequencies of the CH_2-group are shifted from 45.2 ppm to 54.7 ppm in the ^{13}C-spectra and from 4.80 ppm to 5.48 ppm in the ^{1}H-spectra. In the IR spectra a sharp carbonyl absorption band at 1775 cm^{-1} was detected. Triethylamine caused decomposition of this salt.

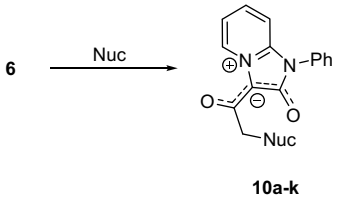
The chlorine atom of **6** is susceptible to a variety of nucleophilic substitutions. Thus, **10a–k** were prepared (Scheme 5, Table 1). Reactions of **6** with amines were realised without any base or catalyst. Conversions of **6** with alcohols needed sodium alcoholate or



Scheme 3. Proposed mechanism for the formation of **6**.



Scheme 4. Formation of salt **9**.



Scheme 5. Nucleophilic substitutions.

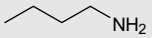
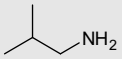
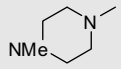
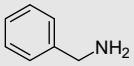
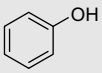
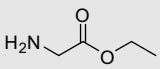
potassium carbonate as bases. The *N*-methylpiperazine derivative has been described[10a] as a derivative of 4-oxopyrimidinium-5-olate **3** so that its structure has also to be revised to**10c**. Compound **10j** is a pyridinium salt with chloride as anion.

The structure **10h** was confirmed by an X-ray single crystal analysis. Single crystals were obtained by slow evaporation of **10h** in methanol (Fig. 3). One of the two independent crystallographic molecules is shown. The minor component of the disordered allyloxy-group is omitted for clarity, and data for the second molecule are given in brackets.

The dihedral angles of C2–N1–C11–C16 (crystallographic numbering) and C7A–N1–C11–C12 are −48.7(4)° and −51.3(4)° [−50.6(4)° and −51.5(4)°], respectively. Moreover, torsion angles of 4.7(5)° [5.8(4)°] [O2–C2–C3–C31] and −3.0(4)° [−4.2(6)°] [C31–C3–N3A–C4] were determined. In analogy to **6** the allylic derivate **10h** has a delocalized negative charge.

In summary, reaction of 2-anilinopyridine with chloroacetyl chloride in the presence of *N*,*N*-dimethylacetamide gives imidazo[1,2-*a*]pyridinium-3-olate instead of 4-oxopyrimidinium-5-olate. We report functionalizations by nucleophilic substitution reactions and present two single crystal X-ray analyses.

Table 1
Substituted mesoions **10a–k**

Entry	Nucleophile	Product	Yield[a] (%)
1		**10a**	53
2		**10b**	51
3		**10c**	97
4		**10d**	62
5		**10e**	21
6		**10f**	79
7	H_3C-OH	**10g**	90
8		**10h**	92
9		**10i**	32
10		**10j**	20
11		**10k**	50

[a] Yields refer to those of pure isolated products.

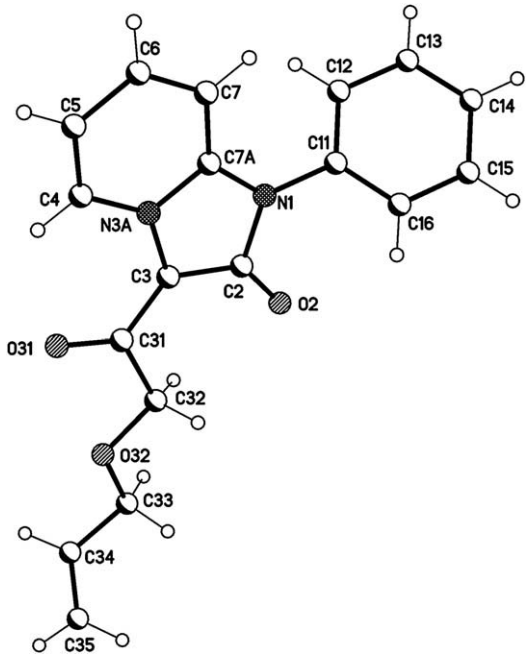


Figure 3. Molecular drawing of mesoion **10h**.

