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Rearrangements of N-Heterocyclic Carbenes of Pyrazole to 4-Aminoquinolines and Benzoquinolines

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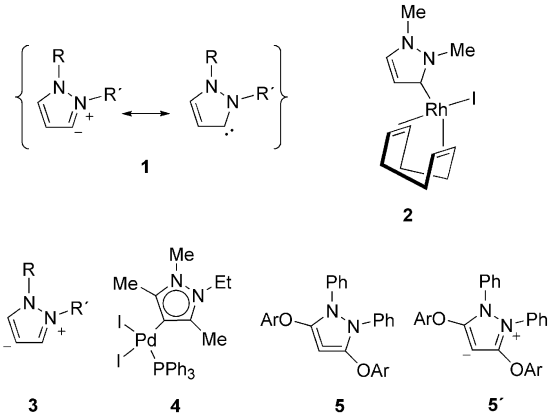
1-Phenyl-substituted pyrazolium salts, formed by quaternization of pyrazoles with benzyl halides or long-chain alkyl halides, deprotonate to pyrazol-3-ylidenes that undergo a sequence of ring-opening, ring-closure, and tautomerization to new substituted 4-aminoquinolines. Similarly, 1-naphthyl-substituted pyrazolium-3-carboxylates decarboxylate on heating in toluene to give benzoquinolines in excellent yields by an analogous reaction pathway. DFT calculations indicate that the ring transformation proceeds through a sequence of intramolecular elimination, imine inversion and 6π-electrocyclization steps.

Introduction

The advance of N-heterocyclic carbenes (NHC) has become one of the most significant developments in modern organic chemistry.[1] The first complexes of imidazolin-2-ylidenes were prepared and isolated as early as 1968 by Öfele and Wanzlick,[2] and, shortly later, Lappert and coworkers described metal complexes of imidazolidin-2-ylidenes.[3] The isolation of stable N-heterocyclic carbenes by Arduengo et al. in 1991,[4] however, initiated intensive investigations into the physical properties,[5] coordination chemistry,[6] and catalytic properties.[7] N-Heterocyclic carbenes have now emerged as a class of ligands with outstanding properties, largely due to their performance in metal-catalyzed reactions such as cross-couplings[8] and second-generation olefin metathesis.[9] In addition, they play important roles in organocatalysis.[10] In contrast to N-heterocyclic carbenes of imidazole,[4] imidazoline,[11] triazole,[12] and benzimidazoline,[12,13] hitherto, less interest has focused on N-heterocyclic carbenes of pyrazole[14] and indazole.[15] Pyrazol-3-ylidene **1** was described as a rhodium complex **2** in 1997,[16] and was identified spectroscopically and by trapping reactions[17] (Scheme 1). In addition, catalytic activities of Iridium,[18] Ruthenium[19] and palladium complexes[20] have been examined. Structure **4** represents a palladium complex of the *remote* N-heterocyclic carbene **3** (*r*NHC[21]), which displays catalytic activities in Suzuki–Miyaura and Mizoroki–Heck reactions.[22] This species has recently been described as a cyclic allene, such as **5**, possessing electron-donating groups in positions **3** and **5** of the pyrazole ring.[23] The zwitterionic structure **5′** has been discussed as an alternative representation of this compound.[24]



Scheme 1. N-Heterocyclic carbenes of pyrazole.

Recently, we described the initial results of a new rearrangement of pyrazol-3-ylidenes **1** (R = Ph or substituted phenyl rings), generated in situ either by thermal decarboxylation of pyrazolium-3-carboxylates or by deprotonation of pyrazolium salts, to new 4-aminoquinolines.[25] Such compounds are of great interest in Malaria research as they represent new substitution patterns and related structures of chloroquine, amodiaquine, and other anti-malarials. Indeed, some new derivatives of 4-aminoquinolines have proven to be highly active,[26] including ring-annelated systems.[27] Simplified, the mechanism of this new rearrange-

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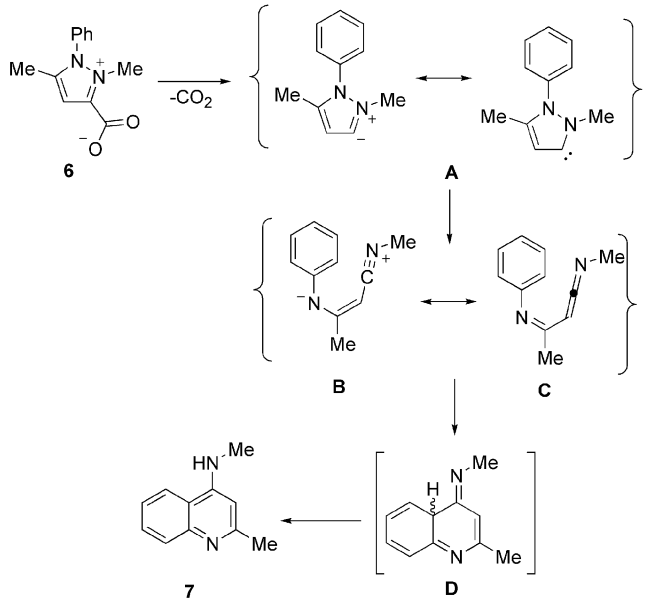
ment can be formulated as shown in Scheme 2: The N-heterocyclic carbene **A**, which is generated in situ, undergoes ring-cleavage to an intermediate that can be represented by two canonical formulae, **B** and **C**. Ring-closure of this intermediate to **D** requires an unsubstituted 2-position of the phenyl ring in the 1-position of the starting material. Intermediate **D** tautomerizes to 4-aminoquinoline **7**. The ring-closure can be regarded either as electrophilic aromatic substitution from **B**, or as a 6π-electrocyclization of the non-polar structure **C**. No experimental evidence has been available to establish the nature of this ring closure.



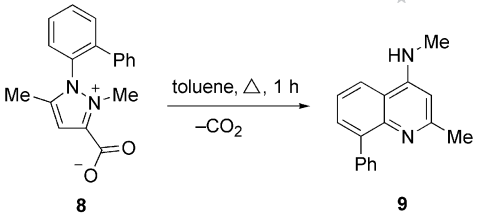
Scheme 2. Rearrangement of pyrazolium-3-carboxylates to 4-aminoquinolines via N-heterocyclic carbenes of pyrazole.

Our first results revealed that this metal-free thermal reaction, which requires no special handling, allows the synthesis of a broad variety of substituted 4-aminoquinolines, among these: bis-, tris-, tetrakis-, and pentakis-substituted derivatives.[25] The scope and limitations of this approach are, however, not yet known.

In a continuation of our interest in N-heterocyclic carbenes in synthesis[28] and catalysis,[29] and in view of the great pharmacological interest in new 4-aminoquinolines and related ring systems, we present here new suitable starting materials for this reaction. DFT calculations offer valuable insights into the mechanism of this new rearrangement.

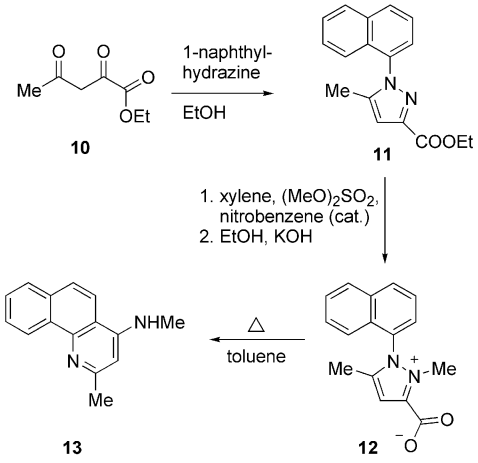
Results and Discussion

One unsubstituted *ortho*-position of the phenyl substituent in position 1 of the starting pyrazolium-3-carboxylate is the *conditio sine qua non* of the thermal decarboxylation/rearrangement sequence to 4-aminoquinolines. Thus, the biphenyl-substituted pyrazolium-3-carboxylate **8**, which is a new representative of the class of pseudo-cross-conjugated heterocyclic mesomeric betaines (PPCMB), gives 8-phenylquinolin-4-amine **9** in 83% yield on heating in toluene (Scheme 3).



