Journal of Organometallic Chemistry 693 (2008) 3063–3073

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

(*N*-Arylaminomethyl)pyridine-*N*-oxides: Synthesis and characterization of potential ligand systems and the formation of their N,O-chelate aluminum complexes

Katrin Nienkemper, Gerald Kehr, Seda Kehr [1], Roland Fröhlich [1], Gerhard Erker *

Organisch-Chemisches Institut der Universität Münster, Corrensstrasse 40, 48149 Münster, Germany

ARTICLE INFO

Article history:
Received 15 January 2008
Received in revised form 9 May 2008
Accepted 26 May 2008
Available online 30 July 2008

Keywords:
Aluminum
Chelate ligands
Pyridine-*N*-oxides
Imines
Arylamines

ABSTRACT

Pyridine-*N*-oxide-2-carbaldehyde (**4a**) was converted to the corresponding imine (**5a**) by treatment with 2,6-diisopropylaniline. Subsequent reduction with a sodium borohydride gave the corresponding (*N*-arylaminomethyl)pyridine-*N*-oxide derivative (**6a**). A series of analogous compounds was prepared starting from the respective (aldimino)quinoline-*N*-oxide (**4b**) or (ketimino)pyridine-*N*-oxide (**10**) systems. Deprotonation of the (aminomethyl)pyridine-*N*-oxides resulted in a series of unexpected reactions, such as coupling, internal redox reactions or fragmentation. Eventually, the N,O-chelate aluminum complexes (**22**, **23**) derived from the (aminoethyl)pyridine-*N*-oxide ligand systems could be obtained by treatment of the respective iminopyridine-*N*-oxides with trimethylaluminum. Many products were characterized by X-ray diffraction.

1. Introduction

Mono-anionic N,O-chelate ligands have found extensive use in homogeneous catalysis. Important examples include the various salicylaldiminato systems (**A**), derivatives of which have found many practical catalytic applications ranging from polymerization reactions [1,2] to asymmetric organic synthesis [3]. In a way the (amidomethyl)pyridine-*N*-oxides (**B**) represent complementary systems to the ubiquitous salicylaldiminates, where formally the negatively charged center was moved from the oxy-arene site to a side-chain nitrogen (see Scheme 1).

We had previously described the synthesis of pyridine-*N*-oxide aldimines [4], the neutral analogues of the negatively charged salicylaldiminates (**A**), and a series of their coordination compounds. We have now investigated a variety of synthetic routes to systems aimed at generating and using the ligands (**B**) in some straightforward fashion. This turned out to be difficult but was eventually successful by making some respective N,O-chelate aluminum complexes of examples of **B** readily available. Some of these developments will be described in this account.

2. Results and discussion

2.1. The parent (aminomethyl)pyridine-N-oxide systems

The synthesis of the parent compound (**6a**, see Scheme 2) started from commercially available 2-(hydroxymethyl)pyridine (**2a**). It was treated with 30% aqueous H_2O_2 in glacial acetic acid to yield the substituted pyridine-*N*-oxide (**3a**, 34% after recrystallization from methanol) [5]. Subsequent oxidation with SeO_2 gave the corresponding pyridine-*N*-oxide carbaldehyde (**4a**) [6] in close to 90% yield. Acid-catalyzed condensation of **4a** with 2,6-diisopropylaniline then gave the respective aldimine derivative **5a** which was eventually reduced to the 2-(*N*-arylaminomethyl)pyridine-*N*-oxide derivative **6a** (54% isolated) by treatment with the $NaBH_4$/CH_3COOH reagent.

Pyridine-*N*-oxide-2-carbaldehyde (**4a**) was also condensed with pentafluoroaniline to yield the pyridine-*N*-oxide carbaldimine derivative **5c**. Its (in situ) reduction with sodium cyanoborohydride eventually furnished the N–C_6F_5-substituted (aminomethyl)pyridine-*N*-oxide derivative **6c** (39% isolated, see Scheme 2).

Both the imine (**5a**) and its reduction product (**6a**) were characterized by X-ray diffraction. Single crystals of **5a** were obtained from methanol. The X-ray crystal structure analysis of **5a** (see Fig. 1, left (values taken from molecule A)) shows a nearly to coplanar arrangement of the imine –C=N– unit (C7–N8 1.261(2) Å) [7] with the pyridine-*N*-oxide nucleus (dihedral angle N1–C2–C7–N8

* Corresponding author. Fax: +49 251 83 36503.
E-mail address: erker@uni-muenster.de (G. Erker).
[1] X-ray crystal structure analyses.

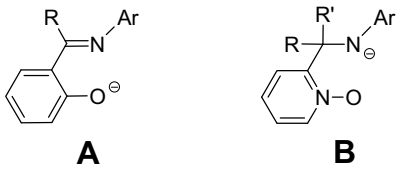
0022-328X/$ - see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2008.05.032

168.5(1)°). The bond lengths around the pyridine-*N*-oxide nitrogen atom amount to N1–O 1.298(2) Å, N1–C2 1.366(2) Å and N1–C6 1.361(2) Å. The imine functional group is E-configurated (C2–C7–N8–C9 174.0(1)°) and the plane of the 2,6-diisopropylphenyl substituent is close to normal to the C=N plane (C7–N8–C9–C14 −99.2(2)°).

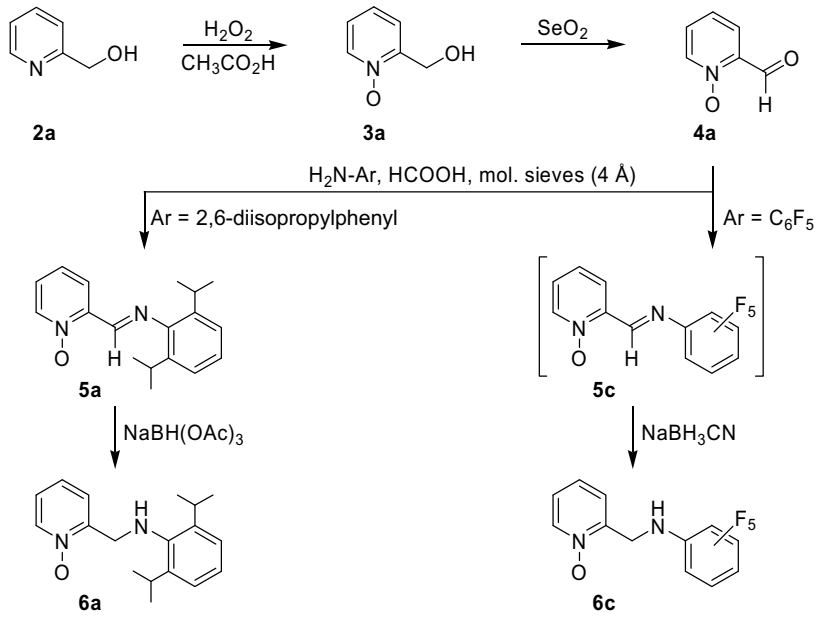
Compound **6a** features a pyridine-*N*-oxide N1–O1 bond length of 1.317(4) Å. The adjacent C2–C7 bond length is found at 1.484(5) Å and the C7–N8 bond (1.469(4) Å) is now in the typical C(sp^3)–N single bond range [7]. The substituents at the central C7–N8 unit in **6a** are found in an anti-periplanar orientation with a dihedral angle of C2–C7–N8–C9 163.6(3)° (N1–C2–C7–N8 179.8(3)°). The plane of the bulky 2,6-diisopropylphenyl substituent at N8 is oriented almost normal to the central pyridine plane (dihedral angle C7–N8–C9–C14 −74.1(5)°).

