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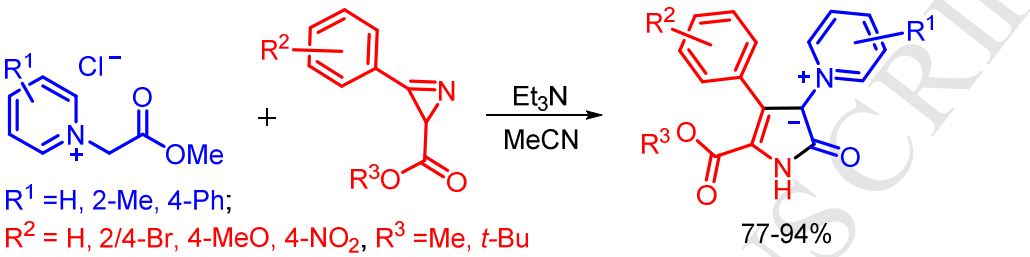
Synthesis and Properties of New Heterocyclic Betaines: 4-Aryl-5-(methoxycarbonyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ides

Liya D. Funt, Mikhail S. Novikov, Galina L. Starova, Alexander F. Khlebnikov*

Saint Petersburg State University, Institute of Chemistry, 7/9 Universitetskaya nab., St. Petersburg, 199034 Russia

Corresponding author. *E-mail address*: a.khlebnikov@spbu.ru (A.F. Khlebnikov).



R^1 =H, 2-Me, 4-Ph;
R^2 = H, 2/4-Br, 4-MeO, 4-NO$_2$, R^3 =Me, *t*-Bu

Abstract: New heterocyclic betaines, 4-aryl-5-(alkoxycarbonyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ides, were synthesized in good yields by the reaction of alkyl 2*H*-azirine-2-carboxylates with 2-methoxy-2-oxo-1-(pyridin-1-ium-1-yl)ethan-1-ides, generated from the corresponding pyridinium salts. The betaines exist as the NH-tautomers both in solution and in the solid state. Two molecules of the betaine form a dimer by hydrogen bonds of the type N-H···O in solid state. According to TD DFT calculations the long-wave absorption band in betaines mainly corresponds to the intramolecular charge transfer between the negatively charged pyrrole unit and the positively charged pyridinium group. The blue shift of the long-wave absorption in protic solvents was adequately described in terms of H-complex formation with the nucleophilic centre of the molecular skeleton.

Keywords: heterocyclic betaines, azirines, pyridinium ylides, solvatochromism

1. Introduction

Heterocyclic betaines, whose unique properties, mainly due to their dipolar character, are of interest for both fundamental and practical reasons.[1] They are applied as starting materials for heterocyclic synthesis and the development of new materials and drugs.[1] In particular properties of pyridinium *N*-phenolate betaine dyes, such as solvatochromism, thermochromism,

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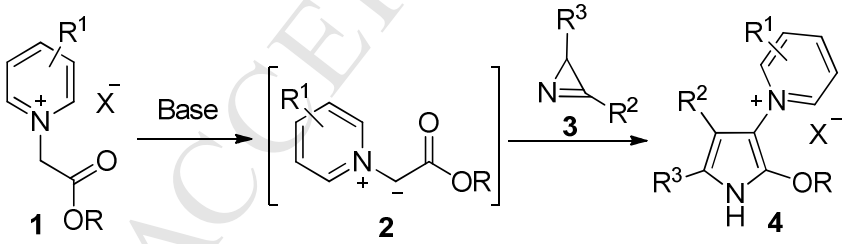
piezochromism, halochromism and perichromism are used to study the properties of solvents and solutions as well as their characterization.[2] One more important recently recognized aspect of betaine chemistry is the possibility of a tautomeric equilibrium with N-heterocyclic carbenes (NHC) and therefore some betaines can be used for the generation of NHC.[1d, 3] Although more than a century has passed since the discovery of the first heterocyclic betaine,[4] a great need still remains to find new types of these zwitterionic molecules. The diversity of betaine structures provides an opportunity to achieve practically useful properties, as well as gain a deeper insight into the relationship between the properties and structure of zwitterionic compounds, which is necessary for developing the principles for their purposeful design.

Pyridinium ylides are versatile building blocks in heterocyclic synthesis.[5] Earlier we discovered the reaction of 2*H*-azirines with *N*-phenacylpyridinium ylides, which gave 1-(1*H*-pyrrol-3-yl)pyridinium salts.[6] The reaction was successfully extended to *N*-phenacyl-imidazolium[3e,7] and *N*-phenacyl-1,2,4-triazolium ylides[3d,f] affording the corresponding pyrrolyl-imidazole/triazole dyads. With the intention of broadening the scope of applicability of the reaction, we decided to vary the type of a substituent in the pyridinium ylide by changing it from benzoyl to alkoxycarbonyl. This would provide a route for the preparation of hardly accessible derivatives of 2-alkoxypyrroles **4** by the route shown in Scheme 1.



Scheme 1. Probable route for the synthesis of 2-alkoxypyrroles **4**

2. Results and discussion

Preliminary experiments revealed, however, that ylide **2a** (R = Me, R^1 = H) does not react with 3-phenyl-2*H*-azirine at room temperature, and gives a complex mixture of unidentified products at higher temperatures. Similar ambiguous results were obtained when 2,3-diphenyl-

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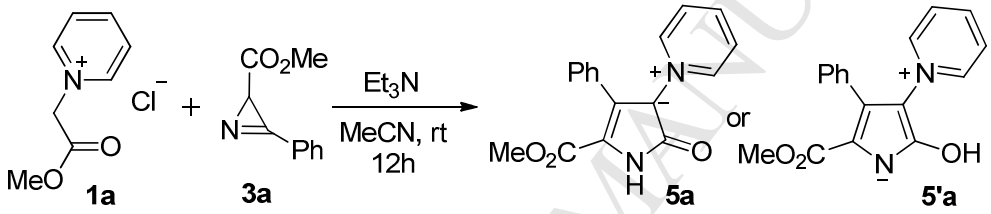
2*H*-azirine was used. We suggested that the presence of an electron-acceptor substituent in the azirine ring may improve the selectivity of the reaction because of increased electrophilicity toward nucleophile **2** and due to stabilization of the pyrrole ring. More electrophilic azirines were, therefore, tested. The reaction of 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1a** with methyl 3-phenyl-2*H*-azirine-2-carboxylate **3a** in the presence of triethylamine as a base (ca.1 equiv), leads, according to ^{1}H NMR and HRMS data, to the pyrrole-type product **5a** (NH-tautomer) or **5'a** (NH-tautomer) in 77% yield (Scheme 2). The use of a 2- or 3-fold excess of triethylamine does not affect the yield. The isolation of the precipitated product consists simply of filtering off and washing, making acetonitrile the solvent of choice due to the lower solubility of the product in this solvent.



Scheme 2. Reaction of azirine **3a** with pyridinium salt **1a**

An analysis of HSQC ^{1}H-^{15}N NMR spectra makes it possible to distinguish between tautomers **5a** and **5'a** (See the Supporting information). The pyrrole-type nitrogen, with chemical shift of 137.7 ppm, has an intensive cross-peak with the proton at 9.67 ppm. Consequently this proton is connected to the pyrrole-type nitrogen. According to the DFT calculations at the B3LYP/6-31G+(d,p) level with the PCM model for DMSO at 298 K, the tautomer **5a** in solution in DMSO is much more stable than tautomer **5'a** (by 12.2 kcal/mol). Thus, the reaction of 2-methoxy-2-oxo-1-(pyridin-1-ium-1-yl)ethan-1-ide **2a** with methyl 3-phenyl-2*H*-azirine-2-carboxylate **3a** provides an access to the new type of betaines **5**. To obtain more information about the structure of the zwitterionic molecule **5a** a single crystal was grown from $CDCl_3$ by slow evaporation of the solvent and studied by single crystal X-ray analysis (Figure 1).