3. Experimental

3.1. General

The ^1H and ^{13}C NMR spectra were recorded on Bruker ARX-400 and DPX-200 spectrometers and were taken in $CDCl_3$ and DMSO-d_6 at 200 and 400 MHz at 20 °C. The chemical shifts are reported in ppm relative to internal tetramethylsilane (δ=0.00). Multiplicities are described by using the following abbreviations: s=singlet, d=doublet, t=triplet, q=quadruplet, h=heptet, m=multiplet, br=broad. The

mass spectra (EIMS) were measured with a Hewlett-Packard HP 5989B or a Varian SAT2100T with GC3900. Melting points are uncorrected. The CHN analyses were performed in the Institute of Technical Chemistry of the Clausthal University of Technology.

3.2. X-ray crystal structure analyses of 6 and 10h

6: colorless crystals, $C_{15}H_{11}ClN_2O_2$, M=286.71, crystal size 0.40×0.20×0.05 mm, monoclinic, space group $P2_1/c$ (no. 14): a=3.896(1) Å, b=22.380(3) Å, c=14.444(1) Å, β=97.73(1)°, V=1247.9(4) Å^3, Z=4, ρ(calcd)=1.526 Mg m^{-3}, F(000)=592, μ=0.308 mm^{-1}, 9231 reflections ($2\theta_{max}$=50°) measured on a Bruker-Nonius Kappa-CCD diffractometer at 123(2) K using MoKα radiation (λ=0.71073 Å), 2203 unique [R_{int}=0.1049] used for structure solution (Direct Methods, SHELXS-97[23]) and refinement (full-matrix least-squares on F^2, SHELXL-97[23]) with 181 parameters, H-atoms with a riding model, $R1$ ($I>2\sigma(I)$)=0.0704, $wR2$ *(all data)*=0.1725, largest diff. peak and hole 0.449 and −0.413 e Å^{-3}.

10h: colorless crystals, $C_{18}H_{16}N_2O_2\cdot 0.25$ MeOH, M=316.34, crystal size 0.50×0.25×0.15 mm, triclinic, space group P-1 (no. 2): a=10.036(1) Å, b=12.566(3) Å, c=12.680(1) Å, α=89.79(1)°, β=85.74(1)°, γ=72.30(1)°, V=1518.9(2) Å^3, Z=4, ρ(calcd)=1.383 Mg m^{-3}, F(000)=666, μ=0.096 mm^{-1}, 15,602 reflections ($2\theta_{max}$=55°) measured on a Bruker-Nonius Kappa-CCD diffractometer at 123(2) K using MoKα radiation (λ=0.71073 Å), 6815 unique [R_{int}=0.0265] used for structure solution (Direct Methods, SHELXS-97[23]) and refinement (full-matrix least-squares on F^2, SHELXL-97[23]) with 424 parameters and 56 restraint, H-atoms with a riding model, $R1$ ($I>2\sigma(I)$)=0.0669, $wR2$ *(all data)*=0.1539, largest diff. peak and hole 0.658 and −0.611 e Å^{-3}. The allyloxy groups are disordered.

Crystallographic data (excluding structure factors) for the structures reported in this work have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-729165 (**6**) and CCDC-729166 (**10h**). Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge DB2 1EZ, UK (Fax: +1223 336–033; e-mail:deposit@ccdc.cam.ac.uk).

3.3. 3-(2-Chloroacetyl)-1-phenyl-1*H*-imidazo[1,2-*a*]-pyridinium-2-olate 6

A sample of 0.851 g (5 mmol) of 2-anilinopyridine was suspended in 5 mL of anhyd benzene. After addition of 1.07 mL (1.0 g, 11.5 mmol) of *N*,*N*-dimethylacetamide, 0.92 mL (1.3 g, 11.5 mmol) of 2-chloroacetyl chloride was added dropwise over a period of 10 min. The reaction mixture was heated at 50 °C for 1 h. After evaporation of the solvent in vacuo the residue was dissolved in chloroform and washed two times with water and dried over Na_2SO_4. Evaporation of the solvent in vacuo gave a solid which was purified by recrystallisation from ethanol.