The related compound **6c** was also characterized by X-ray diffraction (single crystals from methanol/triethylamine by evaporation). It features similar structural parameters of the pyridine-*N*-oxide core (N1–O1 1.318(2) Å, C2–C7 1.503(2) Å, N1–C2–C7–N8 −178.6(1)°, see Fig. 2) but exhibits a markedly different conformational arrangement of the attached *N*-pentafluorophenylaminomethyl substituent. While the C_6F_5 group is rotated almost perpendicular from the pyridine plane (C2–C7–N8–C9 86.4(2)°), its plane is found almost coplanar with the adjacent C7–N8 vector (C7–N8–C9–C10 −8.8(2)°).

The conformation of **5a** in the crystal contains an element of axial prochirality at the N8–C9 vector. However, in solution diastereotopic splitting of the methyl NMR resonances of the attached pair of isopropyl groups was not observed [^{1}H/^{13}C: δ 1.16 (d, 12H)/23.4 CH(CH_3)$_2$]. Similarly, compound **6a** features one set of ^{1}H/^{13}C NMR isopropyl methyl resonances (δ 1.19/24.3).



Scheme 1.



Scheme 2.

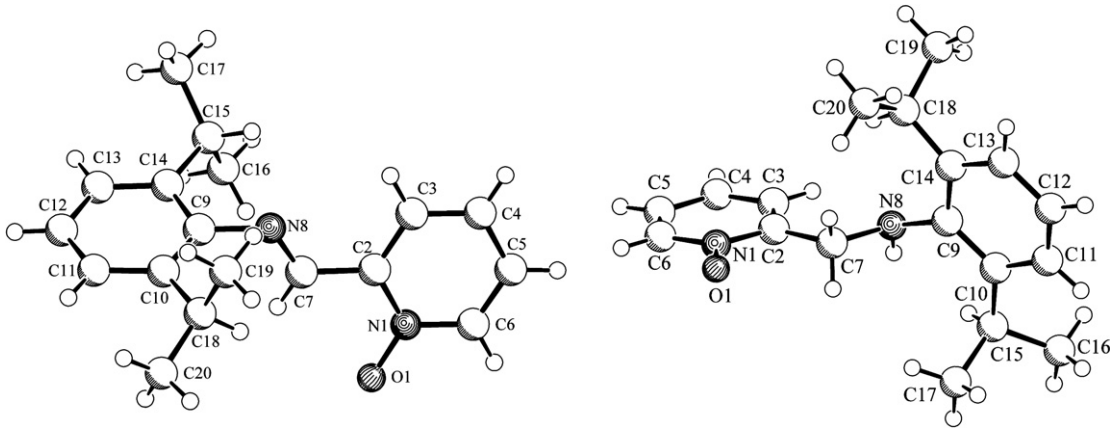


Fig. 1. Views of the molecular structures of the compounds **5a** (left) and **6a** (right).

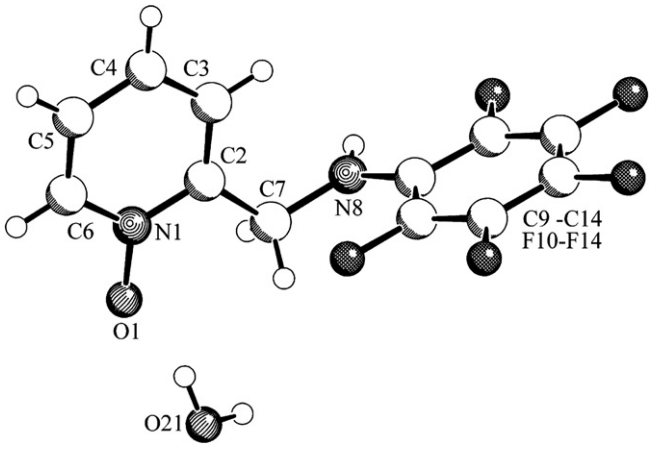


Fig. 2. Molecular geometry of **6c**.

The synthesis of the related quinoline-*N*-oxide derivatives started from 2-methyl-quinoline-*N*-oxide (**1b**), which was obtained by oxidation (*m*-CPBA in chloroform) of chinaldine according to the literature procedure [8]. It was converted to 2-hydroxymethylquinoline (**2b**) by a Boekelheide reaction [9] by treatment with trifluoroacetic anhydride (for a mechanistic scheme see the Supplementary material). Then, first the quinoline nitrogen was oxidized with *meta*-chloroperbenzoic acid to get **3b** and subsequent oxidation with SeO_2 gave the corresponding aldehyde (**4b**) [10], which was then converted to the imine (**5b**) by treatment with 2,6-diisopropylaniline (see Scheme 3). The imine **5b** was isolated in ca. 80% after crystallization from methanol. Reduction of **5b** was carried out with $NaBH_4/CH_3COOH$ to eventually yield **6b** (86% isolated).

Both compounds **5b** and **6b** were characterized by X-ray crystal structure analyses (see Fig. 3). Single crystals were obtained by crystallization from methanol (**5b**) or by a slow evaporation of solvent from a methanol/triethylamine solution (**6b**).

Compound **5b** features a N1–O1 bond length of 1.287(2) Å. The C=N unit (C7–N8 1.266(2) Å) is E-configurated (dihedral angles N1–C2–C7–N8 178.4(2)°, C2–C7–N8–C9 176.5(2)°) and the aryl substituent at N8 is oriented close to orthogonal (C7–N8–C9–C14 94.0(2)°) (values are taken from molecule A).

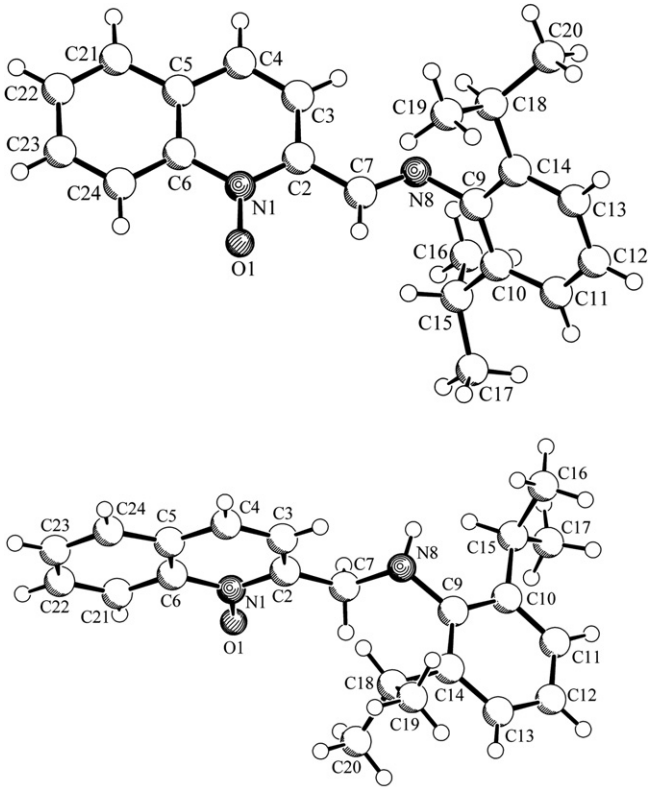
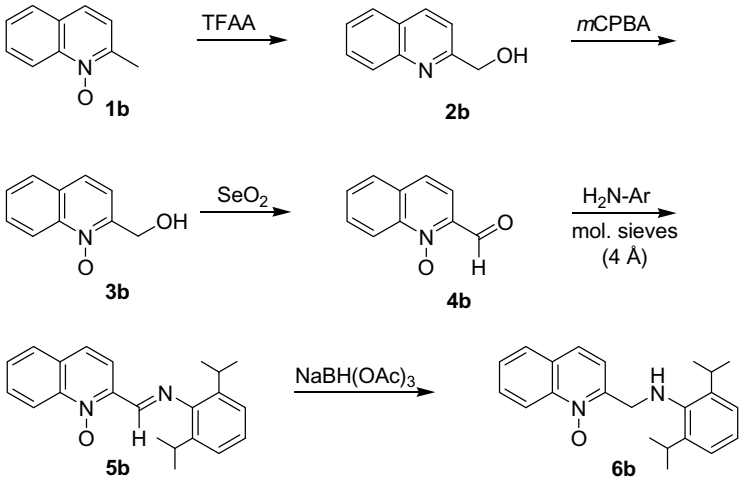


Fig. 3. Projections of the molecular structures of compounds **5b** (top) and **6b** (bottom).

