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New Pyrazolium-carboxylates as Structural Analogues of the Pseudo-Cross-Conjugated Betainic Alkaloid Nigellicine

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Pyrazolium-3-carboxylates were examined as relatives of the betainic alkaloid Nigellicine and as new examples of the sparsely populated class 16 of heterocyclic pseudo-cross-conjugated mesomeric betaines (PCCMB). The title compounds were prepared in a 4-step procedure starting from β-diketo compounds **8** which were cyclized with substituted hydrazines. The resulting isomeric pyrazole esters **9** and **10** were separated and subsequently quaternized with dimethyl sulfate in the presence of nitrobenzene to pyrazolium esters **11** and **12**. Saponification was best accomplished in diluted sulfuric acid, which resulted in the formation of the pseudo-cross-conjugated mesomeric betaines **13** and **14** in one step. Protonation to the corresponding carboxylic acids required the treatment of the betaines with tetrafluoroboric acid in dichloromethane. The effect of negative solvatochromism proves the charge separation in the ground state of the molecules. X-ray crystallographic analyses, semiempirical calculations, and ESI mass spectrometric measurements were performed to gain knowledge about the phenomenon of pseudo-cross-conjugation.

Introduction

Alkaloids, which belong to the class of heterocyclic mesomeric betaines, form a relatively small group of natural products with interesting biological and chemical properties[1] between the large group of cationic alkaloids on one hand (e.g. pyridinium-, quinolinium-, and isoquinolinium-alkaloids) and the very small group of anionic alkaloids on the other.[2−4] Mesomeric alkaloid betaines are dipolar molecules with opposite charges delocalized within a common π-electron system. It has been recognized that heterocyclic mesomeric betaines can be divided into four major classes depending on their type of conjugation, i.e. conjugated (CMB), cross-conjugated (CCMB), pseudo-cross-conjugated (PCCMB) heterocyclic mesomeric betaines, and heterocyclic *N*-ylides which are related to CMB. A subdivision on the basis of the isoconjugate equivalents led to 4 subclasses, respectively, i.e. to at least 16 distinct structural classes of heterocyclic mesomeric betaines.[5] The charges in CMB are in mutual conjugation and common atoms for the negative and the positive charge can be realized by an inspection of the canonical formulas. Examples are the well-known five-membered mesoions such as sydnones,[6] münchnones,[7] and derivatives, and six-membered systems such as 1-alkyl-pyridinium-3-olates.[8] Most synthetic or natural heterocyclic mesomeric betaines known to date belong to this class of compounds,[1] which are versatile 1,3-dipoles[9] and valuable starting materials for heterocyclic synthesis.[10] *N*-Ylides (best represented as 1,2-dipoles) form the second class of heterocyclic mesomeric betaines. Several alkaloids belonging to this class of compounds have been isolated from natural sources.[1] In molecules which belong

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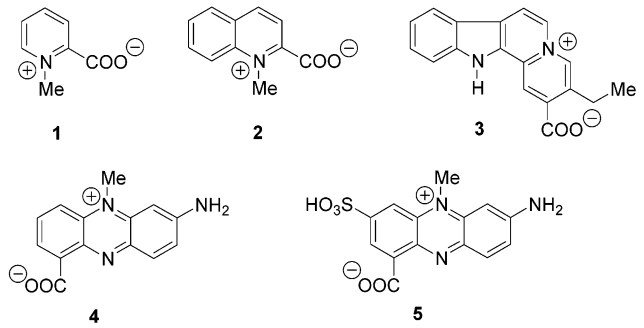
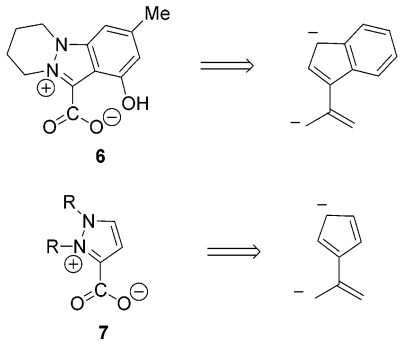
SCHEME 1. Alkaloids that Belong to the Class of Pseudo-Cross-Conjugated Heterocyclic Mesomeric Betaines