Yield: 0.714 g (2.5 mmol, 50%); mp: 192–193 °C (lit[10a]: 193.5–195.5 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.84 (s, 2H, CH_2Cl), 7.15 (dt, J=8.61, 1.08 Hz, 1H, 8-H), 7.23–7.27 (m, 1H, 6-H), 7.44–7.46 (m, 2H, 2′-H), 7.50–7.54 (m, 1H, 4′-H), 7.56–7.61 (m, 3H, 3′-H, 7-H), 10.13 (dt, J=6.65, 0.93 Hz, 1H, 5-H). ^{13}C NMR (100 MHz, $CDCl_3$: δ=46.5 (CH_2Cl), 102.1 (C-3), 106.9 (C-8), 116.9 (C-6), 127.0 (2C, C-2′), 129.5 (C-4′), 130.0 (3C, C-3′, C-5), 131.5 (C-1′), 133.1 (C-7), 137.2 (C-9), 158.3 (C-2), 179 (C=O). ^{15}N NMR (40 MHz, $CDCl_3$): δ=−184.5 (N-5), −218.9 (N-1). MS: m/z (%)=286 (70)[M$^+$], 237 (100), 208 (5), 181 (15), 168 (5), 119 (5), 77 (60). IR (KBr)=3084, 1678, 1633, 1509, 1440, 1385, 1303, 1269, 1240, 1204, 1121, 1076, 772, 703 cm^{-1}. HR-ESI-MS calcd for $C_{15}H_{11}N_2O_2Cl$: 286.0509; found: 286.0509. Anal. Calcd for $C_{15}H_{11}N_2O_2Cl$: C, 62.84; H, 3.87; N, 9.77. Found: C, 62.69; H, 3.33; N, 9.40.

3.4. 2-Oxo-1-phenyl-2,3-dihydro-1*H*-imidazo[1,2-*a*]-pyridinium (9)

A sample of 0.143 g (0.5 mmol) of the betaine **6** was dissolved in 2 mL of chloroform and then treated with tetrafluoroboric acid (40%, 0.5 mL). After the mixture had been stirred for 30 min at room temperature the solvents were evaporated to leave a reddish solid which was recrystallized from ethanol.

Yield: quantitative; ^{1}H NMR (400 MHz, MeOD): δ=5.45 (s, 2H, C-3), 7.33 (d, J=8.8 Hz, 1H, 8-H), 7.49 (m, 2H, 2′-H), 7.58–7.69 (m, 4H, 3′-H, 4′H, 6-H), 8.38 (t, J=8.2 Hz, 1H, 7-H), 8.83 (d, J=6 Hz, 1H, 5-H). ^{13}C NMR (100 MHz, MeOD): δ=55.1 (C-3), 110.5 (C-8), 120.2 (C-6), 127.6 (2C, C-2′), 130.6 (C-1′), 139.8 (3C, C-3′, C-4′), 139.9 (C-5), 148.0 (C-7), 153.5 (C-9), 167.8 (C-2). IR (KBr): $\tilde{\nu}$ = 3332, 1772, 1646, 1586, 1514, 1397, 1339, 1310, 1225, 1065, 1025, 766 cm^{-1} ESI-MS: m/z (%)=211.1 (100), 509 (35).

3.5. General procedure for the nucleophilic substitutions on imidazo[1,2-*a*]pyridinium-3-olate 6 to 10a–k

3.5.1. Amine derivates

Samples of 0.143 g (0.5 mmol) of betaine **6** and 1.5 mmol of the corresponding amine were dissolved in 5 mL of chloroform. The reaction mixture was then heated for 1 h at 50 °C. Evaporation of the solvent in vacuo gave a solid residue which was purified by flash column chromatography [silica gel, ethyl acetate] yielding the products **10a–d**.

