A Novel Pathway to Imidazo[1,2-*a*]pyridines. Access through Imino Pyridinium Salts

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A new synthetic strategy for the preparation of imidazo[1,2-*a*]pyridines **10** is reported, which is based on the electrocyclization reaction of imino pyridinium salts **7** upon treatment with a strong base. The starting materials are easily prepared from 2-aminopyridine (**3**) by imine condensation and subsequent alkylation at the pyridine nitrogen atom. The ring closure reaction of the zwitterionic intermediate **8** to give a five-membered ring proceeds in low yield forming first the dihydro compound **9**, which under the reaction conditions is transformed into the corresponding aromatic compounds **10** and **11** by air oxidation. The mechanism of the electrocyclization reaction is interpreted in detail by quantum-chemical calculations.

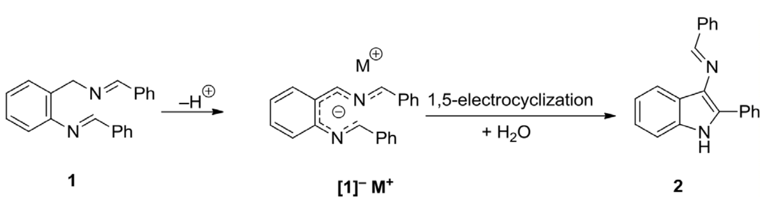
Key words: Imines, Pyridinium Salts, Electrocyclization, Imidazo[1,2-*a*]pyridines, Quantum-chemical Calculations

Introduction

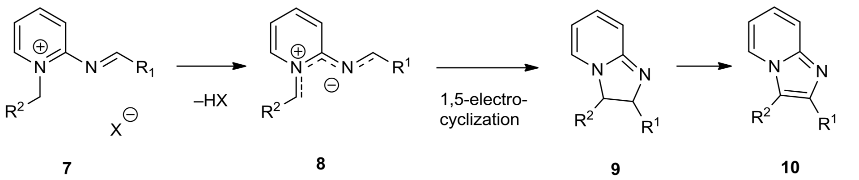
Imidazo[1,2-*a*]pyridines are examples of bridgehead nitrogen compounds, being of interest not only due to their manifold pharmaceutical activities [1] but also in view of their electronic properties, *e. g.* the use as chromophores [2,3]. Several elegant methods for the synthesis of such compounds are reported in the literature [4, 5]. For pharmaceutical purposes it is of importance to have access to diverse substitution patterns. Often, this is a difficult task which requires several reaction steps [6].

In the context of our previous work on the synthesis of five- and seven-membered nitrogen heterocycles by ionic electrocyclization reactions of azapolyenyl anions or cations, we became interested in the synthesis of imidazo[1,2-*a*]pyridines by such an electrocyclization route. For example Hunter *et al.* [7] and our group[8] reported on aza- and diazapolyenyl metal compounds which – depending on the position of the nitrogen atom(s) – underwent electrocyclic ring closure reactions. Thus, polyenyl metal compounds with nitrogen atoms in even positions were found to be destabilized. They show a high tendency to transform into the more stable *N*-heterocyclic isomers [9]. Based on this concept we have described *inter alia* the efficient synthesis of 3-aminoindoles (**2**) starting from 2,6-diazaheptatrienyl metal compounds ($[\mathbf{1}]^-\mathbf{M}^+$) (Scheme 1) [10].

Herein we investigate the utility of related zwitterionic compounds with nitrogen atoms in position 2 and 4 for heterocyclic synthesis (Scheme 2). Here, imino pyridinium salts **7** were chosen as starting materials, which were expected to generate the zwitterionic intermediate **8** upon treatment with base. The positive charge of **7** was assumed to facilitate the deprotonation, leading to an overall neutral equivalent of the previously investigated highly reactive 2-azapolyenyl anions. Similar to those, compounds **8** were expected to be destabilized intermediates, thus enabling a cycliza-



Scheme 1. 2,6-Diazaheptatrienyl metal compounds ($[\mathbf{1}]^-\mathbf{M}^+$) in the synthesis of 3-aminoindole derivatives **2**.



Scheme 2. Proposed reaction of 2,4-diazaheptatrienyl zwitterions **7** upon deprotonation to give imidazo[1,2-*a*]pyridines **10**.

tion reaction for stabilization to give the cyclic products **9**. In this article we report on imidazo[1,2-*a*]pyridines of type **10**, which were found to be the products of this ring closure reaction upon air oxidation of the initially formed dihydro compounds **9**.

Table 1. Yields for compounds **5**.

Compound	R^1	Yield (%)
5a	Ph	98
5b	2-Naphth	87
5c	4-Cl-Ph	89
5d	4-Me-Ph	86

Results and Discussion

Synthesis of precursors

The 2-alkylideneamino-pyridinium salts **7**, which were used as starting materials for the cyclization reaction, were synthesized by a two step procedure starting from the commercially available 2-aminopyridine **3** (Scheme 3). Condensation reaction [11] of **3** with various arylaldehydes **4** (2.0 eq.) led to imino pyridines **5**. The excess of aldehyde was removed by Kugelrohr distillation. In some cases recrystallization was necessary for purification. Some compounds of type **5** have already been described in the literature [12, 13]. We were able to increase the yield of the imine products in several cases by the indicated reaction conditions (Table 1).

In the second step pyridinium salt (**7**) formation was achieved by pyridine-*N*-alkylation using various benzyl or allyl halides **6** in 10-fold excess. The yields ranged from moderate to excellent (Table 2). The benzyl derivatives (**7a**, **b**) were investigated with respect to a possible five-membered ring formation, the allyl derivatives (**7c**–**f**) might also be suitable for the corresponding seven-membered products.

All 2-alkylideneamino-pyridinium salts **7** turned out to be very hygroscopic, which in some cases is fatal since their imine functionality is highly sensitive towards moisture and thus prone to hydrolysis. In any case, these compounds are very sensitive and have

Table 2. Yields for compounds **7**.

Compounds	R^1	R^2	X^-	Yield (%)
7a	Ph	Ph	Br^-	93
7b	2-Naphth	Ph	Br^-	50
7c	Ph	$CH{=}CH_2$	Br^-	60
7d	Ph	$CH{=}CH_2$	I^-	99
7e	4-Cl-Ph	$CH{=}CH_2$	Br^-	38
7f	4-Me-Ph	$CH{=}CH_2$	Br^-	33

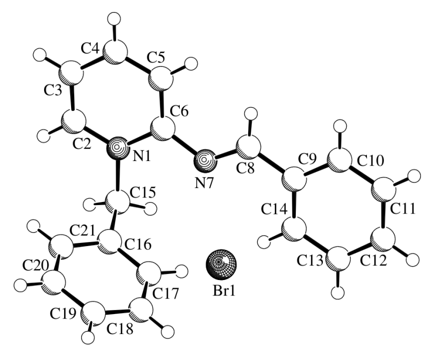
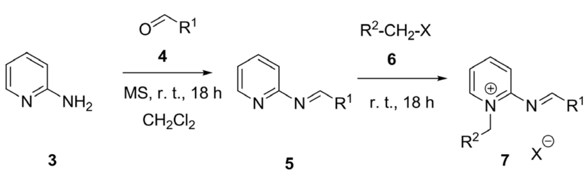


Fig. 1. Molecular structure of **7a** in the crystalline state (SCHAKAL [14]).