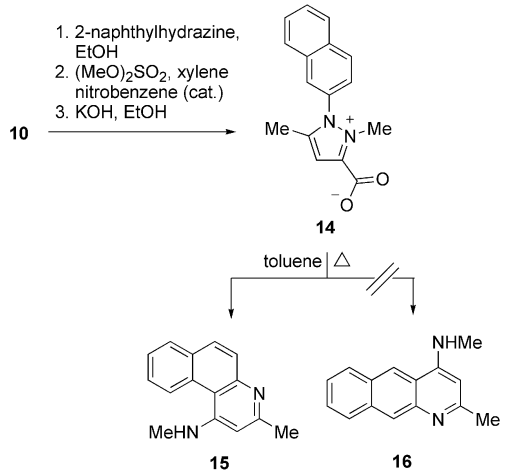
Scheme 3. Synthesis of 4-aminoquinolines.

Next, we became interested in the synthesis of enlarged ring systems. We therefore started a sequence of reactions with the condensation of 1-naphthyl hydrazine and the 2,4-dioxoester **10** to give pyrazole ester **11**, which proceeded in 53% yield. Its isomeric species was easily separated by column chromatography in 9% yield. Methylation, followed by ester cleavage gave the pyrazolium betaine **12** in excellent yield (98%) as a stable yellow solid. On heating in toluene, rearrangement to the benzo[*h*]quinolin-4-amine **13** occurred in 93% yield (Scheme 4).



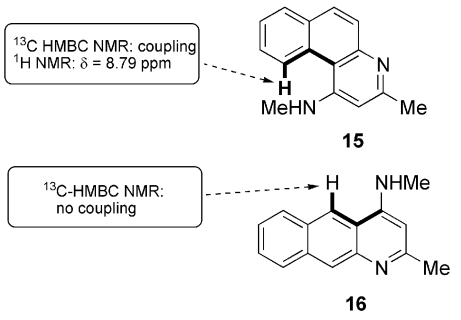
Scheme 4.

An analogous series of reactions was performed starting from 2-naphthyl hydrazine, which was subsequently converted into the pyrazole betaine **14** (Scheme 5). Only one

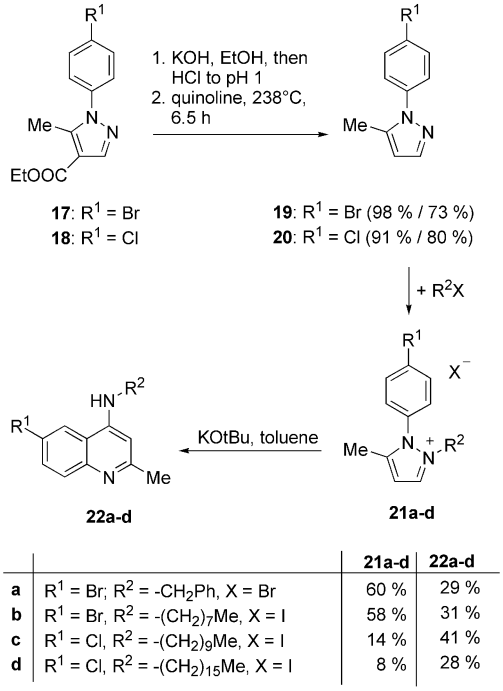


Scheme 5. Regioselective rearrangement to benzo[*f*]quinolin-1-amine.

product was formed by rearrangement in 77% yield: benzo[*f*]quinoline-1-amine **15**. No traces of the isomeric benzo[*g*]quinolin-4-amine **16** were isolated. Scheme 6 shows some diagnostic NMR results, which were obtained by a series of NOESY, HMBC, and HSQC NMR measurements for unambiguous peak assignments. Thus, in agreement with structure **15**, 10-H couples to C-10b as shown, and the resonance frequency of 10-H is shifted downfield as predicted. On the other hand, no coupling is observed between 5-H and C-4 as would be present in the hypothetical structure **16**.



Scheme 6. Diagnostic NMR results.



		21a-d	22a-d
a	R^1 = Br; R^2 = -CH_2Ph, X = Br	60 %	29 %
b	R^1 = Br, R^2 = -$(CH_2)_7$Me, X = I	58 %	31 %
c	R^1 = Cl, R^2 = -$(CH_2)_9$Me, X = I	14 %	41 %
d	R^1 = Cl, R^2 = -$(CH_2)_{15}$Me, X = I	8 %	28 %

Scheme 7. Rearrangements starting from pyrazolium salts.

Only a very few pieces of information on pyrazolium salts are available in the literature. We therefore started a series of reactions as follows: Ester cleavage of the pyrazole esters **17** and **18** followed by decarboxylation in quinoline gave the pyrazoles **19** and **20**, respectively, in very good yields (Scheme 7). According to a modified literature procedure,[30] pyrazole **19** was treated with benzyl bromide under microwave conditions to give the benzyl-substituted pyrazolium salt **21a** in good yield. We next tried to quaternize **19** and **20** with long-chain aliphatic residues. Thus, substitution starting from iodooctane was accomplished on heating to 140 °C over a period of 11 h to give the salt **21b** in 58% yield. The reaction with iododecane, however, required a longer reaction time, a higher temperature and gave a considerably lower yield of the desired pyrazolium salt **21c**. Because thermal conditions failed, microwave irradiation was then applied to quaternize pyrazole **20** with iodohexadecane to give **21d**; the yield, however, was low. Rearrangements of **21a**–**d** to the new 4-aminoquinolines **22a**–**d** (Scheme 7) were accomplished by mixing potassium *tert*-butoxide with the corresponding pyrazolium salts, and adding these mixtures to boiling anhydrous toluene. In spite of only moderate yields for the rearrangement, this approach enabled the synthesis of 4-aminoquinolines possessing benzyl or long-chain alkyl groups at the amino group.

To obtain further insights into the mechanism of these rearrangements, we carried out quantum chemical calculations for the reaction pathway depicted in Scheme 2.

Starting from **6**, the C–C bond was found to be cleaved directly in a single step to yield **A** + CO_2. This process is endergonic and occurs without any kinetic barrier (i.e., the reverse reaction of **A** + CO_2 to **6** is barrierless). The predicted endergonicity for the CO_2 dissociation is fairly large (ΔG = +18.1 kcal/mol); however, the equilibrium between **6** and **A** + CO_2 is shifted towards **A** if carbon dioxide is removed from the solution, which is the case under the applied reaction conditions.

For the initial step of the reaction, we also considered the possibility of N–N cleavage before or along with the CO_2 extrusion; the latter pathway would correspond to a Grob-type fragmentation. Our attempts to find transition states for these pathways were unsuccessful, which corroborates the idea that carbene **A** is indeed an intermediate in the overall process.

The results of our computations for the further steps from **A** towards product **7** are summarized in Figure 1 in the form of a solvent-phase free energy diagram. The N–N bond of **A** can be cleaved via the low-lying transition state $\mathbf{TS}_{N-N}$, producing the *E* isomer of intermediate **C**. The *cis*–*trans* isomerism barrier arises due to the π-bonds in **C** causing restricted rotation around the C=N moiety.[31] Subsequent cyclization can only proceed from the *Z*-**C** isomer, an inversion of the imine nitrogen is therefore required ($\mathbf{TS}_{C=N}$). Starting from *Z*-**C**, two different transition states for C–C bond formation can be identified ($\mathbf{TS}_{C-C,E}$ and $\mathbf{TS}_{C-C,Z}$, Figure 2). The two pathways correspond to attack on two different atoms of the phenyl group, and lead to two cyclized products (*E*-**D** and *Z*-**D**) differing in the resulting configuration of a C=N bond, which was initially part of the azaallenic system. Interestingly, the higher-lying transition state leads to the lower-lying product.