*3.5.2. 3-(2-(Butylamino)acetyl)-1-phenyl-1H-imidazo[1,2-a]-pyridinium-2-olate (**10a**)*

n-Butylamine was used; yield: 0.09 g (53 %), mp: 120–123 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.91 (t, J=7.2 Hz, 3H, 7*-H), 1.23–1.43 (m, 2H, 6*-H), 1.48–1.63 (m, 2H, 5*-H), 2.56 (br s, 1H, N*H*), 2.69 (t, J=7.0 Hz, 2H, 4*-H), 4.11 (s, 2H, 2*), 7.08–7.32 (m, 2H, $H_{arom.}$), 7.46–7.65 (m, 6H, $H_{arom.}$), 10.18 (d, J=8.2 Hz, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=14.0 (C-7*), 20.4 (C-6*), 32.4 (C-5*), 49.5 (C-4*), 55.9 (C-2*), 102.4 (C-3), 106.7 (C-8), 116.6 (C-6), 127.1 (2C, C-2′), 129.3 (C-4′), 129.7 (C-5), 129.9 (2C, C-3′), 131.8 (C-1′), 132.1 (C-7), 136.6 (C-9), 158.3 (C-2), 186.8 (C=O). IR (KBr): $\tilde{\nu}$ = 3420, 2042, 2926, 2868, 1658, 1610, 1510, 1441, 1308, 1241, 1206, 1116, 1079, 1049, 921, 771, 711 cm^{-1}. MS: 324 [M+H$^+$](100), 252 (90), 237 (20), 210 (75), 181 (20), 77 (45). HR-ESI-MS calcd for $C_{19}H_{22}N_3O_2$: 324.1712; found: 324.1711. Anal. cCalcd for $C_{19}H_{21}N_3O_2\cdot 2H_2O$: C, 63.7; H, 7.0; N, 11.7. Found: C, 64.2; H, 5.7; N, 11.4.

*3.5.3. 3-(2-(Isobutylamino)acetyl)-1-phenyl-1H-imidazo[1,2-a]-pyridinium-2-olate (**10b**)*

iso-Butylamine was used; yield: 0.083 g (0.256 mmol, 51%) mp: 142–145 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.95 (d, J=6.6 Hz, 6H, CH_3), 0.96 (s, 3H, CH_3), 1.69–1.92 (m, 1H, CH), 2.09 (br s, 1H, NH), 2.51 (d, J=6.8 Hz, 2H, 4*-H), 4.11 (s, 2H, 1*-H), 7.05–7.25 (m, 2H, $H_{arom.}$), 7.43–7.65 (m, 6H, $H_{arom.}$), 10.20 (d, J=6.8 Hz, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=20.7 (2C, CH_3), 27.0 (CH), 56.2 (CH_2), 57.9 (CH_2), 102.4 (C-3), 106.7 (C-8), 116.5 (C-6), 127.1 (2C, C-2′), 129.3 (C-4′), 129.7 (C-5), 129.9 (2C, C-3′), 131.9 (C-1′), 132.0 (C-7), 136.5 (C-9), 158.3 (C-2), 187.0 (C=O). IR (KBr): $\tilde{\nu}$ = 3419, 3047, 2951, 1661, 1608, 1510, 1439, 1307, 1240, 1206, 1114, 1079, 1048, 770, 711 cm^{-1}. MS: 323 [M$^+$](20), 280 (10), 252 (90), 237 (40), 223 (70), 210 (100), 181 (20), 77 (90). HR-ESI-MS calcd for $C_{19}H_{22}N_3O_2$: 324.1712; found: 324.1711. Anal. cCalcd for $C_{19}H_{21}N_3O_2\cdot 2.5H_2O$: C, 61.94; H, 7.11; N, 11.40. Found: C, 61.71; H, 5.41; N, 11.03.

*3.5.4. 3-(2-(4-Methylpiperazin-1-yl)acetyl)-1-phenyl-1H-imidazo[1,2-a]pyridinium-2-olate (**10c**)*

1-Methylpiperazine was used; yield: 0.170 g (0.485 mmol, 97%) mp: 167 °C (dec); ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.30 (s, 3H, CH_3),