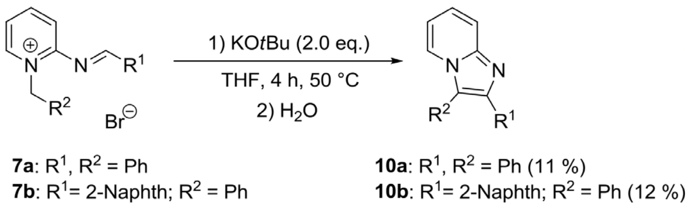
to be stored under argon. For the imino pyridinium salt **7a**, we were able to grow crystals suitable for X-ray diffraction (Fig. 1). The benzylideneamino substituent is in plane with the pyridine framework. A value of 1.259(4) Å was found for the *E*-configured imine bond. The phenyl ring of the benzyl group is placed out of plane with a dihedral angle of 84.4(3)° [C(6)–N(1)–C(15)–C(16)].

Synthesis of imidazo[1,2-a]pyridines

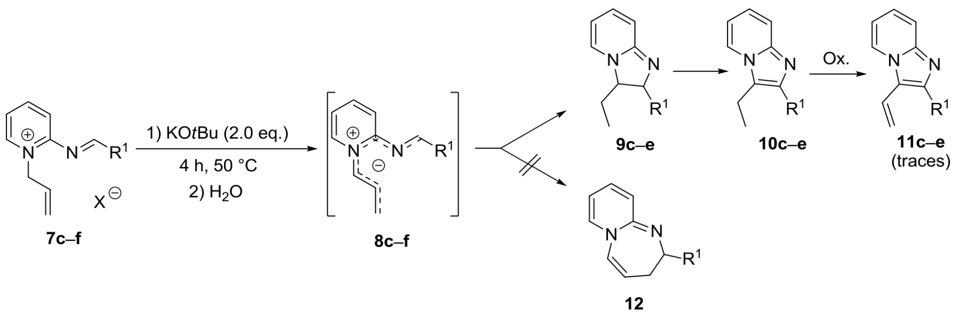
To generate the reactive 2,4-diazaheptatrienyl zwitterionic compounds **8** the imino pyridinium salts **7a**, **b** were deprotonated using KO*t*Bu in THF (Scheme 4). After stirring at 50 °C for 4 h while monitoring by TLC and NMR, the imidazo[1,2-*a*]pyridines **10a**, **b** were ob-



Scheme 3. Synthesis of 2-alkylideneamino-pyridinium salts **7**.



Scheme 4. Synthesis of imidazo[1,2-*a*]pyridines **10a**, **b**.



Scheme 5. Synthesis of imidazo[1,2-*a*]pyridines **10c**, **e** and oxidation to **11c**, **e**.

Table 3. Synthesis of imidazo[1,2-*a*]pyridines **10c** – **f**.

Starting Material	Product	R^1	Yield (%)
7c	**10c**	Ph	18[a]
7d	**10c**	Ph	11[a]
7e	**10d**	4-Cl-Ph	–[b]
7f	**10e**	4-Me-Ph	13[a]

[a] Mixture of **10** (major product) and **11** (traces); [b] no isolation possible, fast decomposition of starting material.

tained in low yield after purification by column chromatography. Interestingly, compounds **10a**, **b** are products of an oxidation process, most likely due to the workup under air.

Similarly, the allyl derivatives **7c** – **f** were deprotonated using KO*t*Bu under the same reaction conditions as described above. Here, the major products were imidazo[1,2-*a*]pyridines **10c** and **10e**, which were found in 11 – 18 % yield. Products of the formation of species with seven-membered rings (**12**) were not observed. The formation of compounds **10c** and **10e** may be traced back to an internal redox process (hydrogen transfer from the newly formed heterocycle to the allyl system) (Scheme 5). Additionally, traces of oxidized compounds **11c** and **11e** were detected by ^{1}H NMR spectroscopy in admixtures with **10c** and **10e** (Table 3), again possibly formed due to workup under air. In case of **7e** we were not able to isolate any products (*e. g.* **10d**), because of the fast decomposition of the starting material.

In case of **10b** it was possible to grow single crystals for X-ray diffraction. Compound **10b** has already been mentioned in the literature, but no analytical data was given [3]. The framework of the imidazo[1,2-*a*]pyridine is planar (Fig. 2). The naphthalen-2-yl substituent is twisted relative to the core structure by a torsion angle of 23.8(3)° (N7–C8–C10–C11). The torsion angle between the phenyl substituent and the imidazopyridine substructure amounts to 55.3(3)° (C8–C9–C20–C21). For the imidazole substructure, the lengths of the C–N bonds amount to 1.392(2) Å (N1–C6), 1.391(2) Å (N1–C9), 1.328(2) Å (C6–N7), and 1.376(2) Å (N7–C8), respectively.

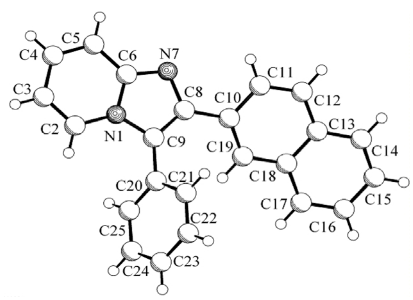
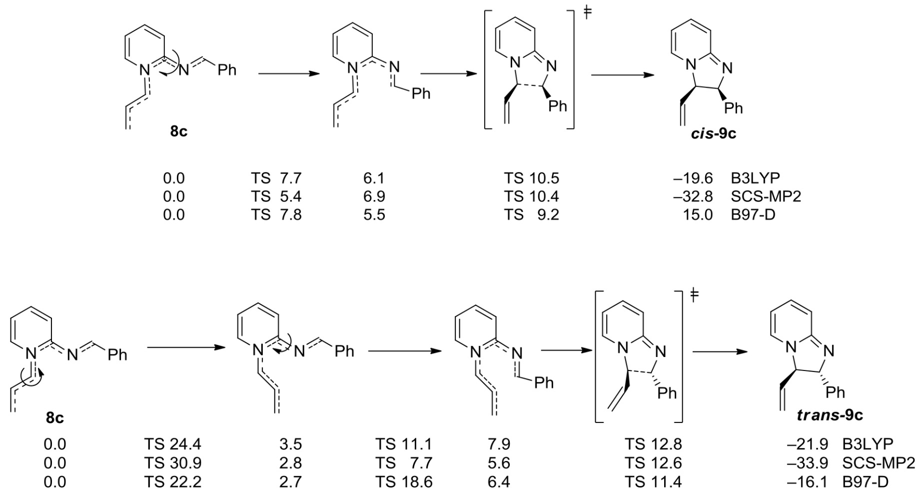


Fig. 2. Molecular structure of compound **10b** in the crystalline state (SCHAKAL [14]).