A proton transfer, which was not investigated in detail, may ultimately convert *E*-**D** and *Z*-**D** into **7**, with a large gain in free energy and loss of stereochemical information.

Beyond revealing the reaction pathway, our calculations provided the possibility of a deeper understanding of the

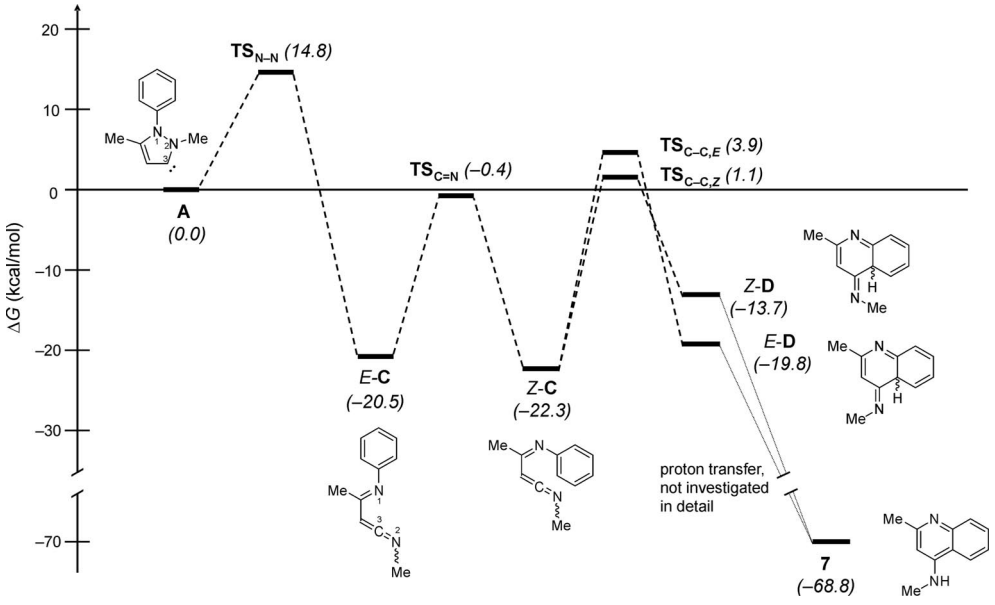


Figure 1. Calculated solvent-phase Gibbs free energy profile for the conversion of **A** into **7**. Atom numbering used in text is indicated.

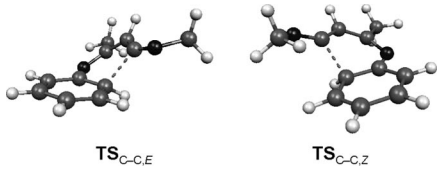


Figure 2. Geometries of the ring-closing transition states **TS**$_{C–C,E}$ and **TS**$_{C–C,Z}$.

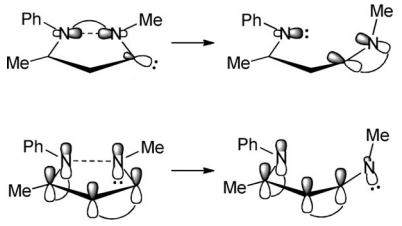


Figure 3. Reorganization of σ (top) and π (bottom) electrons of **A** upon ring opening. Curved lines and dots indicate bonding and nonbonding pairs according to one of the high-weight resonance forms.

mechanism through an analysis of the structural and electronic properties. Starting on the reactant side of this rearrangement process, a simple heterolytic C–C bond breaking in **6** initiates the reaction. The resulting carbene **A** has a five-membered ring with almost planar ring atoms (the smallest sum of angles is 354.1° at N1), which indicates a significant degree of cyclic π-delocalization, i.e., a high contribution of the zwitterionic resonance forms.

A remarkable feature of the ring-opening reaction of **A** is that the C3–N2–Me angle first significantly increases, then decreases again along the reaction route (**A**: 126.5°, **TS**$_{N–N}$: 134.2°, maximum along the intrinsic reaction coordinate: ca. 139°, *E*-**C**: 125.2°). This observation might be rationalized if one considers the reorganization of electrons, as shown in Figure 3.

The N–N σ-bond is cleaved upon interaction with the carbene lone pair, in a process resembling the second step of a unimolecular elimination with a conjugate base (E1cB). The 5-orbital, 6-electron cyclic π-system undergoes a simple, smooth cleavage to an open-chain structure. The two participating orbitals on N2 allow this atom to continuously keep a significant degree of bonding both in the σ and in the π systems, which provides a rationale for the low barrier. The widening angle around the TS comes about as a consequence of the rehybridization that takes place to maintain efficient overlap between the two systems.

The resulting open-chain π-system in **C** can be represented as azaallene–imine (**C**) or nitrilium–enamide (**B**) type resonance forms (see Scheme 2). As mentioned in the introduction, the two different forms imply two different mechanistic scenarios for the ring-closing step via **TS**$_{C–C}$ (electrocyclization and electrophilic aromatic substitution for **C** and **B**, respectively). To discriminate between these extremes or characterize the situation as an intermediate between them, we inspected the computed geometry of **C** (Figure 4). The calculated bond lengths suggest a markedly larger contribution from the nonpolar, azaallene–imine structure; the ring closure is thus expected to proceed through a 6 (or 10) electron electrocyclization.

In an attempt to confirm the above descriptions of π-system transformations, we calculated nucleus independent chemical shift (NICS)[32,33] values above the breaking and forming rings[34,35] along the reaction pathway.[36] Ring currents in aromatic systems cause magnetic shielding above and below the ring, which is manifested in significantly negative NICS values; no such effect is expected for nonaromatic rings.[33]

The computed curve for the ring-opening of **A** via **TS**$_{N–N}$ shows a continuous decrease in π-aromaticity that is

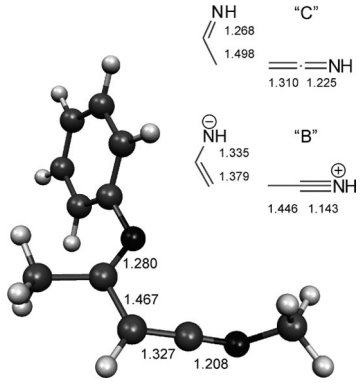


Figure 4. Computed geometry of intermediate *E*-**C**. Calculated bond lengths (Å) of some model compounds formally corresponding to parts of resonance structures **B** and **C** are also given for comparison. Similar results were obtained for *Z*-**C**.

consistent with a gradual cyclic to acyclic transition (Figure 5). In contrast, results for both C–C bond forming pathways show a characteristic minimum near the TS in the NICS versus reaction coordinate plot. Symmetry-allowed pericyclic reactions are known to possess aromatic transition states[37] yielding such minima;[33,36,38] the present ring-closing reaction can thus be concluded to exhibit a significant degree of pericyclic character.

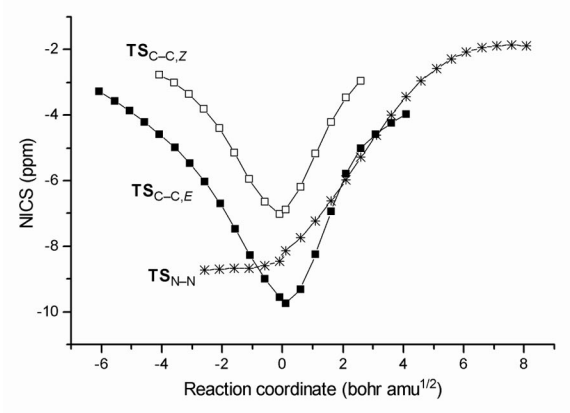


Figure 5. NICS values as a function of the intrinsic reaction coordinate for ring-opening via $\mathbf{TS}_{N-N}$ and ring-closing reactions via $\mathbf{TS}_{C-C,E}$ and $\mathbf{TS}_{C-C,Z}$.