2.52 (br s, 4H, β-Pip-H), 2.76 (br s, 4H, α-Pip-H), 3.94 (s, 2H, CH_2), 7.12–7.30 (m, 2H, $H_{arom.}$), 7.45–7.66 (m, 6H, $H_{arom.}$), 10.23 (d, J=6.8 Hz, 1H, 5-H). ^{13}C NMR: (50 MHz, $CDCl_3$): δ=44.9 (CH_3), 52.6 (2C, α-Pip-C), 53.9 (2C, β-Pip-C), 62.5 (CH_2), 102.0 (C-3), 105.7 (C-8), 115.6 (C-6), 126.1 (2C, C-2′), 128.4 (C-4′), 129.0 (C-5), 129.0 (2C, C-3′), 130.9 (C-1′), 131.1 (C-7), 135.6 (C-9), 157.3 (C-2), 183.8 (C=O). IR (KBr): $\tilde{\nu}$ = 3423, 3111, 3039, 2963, 2927, 2791, 1678, 1613, 1510, 1449, 1344, 1262, 1204, 1101, 1016, 801, 768, 710 cm^{-1}. MS: 351 [M+H$^+$](60), 280 (20), 252 (90), 237 (30), 223 (40), 113 (50), 77 (35), 70 (100). HR-ESI-MS calcd for $C_{20}H_{23}N_4O_2$: 351.1821; found: 351.1821. Anal. cCalcd for $C_{20}H_{23}N_4O_2$: C, 65.20; H, 6.56; N, 15.20. Found: C, 64.84; H, 6.19; N, 15.17.

*3.5.5. 3-(2-(Benzylamino)acetyl)-1-phenyl-1H-imidazo[1,2-a]-pyridinium-2-olate (**10d**)*

Benzylamine was used; yield: 0.109 g (0.31 mmol, 62 %); mp: 148–150 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.61 (s, 1H, N*H*), 3.89 (s, 2H, CH_2), 4.15 (s, 2H, CH_2), 7.05–7.65 (m, 13H, $H_{arom.}$), 10.15–10.19 (m, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=53.7 (CH_2), 55.5 (CH_2), 102.4 (C-3), 106.7 (C-8), 116.6 (C-6), 126.8 (C-8*), 127.1 (2C, C-2′), 128.3 (4C, C-6*, C-7*), 129.4 (C-4′), 129.7 (C-5), 130.0 (2C, C-3′), 131.8 (C-1′), 132.1 (C-7), 136.6 (C-9), 140.3 (C-5*), 158.2 (C-2), 186.4 (C=O). IR (KBr): $\tilde{\nu}$ = 3334, 3054, 2926, 1667, 1606, 1511, 1439, 1239, 1206, 1057, 756, 710 cm^{-1}. MS: *m*/*z* (%)=358 [M+H$^+$](60), 266 (30), 252 (100), 237 (30), 210 (70), 181 (20), 91 (70), 77 (20). HR-ESI-MS calcd for $C_{22}H_{19}N_3O_2$: 358.1556; found: 358.1557. Anal. cCalcd for $C_{22}H_{19}N_3O_2 \cdot 1H_2O$: C, 70.38; H, 5.64; N, 11.12. Found: C, 70.61; H, 4.78; N, 11.02.

3.5.5.1. Aliphatic alcohol derivates. Portions of 0.056 g (2.4 mmol) of sodium were dissolved in 10 mL of the corresponding alcohols. Then, 0.143 g (0.5 mmol) of the betaine **6** was added and the reaction mixture was refluxed for 3 h. Evaporation of the solvent in vacuo gave solids which were purified by flash column chromatography [silica, ethyl acetate] to give the products **10e**–**g**.

*3.5.6. 3-(2-Isopropoxyacetyl)-1-phenyl-1H-imidazo[1,2-a]-pyridinium-2-olate (**10e**)*