Compound **6b** shows a N1–O1 bond length of 1.303(1) Å and an adjacent $C(sp^2)$–$C(sp^3)$ linkage (C2–C7 1.492(2) Å) to the $-CH_2-NH-Ar$ substituent. The C7–N8 single bond (1.462(2) Å) is oriented almost coplanar with the adjacent quinoline-*N*-oxide ring (N1–C2–C7–N8 −177.9(1)°) but the adjacent N–C(ar) vector is markedly rotated out of this plane (C2–C7–N8–C9 141.2(1)°). Again the bulky 2,6-diisopropylphenyl substituent is oriented near to normal to the adjacent C7–N8 vector (dihedral angle C7–N8–C9–C14 −72.8(1)°).

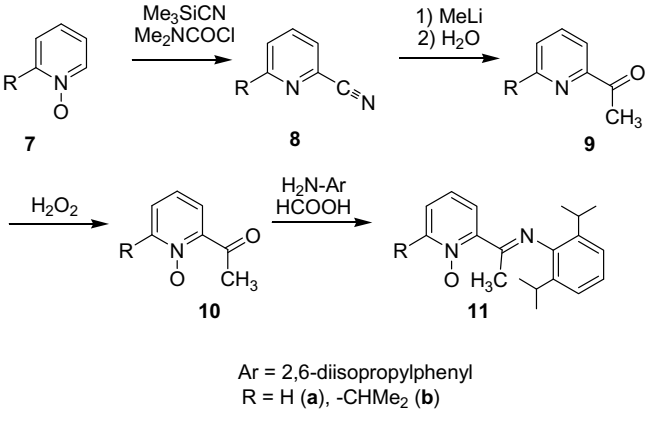


Scheme 3.

In solution compound **5b** features a single set of isopropyl methyl NMR resonances [^{1}H/^{13}C: δ 1.19 (d, ^3J = 6.9 Hz)/23.5] as does **6b** [^{1}H/^{13}C: δ 1.17 (d, ^3J = 6.9 Hz)/24.3].

2.2. Systems derived from 2-acetylpyridine-N-oxide

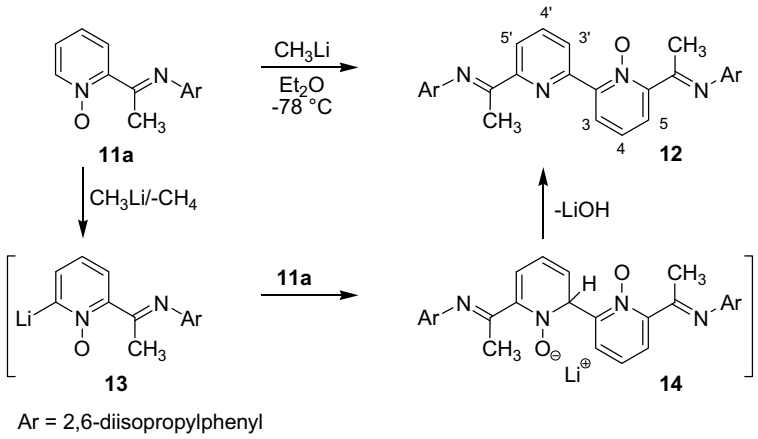
The compounds **11a**/**b** were prepared as was described by us previously [4,11]. The pyridine-*N*-oxides (**7**) were converted to the 2-cyanopyridines (**8**) by a modified Reissert–Henze reaction [12] (for a mechanistic scheme see the Supplementary material). Subsequent nucleophilic methylation, followed by hydrolysis, *N*-oxidation and condensation gave the iminopyridin-*N*-oxide systems (**11**) (see Scheme 4). Their structures in the crystal had previously been determined and described [4].



Scheme 4.

Imines can often be converted to amines by the addition of, e.g. alkyllithium nucleophiles [13], followed by hydrolysis. We have, therefore, treated the ketimino compound **11a** with methyl lithium. Workup gave a new compound (**12**) in ca. 50% yield that clearly was not the corresponding amine but rather a coupled product between two pyridine cores of the starting material (see Scheme 5). This became evident from the observation of two imino ^{13}C NMR signals at δ 167.4 and δ 165.6. The ^{1}H NMR spectrum (see Fig. 4) showed a total of five separated signals originating from the six pyridine protons [δ 9.19, 8.45 (2H), 8.01, 7.63, 7.49 (in THF-d_8)] in addition to a pair of isopropyl CH septets (δ 3.03, δ 2.80) and four corresponding isopropyl methyl doublets (δ 1.26, 1.17, 1.16, 1.14).

The structural assignment of **12** was confirmed by an X-ray crystal structure analysis of the compound (see Fig. 5). It shows the presence of a pyridine ring *ortho*-coupled to a pyridine-*N*-oxide unit [dihedral angle between the units: N1–C6–C22–N23 143.6(4)°]. The C28–N30 imine moiety is close to coplanar to its adjacent pyridine ring (N23–C24–C28–N30 −175.0(4)°) with its attached 2,6-diisopropylphenyl substituent being oriented almost normal to that plane (C28–N30–C31–C36 79.2(5)°). The more bulky pyridine-*N*-oxide forces its attached imine away from coplanarity (N1–C2–C7–N9 127.0(4)°). Both imino-C=N double bonds in **12** are E-configurated. Due to the relatively high *R*-factor



Scheme 5.

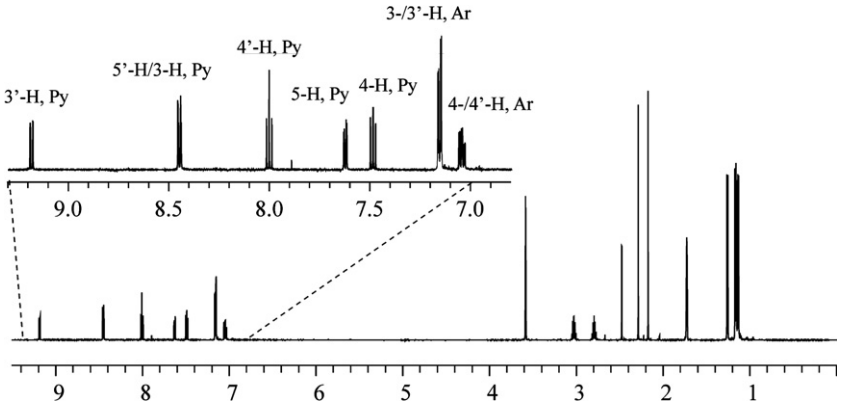


Fig. 4. ^{1}H NMR spectrum of **12** (500 MHz, 298 K, THF-d_8).