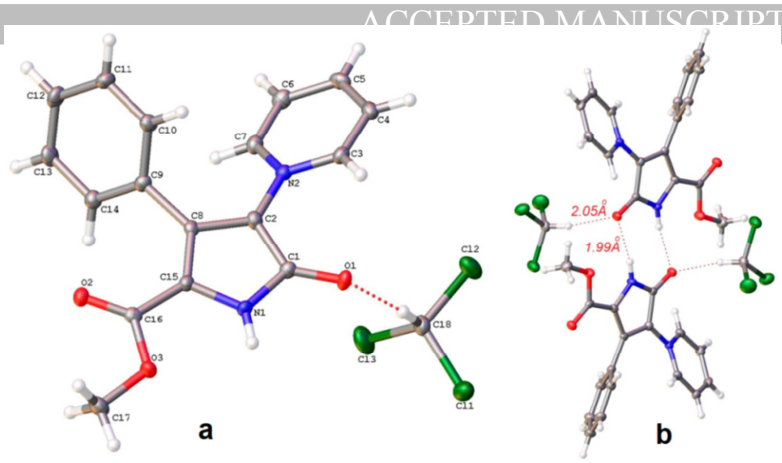


Fig. 1. Molecular structure of **5a** (**a**), and solid-state packing of H-bonded dimer (**b**), showing H···O-contacts.

Compound **5a** crystallizes in a monoclinic space group $P2_1/c$ with four molecules in the unit cell. The solid-state structure of **5a** displays different types of short intermolecular contacts. Two molecules of the compound form a dimer by hydrogen bonds of the type N-H···O, to which the $CDCl_3$ molecules are bound by hydrogen bonds of the type C-H···O. Experimental and calculated selected bond lengths of molecules **5a**, **5'a** are listed in Table 1. Computed at the B3LYP/6-31G+(d,p) level bond lengths of molecules **5a** fit well with the XRD bond lengths, and especially good correspondence is found for the calculated values of the H-bonded dimer of **5a**. Meanwhile, there is a big discrepancy between the computed O1-C1 and N1-C1 bond lengths of molecules **5a'** and the corresponding XRD bond lengths. Thus, the product of the reaction of 2-methoxy-2-oxo-1-(pyridin-1-ium-1-yl)ethan-1-ide **2a** with methyl 3-phenyl-2*H*-azirine-2-carboxylate **3a** exists as the NH-tautomer **5a** both in solution and in the solid state.

Table 1. Experimental and calculated selected bond lengths of molecules **5a**, **5'a**.

Bond	**5a** (XRD)	**5a**[a]/Δ[b]	**5'a**[a]/Δ[b]	H-bonded dimer of **5a**[a]/Δ[b]
O1-C1	1.274(3)	1.247/-0.027	1.368/0.094	1.269/-0.006
C1-C2	1.425(4)	1.459/0.034	1.426/0.001	1.445/0.020
C8-C2	1.421(4)	1.431/0.010	1.434/0.013	1.430/0.009
C8-C15	1.389(4)	1.392/0.003	1.404/0.015	1.392/0.003
N1-C15	1.399(3)	1.396/-0.003	1.390/-0.009	1.396/-0.003
N1-C1	1.368(4)	1.380/0.012	1.309/-0.059	1.368/0.000

[a] Bond lengths computed at the B3LYP/6-31G+(d,p) level.
[b] Δ – difference between the XRD and computed bond length.

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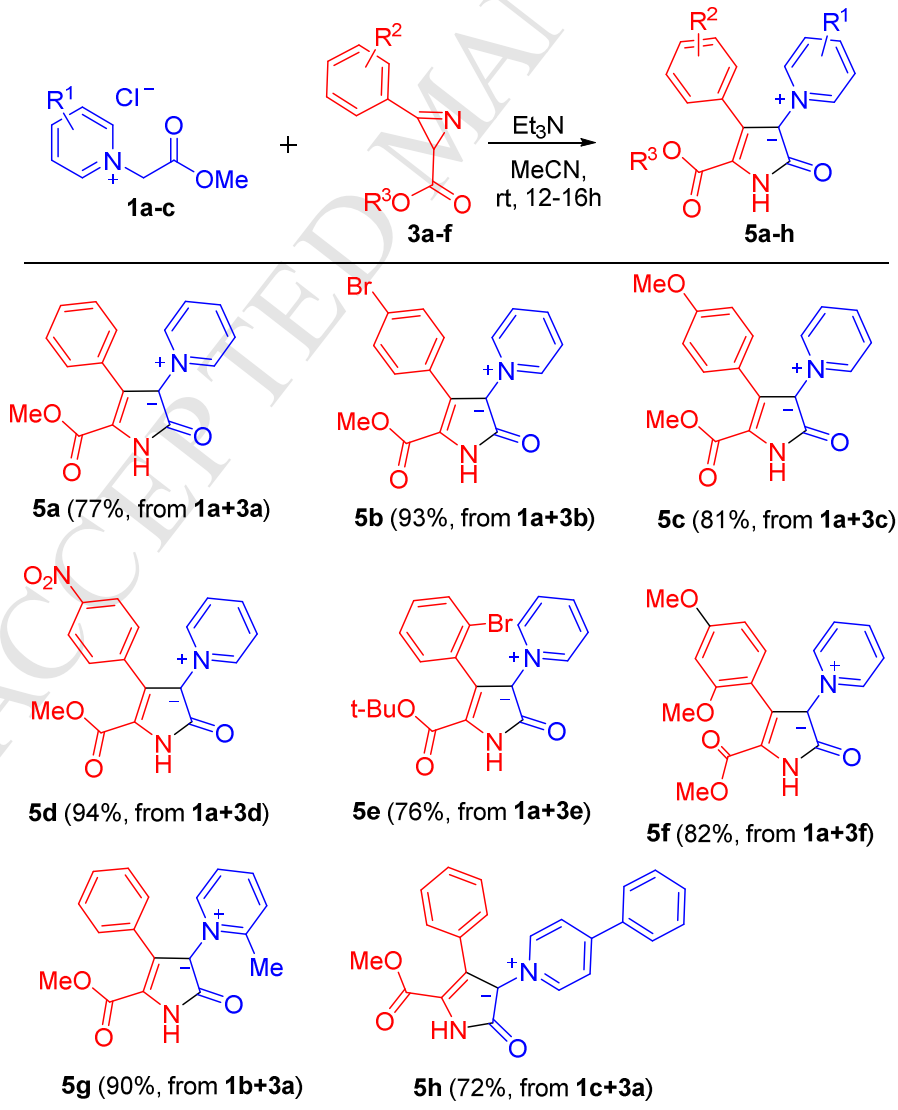
To evaluate the scope of the reaction substituted alkyl azirinecarboxylates **3a-f** were reacted with pyridinium chlorides **1a-c**, 4-(*N*,*N*-dimethylamino)-1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1d**, and 1-(2-methoxy-2-oxoethyl)quinolin-1-ium **1e** and 2-(2-methoxy-2-oxoethyl)isoquinolin-1-ium **1f** chlorides. However, we failed to isolate betaines containing *N*,*N*-dimethylaminopyridine (from **1d**), quinoline (from **1e**) and isoquinoline (from **1f**) moieties and changing the heterocycle from pyridine to imidazole was also not successful. Meanwhile betaines **5a-h** with electron-donating (MeO), electron-withdrawing (NO_2) and halogen (Br) substituents in the phenyl ring were prepared in good yields. *ortho*-Substituents, both in the phenyl and the pyridine rings, do not influence dramatically the yield of the products (Table 1).