Conclusions

In summary, we have investigated the scope and limitations of a new rearrangement of N-heterocyclic carbenes of pyrazole generated in situ, to 4-aminoquinolines and benzoquinolines. The mechanism of the ring transformation was elucidated by calculating the reaction pathway and analyzing the computed geometric, electronic, and magnetic properties. The ring-opening step was found to be an intramolecular E1cB-like elimination, whereas the ring-closure proceeds through a pericyclic reaction; the overall pathway also involves an imine nitrogen inversion.

Experimental Section

General: Compounds **17** and **19** were prepared as described before.[25] The ^{1}H and ^{13}C NMR spectra were recorded with Bruker Avance DPX 200 (200 MHz), Avance 400 (400 MHz), or Avance III (600 MHz) spectrometers and samples were analyzed in [D$_6$]-DMSO, D$_2$O, or CDCl$_3$ at 200, 400, or 600 MHz, respectively. The chemical shifts are reported in ppm relative to internal tetramethylsilane (δ = 0.00 ppm) or HDO (δ = 4.65 ppm). Multiplicities are described by the following abbreviations: s = singlet, d = doublet, t = triplet, m = multiplet; br. = broad. Peak assignments were accomplished by analyzing the results of HMBC-, HSQC-NMR and HH-NOESY measurements. FTIR spectra were obtained with a Bruker Vektor 22 in the range of 400 to 4000 cm^{-1} (2.5% pellets in KBr). The GC–MS spectra (EI) were recorded either with a Varian 320 GC-MS, or with a Varian GC3900 with a SAT2100T mass spectrometer. The ESI mass spectra were measured with an Agilent LCMSD Series HP1100 with APIES. Samples were sprayed from methanol at 0 V fragmentor voltage unless otherwise noted. Melting points were determined with a Boëtius melting apparatus. Yields are not optimized.

1-(Biphenyl-2-yl)-2,5-dimethylpyrazolium-3-carboxylate (8): A sample of ethyl 2,4-dioxopentanoate (1.020 g, 6.45 mmol) was dissolved in ethanol (10 mL), treated with (biphenyl-2-yl)hydrazine (1.188 g, 6.45 mmol), and heated for 1 h at reflux temperature. The solvent was then distilled off in vacuo and the resulting residue was purified by chromatography (petroleum ether/ethyl acetate, 3:1) to give ethyl 1-(biphenyl-2-yl)-5-methylpyrazole-3-carboxylate (44%, 0.860 g) as an orange oil. Its isomer (18%, 0.347 g) was also isolated. ^{1}H NMR (400 MHz, 21 °C, CDCl$_3$, TMS): δ = 7.46–7.55 (m, 4 H, *H*Bp), 7.23–7.27 (m, 3 H, *H*Bp), 7.08–7.11 (m, 2 H, *H*Bp), 6.49 (s, 1 H, 4-*H*), 4.42 (q, *J* = 7.1 Hz, 2 H, CH$_3$C*H*$_2$O), 1.67 (s, 3 H, 5-C*H*$_3$), 1.41 (t, *J* = 7.1 Hz, 3 H, C*H*$_3$CH$_2$O) ppm. ^{13}C NMR (100 MHz, 21 °C, CDCl$_3$, TMS): δ = 162.8, 143.7, 141.7, 139.1, 137.8, 136.8, 130.5, 129.9, 128.9, 128.5, 128.4, 128.3, 127.6, 108.3, 60.9, 14.5, 11.2 ppm. IR (NaCl): $\tilde{\nu}$ = 1732, 1717, 1485, 1432, 1374, 1228, 1152, 1107, 1029, 777, 739, 702 cm^{-1}. HRMS (ESI): calcd. for C$_{19}$H$_{19}$N$_2$O$_2$ [M + H]$^+$ 307.1447; found 307.1443. A sample of this ester (0.784 g, 2.56 mmol) was dissolved in xylene (10 mL) containing one drop of nitrobenzene, and treated with dimethyl sulfate (0.24 mL, 2.56 mmol). After heating at reflux temperature for 2 h and cooling to room temp., the solvent was distilled off in vacuo. The residue was dissolved in 50% sulfuric acid (15 mL) and heated at reflux temperature over a period of 7 h, then neutralized with NaOH, evaporated to dryness, and extracted with EtOH (6 × 10 mL). The solvent was then distilled off and the residue was purified by chromatography (MeOH) to give a beige solid (91%, 0.677 g); m.p. 133 °C (dec.). ^{1}H NMR (400 MHz, 21 °C, [D$_6$]-DMSO): δ = 7.87–7.90 (m, 2 H, *H*Bp), 7.75–7.78 (m, 2 H, *H*Bp), 7.38–7.40 (m, 3 H, *H*Bp), 7.08–7.10 (m, 2 H, *H*Bp), 6.74 (s, 1 H, 4-*H*), 3.96 (s, 3 H, 2-C*H*$_3$), 2.05 (s, 3 H, 5-CH$_3$) ppm. ^{13}C NMR (100 MHz, 21 °C, [D$_6$]DMSO): δ = 156.9, 147.4, 145.9, 140.5, 135.9, 133.1, 131.8, 130.3, 129.7, 129.0, 128.6, 128.2, 127.8, 108.8, 35.4, 11.8 ppm. IR (KBr): $\tilde{\nu}$ = 3479, 1661, 1646, 1481, 1438, 1330, 836, 793, 752, 704 cm^{-1}. HRMS (ESI): calcd. for C$_{18}$H$_{17}$N$_2$O$_2$ [M + H]$^+$ 293.1290; found 293.1290.

***N*,2-Dimethyl-8-phenylquinolin-4-amine (9):** A sample of betaine **8** (205 mg, 0.7 mmol) was suspended in toluene (4 mL) and heated at reflux temperature for 1 h. The solvent was then distilled off in vacuo and the residue was purified by chromatography (MeOH/EtOAc, 1:1). Compound **9** was obtained as a yellow solid (83%, 0.145 g); m.p. 223–224 °C. ^{1}H NMR (600 MHz, 21 °C, CDCl$_3$, TMS): δ = 8.14 (dd, *J* = 8.4, 1.3 Hz, 1 H, *H*Qu), 7.62–7.64 (m, 2

H, *H*Ph), 7.54 (dd, *J* = 7.0, 1.3 Hz, 1 H, *H*Qu), 7.39–7.43 (m, 3 H, *H*Qu, *H*Ph), 7.32–7.35 (m, 2 H, *H*Ph, *H*N), 6.33 (s, 1 H, 3-*H*), 2.89 (d, *J* = 4.2 Hz, 3 H, H_3CN), 2.41 (s, 3 H, 2-CH_3) ppm. ^{13}C NMR (150 MHz, 21 °C, $CDCl_3$, TMS): δ = 158.6, 151.8, 145.4, 140.9, 139.3, 131.1, 130.3, 127.9, 127.0, 123.4, 121.5, 118.3, 98.3, 29.9, 26.0 ppm. IR (KBr): $\tilde{\nu}$ = 3399, 1597, 1543, 1443, 1387, 1364, 1242, 1217, 1189, 1118, 1016, 813, 759, 702 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{17}N_2$ [M + H]$^+$ 249.1392; found 249.1392.