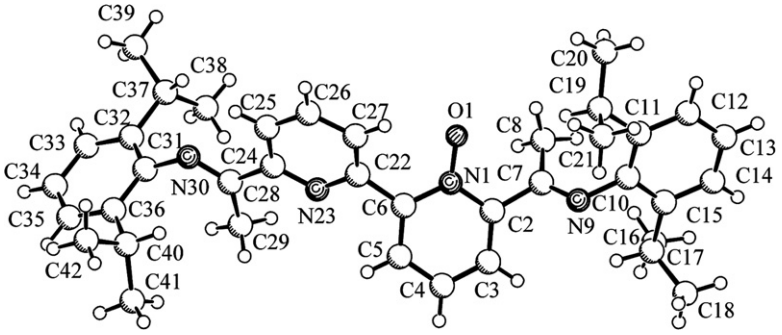


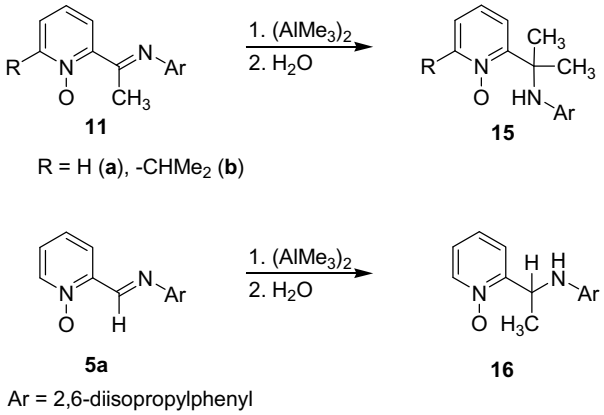
Fig. 5. Molecular structure of **12**.

(9.8%) no further details of the crystal structure analysis of **12** shall be discussed.

A potential mechanistic pathway of the formation of **12** is depicted in Scheme 5. It is well established that pyridine-*N*-oxides are readily deprotonated in the 2-position by treatment with suitable bases [14]. This *o*-lithiation can in some cases [15,16] initiate non-transition metal induced pathways [17] to the formation of bipyridyl-*N*-oxide derivatives. So it may be that *o*-lithiation of **11a** leads to the formation of **13**, which could subsequently undergo nucleophilic attack at the 2-position of a molecule of the starting material (**11a**) to generate **14**. Elimination of lithium hydroxide from this reactive intermediate would then provide a suitable route to the observed product **12** (see Scheme 5) [15].

Since methyl lithium proved to be too basic for the attempted nucleophilic imine to amine conversion we searched for a suited less basic carbon nucleophile for addition to the imine carbon atom of the (ketimino)pyridine-*N*-oxide reagents **11**. We found it in trimethylaluminum. Treatment of **11a** with excess trimethylaluminum followed by aqueous work up furnished the corresponding *N*-aryl-1-methyl-aminoethyl-substituted pyridine-*N*-oxide system (**15a**) in >50% yield. The analogous reaction of **11b** with $(AlMe_3)_2$ gave the corresponding product (**15b**) in >60% yield (see Scheme 6). Compound **15b** features a single ^{1}H NMR isopropyl methyl doublet of the 2,6-diisopropylphenyl substitutent at δ 0.95 (d, ^3J = 6.9 Hz, 12 Hz) plus a corresponding signal of the isopropyl group at the pyridine-*N*-oxide nucleus of half the intensity at δ 1.33 (d, ^3J = 6.9 Hz, 6H). The newly introduced $-C(CH_3)_2-N$ ^{1}H NMR methyl resonance occurs at δ 1.54 (s, 6H) (^{13}C: δ 26.8).

Both the compounds **15a** and **15b** were characterized by X-ray diffraction (see Fig. 6). Compound **15a** (values are taken from molecule A) features a N1–O1 bond length of 1.309(2) Å of the pyridine-*N*-oxide unit. The adjacent C2–C7 bond length is found at



Scheme 6.

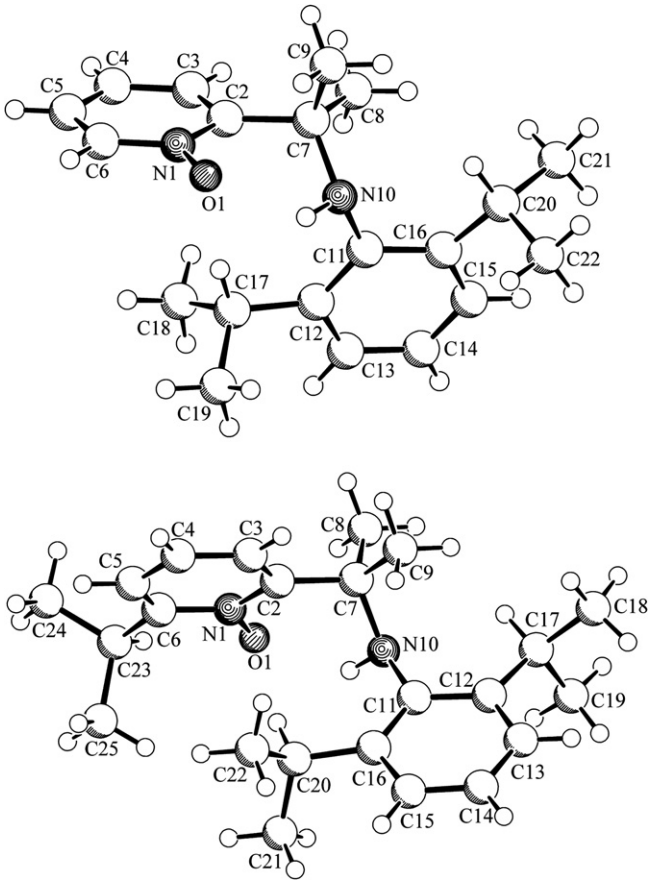


Fig. 6. Views of the molecular structures of the compounds **15a** (top) and **15b** (bottom).

1.533(2) Å and the C7–N10 linkage (1.489(2) Å) is in the typical C(sp^3)–N σ-bond range. It may be that the N–H group forms a weak hydrogen bond to the pyridine-*N*-oxide oxygen atom [O1–H(N10) 2.10(2) Å]. However, the conformation of the respective part of the molecule **15a** is markedly non-planar [dihedral angle N1–C2–C7–N10 55.1(2)°]. The bulky 2,6-diisopropylphenyl group attains a conformational orientation that minimizes steric hindrance (C2–C7–N10–C11 89.7(2)°, C7–N10–C11–C16 93.4(2)°). Compound **15b** exhibits an analogous structure in the crystal (see Fig. 6).

The parent (aldimino)pyridine-*N*-oxide compound **5a** reacts analogously with $(AlMe_3)_2$. After aqueous workup, we have isolated the (aminoethyl)pyridine-*N*-oxide derivative **16** in 75% yield. Compound **16** contains a chiral center [^{1}H NMR: δ 4.00 (1H), δ 1.69 (d, ^3J = 6.9 Hz, 3H), $-CH(CH_3)-N$]. Therefore, a set of diastereotopic

$^{1}H/^{13}C$ NMR isopropyl methyl signals was observed for this compound [^{1}H: δ 3.47 (sept. 1H), 1.18/1.03 (each d, ^{3}J = 6.8 Hz, each 6H)/^{13}C: δ 27.8 ($CHMe_2$), 24.6/24.4 ($CH(CH_3)_2$)].

Compound **16** was also characterized by X-ray diffraction. It features a remarkably different conformation from the related **15a**/**15b** pair of compounds (see Fig. 7). The bond lengths of the characteristic functional groups of compound **16** are in the typical range (N1–O1: 1.312(2) Å, C2–C7 1.512(2) Å, C7–N9 1.464(2) Å), but the C7–N9 vector is rotated away from the pyridine-*N*-oxide moiety (dihedral angles N1–C2–C7–N9 152.3(1)°, C2–C7–N9–C10 −72.6(2)°). Again the bulky 2,6-diisopropylphenyl substituent attains a position that probably minimizes unfavorable steric interaction (C7–N9–C10–C11 −61.0(2)°).