to the third class, i.e. cross-conjugated mesomeric betaines (CCMB), the positive and negative charges are delocalized in separated parts of the common π-electron system.[11] Very little information is available to date concerning stability as well as physical, biological, and chemical properties of pseudo-cross-conjugated systems (PCCMB) which form the fourth class of heterocyclic mesomeric betaines.[11] Nonetheless, the biological role of betainic alkaloids possessing this type of conjugation is apparent. The alkaloid Homarine **1** has been isolated from numerous marine organisms[1,12] and its biological role has been discussed intensively.[13] 1-Methylquinolinium-2-carboxylate (**2**), which belongs to the very rare class 13 of heterocyclic mesomeric betaines, has recently been identified as defense betaine from the fireflies *Photuris versicolor*.[14] Flavocarpine **3** (*Pleiocarpa mutica*)[15] and the closely related structures Vincarpine and Dihydrovincarpine (*Vinca major elegantissima*),[16] as well as Aeruginosine A **4** and B **5** (*Pseudomonas aeruginosa*),[17] are known pseudo-cross-conjugated betainic alkaloids.

On continuation of our work on heterocyclic mesomeric betaines,[18] including alkaloids and nucleobases,[19] we became interested in model compounds of the PCCMB-

SCHEME 2. Nigellicine 6 and Pyrazolium-3-carboxylates 7 as Its Electronically Relevant Partial Structure: Isoconjugate Relationships



alkaloid Nigellicine, isolated from the widely distributed herbaceous plant *Nigella sativa* L. (black cumin, "love in the mist"), which is used as a spice and for the treatment of various diseases.[20] Nigellicine belongs to the extremely rare class of indazole alkaloids. As it is isoconjugate to the 3-isopropenyl-1*H*-indene dianion it represents at the same time a member of class 16 of heterocyclic mesomeric betaines from which to the best of our knowledge only very few stable representatives have been described to date.[21]

The parent heterocyclic ring system of Nigellicine **6** is the pyrazolium-3-carboxylate, from which several canonical formulas can be drawn. Two of them possess electron-sextet structures without internal octet stabilization, which is characteristic for pseudo-cross-conjugated mesomeric betaines. Although these formulas have only a small contribution, if at all, to the overall electronic structure of the molecule, the charges are effectively, but obviously not exclusively delocalized in separated parts of the common π-electron system. The second characteristic feature of PCCMB is the masked 2-oxyallyl 1,3-dipole, which can be dissected from the canonical formulas.[11] Third, the negative partial structure of the pyrazolium-carboxylate is isoconjugate with an odd alternant hydrocarbon anion, the propenyl anion. It is typically joined by a *union bond* through the unstarred, i.e. even-numbered atom, to the cationic structure element.

We present here our results on syntheses and studies of pseudo-cross-conjugated pyrazolium-carboxylates as the electronically relevant partial structure of Nigellicine, structure elucidations by means of X-ray analyses, NOESY-NMR spectroscopy, and the results of semiempirical calculations.

Results and Discussion

The synthesis of the target compounds starts from 2,4-dioxo-pentanoic acid ethyl ester **8** (R^1 = Me) or the 2,4-dioxo-4-phenyl-butyric acid ethyl ester **8** (R^1 = Ph) which are readily available by Claisen-condensation of oxalic acid diethyl ester and 1-phenyl-ethanone or acetone,

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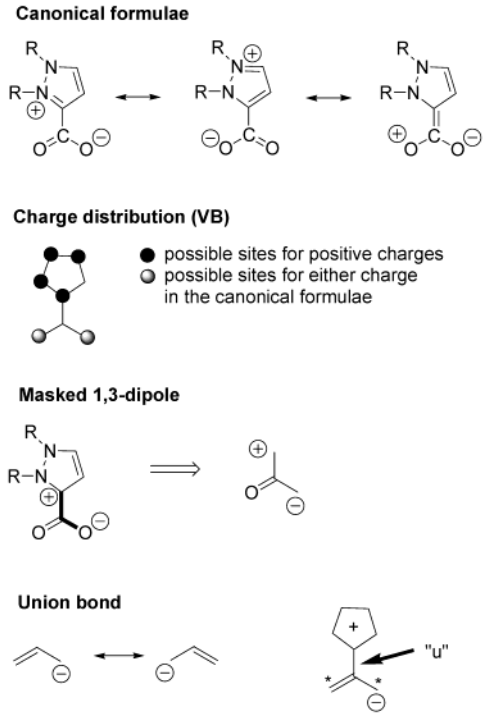
SCHEME 3. Canonical Formulas, Charge Distribution According to the VB Method, and Masked 1,3-Dipole of Pyrazolium-2-carboxylates as Characteristic Features of Pseudo-Cross-Conjugation[a]