iso-Propanol was used; yield: 0.032 g (0.103 mmol, 21%) mp: 126 °C (dec); ^{1}H NMR (200 MHz, $CDCl_3$): δ=1.27 (d, J=6.2 Hz, 6H, C*H*$_3$), 3.73–3.86 (m, 1H, C*H*), 4.82 (s, 2H, CH_2), 7.11–7.26 (m, 2H, $H_{arom.}$), 7.44–7.65 (m, 6H, $H_{arom.}$), 10.09 (d, J=4.6 Hz, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=22.0 (2C, CH_3), 71.0 (CH), 72.2 (CH_2), 101.9 (C-3), 106.7 (C-8), 116.7 (C-6), 127.0 (2C, C-2′), 129.3 (C-4′), 129.7 (C-5), 129.9 (2C, C-3′), 131.8 (C-1′), 132.0 (C-7), 136.7 (C-9), 158.1 (C-2), 185.2 (C=O). IR (KBr): $\tilde{\nu}$ = 3424, 3111, 3053, 2970, 2925, 1691, 1608, 1508, 1454, 1362, 1318, 1240, 1124, 763, 712 cm^{-1}. MS: 311 [M+H$^+$](50), 267 (40), 252 (100), 237 (100), 210 (20), 181 (30), 77 (60). HR-ESI-MS calcd for $C_{18}H_{19}N_2O_3$: 311.1396; found: 311.1396. Anal. cCalcd for $C_{18}H_{18}N_2O_3$ (310.35): C, 69.66; H, 5.85; N, 9.03. Found: C, 69.11; H, 5.43; N, 9.13.

*3.5.7. 3-(2-Ethoxyacetyl)-1-phenyl-1H-imidazo[1,2-a]-pyridinium-2-olate (**10f**)*

Ethanol was used; yield: 0.117 g (0.395 mmol, 79 %) mp: 178–179 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=1.32 (t, J=7.0 Hz, 3H, C*H*$_3$CH$_2$), 3.70 (q, J=7.0 Hz, 2H, CH$_3$C*H*$_2$), 4.81 (s, 2H, CH_2), 7.11–7.29 (m, 2H, $H_{arom.}$), 7.45–7.65 (m, 6H, $H_{arom.}$), 10.19 (d, J=6.6 Hz, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=15.2 (*C*H$_3$CH$_2$), 61.0 (CH$_3$*C*H$_2$), 73.3 (CH_2), 101.9 (C-3), 106.7 (C-8), 116.7 (C-6), 127.0 (2C, C-2′), 129.3 (C-4′), 129.7 (C-5), 130.0 (2C, C-3′), 131.8 (C-1′), 132.1 (C-7), 136.7 (C-9), 158.2 (C-2), 184.8 (C=O). IR (KBr): $\tilde{\nu}$ = 3110, 3061, 2970, 2865, 1685, 1631, 1506, 1457, 1424, 1340, 1319, 1240, 1204, 1121, 1049, 901, 768, 713 cm^{-1}. MS: 297 [M+H$^+$](100), 252 (60), 237 (65), 181 (20), 77 (25). HR-ESI-MS: calcd for $C_{17}H_{17}N_2O_3$: 297.1239; found: 297.1240. Anal. cCalcd for $C_{17}H_{16}N_2O_3$ (296.32): C, 68.91; H, 5.44; N, 9.45. Found: C, 68.41; H, 5.06; N, 9.47.

*3.5.8. 3-(2-Methoxyacetyl)-1-phenyl-1H-imidazo[1,2-a]-pyridinium-2-olate (**10g**)*

Methanol was used; yield: 0.127 g (0.45 mmol, 90 %); mp: 181 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.54 (s, 3H, CH_3), 4.76 (s, 2H, CH_2), 7.13–7.27 (m, 2H, $H_{arom.}$), 7.43–7.65 (m, 6H, $H_{arom.}$), 10.82 (d, J=6.4 Hz, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=59.4 (CH_3), 75.2 (CH_2), 101.8 (C-3), 106.8 (C-8), 116.7 (C-6), 127.0 (2C, C-2′), 129.4 (C-4′), 129.7 (C-5), 129.9 (2C, C-3′), 131.8 (C-1′), 132.2 (C-7), 136.8 (C-9), 158.2 (C-2), 184.4 (C=O). IR (KBr): $\tilde{\nu}$ = 3442, 3107, 3060, 2988, 2945, 2825, 1690, 1604, 1507, 1476, 1458, 1440, 1358, 1323, 1242, 1202, 1107, 1044, 997, 905, 770 cm^{-1}. MS: 283 [M+H$^+$](100), 267 (20), 252 (40), 237 (90), 181 (20), 77 (40). HR-ESI-MS calcd for $C_{16}H_{15}N_2O_3$: 283.1083; found: 283.1084. Anal. cCalcd for $C_{16}H_{14}N_2O_3$ (282.29): C, 68.07; H, 5.00; N, 9.92. Found: C, 67.74; H, 4.51; N, 10.02.