Several attempts were undertaken to optimize the conditions of the cyclization reaction. Changing the solvent from THF to DMF causes a better solubility of the pyridinium salt but the yield was not significantly increased. By use of different bases (LDA, LiTMP, LHMDS), lower temperatures and the explicit application of oxidants like DDQ the yields of **10** (and **11**) could not be increased further. Purification was further attempted by recrystallization and column chromato-



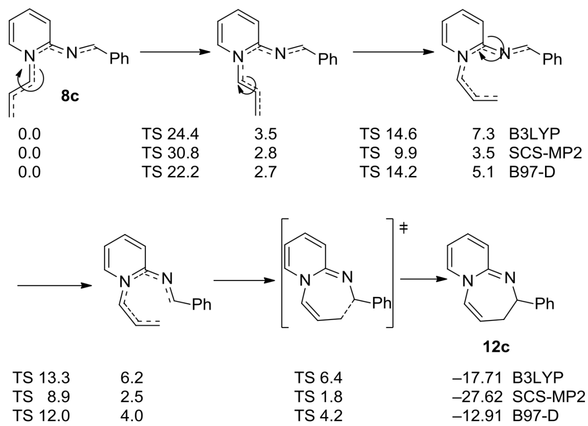
Scheme 6. Proposed reaction steps for the electrocyclization of compound **8c** to give the corresponding *cis* (***cis*-9c**, upper line) and *trans* (***trans*-9c**, lower line) dihydro-imidazo[1,2-*a*]pyridines (energies in kcal mol^{-1}, B3LYP/6-31+G(d)//B3LYP/6-31+G(d)+ZPE, SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d)+ZPE) and B97-D/def2-TZVP//B97-D/def2-TZVP+ZPE).

graphy on either silica gel or aluminum oxide. The analysis of the crude reaction mixture suggested that a high amount of the starting material decomposed prior to the 1,5-electrocyclic ring closure reaction. Typical decomposition products which could be identified were products of imine hydrolysis.

Mechanistic considerations and quantum-chemical calculations

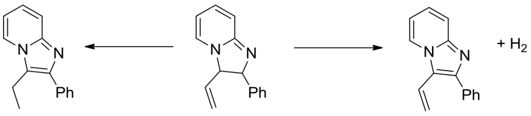
In order to interpret the experimental results, *e. g.* the preferred formation of the five-membered ring over the seven-membered ring from compound **7c**, high-level quantum-chemical calculations were performed. Two levels of methods were employed: The geometries of the species corresponding to minima and transition states were optimized using the B3LYP/6-31+G(d) method [15] as implemented in the program GAUSSIAN 09 [16]. Frequency and IRC calculations were used to characterize the stationary points on the energy hypersurface. Single point energies were obtained using the SCS-MP2 method of S. Grimme [17]. Furthermore B97-D/def2-TZVP geometry optimizations were performed to account for dispersion effects [18]. The methods give similar results, except for the significantly lower relative energy of the final products as calculated by the SCS-MP2 method. All energies reported here contain zero point correction (ZPE).

Schemes 6 and 7 illustrate the proposed mechanism for the cyclization of *N*-allyl compound **7c**.



Scheme 7. Proposed reaction steps for the electrocyclization of compound **8c** to give the experimentally not observed seven-membered ring species **12c** (energies in kcal mol^{-1}, B3LYP/6-31+G(d)//B3LYP/6-31+G(d)+ZPE, SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d)+ZPE) and B97-D/def2-TZVP//B97-D/def2-TZVP+ZPE).

In Scheme 6, the formation of the *cis*- and *trans*-configured five-membered ring systems ***cis***- and ***trans*-9c** is shown. In accordance with the concept of electrocyclization reactions of azapolyenyl anions from previous studies, a quite exothermic reaction enthalpy was calculated for both products with a small preference – as expected – for the *trans* product. Interestingly, several internal rotational changes are necessary to achieve the necessary conformation for the cyclization step. The rotation of the allyl moiety attached to the



10c	**9c**	**11c**	
–54.5	–21.9	–27.3	B3LYP
–64.9	–33.9	–37.3	SCS-MP2
–48.7	–16.1	–24.7	B97-D

Scheme 8. Comparison of the relative energies of products **9c**, **10c**, and **11c** (energies in kcal mol^{-1}, B3LYP/6-31+G(d)//B3LYP/6-31+G(d)+ZPE, SCS-MP2/6-311+G(d,p)//B3LYP/6-31+G(d)+ZPE) and B97-D/def2-TZVP//B97-D/def2-TZVP+ZPE).

pyridinium nitrogen atom affords the highest activation barrier. Thus, the formation of the *trans* products is predicted to be kinetically disfavored. Experimentally, *cis* and *trans* products can not be distinguished due to the immediately following oxidation step. Similarly, the formation of the seven-membered ring system **12c** (Scheme 7) suffers from the barriers of such rotational isomerizations, in spite of the small barrier of the final cyclization step and its exothermicity. In summary, these calculational results are in agreement with the experimental findings and reaction conditions.

In Scheme 8, two products derived of compound **9c** are compared with respect to their relative energies. The formation of the aromatic species **10c** by an intramolecular redox process is highly favored, the dehydrogenated species **11c**, which is observed as minor species, might be formed more likely from **9c** than from **10c**, if dihydrogen is efficiently removed by oxidation.

The transition states, leading to the *cis*- and *trans*-configured five-membered ring systems **9c**, are characterized by the features of a 6π-disrotatory ring closure reaction. They are almost planar with unexpectedly long C$\cdots$C distances of the developing bonds (about 2.6 Å). The terminal carbon atoms show only small charge separation of 0.2 and 0.24 electrons (NBO calculations) [19], the NICS(0) values [20] are quite negative (-11.0 to -11.4 ppm), which is well in accordance with Hückel aromaticity.

The helical transition state, however, leading to the seven-membered ring (**12c**), involves 8π electrons and indicates a conrotatory movement of the two termini. Here, we find significant charge separation between the two reacting carbon atoms (2.49 Å bond length, 0.48 electrons, exclusively located on the allyl terminus) and a NICS(0) value of -8.9 ppm. Thus, we conclude that here the transition state is Möbius-like with significant charge control. These data allow the interesting comparison to our earlier reported anionic cyclization reactions [8, 10], where certainly counterion effects played an important role, which is of no or little influence for the neutral zwitterionic species investigated here.