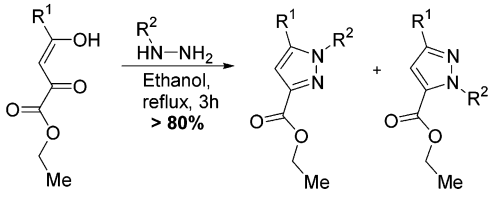
[a] An unstarred position of the isoconjugate equivalent of the anionic segment forms a union bond to the cationic partial structure

respectively.[22] These β-diketo compounds undergo reactions with methyl and phenyl hydrazine, yielding a 2:1 to 1:2 mixture of the two isomeric disubstituted pyrazole-3-carboxylic acid ethyl esters **9** and **10**, respectively. These are readily separable by column chromatography on silica gel. For unambiguous structure elucidation we performed a single-crystal X-ray analysis of **9a**, which allowed us to differentiate between the isomers by means of ^{1}H NMR spectroscopy. The ORTEP plot, given in the Supporting Information, shows an essentially planar molecule. Pyrazol ester **9a** was obtained as an oil that crystallized slowly. In ^{1}H NMR spectroscopy, the *N*-methyl group appears at δ 4.11 ppm. Its isomer **10a** is a pale yellow solid, the *N*-methyl group of which is detectable at δ 3.85 ppm. The esters **9b** and **10b** were obtained as brownish solids. Whereas the *N*-phenyl group of **9b** gives resonance frequencies at δ 7.34−7.50 ppm, the corresponding signals of **10b** were found at δ 7.36−7.45 ppm. Isomer **9c** is a yellow oil [δ(N−Me) 3.95 ppm], whereas **10c** forms a colorless solid [δ(N−Me) 4.23 ppm]. The two phenyl-substituted esters **9d** and **10d**, obtained as brownish solids, displayed no significant differences in the ^{1}H NMR spectra. All structure elucidations were later confirmed by NOESY spectroscopy performed on the target betaines (vide infra).

The *N*-methylation of the pyrazole esters proved to be difficult, as dimethyl sulfate, methyl trifluoromethylsulfonate ("magic methyl"), and trioxonium tetrafluoroborate failed even when vigorous reaction conditions were applied. The quaternization was finally successful with dimethyl sulfate in the presence of nitrobenzene. After heating samples **9b**,**c** and **10b** in a 2:1 mixture of *o*-xylene and nitrobenzene to 140 °C, addition of dimethyl sulfate to the warm solution, and additional heating for 2 h, the new pyrazolium esters **11b**,**c** and **12b** were obtained in high yields as brownish oils and could be used after aqueous workup without further purification. The phenyl derivatives **9d** and **10d**, however, did not react under these conditions, which is presumably due to steric reasons. They were recovered quantitatively. The pyrazole esters **9a** and **10a** decomposed to a black tar from which no identifiable compounds could be extracted. Saponification of the pyrazolium esters was best accomplished on heating **11b**,**c** an **12b** in 50% aqueous sulfuric acid and gave the target compounds in 32−80% yield for the two steps. The betaines could be extracted with nonpolar solvents such as dichloromethane or chloroform. Surprisingly, the betainic structures formed without deprotonation. In neither case were pyrazolium carboxylic acids obtained as hydrogensulfates or sulfates. No saponification could be observed in basic media.