2.3. Metallation reactions

For use of the (aminomethyl)pyridine-*N*-oxide derivatives as ligands in transition metal chemistry it would be desirable to generate the respective anions by deprotonation at the amine nitrogen of the side chain. Therefore, we treated compound **6a** with *n*-butyl lithium in THF. Unexpectedly, this led to the sole formation of the pyridine aldimine product (**19a**). Treatment of **6a** with several other bases (LDA in THF; KH in THF and even $Zr(NMe_2)_4$ in toluene) gave the same result. The reaction of the (aminomethyl)quinoline-*N*-oxide derivative **6b** with LDA (in THF) took the analogous course to yield the quinoline aldimine product **19b**. Both the products **19a** and **19b** were positively identified by comparison with the authentic separately prepared heterocyclic aldimines [18,19]. A potential mechanistic scheme for this intramolecular redox reaction is depicted in Scheme 8. However, this needs to be supported by further specific investigations (see Scheme 7).

We have also reacted the (1-methyl-aminoethyl)pyridine-*N*-oxide derivative **15a** with methyl lithium. In this case, the intramolecular redox reaction is prevented to take place by the presence of the pair of geminal methyl groups at the α-position of the substituent. However, in this case the apparently generated amide anion system proved to be unstable with regard to a fragmentation reaction to yield the acetone imine product (**21**) (see Scheme 9).

In view of these synthetic complications we decided to build up the (amidomethyl)pyridine-*N*-oxide N,O-chelate ligands directly in the coordination sphere of a metal. Since the reactions of the respective imine systems with trimethylaluminum had successfully been used for the alkylated (aminomethyl)pyridine-*N*-oxide synthesis (see above) [20] we decided to use this reaction for the preparation and isolation of the respective (N,O-chelate ligand)aluminum complexes (see Scheme 10).

Treatment of compound **11a** with trimethylaluminum gave the (N,O-chelate)Al complex **23** as a bright yellow solid. It features a ^{1}H NMR singlet for the geminal $C(CH_3)_2$ group inside the chelate ring

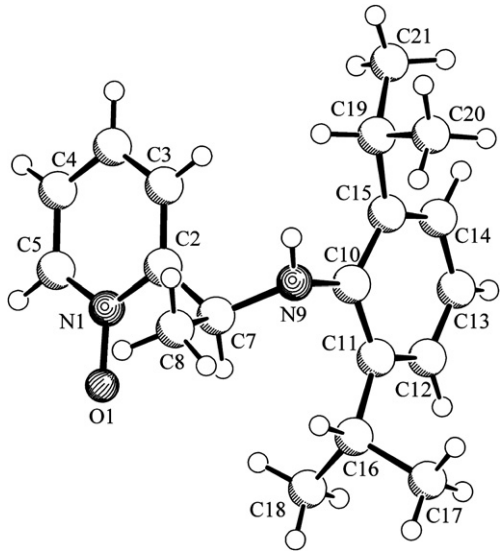
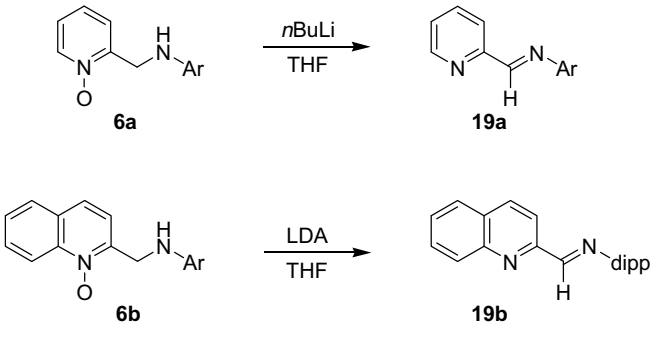
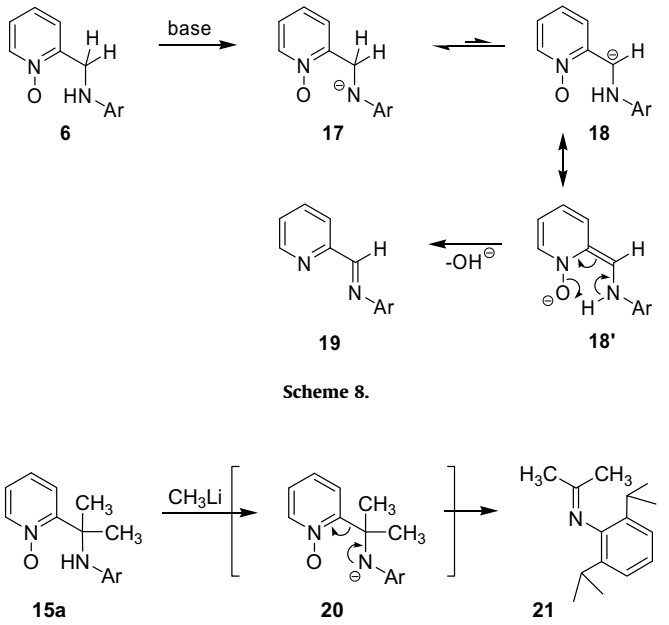


Fig. 7. A projection of the molecular structure of compound **16**.

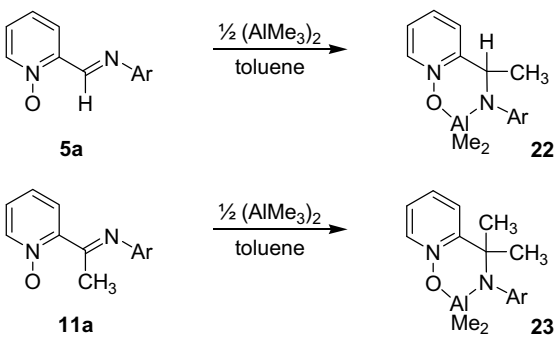


Scheme 7.



Scheme 8.

Scheme 9.



Scheme 10.

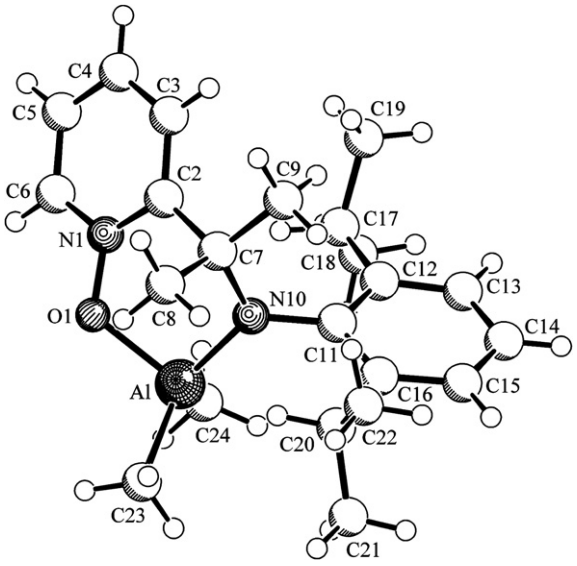


Fig. 8. Molecular structure of the N,O-chelate Al complex **23**.

at δ 1.45 (^{13}C: δ 28.0) and a Al(CH_3)$_2$ resonance at δ −0.23 (^{1}H) (^{13}C: δ −6.9). The *N*-2,6-diisopropylphenyl unit exhibits axial prochirality and, thus, features one isopropyl ^{1}H NMR CH septet (δ 3.37, 2 H intensity) and two CH(CH_3)$_2$ doublets (δ 1.27, δ 1.10) each of 6H intensity [^{13}C: δ 27.8 (*C*HMe$_2$), δ 26.2, 25.1 (CH(*C*H$_3$)$_2$)].