Ethyl 5-Methyl-1-(naphthalen-1-yl)pyrazole-3-carboxylate (11): A sample of ethyl 2,4-dioxopentanoate (1.237 g, 7.82 mmol) was dissolved in ethanol (10 mL), treated with naphthalen-1-ylhydrazine (1.237 g, 7.82 mmol), and heated for 1 h at reflux temperature. The solvent was then distilled off in vacuo and the resulting residue was purified by chromatography (petroleum ether/ethyl acetate, 3:1) to give a yellow solid (53%, 1.162 g). Its isomer (9%, 0.205 g) was also isolated; m.p. 91–92 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$, TMS): δ = 7.99 (d, *J* = 8.0 Hz, 1 H, *H*Np), 7.93 (d, *J* = 8.0 Hz, 1 H, *H*Np), 7.46–7.58 (m, 4 H, *H*Np), 7.21 (d, *J* = 8.0 Hz, 1 H, *H*Np), 6.85 (d, *J* = 0.5 Hz, 1 H, 4-*H*), 4.43 (q, *J* = 7.2 Hz, 2 H, CH_3CH_2O), 2.10 (d, *J* = 0.5 Hz, 3 H, 5-CH_3), 1.40 (t, *J* = 7.2 Hz, 3 H, CH_3CH$_2$O) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$, TMS): δ = 162.8, 144.2, 142.6, 135.4, 134.1, 130.4, 130.1, 128.2, 127.7, 126.8, 125.5, 125.0, 122.6, 108.2, 61.0, 14.5, 11.5 ppm. ESI-MS: *m*/*z* (%) = 281.1 (50) [M + H]$^+$. IR (KBr): $\tilde{\nu}$ = 1707, 1480, 1446, 1426, 1398, 1382, 1233, 1191, 1162, 1106, 1022, 976, 806, 776 cm^{-1}. $C_{17}H_{16}N_2O_2 \cdot 0.5H_2O$ (280.33): calcd. C 70.57, H 5.92, N 9.68; found C 70.79, H 5.32, N 9.66.

2,5-Dimethyl-1-(naphthalen-1-yl)pyrazolium-3-carboxylate (12): A sample of compound **11** (1.068 g, 3.81 mmol) was dissolved in xylene (10 mL) containing one drop of nitrobenzene, and treated with dimethyl sulfate (0.36 mL, 3.81 mmol). After heating at reflux temperature for 2 h, and cooling to room temp., the solvent was distilled off in vacuo. The residue was dissolved in ethanol (10 mL) and then treated with KOH (0.641 g, 11.43 mmol). The solution was heated at reflux temperature over a period of 2 h, then neutralized with HCl, evaporated to dryness, and then extracted with EtOH (6 × 10 mL). The solvent was then distilled off and the residue was purified by chromatography (MeOH) to give a yellow solid (98%, 1.042 g); m.p. 122 °C (dec.). ^{1}H NMR (400 MHz, 21 °C, [D$_6$]DMSO): δ = 8.40 (d, *J* = 8.4 Hz, 1 H, *H*Np), 8.22 (dd, *J* = 7.4, 1.4 Hz, 1 H, *H*Np), 8.09 (dd, *J* = 7.4, 1.0 Hz, 1 H, *H*Np), 7.84 (dd, *J* = 8.4, 7.4 Hz, 1 H, *H*Np), 7.68–7.77 (m, 2 H, *H*Np), 7.12 (dd, *J* = 8.4, 1.0 Hz, 1 H, *H*Np), 7.03 (s, 1 H, 4-*H*), 3.90 (s, 3 H, 2-CH_3), 2.09 (s, 3 H, 5-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, [D$_6$]-DMSO): δ = 157.3, 148.1, 146.7, 133.8, 133.0, 129.6, 129.3, 129.2, 129.0, 127.8, 126.7, 126.0, 120.4, 108.9, 34.9, 11.4 ppm. IR (KBr): $\tilde{\nu}$ = 3419, 1647, 1489, 1418, 1335, 1239, 843, 818, 779, 746 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{15}N_2O_2$ [M + H]$^+$ 267.1134; found 267.1136.

***N*,2-Dimethylbenzo[*h*]quinolin-4-amine (13):** A sample of betaine **12** (266 mg, 1.0 mmol) was suspended in toluene (4 mL) and heated at reflux temperature for 1 h. The solvent was then distilled off in vacuo and the residue was purified by chromatography (MeOH/EtOAc, 1:1). Compound **13** was obtained as a brown solid (93%, 0.207 g); m.p. 109–110 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$, TMS): δ = 9.30 (dd, *J* = 8.3, 1.3 Hz, 1 H, *H*Bq), 7.83 (dd, *J* = 8.3, 1.3 Hz, 1 H, *H*Bq), 7.66 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1 H, *H*Bq), 7.64 (d, *J* = 9.0 Hz, 1 H, *H*Bq), 7.61 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1 H, *H*Bq), 7.54 (d, *J* = 9.0 Hz, 1 H, *H*Bq), 6.45 (s, 1 H, 3-*H*), 5.04 (q, *J* = 5.2 Hz, 1 H, *H*N), 2.99 (d, *J* = 5.2 Hz, 3 H, H_3CN), 2.72 (s, 3 H, 2-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$, TMS): δ = 158.3, 151.0, 145.8, 133.5, 131.6, 127.5, 127.5, 126.6, 125.0, 124.6, 117.0, 113.2, 100.5, 30.1, 25.8 ppm. IR (KBr): $\tilde{\nu}$ = 3394, 1623, 1596, 1565, 1540, 1448, 1360, 1288, 1145, 1078, 818, 797, 756, 717 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{15}N_2$ [M + H]$^+$ 223.1235; found 223.1235.

2,5-Dimethyl-1-(naphthalen-2-yl)pyrazolium-3-carboxylate (14): A sample of ethyl 2,4-dioxopentanoate (0.593 g, 3.75 mmol) was dissolved in ethanol (10 mL), treated with naphthalen-2-ylhydrazine (0.593 g, 3.75 mmol), and heated for 1 h at reflux temperature. The solvent was then distilled off in vacuo and the resulting residue was purified by chromatography (petroleum ether/ethyl acetate, 3:1) to give ethyl 5-methyl-1-(naphthalen-2-yl)pyrazole-3-carboxylate (60%, 0.630 g) as a brown solid. Its isomer (26%, 0.271 g) was also isolated; m.p. 77–78 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$, TMS): δ = 7.87–7.95 (m, 4 H, *H*Np), 7.53–7.60 (m, 3 H, *H*Np), 6.78 (d, *J* = 0.8 Hz, 1 H, 4-*H*), 4.43 (q, *J* = 7.2 Hz, 2 H, CH_3CH_2O), 2.38 (d, *J* = 0.8 Hz, 3 H, 5-CH_3), 1.41 (t, *J* = 7.2 Hz, 3 H, CH_3CH$_2$O) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$, TMS): δ = 162.7, 144.1, 140.8, 136.6, 133.0, 132.8, 129.2, 128.2, 127.9, 127.1, 127.0, 124.0, 123.4, 109.4, 61.0, 14.4, 12.5 ppm. ESI-MS: *m*/*z* (%) = 281.1 (100) [M + H]$^+$. IR (KBr): $\tilde{\nu}$ = 2979, 1719, 1598, 1510, 1478, 1447, 1388, 1235, 1150, 1099, 1026, 869, 833, 773, 749 cm^{-1}. $C_{17}H_{16}N_2O_2$ (280.33): calcd. C 72.84, H 5.75, N 9.99; found C 72.61, H 5.68, N 9.86.