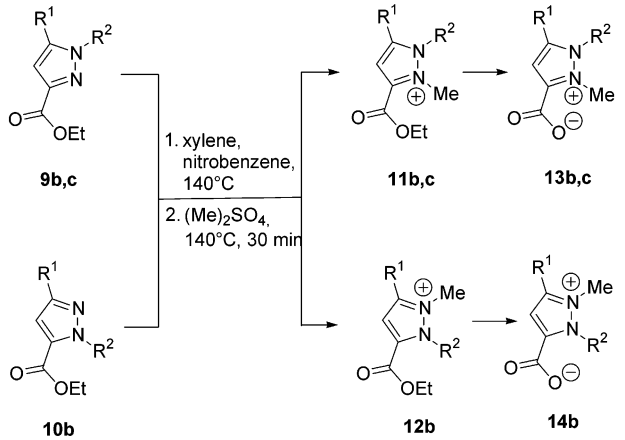
The new pseudo-cross-conjugated mesomeric betaines are stable, brownish to gray compounds at room temperature. Derivative **14b**, which forms a monohydrate on

SCHEME 4. Synthesis of Substituted Pyrazole Esters



9a/10a: $R^1 = R^2$ = Me;
9b/10b: R^1 = Me, R^2 = Ph;
9c/10c: R^1 = Ph, R^2 = Me;
9d/10d: $R^1 = R^2$ = Ph.

SCHEME 5. Quaternization and Saponification to the Target Betaines



9b/11b/13b: R^1 = Me, R^2 = Ph;
9c/11c/13c: R^1 = Ph, R^2 = Me;
10b/12b/14b: R^1 = Me, R^2 = Ph.

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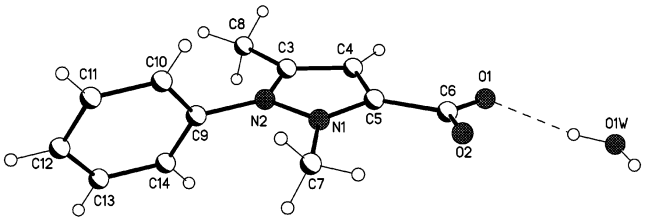
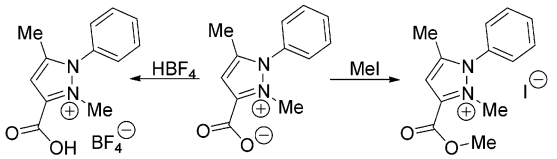


FIGURE 1. Results of the X-ray analysis on PCCMB **13b**.

SCHEME 6. Protonation and Methylation of the PCCMB



15 **13b** **16**

drying in vacuo, is hygroscopic and rapidly picks up water in moist air. For structure elucidation we performed NOESY-NMR spectroscopy, which unambiguously shows interactions between the two methyl groups in **14b**. The phenyl ring interacts with the *N*-methyl group, but not with the 5-methyl group. In contrast, in **13b** interactions of the phenyl group to either methyl group are detectable which are not influencing themselves.

For the sake of a NMR spectroscopic comparison between the betainic and cationic species, we tried protonations and methylations on a representative example, respectively. Conversion of the PCCMB **13b** into the corresponding acids in hydrochloric acid, sulfuric acid, and acetic acid failed. Reaction with tetrafluoroboric acid in dichloromethane, however, gave the 2,5-dimethyl-1-phenyl-pyrazolium-3-carboxylic acid **15** in good yield. The spectroscopic properties of the betaine and its protonated derivative differ significantly (cf. Experimental Section). Thus, the *N*-methyl groups of **13b** shift from δ 1.72 and 3.41 ppm to δ 2.39 and 4.20 ppm on protonation. Treatment of the betaine **13b** with a 5-fold excess of methyl iodide gave the ester **16** as a yellow crystalline solid in almost quantitative yield.

We were able to obtain single crystals of the PCCMB **13b** and performed an X-ray analysis (Figure 1). The betaine crystallizes with one molecule of water of crystallization, which forms a hydrogen bond of 192.2(13) pm length to the carboxylate oxygen atom. The pyrazole ring is essentially planar [$\tau_{min} = 0.17°$, $\tau_{max} = 0.68°$] and the methyl groups are located in the plane. In contrast to this, the carboxylate function is twisted about a torsion angle of $\tau = 167.57°$ [C(4)−C(5)−C(6)−O(2), crystallographic numbering] from the plane of the pyrazole. The bond length of the union bond predicted by the specific architecture of PCCMB (Scheme 3) between the positive and negative partial structures is 152.43(15) pm and is considerably longer than the corresponding bond in ester **9a** [147.46(17) pm]. In addition, due to steric hindrance to the methyl groups the phenyl ring is twisted by $\tau = 73.84°$ from planarity [N(1)−N(2)−C(9)−C(10)] and obviously is not involved in conjugation.