Conclusion

2-Alkylideneamino-pyridinium salts **7** were investigated with respect to their ability as precursors for the synthesis of bridgehead nitrogen heterocyclic compounds like imidazo[1,2-*a*]pyridines. In the literature the synthesis of these compounds usually requires several reaction steps and various expensive starting materials. Using the synthetic pathway described here the starting materials for the cyclization reaction could be obtained in moderate to excellent yields by use of cheap reagents and easy purification. The last reaction step, the 1,5-electrocyclic reaction, turned out to be more difficult, and the products were obtained only in low yield. However, the confirmation of the successful synthesis of the imidazo[1,2-*a*]pyridines by NMR spectroscopy and X-ray diffraction analysis makes this pathway interesting for further investigations. Quantum-chemical calculations of the ring closing process allow valuable comparisons of these zwitterionic systems with the earlier studied azapolyenyl anion cyclization reactions.

Experimental Section

General information

^{1}H and ^{13}C NMR spectra were recorded at 298 K on ARX 300, AV300, WM300 and AMX400 spectrometers from Bruker, on a Jeol AL-400 spectrometer and on Inova 500 and Unity 600 spectrometers from Varian. Chemical shifts are given in parts per million (ppm) and were referenced to the residual proton signal of the solvent. Electron spray ionization (ESI) mass spectra were measured on a quadrupole mass spectrometer Quattro LC-Z from Micromass. Exact masses were measured with a MAT 8200 spectrometer from the same manufacturer. Melting points were determined with a Büchi melting point B-540 apparatus and are uncorrected. Column chromatography was carried out using Merck silica gel 60. Solvents were purified and dried using standard procedures. THF was kept refluxing over potassium and was freshly distilled prior use. Dichloromethane was distilled over phosphorous pentoxide and filtered through alumina before use. Toluene was distilled over sodium and kept over molecular sieves (4 Å).

*General procedure for the synthesis of methylidene-pyridine-2-amines **5***

In a Schlenk flask containing molecular sieves 4 Å, 2-aminopyridine (**3**) (1.0 eq.) was dissolved in dry CH_2Cl_2. Then, 2.0 equivalents of aldehyde **4** were added in pure form or dissolved in dry CH_2Cl_2. The reaction mixture was stirred for a defined period of time and was subsequently filtered through a pad of celite which was washed with CH_2Cl_2 (3×50 mL). The excess of aldehyde was removed by Kugelrohr distillation. For some compounds additional recrystallization was necessary to obtain the pure product.

*(Phenyl-meth-(E)-ylidene)pyridin-2-yl-amine (**5a**)*

13.85 g (0.15 mol) of 2-aminopyridine was dissolved in 100 mL of dry CH_2Cl_2. Subsequently, 29.76 mL (0.30 mmol) of benzaldehyde was added. Recrystallization from pentane gave 25.51 g (0.14 mol, 96 %) of **5a** as colorless crystals. The analytical data correspond to the literature [12].

*(Naphthalen-2-yl-meth-(E)-ylidene)pyridin-2-yl-amine (**5b**)*

0.99 g (10.53 mmol) of 2-aminopyridine was dissolved in 50 mL of dry CH_2Cl_2. Subsequently, 3.29 g (21.07 mmol) of naphthalene-2-carbaldehyde dissolved in 50 mL of dry CH_2Cl_2 was added. 2.14 g (9.20 mmol, 87 %) of **5b** was obtained as a colorless solid, m. p. 95 – 96 °C. – IR (neat): ν = 1612 (s), 1601 (m), 1477 (m), 1435 (m), 1398 (m), 1366 (m), 1348 (m), 1335 (m), 1308 (m), 1275 (w), 1269 (w), 1234 (w), 1196 (m), 1007 (m) cm^{-1}. – ^1H NMR (C_6D_6, 300.13 MHz): δ = 6.62 – 6.67 (m, 1H, $CH_{arom.}$), 7.13 – 7.22 (m, 3H, $CH_{arom.}$), 7.40 – 7.43 (m, 1H, $CH_{arom.}$), 7.50 – 7.58 (m, 3H, $CH_{arom.}$), 7.95 (s, 1H, $CH_{arom.,Naph.}$), 8.42 – 8.49 (m, 2H, $CH_{arom.}$), 9.66 (s, 1H, CH=N). – ^{13}C NMR (C_6D_6, 75.47 MHz): δ = 121.2, 122.0, 124.5, 126.6, 128.2, 128.4, 128.9, 129.2, 133.3 ($CH_{arom.}$), 133.6, 134.6, 135.7 (C_{ipso}), 137.9, 149.3 ($CH_{arom.}$), 161.5 (C_{ipso}) 162.9 (CH=N). – HRMS (ESI): *m/z* = 233.1070 (calcd. 233.1073 for $C_{16}H_{12}N_2H$).

*[(4-Chlorophenyl)-meth-(E)-ylidene)]pyridin-2-yl-amine (**5c**)*

1.94 g (20.64 mmol) of 2-aminopyridine was dissolved in 50 mL of dry CH_2Cl_2. Subsequently, 4.90 g (40.75 mmol) of 4-chlorobenzaldehyde dissolved in 50 mL of dry CH_2Cl_2 was added. 3.95 g (18.33 mmol, 89 %) of compound **5c** was obtained as pale-yellow crystals. The analytical data correspond to the literature [12].

*(p-Tolyl-meth-(E)-ylidene)pyridin-2-yl-amine (**5d**)*

3.30 g (35.00 mmol) of 2-aminopyridine was dissolved in 100 mL of dry CH_2Cl_2. Then, 8.30 mL (70.00 mmol) of 4-methylbenzaldehyde was added. 5.90 g (30.06 mmol, 86 %) of **5d** was obtained as a colorless solid. The analytical data correspond to the literature [12].

*General procedure for the synthesis of 2-alkylideneamino-pyridinium salts **7***

In a Schlenk flask the amino-2-pyridines **5** (1.0 eq.) were reacted with an excess of different halogenides (10.0 eq.). After 48 h of stirring the precipitate was filtered and washed with diethyl ether (3×100 mL). Afterwards the salt was dried *in vacuo*. These very hygroscopic compounds were used for follow-up reaction without further purification.