A sample of this ester (0.510 g, 1.82 mmol) was dissolved in xylene (10 mL) containing one drop of nitrobenzene, and treated with dimethyl sulfate (0.17 mL, 1.82 mmol). After heating at reflux temperature for 2 h and cooling to room temp., the solvent was distilled off in vacuo. The residue was dissolved in ethanol (10 mL) and then treated with KOH (0.306 g, 5.46 mmol). The solution was heated at reflux temperature over a period of 2 h, then neutralized with HCl, evaporated to dryness, and then extracted with EtOH (6 × 10 mL). The solvent was distilled off and the residue was purified by chromatography (MeOH) to give **14** as a beige solid (88%, 0.425 g); m.p. 137 °C (dec.). ^{1}H NMR (400 MHz, 21 °C, [D$_6$]DMSO): δ = 8.45 (s, 1 H, *H*Np), 8.27 (d, *J* = 8.8 Hz, 1 H, *H*Np), 8.14 (d, *J* = 8.0 Hz, 1 H, *H*Np), 8.08 (d, *J* = 8.0 Hz, 1 H, *H*Np), 7.70–7.81 (m, 3 H, *H*Np), 6.91 (s, 1 H, 4-*H*), 4.05 (s, 3 H, 2-CH_3), 2.22 (s, 3 H, 5-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, [D$_6$]DMSO): δ = 157.4, 147.5, 145.8, 133.8, 132.5, 130.4, 129.3, 128.7, 128.7, 128.3, 128.0, 127.7, 124.8, 108.6, 35.5, 11.9 ppm. IR (KBr): $\tilde{\nu}$ = 3406, 1645, 1435, 1335, 831, 788, 757 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{15}N_2O_2$ [M + H]$^+$ 267.1134; found 267.1131.

***N*,2-Dimethylbenzo[*f*]quinolin-4-amine (15):** A sample of betaine **14** (266 mg, 1.0 mmol) was suspended in toluene (4 mL) and heated at reflux temperature for 1 h. The solvent was then distilled off in vacuo and the residue was purified by chromatography (MeOH/EtOAc, 1:1). Compound **15** was obtained as a yellow solid (77%, 0.172 g); m.p. 150–151 °C. ^{1}H NMR (600 MHz, 21 °C, $CDCl_3$, TMS): δ = 8.79 (dd, *J* = 8.4, 1.2 Hz, 1 H, *H*Bq), 7.89 (dd, *J* = 8.0, 1.5 Hz, 1 H, *H*Bq), 7.82 (s, 2 H, *H*Bq), 7.56 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1 H, *H*Bq), 7.51 (ddd, *J* = 8.0, 7.0, 1.2 Hz, 1 H, *H*Bq), 6.55 (s, 1 H, 3-*H*), 5.55 (q, *J* = 5.4 Hz, 1 H, *H*N), 2.99 (d, *J* = 5.4 Hz, 3 H, H_3CN), 2.66 (s, 3 H, 2-CH_3) ppm. ^{13}C NMR (150 MHz, 21 °C, $CDCl_3$, TMS): δ = 158.0, 153.6, 149.1, 131.8, 130.2, 129.6, 129.2, 128.5, 126.5, 125.3, 123.9, 112.8, 102.3, 30.9, 25.0 ppm. ESI-MS: *m*/*z* (%) = 223.1 (100) [M + H]$^+$. IR (KBr): $\tilde{\nu}$ = 3341, 1625, 1584, 1557, 1531, 1506, 1447, 1389, 1350, 1207, 997, 836, 759 cm^{-1}. $C_{15}H_{14}N_2 \cdot H_2O$ (222.29): calcd. C 74.97, H 6.71, N 11.66; found C 74.93, H 6.36, N 12.22.

Ethyl 1-(4-Chlorophenyl)-5-methylpyrazole-4-carboxylate (18): A sample of ethyl 2-(dimethylamino)methylen-3-oxobutanoate (870 mg, 4.702 mmol) was dissolved in ethanol (16 mL) with (4-chlorophenyl)hydrazine (670 mg, 4.702 mmol) and stirred for 2.5 h

at 78 °C. After cooling, the solvent was distilled off and the resulting residue was purified by chromatography (silica gel; petroleum ether/ethyl acetate, 8:1) to give **18** as an orange solid (80%, 1.033 g); m.p. 56 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 8.02 (s, 1 H, 3-*H*), 7.48 (d, *J* = 8.4 Hz, 2 H, *H*Ar), 7.38 (d, *J* = 8.4 Hz, 2 H, *H*Ar), 4.33 (q, *J* = 7.1 Hz, 2 H, CH_3CH_2O), 2.57 (s, 3 H, 5-CH_3), 1.38 (t, *J* = 7.1 Hz, CH_3CH_2O) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 163.7, 143.6, 142.2, 137.4, 134.5, 129.5, 126.7, 113.3, 60.1, 14.4, 12.0 ppm. IR (KBr): $\tilde{\nu}$ = 3072, 3001, 2981, 2939, 2906, 1713, 1558, 1504, 1414, 1228, 1099, 1021, 832, 772 cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_{14}ClN_2O_2$ $[M + H]^+$ 265.0744; found 265.0745.

1-(4-Chlorophenyl)-5-methylpyrazole (20) – A. Ester Cleavage: A sample of ethyl 1-(4-chlorophenyl)-5-methylpyrazole-4-carboxylate (3.089 g, 11.680 mmol) was dissolved in ethanol (40 mL) with KOH (1.962 g, 35.040 mmol) and stirred for 3.5 h at 78 °C. The solvent was distilled off in vacuo and the residue was dissolved in H_2O (50 mL) and acidified to pH 1 with HCl. The resulting 1-(4-chlorophenyl)-5-methylpyrazole-4-carboxylic acid was filtered and washed with water (80 mL), and finally dried to give a white solid (91%, 2.516 g); m.p. 195 °C. ^{1}H NMR (400 MHz, 21 °C, [D_6]-DMSO): δ = 12.76 (s, 1 H, O*H*), 7.98 (s, 1 H, 3-*H*), 7.63–7.57 (AA′BB′, *J* = 8.9 Hz, 4 H, *H*Ar), 2.51 (s, 3 H, 5-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 164.4, 143.4, 141.8, 137.4, 133.0, 129.3, 127.0, 113.2, 11.4 ppm. IR (KBr): $\tilde{\nu}$ = 2972, 2693, 2606, 2361, 2343, 1698, 1663, 1562, 1501, 1290, 1255, 1095, 936, 830, 781 cm^{-1}. HRMS (ESI): calcd. for $C_{11}H_{10}ClN_2O_2$ $[M + H]^+$ 237.0431; found 237.0427.

B. Decarboxylation: A sample of 1-(4-chlorophenyl)-5-methylpyrazole-4-carboxylic acid (2.492 g, 10.537 mmol) was mixed with quinoline (2.845 mL, 24.235 mmol) and stirred for 6.5 h at 238 °C. The reaction mixture was then purified by chromatography (silica gel; petroleum ether/ethyl acetate, 8:1) to give a light-brown liquid (80%, 1.600 g). ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 7.60 (d, *J* = 1.2 Hz, 1 H, 3-*H*), 7.48–7.42 (AA′BB′, *J* = 8.5 Hz, 4 H, *H*Ar), 6.23 (d, *J* = 1.2 Hz, 1 H, 4-*H*), 2.37 (s, 3 H, 5-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 140.2, 138.7, 138.5, 133.3, 129.2, 126.0, 107.3, 12.5 ppm. IR (NaCl): $\tilde{\nu}$ = 1545, 1500, 1468, 1444, 1410, 1389, 1206, 1095, 1011, 921, 833, 780, 537 cm^{-1}. HRMS (ESI): calcd. for $C_{10}H_{10}ClN_2$ $[M + H]^+$ 193.0533; found 193.0531.