To prove the charge separation in the ground state of the molecules we examined the effect of negative solvatochromism. Indeed, with increasing solvent polarity the UV−vis absorption maxima of these compounds shift in a linear free enthalpy relationship to shorter wavelengths. This is mainly due to the decreasing permanent dipole moment on electronic excitation. The dipolar ground state is obviously better stabilized by polar than by nonpolar solvents, so that the absorption maxima of the compounds show a blue shift on changing polar solvents to nonpolar solvents. The dependence of the $\pi \rightarrow \pi^*$ transitions on the solvent polarity E_T^N between $E_T^N = 0.259$ (chloroform) and $E_T^N = 1.000$ (water) is presented in Figure 2. The absorption maxima were found between 277 and 245 nm depending on the solvent polarity. In agreement with this observation, the semiempirically calculated permanent dipole moment in the ground state is considerably larger than in the first excited state [$\Delta\mu$(PM3) = 4.7 D] (Figure 3).

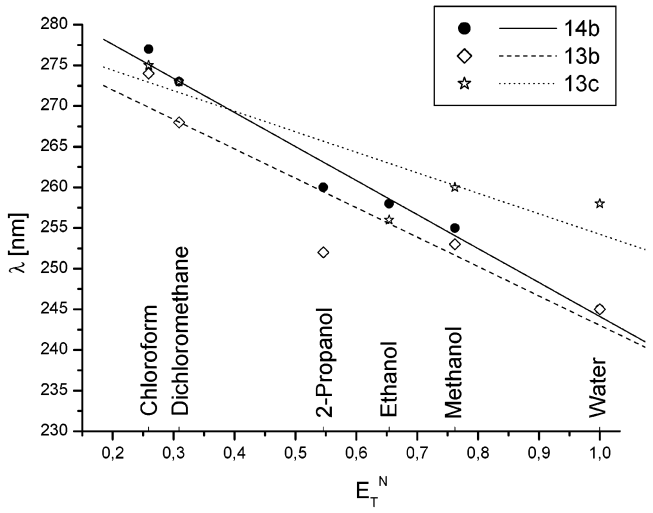


FIGURE 2. Effect of negative solvatochromism of the PCCMBs **13b**,**c** and **14b**.

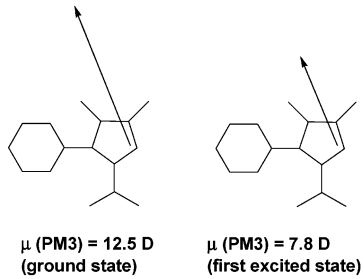


FIGURE 3. Semiempirically calculated dipole moments of the PCCMB **14b**.

Electrospray-ionization mass spectrometry (ESI-MS) proved to be a valuable tool to determine the betainic structures. The spectra were taken on spraying methanolic solutions of the betaines **13b**,**c** and **14b** from methanol.[23] As examples, the ESI mass spectra at 0 V fragmentor voltage display the peaks of the protonated betaine, i.e. the pyrazolium-3-carboxylic acid at *m*/*z* 217.0 amu (18%). The betaine gives a peak as sodium adduct at *m*/*z* 239 amu (82%). An additional prominent peak is

(23) The samples were dissolved in anhydrous MeOH and sprayed from MeOH. Capillary voltage 3000 V; drying gas temperature 300°C; 35 psig drying gas pressure; 0 V fragmentor voltage; direct injection.

FIGURE 4. Most stable conformation according to a semiempirical calculation on the PCCMB **14b.**

detectable at *m*/*z* 173 amu (62%), which corresponds to the decarboxylated derivative, i.e. the 2,5-dimethyl-1-phenyl-pyrazolium salt formed via an ylidic species. On increasing the fragmentor voltage to 20 and 40 V, the peak at 173 amu increases and forms the base peak of the spectrum as can be expected, whereas the peaks at *m*/*z* 217.0 and 239 decrease to the relative intensity of 7% and 30%, respectively. A dimerized ylide (2 × 172 amu) can be detected as protonated species at *m*/*z* 345 amu.