Table 1. Synthesis of betaines **5a-h**



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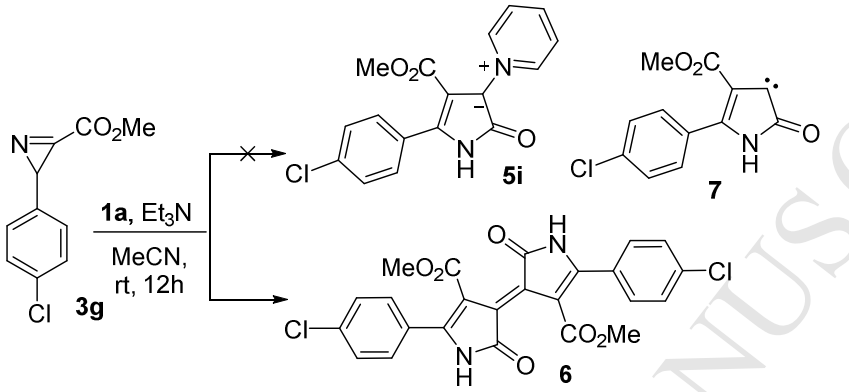
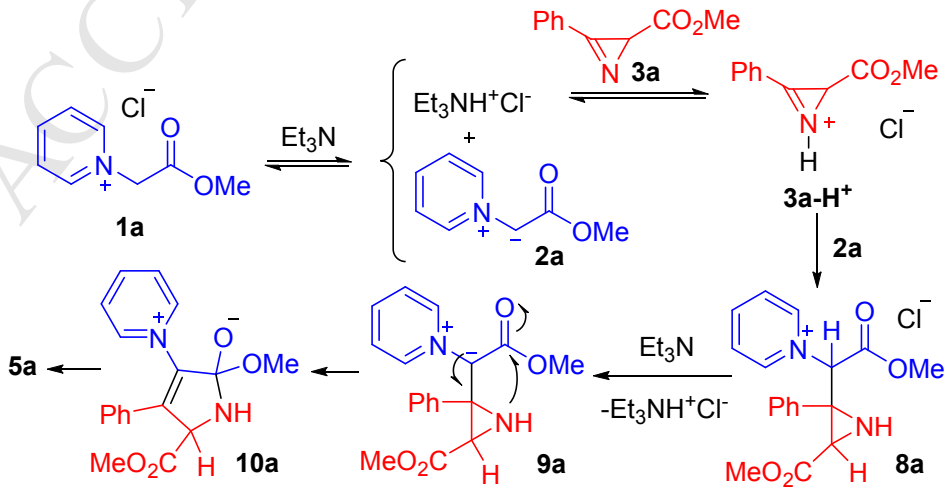
Having decided to evaluate the reactivity of azirines with the opposite location of the aryl and methoxycarbonyl substituents, we synthesized azirine **3g** and reacted it with salt **1a** under the standard conditions. However, instead of the betaine product **5i**, the product **6** of formal dimerization of carbene **7** was unexpectedly isolated in 18% yield (Scheme 3). According to the DFT calculations at the B3LYP/6-31G+(d,p) level with the PCM model for MeCN at 298 K, the E-isomer of **6** is more stable than the Z-isomer by 4.4 kcal/mol.



Scheme 3. Reaction of pyridinium salt **1a** with methyl 2-(4-chlorophenyl)-2*H*-azirine-3-carboxylate **3g**

The proposed mechanism of the formation of betaine **5a** (Scheme 4) involves generation of pyridinium ylide **2a**, nucleophilic attack of the latter on the C=N bond of the protonated azirine (**3a-H**$^+$) with the formation of aziridine intermediate **8a** followed by dehydrohalogenation of **8a** to aziridinyl-substituted pyridinium ylide **9a**. A rearrangement of **9a** to betaine **10a**, followed by an elimination of MeOH leads to betaine **5a**.



Scheme 4. Proposed mechanism of formation of betaines **5**

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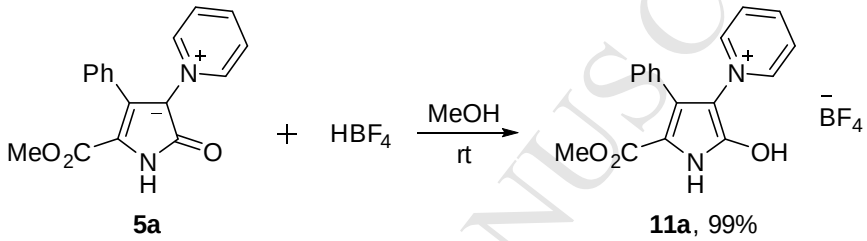
All new compounds were characterized by ^{1}H, ^{13}C NMR and HRMS methods. Betaines **5** and dimer **6** are non-hygroscopic, air-unstable high-melting intensively colored crystalline solids, which fade when kept in air for a long time, probably due to the formation of a carbonate (*vide infra*). Substances **5a-h** and **6** possess poor solubility in dichloromethane, methanol, dimethyl sulfoxide and very poor solubility in acetonitrile and water. Betaines **5** are weak bases and reaction with hydrochloric or hydrobromic acids was accompanied by tarring of the reaction mixture, but the reaction with aq HBF_4 led quantitatively to hydroxypyrrole **11a** (Scheme 5).



5a **11a**, 99%

Scheme 5. Synthesis of 1-(2-hydroxy-5-(methoxycarbonyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridin-1-ium tetrafluoroborate **11a**

Compound **11a** was characterized by spectroscopic methods (^{1}H, ^{13}C, HSQC ^{1}H-^{13}C, HMBC ^{1}H-^{13}C NMR and HRMS). Its structure was also confirmed by single crystal X-ray analysis (Fig. 2).

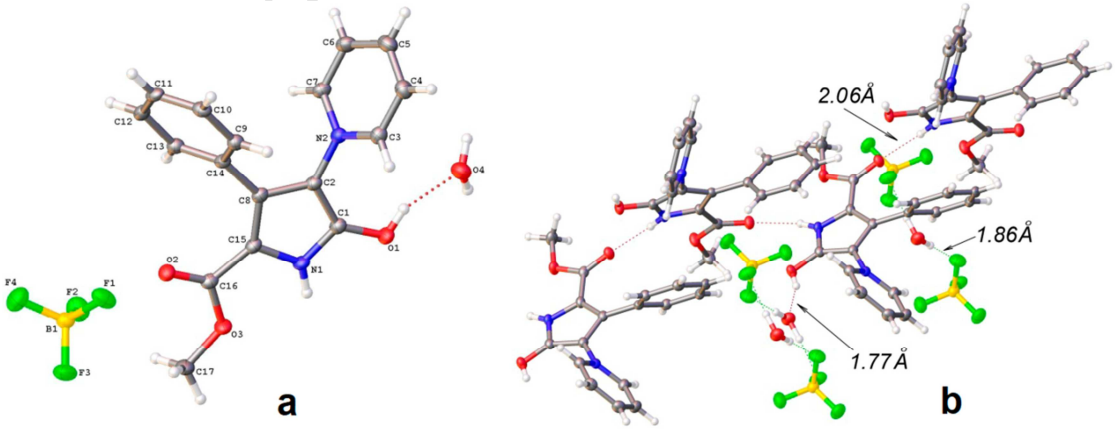


Fig. 2. Molecular structure of **11a** (**a**), and solid-state packing of **11a** (**b**), showing H···O- and H···F-contacts.

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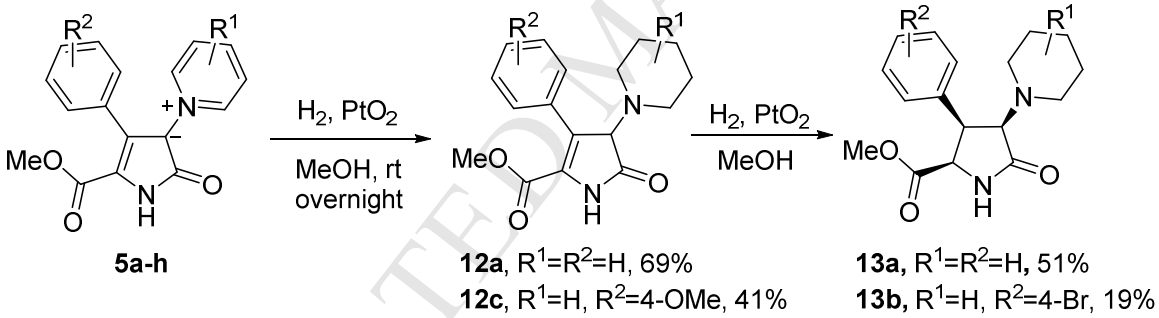
Salt **11a** crystallizes in a monoclinic space group $P2_1/c$ with four molecules in the unit cell. The solid-state structure of **11a** displays different types of short intermolecular contacts. 1-(2-Hydroxy-5-(methoxycarbonyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridin-1-ium ions interacting with each other through hydrogen bonds of the N-H···O type and with water molecules (via a hydrogen bond of the C-H···O type) form one of the layers that is interleaved by the $^{-}BF_4$ layers that have contact both with the pyridin-1-ium ions and with water molecules through hydrogen contacts of the type O-H···F.

The selective hydrogenation of the pyridinio-substituents in some cases allows them to be considered as synthetic equivalents of the pyrrolidin-1-yl substituents.[6a,b] We tried to carry out this reaction for betaines **5** under heterogeneous hydrogenation conditions. It turned out that they can be hydrogenated in methanol at atmospheric pressure of H_2 in the presence of Adams' catalyst either to 1,3-dihydro-2*H*-pyrrol-2-ones **12**, or to pyrrolidin-2-ones **13** (Scheme 6).