Complex **23** was characterized by X-ray diffraction (single crystals from pentane at −20 °C). The structural analysis confirms that a methyl anion equivalent was added to the former imine carbon center of the starting material (**11a**). The aluminum atom is coordinated to both the nitrogen atom of the side chain and the oxygen atom of the pyridine-*N*-oxide subunit (bond lengths Al–N10 1.844(2) Å, Al–O1: 1.859(2) Å). This coordination has resulted in a marked lengthening of the pyridine-*N*-oxide N1–O1 bond (**23**: 1.355(3) Å, cf. **11a**: 1.301(1) Å [4]). The Al atom in **23** features a distorted pseudotetrahedral coordination sphere [bond angles N10–Al–O1 94.2(1)°, N10–Al–C24 114.6(1)°, O1–Al–C24 109.7(1)°, N10–Al–C23 120.6(1)°, O1–Al–C23 102.9(1)°, C24–Al–C23 112.0(2)°]. The metallacyclic six-membered chelate ring adopts a shallow envelope-like conformation (C2–C7–N10–Al −59.5(3)°, N1–C2–C7–N10 52.4(3)°, O1–N1–C2–C7 2.7(4)°). The bulky 2,6-diisopropylphenyl substituent at N10 is markedly rotated out of the mean central plane of **23** (C7–N10–C11–C12 −89.2(3)°) (see Fig. 8).

Treatment of the aldimino-substituted pyridine-*N*-oxide system (**5a**) with trimethylaluminum yielded the corresponding six-membered N,O-chelate Al complex **22** (see Scheme 10). In this case, the ring contains a newly formed chirality center. Consequently we have observed a pair of ^{1}H NMR isopropyl CH septets (at δ 3.86, 3.09) and four –CH(*C*H$_3$)$_2$ doublets (δ 1.18, 1.17, 1.10, 1.04) of the orthogonally oriented 2,6-diisopropylphenyl substituent. Complex **22** features a pair of Al(CH_3) ^{1}H NMR resonances at δ −0.54 and −0.77 (^{13}C: −7.2, −9.4; both are very broad).

3. Conclusions

This study has shown that a variety of (aminomethyl)pyridine-*N*-oxide systems is readily available via their respective aldimines or ketimines. Reduction can be effected by treatment with sodium borohydride reagents. Alternatively, treatment with trimethylaluminum leads to a clean transfer of a methyl anion equivalent. Subsequent hydrolysis then liberates the corresponding (aminoethyl)pyridine-*N*-oxide derivatives. Unexpectedly, the deprotonation of these systems resulted in reactive amide anions that were unstable with regard to either an intramolecular redox reaction or the formation of a coupling product or fragmentation. Under the reaction conditions applied by us in this study this has prohibited the usual use and application of such ligands by means of employment of their amide anions (i.e. their alkali metal compounds). A potential synthetic solution of this serious problem was eventually provided by the clean reaction of the pyridine-*N*-oxide aldimines or ketimines with trimethylaluminum; from these reaction mixtures the corresponding N,O-chelate (amidoethyl)pyridine-*N*-oxide Al complexes could be obtained. It will be seen if such Al systems might prove useful, be it as reagents for transmetallation to transition metals or themselves as catalysts, e.g. in polymerization reactions [21,22].

4. Experimental

All reactions involving air or moisture sensitive compounds were carried out under inert atmosphere using *Schlenk*-type glassware or in a glovebox. Solvents were dried and distilled prior to use. The following instruments were used for physical characterization of the compounds: Melting points, DSC 2010 TA-instruments; elemental analyses, Foss-Heraeus CHNO-Rapid; MS, Micromass Quattro LC-Z electrospray mass spectrometer; NMR, Bruker AC 200 P (^{1}H: 200 MHz), Bruker AV 400 (^{1}H: 400 MHz), Varian INOVA NMR spectrometer (^{1}H: 500 MHz, ^{13}C: 126 MHz), or Varian UNITY plus NMR spectrometer (^{1}H: 600 MHz, ^{13}C: 151 MHz, ^{19}F 564 MHz). X-ray crystal structure determinations: Data sets were collected with Nonius KappaCCD diffractometers, in case of Mo-radiation a rotating anode generator was used. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN (Z. Otwinowski, W. Minor, Methods in Enzymology, 1997 (276) 307), absorption correction SORTAV (R.H. Blessing, Acta Crystallogr., Sect. A, 1995 (51) 33; R.H. Blessing, J. Appl. Crystallogr. 1997 (30) 421) and Denzo (Z. Otwinowski, D. Borek, W. Majewski, W. Minor, Acta Crystallogr., Sect. A, 2003 (59) 228), structure solution SHELXS-97 (G.M. Sheldrick, Acta Crystallogr., Sect. A, 1990 (46) 467), structure refinement SHELXL-97 (G.M. Sheldrick, Universität Göttingen, 1997), graphics SCHAKAL (E. Keller, Universität Freiburg, 1997).

The (ketimino)pyridine-*N*-oxides **11a** and **11b** [4] were synthesized according to procedures reported in the literature.

4.1. 2-{[(*E*)-2,6-Diisopropylphenylimino]methyl}pyridine-*N*-oxide (*5a*)

2,6-Diisopropylaniline (3.01 g, 17.0 mmol) and a catalytic amount of formic acid were added to a solution of **4a** (2.00 g, 16.2 mmol) in dichloromethane (50 mL). After refluxing the reaction mitxture in the presence of moleculare sieve (4 Å) for 4 h, it was filtered and then the solvent was removed in vacuo to yield a yellow solid. Crystallisation from methanol gave the pure product (2.80 g, 61%) as a shiny yellow crystalline solid. Fractional crystallization from methanol gave crystals suitable for X-ray diffraction. M.p. 133 °C (DSC). MS-ESI (*m*/*z*, ES+, in methanol): 283.2 [M+H]$^+$, 305.2 [M+Na]$^+$, 587.3 [2M+Na]$^+$. Anal. Calc. for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.47; H, 7.94; N, 9.81%. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 8.89 (s, 1H, N=C*H*), 8.23 (m, 1H, 6-H^{Py}), 8.18 (m, 1H, 3-H^{Py}), 7.35 (m, 1H, 5-H^{Py}), 7.33 (m, 1H, 4-H^{Py}), 7.15 (m, 2H, 3-H^{Ar}), 7.11 (m, 1H, 4-H^{Ar}), 2.91 (sept, ^3J = 6.9 Hz, 2H, C*H*(CH$_3$)$_2$), 1.16 (d, ^3J = 6.9 Hz, 12H, CH(C*H*$_3$)$_2$). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 298 K): δ = 155.1 ($^1J_{CH}$ = 176 Hz, N=*C*H), 148.3 (C1^{Ar}), 145.5 (C2^{Py}), 140.0 (C6^{Py}), 137.2 (C2^{Ar}), 127.3 (C5^{Py}), 125.4 (C4^{Py}), 124.9 (C4^{Ar}), 124.5 (C3^{Py}), 123.1 (C3^{Ar}), 28.0 (*C*H(CH$_3$)$_2$), 23.4 (CH(*C*H$_3$)$_2$).