The betaines can unambiguously be differentiated from the corresponding protonated species **15**. Independent of the fragmentor voltage in the range between 0 and 40 V, the spectrum constists only of two peaks at *m*/*z* 217.1 (95%) and 433.1 amu (100%) which are due to the salt or to its dimer (*m*/*z* = 434/2 = 217 amu). The semideprotonated salt causes the second peak of the spectrum.

To gain additional insight into the electronic structure of the PCCMB, we performed semiempirical calculations[24] on the PCCMB **14b** and found a most stable conformation with the phenyl group twisted by 143.2° from planarity (ΔH_f (PM3) = 103.61 kJ/mol). The carboxyl group and the *N*-methyl group are twisted by 36.8° and 30.4° from the plane of the pyrazolium ring, respectively. Thus, the substituents do not adopt a propeller-like conformation. On one hand, steric hindrance between the *N*-methyl group and the phenyl ring causes the twisted conformation. On the other hand, an attractive interaction is observed between one carboxy oxygen and the aromatic C(2)−H group of the phenyl ring, which have a distance of 177.3 pm. The most stable conformation is presented in Figure 4.

As expected for a pseudo-cross-conjugated system, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) are essentially located in separated parts of the π-electron system (Figure 5). The anionic partial structure is joined to the cationic through a nodal position of the HOMO, which consists mainly of the lone pairs of the oxygen atoms. Thus, the carboxy carbon atom serves as an isolator, which prevents the charge neutralization in the ground state of the molecule. The resulting charge

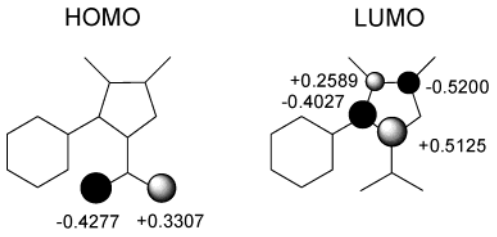


FIGURE 5. Frontier orbital profile of PCCMB **14b**.

separation in the ground state was proved by the effect of negative solvatochromism (Figure 2).

Experimental Section

Modified Procedure for the Preparation of 2,4-Dioxo-4-phenyl-butyric Acid Ethyl Ester (8) (R = Ph). A suspension of sodium (0.18 mol, 4.14 g) in 200 mL of anhydrous toluene was heated to approximately 80 °C and stirred vigorously, until the sodium was molten. After the mixture was cooled to 50 °C anhydrous ethanol was added slowly until all traces of sodium had reacted. The resulting emulsion, cooled to room temperature, was first treated dropwise with oxalic acid diethyl ester (0.15 mol, 20.3 mL) then with 1-phenyl-ethanone (0,15 mol, 17.5 mL), whereupon the color changed to brownish-red. The mixture was stirred overnight and then treated with 100 mL of concentrated acetic acid and water, respectively. The aqueous layer was extracted several times with diethyl ether and the combined organic layers and the etheral phases were concentrated in vacuo. On cooling to −20 °C, the precipitated product was finally recrystallized from methanol. The desired compound **8** (R = Ph) (0.14 mol, 31.85 g) was obtained as a yellow solid in 96.4% yield; mp 39−41 °C. ^{1}H NMR ($CDCl_3$) δ 7.99 (m, 2 H; Ar−H), 7.42−7.67 (m, 3 H; Ar−H), 7.08 (s, 1 H; CH), 4.40 (q, 2 H, J = 7.15 Hz; CH_2), 1.41 (t, 3 H, J = 7.15 Hz; CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 190.7, 169.8, 162.2, 134.9, 133.8, 128.9, 127.9, 98.0, 62.6, 14.1 ppm. The spectroscopic data are identical with the reported data.[22]