*1-Benzyl-2-[(1-phenyl-meth-(E)-ylidene)amino]pyridinium bromide (**7a**)*

2.90 g (16.00 mmol) of **5a** was reacted with 13.85 mL (160 mmol) of benzyl bromide. Yield: 93 % (5.25 g, 14.86 mmol), colorless, hygroscopic solid, m. p. 190 °C. – IR (neat): ν = 3042 (w), 3013 (w), 2994 (m), 1659 (w), 1614 (vs), 1597 (m), 1585 (w), 1578 (w), 1560 (vs), 1530 (w), 1512 (vs), 1501 (vs), 1450 (vs), 1395 (s), 1364 (w), 1331 (w), 1315 (m), 1298 (m), 1285 (s), 1209 (vs), 1171 (vs), 1146 (vs), 1109 (w), 1080 (w), 1074 (w), 1038 (w), 1022 (w), 1013 (w) cm^{-1}. – ^1H NMR ($CDCl_3$, 599.55 MHz): δ = 6.10 (s, 2H, CH_2), 7.26 – 7.31 (m, 3H, $CH_{arom.}$), 7.45 – 7.47 (m, $CH_{arom.}$), 7.55 (t, ^3J = 7.8 Hz, 2H, $CH_{arom.}$), 7.66 (t, ^3J = 7.5 Hz, $CH_{arom.}$), 7.77 (t, ^3J = 7.5 Hz, 1H, $CH_{arom.}$), 8.05 (dd, ^3J = 7.2 Hz, ^4J = 1.2 Hz, 1H, $CH_{arom.}$), 8.11 (dd, ^3J = 8.4 Hz, ^4J = 1.2 Hz, 2H, $CH_{arom.}$), 8.46 (td, ^3J = 8.4 Hz, ^4J = 1.8 Hz, 1H, $CH_{arom.}$), 9.24 (s, 1H, CH=N), 9.51 (dd, ^3J = 6.3 Hz, ^4J = 1.2 Hz). – ^{13}C NMR ($CDCl_3$, 150.77 MHz): δ = 78.9 (CH_2), 111.7, 115.3, 117.4, 120.1, 128.4, 128.5, 128.7, 129.0, 132.2, 133.2, 133.4 ($CH_{arom.}$), 140.2, 140.7 (C_{ipso}), 148.1 ($C_{ipso,Py.}$), 166.1 (CH=N). – HRMS (ESI): *m/z* = 273.1383 (calcd. 273.1386 for $C_{19}H_{17}N$). For crystal structure data, see Table 4.

*1-Benzyl-2-[(1-naphthalen-2-yl-meth-(E)-ylidene)amino]-pyridinium bromide (**7b**)*

2.90 g (12.48 mmol) of **5b** was reacted with 10.80 mL (124.80 mmol) of benzyl bromide. An orange solid was obtained. Yield: 50 % (2.52 g, 6.25 mmol), orange, hygroscopic solid, m. p. 198 °C. – IR (neat): ν = 3235 (w), 3100 (w), 3038 (m), 3003 (m), 2980 (m), 2920 (w), 1693 (vw), 1659 (m), 1632 (w), 1609 (s), 1595 (s), 1580 (m), 1557 (vs), 1528 (m), 1514 (s), 1497 (m), 1468 (w), 1450 (s), 1437 (m), 1395 (w), 1387 (w), 1369 (w), 1358 (m), 1331 (w), 1315 (w), 1294 (m), 1273 (m), 1244 (w), 1207 (m), 1169 (s), 1138 (m), 1126 (m), 1115 (m), 1078 (w), 1065 (w), 1028 (m) cm^{-1}. – ^1H NMR (CD_2Cl_2, 300.13 MHz): δ = 6.15 (s, 2H, CH_2), 7.29 – 7.31 (m, 3H, $CH_{arom.}$), 7.49 –

7.52 (m, 2H, $CH_{arom.}$), 7.57 – 7.63 (m, 1H, $CH_{arom.}$), 7.66 – 7.71 (m, 1H, $CH_{arom.}$), 7.74 – 7.79 (m, 1H, $CH_{arom.}$), 7.93 – 8.04 (m, 3H, $CH_{arom.}$), 8.09 – 8.12 (m, 1H, $CH_{arom.}$), 8.18 – 8.21 (m, 1H, $CH_{arom.}$), 8.42 – 8.48 (m, 1H, $CH_{arom.}$), 8.60 (s, 1H, $CH_{arom.,Naph.}$), 9.29 (s, 1H, CH=N), 9.58 – 9.61 (m, 1H, $CH_{Py.}$). – ^{13}C NMR (CD_2Cl_2, 75.48 MHz): δ = 59.0 (CH_2), 119.4, 124.1, 124.5, 127.9, 128.6, 128.8, 129.5, 129.7, 129.7, 129.9, 130.3, 130.3 ($CH_{arom.}$), 132.2, 133.2, 134.1, 137.0 (C_{ipso}), 137.5, 145.1, 147.6 ($CH_{arom.}$), 158.2 (C_{ipso}), 171.5 (CH=N). – HRMS (ESI): *m/z* = 323.1542 (calcd. 323.1543 for $C_{23}H_{19}N_2$).

*1-Allyl-2-[(1-phenyl-meth-(E)-ylidene)amino]pyridinium bromide (**7c**)*

3.64 g (20.00 mmol) of pyridine imine **5a** was reacted with 17.30 mL (200.00 mmol) of allyl bromide. Yield: 60 % (3.62 g, 11.94 mmol), light-yellow, hygroscopic solid, m. p. 207 °C. – IR (neat): ν = 3071 (w), 3057 (w), 3034 (w), 2988 (w), 1693 (vw), 1661 (w), 1614 (s), 1599 (m), 1576 (w), 1560 (s), 1524 (m), 1508 (s), 1449 (s), 1410 (w), 1393 (m), 1356 (m), 1317 (m), 1300 (m), 1211 (s), 1177 (m), 1163 (s), 1152 (m) cm^{-1}. – ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 5.17 (d, ^3J = 5.5 Hz, 1H, CH=CH_2), 5.38 (d, ^3J = 5.5 Hz, 1H, CH=CH_2), 5.51 (d, ^3J = 6.0 Hz, 2H, CH_2), 5.94 – 6.12 (m, 1H, CH=CH_2), 7.52 (t, ^3J = 7.2, 2H, $CH_{arom.}$), 7.58 – 7.70 (m, 1H, $CH_{arom.}$), 7.83 – 7.90 (m, 1H, $CH_{arom.}$), 8.09 – 8.13 (m, 3H, $CH_{arom.}$), 8.55 (t, ^3J = 8.0 Hz, 1H, $CH_{arom.}$), 9.33 (s, 1H, CH=N), 9.40 (dd, ^3J = 6.3 Hz, ^4J = 1.2 Hz, 1H, CH_{Py}). – ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ = 58.0 (CH_2), 119.1 (CH=CH_2), 122.6 (CH=CH_2), 124.4, 129.4, 130.0, 131.4, 134.0, 135.2, 144.5, 147.7 ($CH_{arom.}$), 154.5, 157.6 (C_{ipso}), 171.6 (CH=N). – HRMS (ESI): *m/z* = 223.1232 (calcd. 223.1230 for $C_{15}H_{15}N_2$).