Scheme 6. Catalytic hydrogenation of betaines **5**

In the case of betaine **5a** it was possible to obtain both reduction products, 1,3-dihydro-2*H*-pyrrol-2-one **12a** and pyrrolidin-2-one **13a**. The second product was obtained by use of an additional portion of catalyst and stirring for another 24 h. Betaine **5b**, however, was reduced immediately to pyrrolidin-2-one **13b**. Betaine **5c** gave only the first step reduction product **12c**. Nitro-substituted compound **3d** gave a mixture of compounds, **12d** and the amino-substituted product by reduction of the nitro-group in **12d** (30:70 ratio, 33% overall yield). Betaines **5e-g** gave unstable products which could not be obtained as individual compounds. Betaine **5h** after 5

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days of stirring in an atmosphere of hydrogen gave **13h** and the product of hydrogenation of one of the phenyl ring (68:32 ratio, 70% overall yield). Unfortunately, we were unable to find conditions for the chromatographic separation of these mixtures. It has to be noted that substances **13a** and **13b** have 3 stereogenic centers, but they were obtained as a single diastereomer, which has all-cis-configuration. This was confirmed by single crystal X-ray analysis of **13a** (Fig. 3).

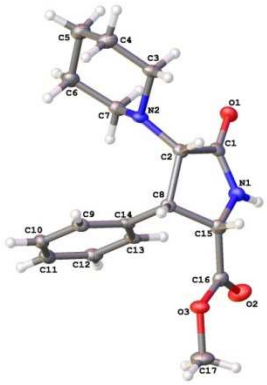

Fig. 3. Molecular structure of **13a**

The UV spectra of solutions of compounds **5** are characterized by a long-wave absorption band (Table 2), which is responsible for the color of these compounds (from purple to dark-brown). The position of this band is hardly affected by changing the solvent. Compounds **5a,c,d** show a hypsochromic shift by about 30–40 nm on changing the solvent from polar aprotic acetonitrile to a polar protic solvent such as water or methanol. To elucidate the nature of the long-wave absorption band and the solvent effect on the band position, the geometry of **5a,c,d** was optimized at the B3LYP/6-31+g(d,p) level with PCM model for the corresponding solvent and then single point calculations at the TD-DFT B3LYP/6-31+G(d,p)/PCM and SMD, M062X/6-31+G(d,p)/PCM and SMD, CAM-B3LYP/6-31+G(d,p)/SMD level of theory were performed (Table 2). For details of the computations see Supporting information. The best fit between the experimental and calculated wave length for compounds **5a,c,d** (the long-wave band) is observed for the TD-DFT B3LYP/6-31+G(d,p) level with SMD solvation model (Δ12-14 nm for MeCN, Δ10-63 nm for H_2O, Δ25 nm for MeOH; Table 2). The TD-DFT B3LYP/6-

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31+G(d,p)/SMD calculation results demonstrate that the long-wave absorption of the compounds **5a,c** mainly arises from HOMO to LUMO transitions (coefficient of the wave function >0.7) (Fig. 4). For compound **5d** the HOMO to LUMO transition has an oscillator strength of only 0.03 and was not observed, whereas the observed long-wave absorption correspond to the HOMO to LUMO+1 transition (f = 0.23, coefficient of the wave function >0.7). Thus, the long-wave absorption of compounds **5a,c,d** is mainly corresponding to the intramolecular charge transfer excitation between the negatively charged pyrrole unit and the positively charged pyridinium group. The second possibility for the compound **5d** charge transfer from the negatively charged pyrrole unit (LUMO) to the positively charged nitro-substituted phenyl group (HOMO) has a too low intensity.

Table 2. Data of experimental absorption spectra and calculated by TD-DFT long wavelengths and oscillator strengths of compounds **5a,c,d**.

5	solvent	absorbance, λ_{max}, nm (ε, $10^{-3} \cdot M^{-1}\ cm^{-1}$)	B3LYP/6-31+G(d,p) PCM	B3LYP/6-31+G(d,p) SMD	M062X/6-31+G(d,p) PCM	M062X/6-31+G(d,p) SMD	CAM-B3LYP/6-31+G(d,p) SMD
			λ max (nm), f (HOMO→LUMO transition)				
a	MeCN	330 (8.4), 515 (8.9)	535/0.237	527/0.246	440/0.335	432/0.348	430/0.345
a	H_2O	288 (21.5), 359 (15.5), 475 (6.0)	533/0.233	493/0.246	437/0.330	403/0.369	401/0.367
c	MeCN	329 (11.8), 517 (9.9)	539/0.228	531/0.237	441/0.329	434/0.340	432/0.338
c	MeOH	318 (12.3), 476 (5.5)	539/0.227	501/0.238	441/0.327	408/0.363	406/0.361
c	H_2O	320 (14.7), 436 (4.9)	538/0.223	497/0.234	441/0.323	404/0.361	402/0.359
d	MeCN	320 (17.8), 513 (9.2)	722/0.035 533/0.221[a]	741/0.034 525/0.228[a]	447/0.291 426/0.068[a]	447/0.224 423/0.141[a]	445/0.232 420/0.134[a]
d	H_2O	355 (19.3), 482 (5.1)	723/0.034 532/0.217[a]	721/0.034 492/0.227[a]	446/0.276 425/0.076[a]	430/0.172 396/0.211[a]	428/0.177 395/0.209[a]

[a] HOMO→LUMO+1.

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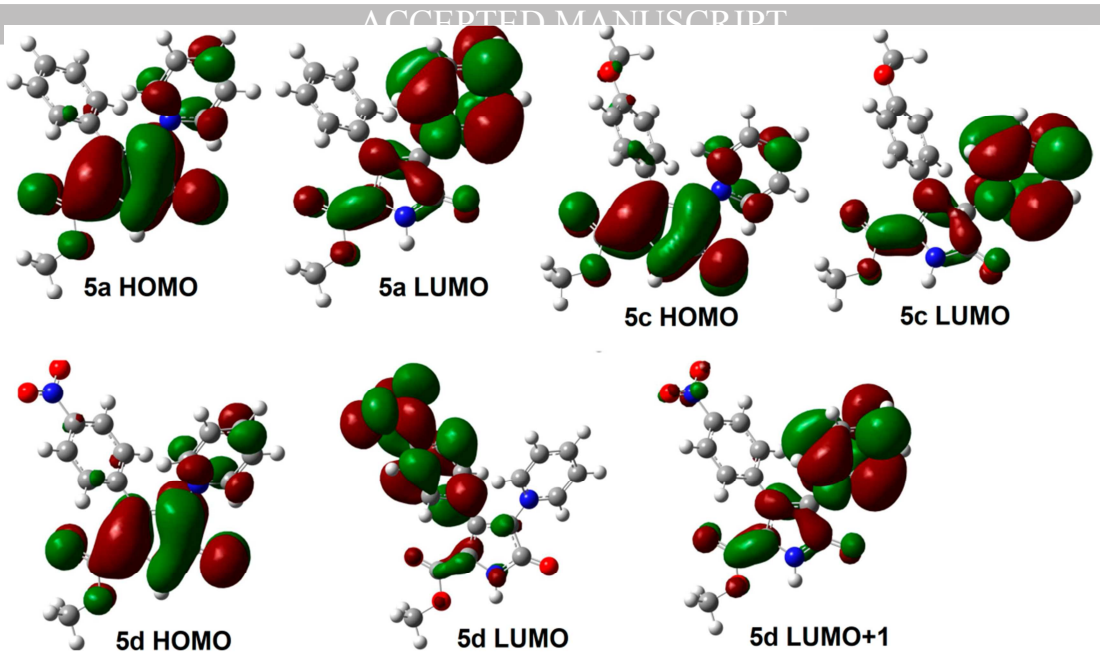

Fig. 4. Contour surface plots of the frontier orbital of compounds **5a,c,d** (isovalue is 0.02 a.u.)

Since the betaines **5** are of a basic nature (*vide supra*), we assumed that complexes with a hydrogen bond can be formed in proton solvents (water, methanol), and accepting this to be true we can obtain a better agreement between the experimental and calculated maxima of the long-wave bands. Indeed, as can be seen from Table 3, the calculated data for such complexes correspond better to the experimental spectra. Thus, the formation of H-complexes **5-HOR** leads to the blue shift of the calculated absorption. This is mainly due to the higher ground state stabilization upon H-complex formation compared to the first exited state (Fig. 5).