X-ray crystal structure analysis for ***5a***: formula $C_{18}H_{22}N_2O$, $M = 282.38$, yellow crystal $0.40 \times 0.25 \times 0.15$ mm, $a = 10.9335(3)$, $b = 22.6543(7)$, $c = 13.4702(5)$ Å, $\beta = 100.451(1)°$, $V = 3281.09(18)$ Å^3, $\rho_{calc} = 1.143$ g cm^{-3}, $\mu = 0.557$ mm^{-1}, empirical absorption correction ($0.808 \leqslant T \leqslant 0.921$), $Z = 8$, monoclinic, space group $P2_1/n$, (No. 14), $\lambda = 1.54178$ Å, $T = 223$ K, ω and ϕ scans, 27251 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.60$ Å^{-1}, 5859 independent ($R_{int} = 0.042$) and 5194 observed reflections [$I \geqslant 2\sigma(I)$], 387 refined parameters, $R = 0.050$, $wR^2 = 0.139$, max. residual electron density 0.54 (−0.37) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

4.2. 2-{[(E)-2,6-Diisopropylphenylimino]methyl}quinoline-N-oxide (*5b*)

2,6-Diisopropylaniline (1.09 mL, 5.80 mmol) was added to a solution of **4b** (1.00 g, 5.80 mmol) in dichloromethane (30 mL) with moleculare sieve (4 Å). After refluxing the reaction mitxture for 4 h, it was filtered and then the solvent was removed in vacuo to yield a yellow solid. Crystallisation from methanol gave the pure product (1.58 g, 81%) as a shiny yellow solid. Fractional crystallization from methanol gave crystals suitable for X-ray diffraction. M.p. 133 °C (DSC). MS-ESI (*m*/*z*, ES+, in methanol): 333.2 $[M+H]^+$, 355.2 $[M+Na]^+$, 687.4 $[2M+Na]^+$. Anal. Calc. for $C_{22}H_{24}N_2O$: C, 79.48; H, 7.28; N, 8.43. Found: C, 78.57; H, 7.14; N, 8.33%. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): $\delta = 9.14$ (s, 1H, N=C*H*), 8.78 (d, $^3J = 8.8$ Hz, 1H, 8-H^{Ch}), 8.22 (d, $^3J = 8.8$ Hz, 1H, 3-H^{Ch}), 7.88 (d, $^3J = 8.1$ Hz, 1H, 5-H^{Ch}), 7.77 (ddd, $^3J = 8.8$ Hz, $^3J = 7.0$ Hz, $^4J = 1.3$ Hz, 1H, 7-H^{Ch}), 7.76 (d, $^3J = 8.8$ Hz, 1H, 4-H^{Ch}), 7.68 (ddd, $^3J = 8.1$ Hz, $^3J = 7.0$ Hz, $^4J = 1.2$ Hz, 1H, 6-H^{Ch}), 7.18 (m, 2H, 3-H^{Ar}), 7.14 (m, 1H, 4-H^{Ar}), 2.98 (sept, $^3J = 6.9$ Hz, C*H*(CH$_3$)$_2$), 1.19 (d, $^3J = 6.9$ Hz, CH(C*H*$_3$)$_2$).

X-ray crystal structure analysis for ***5b***: formula $C_{22}H_{24}N_2O$, $M = 332.43$, yellow crystal $0.25 \times 0.15 \times 0.15$ mm, $a = 8.578(1)$, $b = 10.941(1)$, $c = 20.396(8)$ Å, $\alpha = 79.58(1)°$, $\beta = 83.87(1)°$, $\gamma = 80.30(1)°$, $V = 1850.0(3)$ Å^3, $\rho_{calc} = 1.194$ g cm^{-3}, $\mu = 0.572$ mm^{-1}, empirical absorption correction ($0.870 \leqslant T \leqslant 0.919$), $Z = 4$, triclinic, space group $P\bar{1}$, (No. 2), $\lambda = 1.54178$ Å, $T = 223$ K, ω and ϕ scans, 20302 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.60$ Å^{-1}, 6416 independent ($R_{int} = 0.037$) and 5520 observed reflections [$I \geqslant 2\sigma(I)$], 489 refined parameters, $R = 0.050$, $wR^2 = 0.139$, max. residual electron density 0.70 (−0.17) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

4.3. 2-[(2,6-Diisopropylphenylamino)methyl]pyridine-N-oxide (*6a*)

Sodium borohydride (1.24 g, 32.7 mmol) was added carefully to a solution of THF (49 mL) and glacial acetic acid (19 mL) at 0 °C in a way that the temperature was always below 20 °C. After the hydrogen evolution has stopped, the rection mixture was cooled to −78 °C and a solution of **5a** (3.09 g, 10.9 mmol) in THF (10 mL) was added. Then the reaction mixture was stirred over night at room temperature. The solvent was removed in vacuo and the residue was dissolved in dichloromethane (100 mL). Aqueous Na_2CO_3 solution was added, the organic phase was separated, dried over $MgSO_4$, and the solvent was removed in vacuo. The product was obtained after column chromatography (SiO_2; pentane/methanol/dichloromethane/triethyl-amine 15:1:1:1) as a white solid (1.66 g, 54%). Crystallization from a chloroform/methanol/triethylamine mixture gave crystals suitable for X-ray diffraction. M.p. 92 °C (DSC). MS-ESI (*m*/*z*, ES+, in methanol): 285.1 $[M+H]^+$, 307.1 $[M+Na]^+$, 591.4 $[2M+Na]^+$. Anal. Calc. for $C_{18}H_{24}N_2O$: C, 76.02; H, 8.51; N, 9.85. Found: C, 75.98; H, 8.43; N, 9.77%. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): $\delta = 8.27$ (m, 1H, 6-H^{Py}), 7.32 (m, 1H, 3-H^{Py}), 7.21 (m, 2H, 4-/5-H^{Py}), 7.06 (m, 3H, 3-/4-H^{Ar}), 4.47 (br s, 1H, N*H*), 4.20 (s, 2H, NCH_2), 3.32 (sept, $^3J = 6.9$ Hz, 2H, C*H*(CH$_3$)$_2$), 1.19 (d, $^3J = 6.9$ Hz, CH(C*H*$_3$)$_2$). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 298 K): $\delta = 149.7$ (C2^{Py}), 143.0 (C2^{Ar}), 142.1 (C1^{Ar}), 139.6 (C6^{Py}), 126.0 (C4^{Py}), 125.6 (C3^{Py}), 124.6 (C5^{Py}), 124.2 (C4^{Ar}), 123.6 (C3^{Ar}), 51.5 (NCH_2), 27.5 (C*H*(CH$_3$)$_2$), 24.3 (CH(C*H*$_3$)$_2$).

X-ray crystal structure analysis for ***6a***: formula $C_{18}H_{24}N_2O$, $M = 284.39$, light yellow crystal $0.30 \times 0.06 \times 0.03$ mm, $a = 35.478(2)$, $b = 5.819(1)$, $c = 15.606(1)$ Å, $V = 3221.8(6)$ Å^3, $\rho_{calc} = 1.173$ g cm^{-3}, $\mu = 0.567$ mm^{-1}, empirical absorption correction ($0.848 \leqslant T \leqslant 0.983$), $Z = 8$, orthorhombic, space group *Pbcn*, (No. 60), $\lambda = 1.54178$ Å, $T = 223$ K, ω and ϕ scans, 13626 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.59$ Å^{-1}, 2243 independent ($R_{int} = 0.068$) and 1182 observed reflections [$I \geqslant 2\sigma(I)$], 198 refined parameters, $R = 0.061$, $wR^2 = 0.213$, max. residual electron density 0.28 (−0.28) e Å^{-3}, hydrogen atom at N8 from difference fourier map, other calculated and refined as riding atoms.