*1-Allyl-2-[(1-phenyl-meth-(E)-ylidene)amino]pyridinium iodide (**7d**)*

2.02 g (11.09 mmol) of compound **5a** was reacted with 9.60 mL (110.90 mmol) of allyl iodide. Yield: 99 % (3.86 g, 11.02 mmol), yellow, hygroscopic solid, m. p. 141 °C. – IR (neat): ν = 3296 (m), 3256 (w), 3117 (s), 3078 (m), 3057 (m), 3032 (m), 3011 (m), 2988 (s), 2955 (w), 2905 (w), 1699 (m), 1655 (s), 1612 (vs), 1597 (vs), 1584 (vs), 1558 (vs), 1526 (vs), 1518 vs), 1504 (vs), 1447 (vs), 1433 (vs), 1408 (s), 1391 (vs), 1344 (m), 1337 (m), 1323 (w), 1312 (vs), 1296 (vs), 1265 (m), 1206 (vs), 1180 (s), 1165 (vs), 1150 (vs), 1130 (s), 1096 (m), 1072 (m), 1061 (m), 1024 (m), 1013 (m) cm^{-1}. – ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 5.43 – 5.45 (m, 2H, CH_2), 5.47 – 5.48 (m, 1H, CH=CH_2), 6.01 – 6.14 (m, 1H, CH=CH_2), 7.52 – 7.57 (m, 2H, $CH_{arom.}$), 7.63 – 7.67 (m, 1H, $CH_{arom.}$), 7.83 – 7.88 (m, 1H, $CH_{arom.}$), 8.07 – 8.14 (m, 3H, $CH_{arom.}$), 8.52 – 8.58 (m, 1H, $CH_{arom.}$), 9.18 (dd, ^3J = 6.3 Hz, ^4J = 1.2 Hz, 1H, $CH_{arom.}$), 9.33 (s, 1H, CH=N). – ^{13}C NMR ($CDCl_3$, 75.48 MHz): δ = 58.1 (CH_2), 119.4 (CH=CH_2), 122.9 (CH=CH_2), 123.0 (C_{ipso}), 124.4, 129.5, 129.7, 131.5 ($CH_{arom.}$), 133.9 (C_{ipso}), 135.3, 144.0, 147.7 ($CH_{arom.}$), 171.5 (CH=N). – HRMS (ESI): *m/z* = 223.1234 (calcd. 223.1230 for $C_{15}H_{15}N_2$).

*1-Allyl-2-[(1-(4-chlorophenyl)-meth-(E)-ylidene)amino]pyridinium bromide (**7e**)*

2.20 g (10.00 mmol) of compound **5c** was dissolved in 8.70 mL (100.00 mmol) of allyl bromide. A light-yellow solid was obtained, which was contaminated with products of hydrolysis. Yield: 38 % (1.29 g, 3.81 mmol), light-yellow, hygroscopic solid, m. p. 212 °C. – IR (neat): ν = 3078 (m), 3065 (m), 3055 (w), 3042 (m), 3034 (m), 3015 (m), 2980 (s), 2947 (w), 2907 (w), 2880 (w), 1626 (vs), 1618 (vs), 1589 (vs), 1560 (vs), 1526 (m), 1503 (vs), 1485 (vs), 1447 (vs), 1433 (vs), 1414 (m), 1391 (s), 1381 (s), 1354 (m), 1337 (w), 1327 (w), 1302 (vs), 1211 (vs), 1161 (vs), 1148 (vs), 1103 (m), 1088 (vs), 1061 (m), 1011 (vs) cm^{-1}. – ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 5.41 – 5.44 (m, 2H, CH_2), 5.48 – 5.50 (m, 2H, CH=CH_2), 6.01 – 6.14 (m, 1H, CH=CH_2), 7.52 (d, ^3J = 9.0 Hz, 2H, $CH_{arom.}$), 7.84 (t, ^3J = 9.0 Hz, 1H, $CH_{arom.}$), 8.10 (d, ^3J = 9.0 Hz, 2H, $CH_{arom.}$), 8.16 (d, ^3J =9.0 Hz, 1H, $CH_{arom.}$), 8.51 (t, ^3J = 9.0 Hz, 1H, $CH_{arom.}$), 9.25 (d, ^3J = 6.0 Hz, 1H, $CH_{arom.,Py.}$), 9.47 (s, 1H, CH=N). – ^{13}C NMR: not possible due to rapid decomposition. – HRMS (ESI): *m/z* = 275.0835 (calcd. 275.0840 for $C_{15}H_{14}ClN_2$). – $C_{15}H_{14}BrClN_2$ (337.64): calcd. C 53.36, H 4.18, N 8.30; found C 52.86, H 3.99, N 8.46.

*1-Allyl-2-[(1-p-tolylmeth-(E)-ylidene)amino]pyridinium bromide (**7f**)*

1.29 g (6.57 mmol) of compound **5d** was reacted with 5.69 mL (65.70 mmol) of allyl bromide. Yield: 33 % (0.69 g, 2.16 mmol), light-yellow, hygroscopic solid, m. p. 217 °C. – IR (neat): ν = 3082 (m), 3067 (m), 3057 (m), 3042 (m), 3030 (m), 3013 (m), 2982 (s), 2945 (m), 2909 (w), 1663 (m), 1641 (w), 1622 (vs), 1605 (vs), 1582 (m), 1560 (vs), 1526 (s), 1516 (vs), 1501 (vs), 1449 (vs), 1433 (vs), 1393 (s), 1354 (m), 1339 (w), 1302 (vs), 1217 (vs), 1209 (vs), 1173 (vs), 1161 (vs), 1150 (vs), 1111 (m), 1105 (m), 1063 (m), 1036 (m), 1016 (m), 1009 (s cm^{-1}). – ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 2.45 (s, 3H, CH_3), 5.19 – 5.46 (m, 2H, CH_2), 5.53 (d, ^3J = 6.0 Hz, 1H, CH=CH_2), 5.98 – 6.09 (m, 1H, CH=CH_2), 7.34 (d, ^3J = 9.0 Hz,2H, $CH_{arom.}$), 7.78 – 7.83 (m, 1H, $CH_{arom.}$), 8.00 (d, ^3J = 9.0 Hz,2H, $CH_{arom.}$), 8.07 (dd, ^3J = 9.0 Hz, ^4J = 1.0 Hz, 1H, $CH_{arom.}$), 8.49 – 8.55 (m, 1H, $CH_{arom.}$), 9.23 (s, 1H, CH=N), 9.45 (dd, ^3J = 6.0 Hz, ^4J = 1.3 Hz, 1H, $CH_{arom.}$). – ^{13}C NMR ($CDCl_3$, 75.48 MHz): δ = 22.3 (CH_3), 57.9 (CH_2), 118.9 (CH=CH_2), 122.6 (CH=CH_2), 124.0 (C_{ipso}), 130.1, 130.3, 131.6, 131.6 ($CH_{arom.}$), 144.6 (C_{ipso}), 147.0, 147.4 ($CH_{arom.}$),

157.8 (C_{ipso}), 171.1 (*C*H=N). – HRMS (ESI): *m*/*z* = 237.1386 (calcd. 237.1386 for $C_{16}H_{17}N_2$).