Preparation of 5-Methyl-1-phenyl-pyrazole-3-carboxylic Acid Ethyl Ester (9b) and 5-Methyl-2-phenyl-pyrazole-3-carboxylic Acid Ethyl Ester (10b). 2,4-Dioxo-4-phenyl-butyric acid ethyl ester (1.0 mmol, 0.14 mL) in 10 mL of ethanol was treated dropwise with phenyl hydrazine (1.2 mmol, 0.12 mL) and the resulting solution was heated at reflux temperature over a period of 3 h. After the mixture was cooled to room temperature, the solvent was distilled off in vacuo. The residue was purified by means of column chromatography (silica gel; petroleum ether:ethyl acetate 4:1). Ester **9b** (140 mg, 0.61 mmol; 60.8%) was isolated as a pale brownish solid; mp 37 °C. ^{1}H NMR ($CDCl_3$) δ 7.34−7.50 (m, 5 H; Ar−H), 6.73 (q, 1 H, J = 0.65 Hz; C*H*), 4.41 (q, 2 H, J = 7.13 Hz; CH_2), 2.32 (d, 3 H, J = 0.65 Hz; CH_3), 1.39 (t, 3 H, J = 7.13 Hz; CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 169.9, 144.1, 140.9, 139.5, 129.5, 128.9, 125.8, 109.5, 61.2, 14.8, 12.7 ppm; IR (KBr) 1721, 1235 cm^{-1}; MS (70 eV) *m*/*z* 77 (26.2%), 158 (100%), 185 (67.2%), 230 (50.8%). Anal. Calcd.: C, 67.81; N, 12.17; H, 6.13. Found: C, 67.87; N, 12.16; H, 6.10.

Ester **10b** (82 mg; 0.36 mmol; 35.6% yield) was isolated as a pale yellow solid; mp 39−40 °C; ^{1}H NMR ($CDCl_3$) δ 7.36−7.45 (m, 5 H; Ar−H), 6.81 (q, 1 H, J = 0.42 Hz; C*H*), 4.21 (q, 2 H, J = 7.13 Hz; CH_2), 2.35 (d, 3 H, J = 0.42 Hz; CH_3), 1.41 (t, 3 H, J = 7.13 Hz; CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 159.6, 149.3, 140.8, 134.3, 128.9, 128.8, 126.4, 112.5, 61.4, 14.4, 13.8 ppm; IR (KBr) 1732, 1286, 1234 cm^{-1} ; EIMS (70 eV) *m*/*z* 77 (45.9%), 158 (47.5%), 185 (63.9%), 230 (100%). Anal. Calcd.: C, 67.81; N, 12.17; H, 6.13. Found: C, 67.76; N, 12.22; H, 6.12.

Preparation of 3-Ethoxycarbonyl-1,5-dimethyl-2-phenyl-pyrazolium Sulfate (12b). Pyrazole ester **10b** (2.24 g, 9.7 mmol) was dissolved in a mixture of 20 mL of *o*-xylene and 10 mL of nitrobenzene and heated at 140 °C over a period of 2 h.

(24) Semiempirical calculations were carried out with MOPAC 6.0[25] on a IBM workstation RS/6000, AIX V 4.3 to perform the PM3 calculations.[26] The structures were first optimized with the default gradient requirements and subsequently refined with the options EF DMAX = 0.01, GNORM = 0.01, SCFCRT = 1 × 10^{-10}. The absolute minima were proved by a force calculation. The first exited state was calculated with the ground-state geometry and the option EXITED.

(25) Stewart, J. J. P. *QPCE*, No 455, Department of Chemistry, Bloomington, IN, 1989.

(26) Stewart, J. J. P. *J. Comput. Chem*. **1989**, *10*, 209.

The reaction mixture was then treated with dimethyl sulfate (10 mL, 10.5 mmol), heated for an additional hour to 140 °C, and stirred overnight at room temperature. The reaction mixture was then treated with 40 mL of water and stirred for 30 min. The organic layer was separated and the aqueous layer was extracted several times with 10 mL of diethyl ether, respectively. The aqueous layer was then evaporated to dryness to give a brown oil of pyrazolium sulfate **12b** (2.05 g, 6.0 mmol, 61.8%). ^{1}H NMR (DMSO-d_6) δ 7.83−7.64 (m, 5 H; Ar−H), 7.54 (s, 1 H; C*H*), 4.18 (q, 2 H, J = 7.12 Hz; CH_2), 3.68 (s, 3 H; CH_3), 2.60 (s, 3 H; CH_3), 1.01 (t, 3 H, J = 7.12 Hz; CH_3) ppm; ^{13}C NMR (DMSO-d_6) δ 155.9, 148.4, 136.7, 132.5, 132.3, 129.8, 128.7, 111.5, 62.5, 35.1, 13.4, 11.9 ppm; ESIMS *m*/*z* 217.1 (25.7%), 231.1 (62.8%), 245.1 (100%) amu.