Table 3 Data of experimental absorption spectra and calculated by TD-DFT B3LYP/6-31+G(d,p)/PCM and SMD[a]

compound	solvent	exp. λ_{max}, nm	calcd, λ_{max}, nm (PCM/SMD)
5a	H_2O	475	533/493
5a-H_2O			521/484
5c	H_2O	436	538/497
5c-H_2O			525/487
5c	MeOH	476	539/501
5c-MeOH			528/492
5d	H_2O	482	532/492
5d-H_2O			519/482

[a] Geometry of **5a,c,d** was optimised at the B3LYP/6-31+g(d,p) level with PCM model for the corresponding solvent

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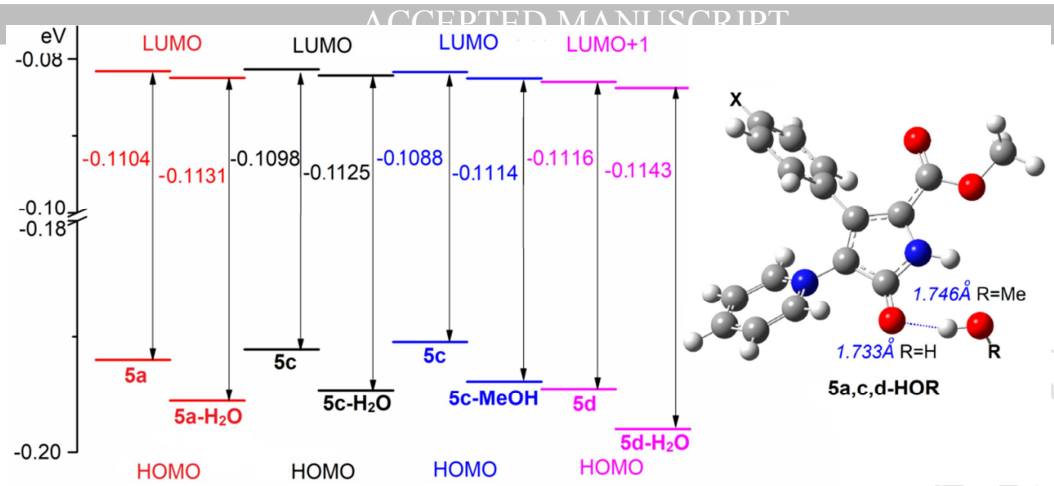

Fig. 5. Energies of frontier MO of **5a,c,d** and their complexes with ROH

Titration of an aprotic acetonitrile solution of **5c** with water (Fig. 6) shows clear cut isosbestic points in the absorption spectra that is indicative of a chemical equilibrium between the solvated (with water) and unsolvated forms of **5c**.

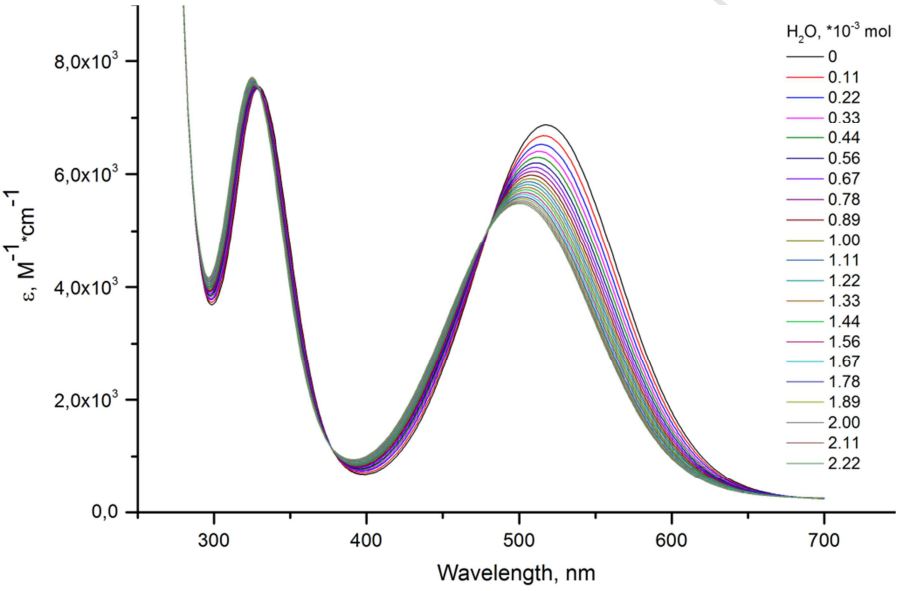

Fig. 6. Titration of the solution of **5c** in MeCN ($1.54 \cdot 10^{-4}$ mol/l) with water at rt

3. Conclusion

New heterocyclic betaines, 4-aryl-5-(alkoxycarbonyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ides, were synthesized in good yields by reaction of alkyl 2*H*-azirine-2-carboxylates with 2-methoxy-2-oxo-1-(pyridin-1-ium-1-yl)ethan-1-ides, generated from the corresponding pyridinium salts. The betaines exist as the NH-tautomers both in solution and in

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the solid state. In the solid state two molecules of the betaine form the dimer by hydrogen bonds of the type N-H···O. Catalytic reduction of betaines **5** in methanol in H_2 at the atmospheric pressure in the presence of Adams' catalyst give either 1,3-dihydro-2*H*-pyrrol-2-ones **12** or pyrrolidin-2-ones **13**. The long-wave absorption of the betaines corresponds, according to the TD DFT calculations, to the intramolecular charge transfer excitation between the negatively charged pyrrole unit and the positively charged pyridinium group. The blue shift of the long-wave absorption in protic solvents was adequately described in terms of H-complex formation with the nucleophilic centre of the molecular skeleton.

4. Experimental section

4.1. General Information and Methods

Melting points were determined on a capillary melting point apparatus Stuart® SMP30. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded in $CDCl_3$, DMSO-d_6 or methanole-d_4 with Bruker AVANCE III 400 spectrometer. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane (TMS δ 0.00). ^{1}H NMR spectra were calibrated according to the residual peak of $CHCl_3$ (7.26 ppm), DMSO-d_6 (2.50 ppm) or methanole-d_4 (3.31 ppm). $^{13}C\{^{1}H\}$ and ^{13}C DEPT-135 were calibrated according to the peak of $CDCl_3$ (77.00 ppm), DMSO-d_6 (39.51 ppm) or methanole-d_4. Mass spectra were recorded on a Bruker maXis HRMS-ESI-QTOF, electrospray ionization, positive mode. Thin-layer chromatography (TLC) was conducted on aluminum sheets with 0.2 mm silica gel (fluorescent indicator, Macherey-Nagel) and Macherey-Nagel Silica 60 M was used for column chromatography. Suitable crystals of **5a**, **11a**, **13a** were selected and studied on an Xcalibur, Eos diffractometer, SuperNova, Single source at offset/far, HyPix3000 diffractometer and SuperNova, Dual, Cu at zero, Atlas diffractometer. The crystal was kept at 100(2) K during data collection. Using Olex2,[8] the structure was solved with the Superflip[9a-c] structure solution programme using Charge Flipping (for **5a** and **13a**) or with the ShelXS[10] structure solution

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program using Direct Methods (for **11a**) and refined with the ShelXL[11] refinement package using Least Squares minimisation. Crystallographic data for structures **5a**, **11a**, **13a** have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1819078, 1816088, 1586949, respectively). Compounds **1a-c**[12] and **3a-d**,[13a] **3e**,[13b] and **3g**[13c] were prepared by the reported procedures.

4.2. Calculation details

All calculations were performed by using the Gaussian 16 suite of quantum chemical programmes[14] at Resource Centre "Computer Centre of Saint Petersburg State University". Geometry optimizations of molecules were performed with the B3LYP density functional method[15] and 6-31+G(d,p) basis set using PCM solvent model.[16] Stationary points on the respective potential-energy surfaces were characterized at the same level of theory by evaluating the corresponding Hessian indices. The absorption spectra were investigated for the optimized DFT/B3LYP/6-31+G(d,p)/PCM geometry with time dependent density function theory (TD-DFT)[17] using B3LYP[15], CAM-B3LYP[18] and M062X[19] functionals and 6-31+G(d,p) basis set with PCM[16] or SMD[20] solvent models.