*General procedure for the synthesis of imidazo[1,2-a]pyridines **10/11***

In a Schlenk flask a solution of KO*t*Bu (2.0 eq., 1 M solution or solid) was dissolved in dry THF. The solution was heated to 50 °C. Then, 1.0 eq. of pyridinium salt **7** dissolved in dry THF was added slowly to the stirred mixture. A deep brown color appeared. After a defined period of time at 50 °C, 10 mL of distilled H_2O were added. Immediately the color of the solution faded. The yellow mixture was extracted with diethyl ether (3 × 50 mL), and the organic layer was dried over $MgSO_4$. After removal of the solvent, the crude product was purified by column chromatography.

*4,5-Diphenylimidazo[1,2-a]pyridine (**10a**)*

0.57 g (5.10 mmol) of KO^{t}Bu was dissolved in 20 mL of dry THF. Then, 0.90 g (2.55 mmol) of **7a** in 20 mL of dry THF was added slowly. The mixture was stirred for 4 h at 50 °C. The crude product was purified by column chromatography (R_f = 0.42, SiO_2, cyclohexane-ethyl acetate 1 : 1). Yield: 11 % (0.07 g, 0.27 mmol), brown solid, m. p. 152 °C. – IR (neat): ν = 3063 (w), 2955 (w), 2924 (m), 2855 (w), 1601 (w), 1543 (w), 1504 (m), 1472 (w), 1445 (m), 1437 (m), 1385 (s), 1360 (m), 1341 (m), 1312 (w), 1271 (m), 1236 (s), 1213 (w), 1179 (w), 1148 (w), 1111 (w), 1072 (m), 1028 (w) cm^{-1}. – ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 6.73 (td, ^3J = 6.9 Hz, ^4J = 1.2 Hz, 1H, C*H*), 7.17 – 7.31 (m, 4H, C*H*/C$H_{arom.}$), 7.44 – 7.56 (m, 5H, C$H_{arom.}$), 7.65 – 7.70 (m, 3H, C$H_{arom.}$), 7.96 (d, ^3J = 6.9 Hz, 1H, C*H*-N). – ^{13}C NMR ($CDCl_3$, 75.48 MHz): δ = 112.4, 117.6 (*C*H), 121.2 ($C_{quat.}$), 123.4, 124.8 (*C*H), 127.6, 128.2, 128.4, 129.0, 129.7 ($CH_{arom.}$), 130.0 (C_{ipso}), 130.8 ($CH_{arom.}$), 134.3, 142.5, 144.9 (C_{ipso}). – HRMS (ESI): *m*/*z* = 271.1228 (calcd. 271.1230 for $C_{19}H_{15}N_2$).

*2-Naphthalen-2-yl-3-phenylimidazo[1,2-a]pyridine (**10b**)*

0.48 g (1.20 mmol) of pyridinium salt **7b** dissolved in 70 mL dry THF was added to a stirred solution of 0.27 g (2.39 mmol) KO*t*Bu in 50 mL of dry THF. The mixture was heated for 4 h at 50 °C. The product was purified by column chromatography (R_f = 0.16 SiO_2, pentane-diethyl ether 2 : 1) and subsequent recrystallization from CH_2Cl_2. Yield: 12 % (0.04 g, 0.14 mmol), light-yellow crystals, m. p. 134 °C. – IR(neat): ν = 3076 (w), 3051 (m), 3038 (m), 2988 (w), 2959 (w), 2947 (w), 2922 (m), 2868 (w), 2851 (w), 1692 (m), 1634 (s), 1601 (s), 1576 (m), 1547 (m), 1526 (m), 1504 (vs), 1485 (s), 1466 (m), 1450 (s), 1435 (s), 1396 (m), 1379 (m), 1362 (vs), 1344 (vs), 1308 (m), 1273 (vs), 1248 (s), 1238 (vs), 1217 (s), 1196 (s), 1177 (m), 1161 (m), 1148 (s), 1136 (s), 1124 (m), 1099 (s), 1070 (s), 1028 (s), 1018 (s), 1013 (s) cm^{-1}. – ^{1}H NMR (CD_2Cl_2, 300.13 MHz): δ = 6.77 (td, ^3J = 6.9 Hz, 1H, C*H*), 7.21 – 7.27 (m, 1H, C*H*), 7.40 – 7.46 (m, 2H, C*H*/C$H_{arom.}$), 7.49 – 7.60 (m, 5H, C*H*/C$H_{arom.}$), 7.66 (dt, ^3J = 9.0 Hz, ^4J = 1.2 Hz, 1H, C$H_{arom.}$), 7.73 – 7.82 (m, 4H, C$H_{arom.}$), 7.92 – 8.06 (m, 1H, C$H_{arom.}$), 8.22 (s, 1H, C$H_{arom.,Naph.}$). – ^{13}C NMR (CD_2Cl_2, 100.62 MHz): δ = 112.7, 117.9, 124.0, 125.3, 126.4, 126.5, 126.6, 127.4, 128.0, 128.1, 128.7, 129.5, 130.1, 130.6, 131.4, 133.3, 134.0. – HRMS (ESI): *m*/*z* = 321.1396 (calcd. 321.1386 for $C_{23}H_{17}N_2$). For crystal data, see Table 4.

*3-Ethyl-2-phenylimidazo[1,2-a]pyridine (**10c**) and 2-phenyl-3-vinylimidazo[1,2-a]pyridine (**11c**)*