2-Benzyl-1-(4-bromophenyl)-5-methylpyrazolium Bromide (21a): A sample of 1-(4-bromophenyl)-5-methylpyrazole (**19**; 153 mg) was dissolved in benzyl bromide (1.7 mL) and then subjected to microwave irradiation under vigorous stirring. Conditions were as follows: 10 min at 120 °C, 10 min at 130 °C, 20 min at 140 °C, then 70 min at 150 °C (max. power: 400 W). The reaction mixture was then purified by chromatography (silica gel; dichloromethane/EtOH, 9:1) to give a colorless solid (60%, 0.157 g); m.p. 170 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 9.22 (d, *J* = 2.9 Hz, 1 H, 3-*H*), 7.67 (d, *J* = 8.7 Hz, 2 H, *H*Ar), 7.44 (d, *J* = 8.7 Hz, 2 H, *H*Ar), 7.28–7.24 (m, 3 H, *H*Ar), 7.00 (d, *J* = 6.9 Hz, 2 H, *H*Ar), 6.77 (s, *J* = 2.9 Hz, 1 H, 4-*H*), 5.80 (s, 2 H, CH_2), 2.27 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 148.7, 139.7, 134.0, 131.7, 130.8, 129.7, 129.4, 129.3, 128.6, 127.6, 108.3, 55.5, 12.8 ppm. IR (KBr): $\tilde{\nu}$ = 3109, 3051, 2988, 2929, 1635, 1532, 1516, 1484, 1456, 1402, 1387, 1363, 1222, 1186, 1070, 1004, 834, 705, 696, 551 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{16}BrN_2$ $[M]^+$ 327.0497; found 327.0491.

1-(4-Bromophenyl)-5-methyl-2-octylpyrazolium Iodide (21b): A sample of 1-(4-bromophenyl)-5-methylpyrazole (**19**; 105 mg) was dissolved in 1-iodooctane (532 mg, 2.214 mmol) and stirred for 11 h at 140 °C. After cooling, the mixture was purified by chromatography (silica gel; dichloromethane/EtOH, 15:1) to give a colorless solid (58%, 122 mg); m.p. 122 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 8.72 (d, *J* = 3.0 Hz, 1 H, 3-*H*), 7.85 (d, *J* = 8.7 Hz, 2 H, *H*Ar), 7.76 (d, *J* = 8.7 Hz, 2 H, *H*Ar), 6.81 (d, *J* = 3.0 Hz, 1 H, 4-*H*), 4.35 (t, *J* = 7.6 Hz, 2-CH_2), 2.34 (s, 3 H, 5-CH_3), 1.79–1.72 (m, 2 H, *H*Alk), 1.26–1.19 (m, 10 H, *H*Alk), 0.86 (t, *J* = 6.8 Hz, 3 H, Alk-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 148.4, 138.3, 134.5, 130.9, 129.5, 128.0, 108.7, 52.0, 31.7, 29.1, 29.0, 28.8, 26.1, 22.7, 14.2, 13.2 ppm. IR (KBr): $\tilde{\nu}$ = 3084, 3018, 2954, 2925, 2855, 1695, 1636, 1518, 1487, 1467, 1397, 1226, 1069, 1007, 842, 785 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{26}BrN_2$ $[M]^+$ 349.1279; found 349.1269.

1-(4-Chlorophenyl)-2-decyl-5-methylpyrazolium Iodide (21c): A sample of 1-(4-chlorophenyl)-5-methylpyrazole (**20**; 400 mg, 2.078 mmol) was dissolved in 1-iododecane (2.786 g, 10.390 mmol) and stirred for 48 h at 132 °C. After cooling, the mixture was purified by chromatography (silica gel; dichloromethane/ethanol, 15:1) to give a light-brown solid (14%, 0.133 g); m.p. 56.8 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 8.64 (d, *J* = 2.7 Hz, 1 H, 3-*H*), 7.78–7.59 (AA′BB′, *J* = 8.7 Hz, 4 H, *H*Ar), 6.72 (d, *J* = 2.7 Hz, 1 H, 4-*H*), 4.22 (t, *J* = 7.6 Hz, 2 H, 2-CH_2-Alk), 2.27 (s, 3 H, 5-CH_3), 1.64 (quint, *J* = 7.6 Hz, 2 H, *H*Alk), 1.16–1.06 (m, 14 H, *H*Alk), 0.75 (t, *J* = 7.0 Hz, 3 H, Alk-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 148.5, 139.3, 138.0, 131.3, 130.7, 128.6, 108.5, 51.6, 31.7, 29.3, 29.1, 29.0, 28.6, 25.9, 22.5, 14.0, 13.3 ppm. IR (KBr): $\tilde{\nu}$ = 3457, 3078, 3021, 2925, 2854, 1516, 1491, 1464, 1391, 1091, 1009, 845 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{30}ClN_2$ $[M]^+$ 333.2098; found 333.2094.

1-(4-Chlorophenyl)-2-hexadecyl-5-methylpyrazolium Iodide (21d): A sample of 1-(4-chlorophenyl)-5-methylpyrazole (250 mg, 1.299 mmol) was dissolved in 1-iodohexadecane (2.289 g, 6.494 mmol) and then subjected to microwave irradiation under vigorous stirring. Conditions were as follows: 30 min at 130 °C, 30 min at 150 °C, 70 min at 170 °C, 35 min at 180 °C, 240 min at 190 °C, then 420 min at 200 °C. The mixture was then purified by chromatography (silica gel; dichloromethane/ethanol, 15:1) to give a brown solid (8%, 0.057 g); m.p. 79 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 8.70 (d, *J* = 2.5 Hz, 1 H, 3-*H*), 7.84–7.68 (AA′BB′, *J* = 8.7 Hz, 4 H, *H*Ar), 6.81 (d, *J* = 2.5 Hz, 1 H, 4-*H*), 4.34 (t, *J* = 7.5 Hz, 2 H, 2-CH_2-Alk), 2.34 (s, 3 H, 5-CH_3), 1.76 (qu, *J* = 7.2 Hz, 2 H, *H*Alk), 1.34–1.19 (m, 26 H, *H*Alk), 0.88 (t, *J* = 6.5 Hz, 3 H, Alk-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 148.4, 139.7, 138.2, 131.4, 130.7, 128.8, 108.6, 51.9, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.1, 28.8, 26.1, 22.7, 14.1, 13.1 ppm. IR (KBr): $\tilde{\nu}$ = 3425, 2920, 2851, 1512, 1493, 1467, 1441, 1383, 1234, 1090, 837, 822 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{42}ClN_2$ $[M]^+$ 417.3037; found 417.3036.

***N*-Benzyl-6-bromo-2-methylquinolin-4-amine (22a):** A sample of 2-benzyl-1-(4-bromophenyl)-5-methylpyrazolium bromide (**21a**; 60 mg, 0.147 mmol) was mixed with potassium *tert*-butoxide (19 mg, 0.176 mmol) and added rapidly into hot anhydrous toluene (2 mL). Heating at reflux temperature was continued for 1 h. After cooling, the solvent was distilled off and the resulting residue was purified by chromatography (silica gel; MeOH/EtOAc, 1:10) to give **22a** (29%, 0.014 g); m.p. 195 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 7.84 (d, *J* = 2.1 Hz, 1 H, 5-*H*), 7.81 (d, *J* = 8.9 Hz, 1 H, 8-*H*), 7.67 (dd, *J* = 8.9, 2.1 Hz, 1 H, 7-*H*), 7.42–7.36 (m, 5 H, *H*Ar), 6.39 (s, 1 H, 3-*H*), 5.15 (s, 1 H, N*H*), 4.51 (d, *J* = 5.1 Hz, 2 H, CH_2), 2.58 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 160.0, 148.9, 146.7, 137.3, 132.6, 130.7, 129.1, 128.1, 127.8, 122.3, 118.8, 117.8, 100.3, 47.7, 25.7 ppm. IR (KBr): $\tilde{\nu}$ = 2924, 1631, 1590, 1562, 1488, 1445, 1410, 1350, 1249, 1128, 826,

572 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{16}BrN_2$ $[M + H]^+$ 327.0497; found 327.0494.