4.3. 3-(2,4-Dimethoxyphenyl)isoxazol-5(4H)-one

Hydroxylamine hydrochloride (827 mg, 1.19 mmol, 3 equiv) was added to a heterogeneous mixture of ethyl 3-(2,4-dimethoxyphenyl)-3-oxopropanoate (1 g, 3.97 mmol, 1 equiv) and 10 mL of water and the resulting mixture was kept at 100 °C for 5 min. Then approximately 20 mL of ethanol (till homogenization) was added and the solution was heated at reflux for 1 h, cooled, the precipitate formed was filtered off, washed with cold mixture of ethanol and water (1:1) and dried to obtain pure product. Colorless solid, 470 mg (54%), mp 158-160 °C. Product (in DMSO) is a mixture of tautomers: 3-(2,4-dimethoxyphenyl)isoxazol-5(4*H*)-one and 3-(2,4-dimethoxyphenyl)isoxazol-5-ol at 1:2 ratio. ^{1}H NMR (DMSO-d_6): δ 3.84 (s, 6H), 3.89 (s, 3H), 4.19 (s, 1H), 5.55 (s, 1H), 6.51-6.83 (m, 3H), 7.41-7.61 (m, 1H), 7.62-7.74 (m, 0.5H), 12.27 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 37.2 (CH_2), 55.6 (CH_3), 55.8 (CH_3), 55.9

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(CH_3), 84.2 (CH), 98.8 (CH), 106.2 (CH), 106.4 (CH), 107.3 (C), 109.1 (C), 129.1 (CH), 129.6 (CH), 158.9 (C), 159.3 (C), 161.4 (C), 162.6 (C), 163.3 (C), 163.5 (C), 172.0 (C), 176.7 (C). HRMS (ESI) m/z: 222.0761 calcd for $C_{11}H_{12}NO_4^+$ $[M + H]^+$, found 222.0764.

4.4. 3-(2,4-Dimethoxyphenyl)-5-methoxyisoxazole

A suspension of 3-(2,4-dimethoxyphenyl)isoxazol-5-ol (0.6 g, 2.71 mmol, 1 equiv) in 10 mL of diethyl ether was cooled with ice bath and a solution of diazomethane (obtained from 0.84 g of 1-methyl-1-nitrosourea and 1.52 g of potassium hydroxide) in 30 mL of diethyl ether was added dropwise. The resulting mixture was stirred at rt for 1 h and quenched with acetic acid. The homogeneous solution was concentrated in vacuo and purified by column chromatography (hexane:ethyl acetate, 1.5:1). Colorless solid, 312 mg (49%), mp 56-58 °C. ^{1}H NMR ($CDCl_3$): δ 3.84 (s, 3H), 3.87 (s, 3H), 5.69 (s, 1H), 6.50-6.50 (m, 2H), 7.78 (d, 1H, J = 8.5 Hz). ^{13}C NMR ($CDCl_3$): δ 55.6 (CH_3), 55.7 (CH_3), 58.8 (CH_3), 78.7 (CH), 99.0 (CH), 105.2 (CH), 111.6 (C), 130.0 (CH), 158.7 (C), 161.8 (C), 162.4 (C), 173.8 (C). HRMS (ESI) m/z: 236.0917 calcd for $C_{12}H_{14}NO_4^+$ $[M + H]^+$, found 236.0928.

4.5. Methyl 3-(2,4-dimethoxyphenyl)-2H-azirine-2-carboxylate **3f**

Iron(II) chloride tetrahydrate (24 mg, 0.12 mmol, 10 mol%) was added to a stirred solution of 3-(2,4-dimethoxyphenyl)-5-methoxyisoxazole (280 mg, 1.19 mmol) in 8 mL of dry acetonitrile under inert atmosphere and the resulting mixture was stirred for 2 h at rt (monitoring by TLC, hexane:ethyl acetate, 2:1). After completion of the reaction the solution was filtered through celite, concentrated in vacuo and purified by flash column chromatography (hexane:ethyl acetate, 1:1). Colorless solid, 280 mg (100%), mp 70-72 °C. ^{1}H NMR ($CDCl_3$): δ 2.64 (s, 1H), 3.70 (s, 3H), 3.88 (s, 3H), 3.95 (s, 3H), 6.46-6.56 (m, 1H), 6.60 (dd, J = 8.5, 2.2 Hz, 1H), 7.53 (d, J = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 27.2 (CH), 52.2 (CH_3), 55.9 (CH_3), 56.1 (CH_3), 98.7 (CH), 104.3 (C), 105.8 (CH), 134.8 (CH), 153.9 (C), 162.0 (C), 166.1 (C), 173.0 (C). HRMS (ESI) m/z: 258.0737 calcd for $C_{12}H_{13}NNaO_4^+$ $[M + Na]^+$, found 258.0746.

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*4.6. Typical procedure for the preparation of betaines **5a-h***

Triethylamine (26 mg, 0.26 mmol, 1.05 equiv) was added to a suspension of 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride (50 mg, 0.25 mmol) and methyl 3-phenyl-2*H*-azirine-2-carboxylate (65 mg, 0.37 mmol, 1.5 equiv) in 1 mL of dry acetonitrile and the reaction mixture was stirred at rt for 12 h. Then the precipitate formed was filtered off, washed with 1 mL of dry acetonitrile and dried to obtain pure product.

*4.6.1. 5-(Methoxycarbonyl)-2-oxo-4-phenyl-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1H-pyrrol-3-ide (**5a**)*

Compound **5a** (56 mg, 77%) was prepared from 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1a** (50 mg, 0.25 mmol), methyl 3-phenyl-2*H*-azirine-2-carboxylate **3a** (65 mg, 0.37 mmol) and triethylamine (26 mg, 0.26 mmol) according to the typical procedure. Dark brown solid, mp 211–213 °C. ^{1}H NMR (DMSO-d_6): δ 3.46 (s, 3H), 7.18-7.35 (m, 5H), 7.67-7.81 (m, 2H), 7.90-8.06 (m, 1H), 8.44-8.64 (m, 2H), 9.67 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 49.9 (CH_3), 102.9 (C), 108.6 (C), 124.2 (C), 126.5 (CH), 127.0 (CH), 128.0 (CH), 129.8 (CH), 132.9 (C), 137.8 (CH), 140.2 (CH), 155.8 (C), 160.0 (C). HRMS (ESI) m/z: 295.1077 calcd for $C_{17}H_{15}N_2O_3^+$ $[M + H]^+$, found 295.1064. IR (KBr, cm^{-1}): ν 1132, 1428, 1482, 1588, 1618, 1680.

*4.6.2. 4-(4-Bromophenyl)-5-(methoxycarbonyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1H-pyrrol-3-ide (**5b**)*

Compound **5b** (87 mg, 93%) was prepared from 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1a** (50 mg, 0.25 mmol), methyl 3-(4-bromophenyl)-2*H*-azirine-2-carboxylate **3b** (95 mg, 0.37 mmol) and triethylamine (26 mg, 0.26 mmol) according to the general procedure. Dark violet solid, mp 196–198 °C. ^{1}H NMR (methanol-d_4): δ 3.64 (s, 3H), 7.13-7.20 (m, 2H), 7.42-7.47 (m, 2H), 7.82-7.89 (m, 2H), 8.18-8.28 (m, 1H), 8.53-8.60 (m, 2H). ^{13}C NMR (methanol-d_4): δ 51.1 (CH_3), 105.4 (C), 110.9 (C), 122.7 (C), 125.8 (C), 128.4 (CH), 132.5 (CH), 132.7 (C), 133.1 (CH), 142.6 (CH), 145.2 (CH), 155.3 (C), 162.7 (C). HRMS (ESI) m/z: 373.0182 calcd for $C_{17}H_{14}BrN_2O_3^+$ $[M + H]^+$, found 373.0618.

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*4.6.3. 5-(Methoxycarbonyl)-4-(4-methoxyphenyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1H-pyrrol-3-ide (**5c**)*

Compound **5c** (65 mg, 81%) was prepared from 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1a** (50 mg, 0.25 mmol), methyl 3-(4-methoxyphenyl)-2*H*-azirine-2-carboxylate **3c** (76 mg, 0.37 mmol) and triethylamine (26 mg, 0.26 mmol) according to the general procedure. Purple solid, mp 218–219 °C. ^{1}H NMR (DMSO-d_6): δ 3.48 (s, 3H), 3.76 (s, 3H), 6.83-6.92 (m, 2H), 7.10-7.20 (m, 2H), 7.72-7.81 (m, 2H), 7.95-8.03 (m, 1H), 8.51-8.60 (m, 2H), 9.57 (s, 1H). ^{13}C NMR (methanol-d_4): δ 51.1 (CH_3), 55.7 (CH_3), 105.3 (C), 111.2 (C), 114.8 (CH), 125.4 (C), 127.2 (C), 128.2 (CH), 132.3 (CH), 142.2 (CH), 145.1 (CH), 155.2 (C), 160.7 (C), 163.0 (C) . HRMS (ESI) m/z: 325.1183 calcd for $C_{18}H_{17}N_2O_4^+$ $[M + H]^+$, found 325.1180.