A solution of 2.00 mL (2.00 mmol) of KO*t*Bu (1.0 M in THF) in 50 mL of dry THF was prepared. Then, 0.30 g (1.00 mmol) of compound **7c** dissolved in 70 mL of dry THF was added slowly. The color of the reaction mixture immediately changed to brown. The solution was stirred for 15 min at 50 °C. By use of column chromatography it was not possible to separate compound **10c** from the minor product **11c** (R_f **10c**: 0.40, R_f **11c**: 0.48 SiO_2, hexane-ethyl acetate 1 : 1). Yield: 18 % (0.04 g, 0.18 mmol), mixture of compound **10c** and **11c**, yellow-brown oil. – IR (neat): ν = 3082 (vw), 3053 (vw), 3032 (vw), 2968 (w), 2932 (vw), 2874 (vw), 2857 (vw), 1634 (w), 1605 (w), 1578 (vw), 1555 (vw), 1528 (vw), 1501 (s), 1489 (m), 1460 (m), 1445 (m), 1393 (s), 1377 (w), 1358 (vs), 1306 (w), 1294 (w), 1267 (vs), 1227 (s), 1177 (w), 1150 (w), 1130 (w), 1109 (vw), 1092 (vw), 1072 (m), 1045 (w), 1024 (w), 1007 (vw) cm^{-1}. – ^{1}H NMR ($CDCl_3$, 399.95 MHz): δ = 1.37 (t, ^3J = 7.2 Hz, 3H, CH_3), 3.12 (q, ^3J = 7.6 Hz, 2H, CH_2), 6.86 (t, ^3J = 6.8 Hz, 1H, C*H*), 7.18 – 7.22 (m, 1H, C*H*/C$H_{arom.}$), 7.35 – 7.38 (m, 1H, C*H*/C$H_{arom.}$), 7.46 – 7.49 (m, 2H, C*H*/C$H_{arom.}$), 7.68 – 7.70 (m, 1H, C$H_{arom.}$), 7.78 – 7.80 (m, 2H, C$H_{arom.}$), 7.97 – 7.99 (d, ^3J = 6.8 Hz, 1H, C$H_{arom.}$). Additional peaks for **11c**: 5.57 (d, ^3J = 16.0 Hz, 1H, CH=CH_2), 5.73 (d, ^3J = 16.0 Hz, 1H, CH=CH_2), 6.86 – 6.96 (m, 1H, C*H*=CH_2). – ^{13}C NMR ($CDCl_3$, 100.40 MHz): δ = 12.3 (*C*H_3), 17.1 (*C*H_2), 112.3, 117.9 (*C*H), 122.0 ($C_{quat.}$), 123.1, 123.9 (*C*H), 127.7, 128.4, 128.8 ($CH_{arom.}$), 135.0, 142.0, 144.5 (C_{ipso}). – HRMS (ESI): *m*/*z* = 223.1226 (calcd. 223.1230 for $C_{15}H_{15}N_2$ (**10c**)); *m*/*z* = 221.1079 (calcd. 221.1073 for $C_{15}H_{13}N_2$ (**11c**)).

*3-Ethyl-2-p-tolyl-imidazo[1,2-a]pyridine (**10e**) and 2-p-tolyl-3-vinylimidazo[1,2-a]pyridine (**11e**)*

2.00 mL (2.00 mmol) of KO*t*Bu (1.0 M solution in THF) in 50 mL of dry THF was prepared. While stirring, 0.32 g (1.00 mmol) of pyridinium salt **7f** was added slowly. By use of column chromatography it was not possible to separate compound **10e** from the minor product **11e** (R_f **10e**: 0.40, R_f **11e**: 0.48 SiO_2, hexane-ethyl acetate 1 : 1). Yield: 13 %

Table 4. Crystal structure data for **7a** and **10b**.

	7a	**10b**
Formula	$C_{19}H_{17}BrN_2$	$C_{23}H_{16}N_2$
M_r	353.26	320.38
Crystal size, mm^3	0.20×0.10×0.05	0.47×0.27×0.10
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$
a, Å	7.6283(4)	6.3013(1)
b, Å	19.9157(9)	17.9472(4)
c, Å	10.7802(5)	14.4155(4)
β, deg	91.272(2)	95.141(1)
V, Å^3	1637.36(14)	1623.70(6)
Z	4	4
D_{calcd}, g cm^{-3}	1.43	1.31
μ, mm^{-1}	3.4 (CuK_α)	0.1 (MoK_α)
$F(000)$, e	720	672
hkl range	$-8\rightarrow9$, ±23, ±12	±8, $-23\rightarrow21$, ±18
$((\sin\theta)/\lambda)_{max}$, Å^{-1}	0.60	0.66
Refl. measured / unique	9830 / 2876	9142 / 3756
R_{int}	0.043	0.039
Param. refined	199	226
$R(F)$ / $wR(F^2)^{a,b}$ (all refl.)	0.039 / 0.095	0.076 / 0.141
GoF $(F^2)^c$	1.037	1.035
$\Delta\rho_{fin}$ (max / min), e Å^{-3}	0.50 / −0.32	0.21 / −0.17

[a] $R = \Sigma\|F_o| - |F_c\|/\Sigma|F_o|$; [b] $wR = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$, $w = [\sigma^2(F_o^2) + (AP)^2 + BP]^{-1}$, where $P = (\text{Max}(F_o^2, 0) + 2F_c^2)/3$; [c] $\text{GoF} = [\Sigma w(F_o^2 - F_c^2)^2/(n_{obs} - n_{param})]^{1/2}$.

(29 mg, 0.12 mmol), brown oil. – IR (neat): ν = 2965 (m), 2926 (w), 2876 (w), 2857 (w), 1724 (w), 1676 (w), 1634 (w), 1607 (w), 1576 (w), 1528 (w), 1503 (s), 1452 (m), 1433 (m), 1412 (w), 1391 (m), 1379 (m), 1360 (s), 1304 (m), 1260 (vs), 1227 (m), 1175 (m), 1148 (m), 1090 (vs), 1063 (vs), 1016 (vs) cm^{-1}. – ^{1}H NMR (C_6D_6, 399.65 MHz): δ = 0.88 (t, ^3J = 7.1 Hz, 3H, CH_2-CH_3), 2.18 (s, 3H, CH_3), 2.62 (q, ^3J = 7.1 Hz, 2H, CH_2-CH_3), 6.16 (t, ^3J = 6.0 Hz, 1H, C*H*), 6.60 – 6.65 (m, 1H, C*H*), 6.92 – 7.19 (m, 2H, C*H*/C$H_{arom.}$), 7.60 – 7.66 (m, 2H, CH/C$H_{arom.}$), 8.05 (d, 2H, C$H_{arom.}$). Additional peaks for **11e**: 5.03 (d, ^3J = 18.0 Hz, 1H, CH=CH_2), 5.15 (d, ^3J = 12.0 Hz, 1H, CH=CH_2), 6.36 – 6.40 (m, 1H, C*H*=CH_2). – ^{13}C NMR (C_6D_6, 75.48 MHz): δ = 12.0 (CH_3), 17.2 (CH_2), 21.3 (Ph-4-CH_3), 111.5, 118.0 (*C*H), 121.4 ($C_{quat.}$), 122.7, 123.0 (*C*H), 127.2, 128.7, 129.6 ($CH_{arom.}$), 133.3, 137.1, 144.6 (C_{ipso}). – HRMS (ESI): *m/z* = 237.1381 (calcd. 237.1386 for $C_{16}H_{17}N_2$ (**10e**)); *m/z* = 235.1223 (calcd. 235.1230 for $C_{16}H_{15}N_2$ (**11e**)).

Crystal structure analyses

Data sets were collected with Nonius KappaCCD diffractometers, in case of Mo radiation equipped with a rotating anode generator. Programs used: data collection COLLECT [21], data reduction DENZO-SMN [22], absorption correction DENZO [23], structure solution SHELXS-97 [24]), structure refinement SHELXS-97 [25], graphics SCHAKAL [14]. Table 4 summarizes the crystal data and numbers pertinent to data collection and structure refeinement.

CCDC 863101 (**7a**) and CCDC 863102 (**10b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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