*3.5.9. 3-(2-Allyloxyacetyl)-1-phenyl-1H-imidazo[1,2-a]-pyridinium-2-olate (**10h**)*

Allylalcohol was used; yield: 0.141 g (0.46 mmol, 92 %); mp: 126–129 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.20 (dt, J=5.8, 1.2 Hz, 2H, 1*-H), 4.83 (s, 2H, CH_2), 5.17–5.40 (m, 2H, 3*-H), 5.92–6.12 (m, 1H, 2*-H), 7.12–7.28 (m, 2H, $H_{arom.}$), 7.41–7.64 (m, 6H, $H_{arom.}$), 10.16–10.20 (m, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=72.5 (C-1*), 72.6 (CH_2), 101.8 (C-3), 106.7 (C-8), 116.7 (C-6), 117.5 (C-3*), 127.0 (2C, C-2′), 129.3 (C-4′), 129.7 (C-5), 130.7 (2C, C-3′), 131.8 (C-1′), 132.1 (C-7), 134.6 (C-2*), 136.7 (C-9), 158.1 (C-2), 184.5 (C=O). IR (KBr): $\tilde{\nu}$ = 3424, 3057, 2859, 1688, 1507, 1456, 1337, 1239, 1204, 1118, 1046, 904, 767, 713 cm^{-1} MS: 309 [M+H$^+$](100), 252 (90), 237 (85), 223 (15), 210 (20), 181 (30), 77 (80). HR-ESI-MS: calcd for $C_{18}H_{16}N_2O_3Na$: 331.1059; found: 331.1068. Anal. cCalcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 69.61; H, 5.25; N, 8.79.

*3.5.10. 3-(2-Phenoxyacetyl)-1-phenyl-1H-imidazo[1,2-a]-pyridinium-2-olate (**10i**)*

A sample of 0.286 g (1 mmol) of the betaine **6** was dissolved in 15 mL of anhyd ethanol. After addition of 0.138 g (1 mmol) of K_2CO_3 and 0.094 g (1 mmol) of phenol the reaction mixture was refluxed for 4 h. Evaporation of the solvent in vacuo gave a solid residue which was purified by flash column chromatography [silica gel, ethyl acetate] to give product **10i**.

Yield: 0.111 g (0.32 mmol, 32 %); mp: 203 °C (dec); ^{1}H NMR (200 MHz, $CDCl_3$): δ=5.39 (s, 2H, CH_2), 6.90–7.09 (m, 3H, $H_{arom.}$), 7.14–7.35 (m, 4H, $H_{arom.}$), 7.46–7.67 (m, 6H, $H_{arom.}$), 10.16 (dt, J=6.6, 1.0 Hz, 1H, 6-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=70.0 (CH_2), 102.0 (C–C=O), 106.9 (C-3), 114.7 (2C, C-II), 116.8 (C-5), 120.8 (C-IV), 127.1 (2C, C-2′), 129.3 (2C, C-III), 129.5 (C-4′), 129.9 (C-6), 130.1 (2C, C-3′), 131.7 (C-1′), 132.5 (C-4), 137.1 (C-2), 158.6 (C-I), 163.1 (C–O$^-$), 182.3 (C=O). IR (KBr): $\tilde{\nu}$ = 3424, 2924, 1675, 1609, 1504, 1456, 1300, 1266, 1235, 1207, 1081, 1053, 1028, 901, 752 cm^{-1}. MS: 344 [M$^+$](90), 237 (100), 210 (80), 181 (40), 169 (20), 94 (15), 77 (90). HR-ESI-MS calcd for $C_{21}H_{16}N_2O_3Na$: 367.1059; found: 367.1063. Anal. cCalcd for $C_{21}H_{16}N_2O_3$ (344.2): C, 73.24; H, 4.68; N, 8.13. Found: C, 72.78; H, 4.26; N, 8.23.

*3.5.11. 1-Phenyl-3-2-(pyridinium)-1H-imidazo[1,2-a]pyridinium-2-olate chloride (**10j**)*

A sample of 0.2 mL (2.5 mmol) of pyridine was added to a solution of 0.143 g (0.5 mmol) of the betaine **6** and 5 mL of chloroform. The reaction mixture was then refluxed for 4 h. After cooling to room temperature the reaction mixture was extracted with 10 mL of water. Evaporation of the solvent in vacuo gave a reddish solid.