*4.6.4. 5-(Methoxycarbonyl)-4-(4-nitrophenyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1H-pyrrol-3-ide (**5d**)*

Compound **5d** (158 mg, 94%) was prepared from 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1a** (100 mg, 0.50 mmol), methyl 3-(4-nitrophenyl)-2*H*-azirine-2-carboxylate **3d** (165 mg, 0.74 mmol) and triethylamine (53 mg, 0.52 mmol) according to the general procedure. Dark brown solid, mp >370 °C. ^{1}H NMR (DMSO-d_6): δ 3.50 (s, 3H), 7.46-7.56 (m, 2H), 7.76-7.82 (m, 2H), 8.02-8.09 (m, 1H), 8.12-8.20 (m, 2H), 8.50-8.59 (m, 2H), 9.99 (s, 1H). ^{13}C NMR (methanol-d_4): δ 51.3 (CH_3), 105.9 (C), 124.3 (CH), 124.7 (C), 128.6 (CH), 132.5 (CH), 140.8 (C), 142.8 (CH), 145.3 (CH), 148.5 (C), 155.5 (C), 162.5 (C). HRMS (ESI) m/z: 340.0928 calcd for $C_{17}H_{14}N_3O_5^+$ $[M + H]^+$, found 340.0939.

*4.6.5. 4-(2-Bromophenyl)-5-(tert-butoxycarbonyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1H-pyrrol-3-ide (**5e**)*

Compound **5e** (94 mg, 76%) was prepared from 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1a** (60 mg, 0.30 mmol), tert-butyl 3-(2-bromophenyl)-2*H*-azirine-2-carboxylate **3e** (132 mg, 0.45 mmol) and triethylamine (32 mg, 0.32 mmol) according to the general procedure. Dark violet solid, mp 198-200 °C. ^{1}H NMR (DMSO-d_6): δ 1.13 (s, 9H), 7.23-7.30 (m, 1H), 7.36-7.40

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(m, 2H), 7.60-7.66 (m, 1H), 7.70-7.76 (m, 2H), 7.85-7.95 (m, 1H), 8.58-8.67 (m, 2H), 9.71 (s, 1H). ^{13}C NMR (methanol-d_4): δ 28.5 (CH_3), 80.7 (C), 108.0 (C), 110.5 (C), 124.3 (C), 125.8 (C), 128.4 (CH), 128.6 (CH), 130.5 (CH), 133.6 (CH), 134.0 (CH), 136.1 (C), 141.9 (CH), 144.0 (CH), 154.8 (C), 162.2 (C). HRMS (ESI) m/z: 415.0652 calcd for $C_{20}H_{20}BrN_2O_3^+$ $[M + H]^+$, found 415.0664.

*4.6.6. 4-(2,4-Dimethoxyphenyl)-5-(methoxycarbonyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1H-pyrrol-3-ide (**5f**)*

Compound **5f** (225 mg, 82%) was prepared from 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1a** (156 mg, 0.77 mmol), methyl 3-(2,4-dimethoxyphenyl)-2*H*-azirine-2-carboxylate **3f** (236 mg, 1.00 mmol, 1.5 equiv) and triethylamine (82 mg, 0.81 mmol, 1.05 equiv) according to the general procedure. Dark violet solid, mp 228-230°C. ^{1}H NMR (DMSO-d_6): δ 3.30 (s, 3H), 3.45 (s, 3H), 3.78 (s, 3H), 6.41-6.49 (m, 1H), 6.52-6.58 (m, 1H), 7.15-7.29 (m, 1H), 7.71-7.79 (m, 2H), 7.90-8.02 (m, 1H), 8.51-8.66 (m, 2H), 9.51 (s, 1H). ^{13}C NMR (methanol-d_4): δ 51.0 (CH_3), 55.6 (CH_3), 55.8 (CH_3), 99.1 (CH), 105.2 (C), 106.3 (CH), 112.0 (C), 114.1 (C), 123.9 (C), 128.1 (CH), 134.7 (CH), 142.0 (CH), 144.4 (CH), 154.7 (C), 158.8 (C), 162.7 (C), 163.0 (C). HRMS (ESI) m/z: 355.3695 calcd for $C_{19}H_{19}N_2O_5^+$ $[M + H]^+$, found 355.1304.

*4.6.7. 5-(Methoxycarbonyl)-2-oxo-4-phenyl-3-(4-phenylpyridin-1-ium-1-yl)-2,3-dihydro-1H-pyrrol-3-ide (**5g**)*

Compound **5g** (86 mg, 90%) was prepared from 1-(2-methoxy-2-oxoethyl)-4-phenylpyridin-1-ium bromide **1b** (80 mg, 0.26 mmol), methyl 3-phenyl-2*H*-azirine-2-carboxylate **3a** (68 mg, 0.39 mmol) and triethylamine (28 mg, 0.27 mmol) according to the general procedure. Dark blue solid, mp 215-217 °C. ^{1}H NMR (DMSO-d_6): δ 3.47 (s, 3H), 7.25-7.37 (m, 5H), 7.89-7.97 (m, 3H), 7.89-7.97 (m, 2H), 8.09-8.15 (m, 2H), 8.50-8.60 (m, 2H), 9.74 (s, 1H). ^{13}C NMR (methanol-d_4): δ 51.1 (CH_3), 105.4 (C), 110.7 (C), 124.8 (CH), 127.3 (C), 128.69 (CH), 128.74 (CH), 129.4 (CH), 130.8 (CH), 131.2 (CH), 132.8 (CH), 133.7 (C), 135.6

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(C), 144.6 (CH), 153.3 (C), 155.4 (C), 162.9 (C). HRMS (ESI) m/z: 371.1390 calcd for $C_{23}H_{19}N_2O_3^+$ $[M + H]^+$, found 371.1408.

*4.6.8. 5-(Methoxycarbonyl)-3-(2-methylpyridin-1-ium-1-yl)-2-oxo-4-phenyl-2,3-dihydro-1H-pyrrol-3-ide (**5h**)*

Compound **5h** (108 mg, 72%) was prepared from 1-(2-methoxy-2-oxoethyl)-2-methylpyridin-1-ium bromide **1c** (120 mg, 0.49 mmol), methyl 3-phenyl-2*H*-azirine-2-carboxylate **3a** (128 mg, 0.73 mmol, 1.5 equiv) and triethylamine (52 mg, 0.51 mmol, 1.05 equiv) according to the general procedure. Dark violet solid, mp 219-221 °C. ^{1}H NMR (DMSO-d_6): δ 2.78 (s, 3H), 3.47 (s, 3H), 7.00-7.12 (m, 2H), 7.12-7.24 (m, 3H), 7.51-7.61 (m, 1H), 7.92-8.04 (m, 1H), 8.07-8.30 (m, 2H), 9.45 (s, 1H). ^{13}C NMR (methanol-d_4): δ 21.0 (CH_3), 51.0 (CH_3), 104.6 (C), 109.44 (C), 125.8 (CH), 128.5 (CH), 129.1 (CH), 129.3 (C), 130.2 (CH), 130.8 (CH), 133.9 (C), 145.3 (CH), 149.6 (CH), 154.6 (C), 159.6 (C), 163.0 (C). HRMS (ESI) m/z: 309.1234 calcd for $C_{18}H_{17}N_2O_3^+$ $[M + H]^+$, found 309.1248.

4.7. Dimethyl 5,5'-bis(4-chlorophenyl)-2,2'-dioxo-1,1',2,2'-tetrahydro-[3,3'-bipyrrolylidene]-4,4'-dicarboxylate (**6**)

Compound **6** (22 mg, 18%) was prepared from 1-(2-methoxy-2-oxoethyl)pyridin-1-ium chloride **1a** (100 mg, 0.50 mmol), methyl 2-(4-chlorophenyl)-2*H*-azirine-3-carboxylate **3g** (156 mg, 0.74 mmol) and triethylamine (53 mg, 0.52 mmol) according to the general procedure. Dark blue solid, mp 335–337 °C. ^{1}H NMR (DMSO-d_6): δ 3.62 (s, 3H), 7.50-7.65 (m, 2H), 7.65-7.77 (m, 2H), 11.25 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 51.4 (CH_3), 108.5 (C), 127.2 (C), 128.4 (C), 128.6 (CH), 130.6 (CH), 136.1 (C), 151.1 (C), 164.3 (C), 167.9 (C). HRMS (ESI) m/z: 499.0458 calcd for $C_{24}H_{17}Cl_2N_2O_6^+$ $[M + H]^+$, found 499.0476.