6-Bromo-*N*-octyl-2-methylquinolin-4-amine (22b): A sample of pyrazolium salt **21b** (60 mg, 0.26 mmol) was mixed with potassium *tert*-butoxide (36 mg, 0.32 mmol) and added rapidly to a hot solution of anhydrous toluene (2 mL). Heating at reflux temperature was continued for 1 h, and then the solvent was distilled off in vacuo and the residue was purified by chromatography (silica gel; MeOH/ethyl acetate, 1:8) to give **22b** (31%, 0.027 g); m.p. 95 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 7.85 (d, J = 1.7 Hz, 1 H, 5-*H*), 7.78 (d, J = 8.9 Hz, 1 H, 8-*H*), 7.64 (dd, J = 8.9, 1.7 Hz, 1 H, 7-*H*), 6.31 (s, 1 H, 3-*H*), 5.01 (s, 1 H, N*H*), 3.28 (q, J = 7.0 Hz, N-CH_2), 2.60 (s, 3 H, 2-CH_3), 1.80–1.72 (m, 2 H, CH_2), 1.49–1.25 (m, 10 H, *H*Alk), 0.90 (t, J = 6.9 Hz, 3 H, Alk-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 159.8, 149.3, 146.4, 132.6, 130.4, 122.2, 118.7, 117.6, 99.7, 43.5, 31.9, 29.5, 29.3, 29.0, 27.3, 25.5, 22.8, 14.2 ppm. IR (KBr): $\tilde{\nu}$ = 2924, 2853, 2361, 1634, 1587, 1560, 1466, 1412, 1355, 1314, 1249, 1197, 1081, 994, 827, 668, 558 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{25}BrN_2$ $[M]^+$ 348.1201; found 348.1199.

6-Chloro-*N*-decyl-2-methylquinolin-4-amine (22c): A sample of 2-decyl-5-methyl-1-(4-chlorophenyl)pyrazolium iodide (**21c**; 51 mg, 0.111 mmol) was mixed with potassium *tert*-butoxide (12.4 mg (0.111 mmol) and added rapidly to a hot solution of anhydrous toluene (2 mL). Heating at reflux temperature was continued for 1 h and then the solvent was distilled off in vacuo and the residue was purified by chromatography (silica gel; ethyl acetate) to give **22c** (41%, 0.015 g) as a brown solid; m.p. 77 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 7.84 (d, J = 8.9 Hz, 1 H, 5-*H*), 7.66 (d, J = 2.2 Hz, 1 H, 8-*H*), 7.51 (dd, J = 8.9, 2.2 Hz, 1 H, 7-*H*), 6.32 (s, 1 H, 3-*H*), 4.87 (s, 1 H, N*H*), 3.28 (t, J = 7.3 Hz, 2 H, N-CH_2-Alk), 2.60 (s, 3 H, 5-CH_3), 1.75 (quint, J = 7.3 Hz, 2 H, *H*Alk), 1.46 (quint, J = 7.3 Hz, 2 H, *H*Alk), 1.39–1.24 (m, 12 H, *H*Alk), 0.88 (t, J = 6.8 Hz, 3 H, Alk-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 149.1, 146.4, 130.5, 129.8, 129.5, 118.7, 118.1, 99.6, 43.3, 31.9, 29.6, 29.4, 29.3, 28.9, 27.2, 25.6, 22.7, 14.1 ppm. IR (KBr): $\tilde{\nu}$ = 3431, 3241, 3061, 2927, 2851, 1589, 1562, 1464, 1411, 1358, 1259, 1091, 840, 829 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{30}ClN_2$ $[M + H]^+$ 333.2098; found 333.2096.

6-Chloro-*N*-hexadecyl-2-methylquinolin-4-amine (22d): A sample of 2-hexadecyl-5-methyl-1-(4-chlorophenyl)pyrazolium iodide (**21d**; 33 mg, 0.061 mmol) was mixed with potassium *tert*-butoxide (8.0 mg, 0.072 mmol) and added rapidly to a hot solution of anhydrous toluene (2 mL). Heating at reflux temperature was continued for 1 h, and then the solvent was distilled off in vacuo. The residue was then purified by chromatography (silica gel; ethyl acetate) to give **22d** (28%, 0.007 g) as a brown solid; m.p. 79 °C. ^{1}H NMR (400 MHz, 21 °C, $CDCl_3$): δ = 7.85 (d, J = 8.9 Hz, 1 H, 5-*H*), 7.66 (d, J = 2.1 Hz, 1 H, 8-*H*), 7.52 (dd, J = 7.5, 2.2 Hz, 1 H, 7-*H*), 6.32 (s, 1 H, 3-*H*), 4.88 (s, 1 H, N*H*), 3.28 (t, J = 7.3 Hz, 2 H, N-CH_2-Alk), 2.61 (s, 3 H, 5-CH_3), 1.76 (quint, J = 7.3 Hz, 2 H, *H*Alk), 1.47 (quint, J = 7.3 Hz, 2 H, *H*Alk), 1.39–1.26 (m, 24 H, *H*Alk), 0.88 (t, J = 6.8 Hz, 3 H, Alk-CH_3) ppm. ^{13}C NMR (100 MHz, 21 °C, $CDCl_3$): δ = 159.7, 149.1, 130.4, 129.8, 129.6, 118.7, 118.0, 99.6, 43.4, 32.0, 29.7, 29.6, 29.4, 28.9, 27.2, 25.5, 22.7, 14.2 ppm. IR (KBr): $\tilde{\nu}$ = 3431, 2926, 2849, 1591, 1561, 1523, 1475, 1460, 1408, 1374, 1253, 1192, 1131, 1087, 990, 881, 840, 823, 811, 731 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{42}ClN_2$ $[M + H]^+$ 417.3034; found 417.3037.

Computational Details: The Gaussian 03 software package[39] was used throughout this study. Stationary points of the potential energy surface were located at the M05–2X/6-31G* level of density functional theory,[40,41] and their nature (minimum or first-order saddle point) was confirmed by harmonic vibrational analysis at the same level (having 0 and 1 imaginary frequency, respectively). Thermodynamic corrections were estimated from unscaled frequencies, using standard formulae in the ideal gas – rigid rotor – harmonic oscillator approximation as implemented in Gaussian, and refer to a standard state of 298.15 K and 1 mol/dm^3 concentration. Relative electronic energies were determined using single-point M05–2X/6-311++G** calculations.[42,43] Free energies of solvation were estimated from the IEF-PCM model[44] with M05-2X/6-31G* wave function, using the in vacuo optimized geometries, UA0 radii, and toluene as solvent. Reported energy values refer to relative Gibbs free energies of solvated species, but the same qualitative trends could be obtained using solely the electronic energies (see comparison in the Supporting Information). Transition states were further analyzed by intrinsic reaction coordinate (IRC) calculations.[45] These usually failed before reaching the respective minima, but they revealed a significant portion of the path. Aromaticity was studied using NICS values[33] calculated 1 Å above the geometrical centers of the forming rings, on the opposite side to the hydrogen atom of the attacked phenyl carbon or to the N2-methyl group. These points were chosen in order to assess the effect of π-electrons, and to minimize the disturbance of the σ-framework.[34,35] Single-point GIAO-B3LYP/6-31+G* calculations[41,43,46,47] were used for this purpose. All DFT calculations were carried out with the "ultrafine" integration grid consisting of 99 radial shells and 590 angular points per shell.

Supporting Information (see also the footnote on the first page of this article): Comparison of electronic and free energies, Cartesian coordinates and total energies of all calculated stationary points.

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