Yield: 0.037 g (0.1 mmol, 20 %); mp: 185 °C (dec); ^{1}H NMR (200 MHz, $CDCl_3$): δ=6.15 (s, 2H, CH_2), 7.24–7.43 (m, 2H, $H_{arom.}$), 7.50–7.73 (m, 5H, $H_{arom.}$), 7.82–7.93 (m, 1H, $H_{arom.}$), 8.10–8.18 (m, 2H, β-Py-H), 8.62–8.73 (m, 1H, γ-Py-H), 8.96–9.00 (m, 2H, α-Py-H), 9.74 (d, J=6.4 Hz, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=67.1 (CH_2), 103.0 (C-3), 109.2 (C-8), 118.9 (C-6), 128.7 (2C, C-2′), 128.8 (2C, β-Py-C),

131.0 (2C, C-4′, C-5), 131.3 (2C, C-3′), 133.0 (C-1′), 136.5 (C-7), 139.9 (C-9), 147.2 (γ-Py-C), 147.7 (2C, α-Py-C), 160–8 (C-2), 175.6 (C═O). IR (KBr): $\tilde{\nu}$ = 3405, 3048, 1670, 1602, 1505, 1446, 1201, 1084, 1045, 764, 708 cm^{-1}. MS: *m*/*z* (%)=330 [M^+](10), 288 (60), 237 (100), 181 (30), 77 (50). HR-ESI-MS calcd for $C_{20}H_{16}N_3O_2$: 330.1243; found: 330.1248. Anal. cCalcd for $C_{20}H_{16}N_3O_2Cl\cdot 3.5H_2O$: C, 56.01; H, 5.36; N, 9.80. Found: C, 56.14; H, 4.73; N, 9.86.

*3.5.12. 3-(2-(2-Ethoxy-2-oxoethylamino)acetyl)-1-phenyl-1H-imidazo-[1,2-a]pyridinium-2-olate (**10k**)*

A sample of 0.143 g (0.5 mmol) of the betaine **6**, 0.140 g (0.5 mmol) of glycine ethyl ester hydrochloride and 0.14 mL (0.101 g, 1 mmol) of triethylamine were suspended in 10 mL of acetonitrile and refluxed for 4 h. Evaporation of the solvent in vacuo gave a solid residue which was purified by flash column chromatography [silica gel, ethyl acetate] to give the product **10k**.

Yield: 0.088 g (0.25 mmol, 50%); mp: 114–116 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=1.27 (t, *J*=6.9 Hz, 3H, CH_2CH_3), 2.45 (s, 1H, N*H*), 3.55 (s, 2H, CH_2), 4.13–4.24 (m, 4H, CH_2CH_3, CH_2), 7.11–7.28 (m, 2H, $H_{arom.}$), 7.43–7.65 (m, 6H, $H_{arom.}$), 10.17 (d, *J*=6.4 Hz, 1H, 5-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=14.2 (CH_2CH_3), 50.7 (CH_2), 55.4 (CH_2), 60.7 (CH_2CH_3), 102.2 (C-3), 106.7 (C-8), 116.6 (C-6), 127.0 (2C, C-2′), 129.3 (C-4′), 129.7 (C-5), 129.9 (2C, C-3′), 131.8 (C-1′), 132.1 (C-7), 136.6 (C-9), 158.2 (C-2), 172.1 (C═O), 185.5 (C═O). IR (KBr): $\tilde{\nu}$ = 3327, 2978, 1729, 1679, 1599, 1505, 1448, 1241, 1204, 1031, 842, 761, 712 cm^{-1}. MS: *m*/*z* (%)=354 [M+H^+](100), 280 (20), 252 (50), 237 (20), 210 (90), 77 (30). HR-ESI-MS: calcd for: $C_{19}H_{20}N_3O_4$: 354.1454; found: 354.1454. Anal. Calcd for $C_{19}H_{19}N_3O_4$: C, 62.97; H, 5.56; N, 11.59. Found: C, 63.16; H, 5.38; N, 11.97.

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