*4.8. 1-(2-Hydroxy-5-(methoxycarbonyl)-4-phenyl-1H-pyrrol-3-yl)pyridin-1-ium tetrafluoroborate (**11a**)*

An excess of tetrafluoroboric acid was added to a suspension of 5-(methoxycarbonyl)-2-oxo-4-phenyl-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ide **5a** (51 mg, 0.17 mmol) in 3

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mL of methanol till the complete change of the color from dark red to bright yellow. Then the solvent was evaporated and the residue treated with diethyl ether, filtered off, washed with additional amount of ether and dried. Bright yellow solid, 65 mg (98%), mp 129-131 °C. ^{1}H NMR (DMSO-d_6): δ 3.60 (s, 3H), 7.10-7.19 (m, 2H), 7.20-7.31 (m, 3H), 7.98-8.19 (m, 2H), 8.47-8.70 (m, 1H), 8.81-8.98 (m, 2H), 11.68 (s, broad, 0.35H, OH), 12.23 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 51.0 (CH_3), 107.3 (C), 109.8 (C), 125.6 (C), 127.8 (CH), 127.9 (CH), 128.0 (CH), 129.7 (CH), 130.6 (C), 143.0 (C), 146.2 (CH), 147.7 (CH), 160.3 (C). HRMS (ESI) m/z: 295.1077 calcd for $C_{17}H_{15}N_2O_3^+$ $[M - BF_4]^+$, found 295.1066. IR (KBr, cm^{-1}): ν 1058, 1300, 1473, 1693, 3253, 3547.

*4.9. Typical procedure for catalytic hydrogenation of pyrrolides **5***

A suspension of 5-(methoxycarbonyl)-2-oxo-4-phenyl-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ide **5a** (89 mg, 0.30 mmol) and PtO_2 (7 mg, 10 mol %) was stirred in hydrogen atmosphere overnight (completion of the reaction was indicated by TLC and disappearance of red color). The resulting colorless solution was filtered from PtO_2, concentrated in vacuo and purified by silica gel column chromatography on silica (dichloromethane/methanol).

*4.9.1. Methyl 5-oxo-3-phenyl-4-(piperidin-1-yl)-4,5-dihydro-1H-pyrrole-2-carboxylate (**12a**)*

Compound **12a** (63 mg, 69%) was prepared from 5-(methoxycarbonyl)-2-oxo-4-phenyl-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ide **5a** (89 mg, 0.30 mmol) and PtO_2 (7 mg, 10 mol%) according to the general procedure. Pale yellow solid, mp 184-186 °C (dichloromethane/diethyl ether). R_f (1% methanol in dichloromethane) 0.53. ^{1}H NMR (DMSO-d_6): δ 1.35-1.50 (m, 6H), 2.67-2.81 (m, 2H), 3.06-3.18 (m, 2H), 3.45 (s, 3H), 4.96 (d, J = 1.2 Hz, 1H), 7.23-7.31 (m, 3H), 7.32-7.39 (m, 2H), 8.69 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 23.7 (CH_2), 25.7 (CH_2), 49.7 (CH_2), 52.0 (CH_3), 59.1 (CH), 123.9 (C), 127.6 (CH), 127.7 (CH), 128.8 (CH), 133.6 (C), 139.3 (C), 170.3 (C), 170.4 (C). HRMS (ESI) m/z: 301.1547 calcd for $C_{17}H_{21}N_2O_3^+$ $[M + H]^+$, found 301.1557.

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*4.9.2. Methyl (2RS,3RS,4RS)-5-oxo-3-phenyl-4-(piperidin-1-yl)pyrrolidine-2-carboxylate (**13a**)*

Compound **13a** (46 mg, 50%) was prepared from obtained from 5-(methoxycarbonyl)-2-oxo-4-phenyl-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ide **5a** (89 mg, 0.30 mmol) and PtO_2 (14 mg, 20 mol%) according to the general procedure, except from that the reaction mixture was stirred 48 h instead of overnight. White solid, mp 179-181 °C (dichloromethane/diethyl ether). R_f (2% methanole in dichloromethane) 0.28. ^{1}H NMR (DMSO-d_6): δ 1.12-1.33 (m, 6H), 2.19-2.32 (m, 2H), 2.56-2.76 (m, 2H), 3.27 (s, 1H), 3.35 (d, J = 7.0 Hz, 1H), 3.94 (t, J = 6.6 Hz, 1H), 4.53 (d, J = 6.1 Hz, 1H), 7.18-7.25 (m, 5H), 8.17 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 24.0 (CH_2), 25.4 (CH_2), 47.6 (CH), 51.3 (CH_3), 51.5 (CH_2), 56.9 (CH), 67.5 (CH), 127.1 (CH), 127.3 (CH), 129.2 (CH), 136.1 (C), 169.4 (C), 174.5 (C). HRMS (ESI) m/z: 303.1703 calcd for $C_{17}H_{23}N_2O_3^+$ $[M + H]^+$, found 303.1713.

*4.9.3. Methyl (2RS,3RS,4RS)-3-(4-bromophenyl)-5-oxo-4-(piperidin-1-yl)pyrrolidine-2-carboxylate (**13b**)*

Compound **13b** (21 mg, 19%) was prepared from 4-(4-bromophenyl)-5-(methoxycarbonyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ide **3b** (106 mg, 0.28 mmol) and PtO_2 (6 mg, 10 mol%) according to the general procedure. White solid, mp 175-177 °C (dichloromethane/diethyl ether). R_f (1% methanole in dichloromethane) 0.41. ^{1}H NMR (DMSO-d_6): δ 1.17-1.30 (m, 6H), 2.17-2.24 (m, 2H), 2.65-2.75 (m, 2H), 3.30-3.35 (m, 4H, here is an overlapping of the H_2O residual peak, signal of methyl group and dublet belonging to one of the pyrrolidine ring protons), 3.96 (t, J = 6.5 Hz, 1H), 4.54 (d, J = 6.1 Hz, 1H), 7.13-7.18 (m, 2H), 7.42-7.48 (m, 2H), 8.23 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 24.0 (CH_2), 25.3 (CH_2), 46.9 (CH), 51.4 (CH_3), 51.6 (CH_2), 56.7 (CH), 67.0 (CH), 120.3 (C), 130.3 (CH), 131.4 (CH), 135.5 (C), 169.3 (C), 174.3 (C). HRMS (ESI) m/z: 381.0808 calcd for $C_{17}H_{22}BrN_2O_3^+$ $[M + H]^+$, found 381.0819.

*4.9.4. Methyl 3-(4-methoxyphenyl)-5-oxo-4-(piperidin-1-yl)-4,5-dihydro-1H-pyrrole-2-carboxylate (**12c**)*

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Compound **12c** (40 mg, 41%) was prepared from 5-(methoxycarbonyl)-4-(4-methoxyphenyl)-2-oxo-3-(pyridin-1-ium-1-yl)-2,3-dihydro-1*H*-pyrrol-3-ide **5c** (100 mg, 0.31 mmol) and PtO_2 (7 mg, 10 mol%) according to the general procedure. Pale yellow solid, mp 129-131 °C (dichloromethane/diethyl ether). R_f (1% methanole in dichloromethane) 0.19. ^{1}H NMR (DMSO-d_6): δ 1.36-1.51 (m, 6H), 2.69-2.82 (m, 2H), 3.04-3.18 (m, 2H), 3.46 (s, 3H), 3.76 (s, 3H), 4.95 (d, J = 1 Hz, 1H), 6.88-6.95 (m, 2H), 7.22-7.29 (m, 2H), 8.60 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 23.7 (CH_2), 25.7 (CH_2), 49.7 (CH_2), 52.0 (CH_3), 55.0 (CH_3), 59.1 (CH), 113.2 (CH), 125.2 (C), 125.5 (C), 130.0 (CH), 138.7 (C), 158.7 (C), 170.3 (C), 170.7 (C). HRMS (ESI) m/z: 331.1652 calcd for $C_{18}H_{23}N_2O_4^+$ $[M + H]^+$, found 331.1662.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http:// dx.doi.org/10.1016/j.tet…

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