Preparation of 1,5-Dimethyl-2-phenyl-pyrazolium-3-carboxylate (14b). Pyrazolium ester **12b** (2.05 g, 6.0 mmol) was dissolved in a mixture of 20 mL of water and 30 mL of concentrated sulfuric acid and heated at reflux temperature over a period of 7 h. The mixture was then neutralized with aqueous sodium hydroxide and then evaporated to dryness. The betaine was extracted from the residue with dichloromethane and chloroform and purified on silica gel (petroleum ether:ethyl acetate 4:1) by means of column chromatography. The betaine was obtained as a yellow solid (1.615 g, 5.8 mmol, 96.7%); decomposition at 101−104 °C. ^{1}H NMR ($CDCl_3$) δ 7.61−7.40 (m, 5 H; Ar−H), 6.74 (s, 1 H; C*H*), 3.60 (s, 3 H; CH_3), 2.52 (s, 3 H; CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 158.1, 149.5, 146.7, 133.4, 131.5, 129.9, 128.5, 108.6, 34.2, 12.5 ppm; ESIMS *m*/*z* 173.1 (41.2%), 217.1 (100%), 239.1 (20.3%), 345.1 (14.2%), 389.1 (10.57%), 433.1 (33.8%), 455.1 (28.4%) amu; IR (KBr) 3130, 1631, 1238 cm^{-1}. Anal. Calcd. for 1.5 mol of water of crystallization: C, 59.24; N, 11.51; H, 6.21. Found: C, 58.65; N, 11.00; H, 5.91.

Preparation of 3-Carboxy-2,5-dimethyl-1-phenyl-pyrazolium Tetrafluoroborate (15). A solution of betaine **13b** (100 mg, 0.46 mmol) in dichloromethane was cooled to 0 °C and then treated with tetrafluoroboric acid (40%, 1 mL). After the mixture was stirred for 30 min at 0 °C the resulting precipitate was filtered off and washed with dichloromethane. The carboxylic acid was obtained as a colorless solid (51 mg, 0.17 mmol, 37.0% yield); decomposition at 265−268 °C. ^{1}H NMR (DMSO-d_6) δ 7.92−7.60 (m, 5 H; Ar−H), 7.44 (s, 1 H; C*H*), 3.94 (s, 3 H; CH_3), 2.26 (s, 3 H; CH_3) ppm; ^{13}C NMR (DMSO-d_6) δ 158.6, 147.4, 138.4, 132.9, 130.7, 130.3, 128.6, 110.7, 37.0, 12.0 ppm; ESIMS *m*/*z* 217.1 (100%), 245.1 (68.7%), 589.0 (39.0%) amu; IR (KBr) 2983, 1644, 1041 cm^{-1}.

Preparation of 3-Methoxycarbonyl-2,5-dimethyl-1-phenyl-pyrazolium Iodide (16). A solution of the betaine **13b** (50 mg, 0.23 mmol) in dichloromethane was treated dropwise with methyl iodide (5 equiv, 0.07 mL) and heated at reflux temperature for 2 h. After evaporation to dryness the ester was obtained as a yellow solid in quantitative yield (82 mg, 0.23 mmol); decomposition at 145−147 °C. ^{1}H NMR ($CDCl_3$) δ 7.84−7.60 (m, 5 H; Ar−H), 7.24 (s, 1 H; C*H*), 4.20 (s, 3 H; CH_3), 4.04 (s, 3 H; CH_3), 2.39 (s, 3 H; CH_3) ppm; ^{13}C NMR ($CDCl_3$) δ 157.3, 148.4, 138.0, 133.4, 131.1, 130.2, 129.3, 111.7, 54.0, 38.5, 13.3 ppm; ESIMS *m*/*z* 217.1 (97.3%), 433.1 (100%) amu; IR (KBr) 1741, 1495, 1252 cm^{-1}. Anal. Calcd.: C, 43.59; N, 7.82; H, 4.22. Found: C, 44.70; N, 7.94; H, 4.84.

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Supporting Information Available: Experimental details, spectroscopic data, ^{1}H NMR spectra of all new compounds. X-ray data, and ORTEP plots. This material is available free of charge via the Internet at http://pubs.acs.org.

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