4.4. 2-[(2,6-Diisopropylphenylamino)methyl]quinoline-N-oxide (*6b*) (according to the procedure described for the synthesis of *6a*)

Sodium borohydride (0.26 g, 6.87 mmol) in THF (15 mL) and glacial acetic acid (5 mL) reacts with a solution of **5b** (0.76 g, 2.29 mmol) in THF (5 mL). The described workup using 50 mL dichloromethane to dissolve the residue was carried out. Finally the product was obtained after column chromatography (SiO_2; pentane/methanol/dichloromethane/triethylamine 30:1:1:1) as a white solid (0.66 g, 86%). Crystallization from a methanol/triethylamine mixture gave crystals suitable for X-ray diffraction. M.p. 124 °C (DSC). MS-ESI (*m*/*z*, ES+, in methanol): 335.2 $[M+H]^+$, 357.2 $[M+Na]^+$. Anal. Calc. for $C_{22}H_{26}N_2O$: C, 79.01; H, 7.84; N, 8.38. Found: C, 78.40; H, 7.83; N, 8.29%. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): $\delta = 8.79$ (d, $^3J = 8.8$ Hz, 1H, 8-H^{Ch}), 7.84 (d, $^3J = 8.2$ Hz, 1H, 5-H^{Ch}), 7.77 (ps t, 1H, 7-H^{Ch}), 7.69 (d, $^3J = 8.5$ Hz, 1H, 4-H^{Ch}), 7.61 (ps t, 1H, 6-H^{Ch}), 7.41 (d, $^3J = 8.5$ Hz, 3-H^{Ch}), 7.08 (m, 3H, 3-/4-H^{Ar}), 4.41 (s, 2H, NCH_2), 3.37 (sept, $^3J = 6.9$ Hz, 2H, C*H*(CH$_3$)$_2$), 1.17 (d, $^3J = 6.9$ Hz, 12H, CH(C*H*$_3$)$_2$). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$, 298 K): $\delta = 146.5$ (C2^{Ch}), 143.0 (C2^{Ar}), 142.2 (C1^{Ar}), 141.6 (C8a^{Ch}), 130.5 (C7^{Ch}), 129.6 (C4a^{Ch}), 128.2 (C6^{Ch}), 128.1 (C5^{Ch}), 125.6 (C4^{Ch}), 124.2 (C4^{Ar}), 123.6 (C3^{Ar}), 121.5 (C3^{Ch}), 119.4 (C8^{Ch}), 52.1 (NCH_2), 27.5 (C*H*(CH$_3$)$_2$), 24.3 (CH(C*H*$_3$)$_2$).

X-ray crystal structure analysis for ***6b***: formula $C_{22}H_{26}N_2O$, $M = 334.45$, light yellow crystal $0.35 \times 0.20 \times 0.06$ mm, $a = 24.044(1)$, $b = 16.651(1)$, $c = 9.290(1)$ Å, $\beta = 95.09(1)°$, $V = 3696.7(5)$ Å^3, $\rho_{calc} = 1.202$ g cm^{-3}, $\mu = 0.572$ mm^{-1}, empirical absorption correction ($0.825 \leqslant T \leqslant 0.967$), $Z = 8$, monoclinic, space group *C*2/*c*, (No. 15), $\lambda = 1.54178$ Å, $T = 223$ K, ω and ϕ scans, 23809 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.60$ Å^{-1}, 3303 independent ($R_{int} = 0.042$) and 3042 observed reflections [$I \geqslant 2\sigma(I)$], 233 refined parameters, $R = 0.040$, $wR^2 = 0.106$, max. residual electron density 0.14 (−0.15) e Å^{-3}, hydrogen atom at N8 from difference fourier map, other calculated and refined as riding atoms.

4.5. 2-(Pentafluorophenylaminomethyl)pyridine-N-oxide (*6c*)

Pentafluoroaniline (811 mg, 4.43 mmol) was added to a solution of **4a** (519 mg, 5.69 mmol) and acetic acid (0.50 mL) in methanol (10 mL). The reaction mixture was refluxed for 24 h in the presence of molecular sieve (3 Å). Subsequently, sodium cyanoborohydride (796 mg, 12.7 mmol) was added carefully and the reaction mixture was refluxed for further two days. Then the reaction was quenched with aqueous $NaHCO_3$ solution. After the separation of the organic phase the aqueous phase was extracted with dichloromethane three times, the combined organic phases were dried over $MgSO_4$ and the solvent was removed in vacuo. Finally the product was obtained after column chromatography (SiO_2; pentane/chloroform/methanol/triethylamine 80:1:1:1) as a white

solid (0.65 g, 39%). Crystallization from a methanol/triethylamine mixture gave crystals suitable for X-ray diffraction. MS-ESI (*m*/*z*, ES+, in methanol): 291.0 $[M+H]^+$, 313.0 $[M+Na]^+$. Anal. Calc. for $C_{12}H_7N_2OF_5$: C, 49.67; H, 2.43; N, 9.65. Found: C, 49.56; H, 2.32; N, 9.57%. ^{1}H NMR (600 MHz, C_6D_6, 298 K): δ = 7.74 (ddd, ^3J = 6.4 Hz, ^4J = 1.2 Hz, ^5J = 0.5 Hz, 1H, 6-H^{Py}), 6.41 (dd, ^3J = 7.7 Hz, ^4J = 1.9 Hz, 1H, 3-H^{Py}), 6.15 (td, ^3J = 7.7 Hz, ^4J = 1.2 Hz, 1H, 4-H^{Py}), 6.06 (ddd, ^3J = 7.7 Hz, ^3J = 6.4 Hz, ^4J = 1.9 Hz, 1H, 5-H^{Py}), 5.60 (br s, 1H, N*H*), 4.21 (d, ^3J = 7.3 Hz, 2H, C*H*$_2$NH). ^{13}C{^{1}H} NMR (151 MHz, C_6D_6, 298 K): δ = 147.9 (C2^{Py}), 139.4 (C6^{Py}), 125.1 (C3^{Py}), 124.7 (C5^{Py}), 123.5 (C4^{Py}), 46.4 (*C*H$_2$NH), n.o. (C_6F_5). ^{19}F NMR (564 MHz, C_6D_6, 298 K): δ = −159.3 (m, 2F, *o*-Ph^F), −164.9 (m, 2F, *m*-Ph^F), −171.6 (m, 1F, *p*-Ph^F).

X-ray crystal structure analysis for ***6c***: formula $C_{12}H_7F_5N_2O \cdot 1/2\ H_2O$, M = 299.20, colorless crystal 0.40 × 0.25 × 0.15 mm, a = 25.262(1), b = 5.629(1), c = 17.097(1) Å, β = 103.22(1)°, V = 2366.8(5) Å^3, ρ_{calc} = 1.679 g cm^{-3}, μ = 0.165 mm^{-1}, empirical absorption correction ($0.937 \leqslant T \leqslant 0.976$), Z = 8, monoclinic, space group *C*2/*c*, (No. 15), λ = 0.71073 Å, T = 198 K, ω and ϕ scans, 7512 reflections collected (±*h*, ±*k*, ±*l*), $[(\sin\theta)/\lambda]$ = 0.67 Å^{-1}, 2834 independent (R_{int} = 0.042) and 1978 observed reflections [$I \geqslant 2\sigma(I)$], 195 refined parameters, R = 0.041, wR^2 = 0.116, max. residual electron density 0.20 (−0.25) e Å^{-3}, hydrogen atom at N8 and water from difference fourier map, other calculated and refined as riding atoms.

4.6. Reaction of *11a* with methyllithium: formation of *12*

Methyllithium (1.6 M in diethylether, 4.6 mL, 7.30 mmol) was added to a solution of **11a** (2.06 g, 6.95 mmol) in diethylether (100 mL) at −78 °C. Subsequently, the reaction mixture was stirred for 2 h at −78 °C then for 12 h at room temperature. After addition of aqueous ammonium chloride solution, the phases were separated and the aqueous phase was extracted with dichloromethane (30 mL). The combined organic phases were dried over $MgSO_4$, filtered, and the solvent was removed in vacuo. The obtained yellow oil was purified by column chromatography (SiO_2; cyclohexane/ethyl acetate/triethylamine 30:1:1) to yield the product as a yellow, crystalline solid (1.05 g, 53%). Crystallization from a pentane/chloroform/methanol/triethylamine mixture gave crystals suitable for X-ray diffraction. M.p. 189 °C (DSC). MS-ESI (*m*/*z*, ES+, in methanol): 575.4 $[M+H]^+$, 597.4 $[M+Na]^+$. Anal. Calc. for $C_{38}H_{46}N_4O$: C, 79.40; H, 8.07; N, 9.75. Found: C, 78.73; H, 7.93; N, 9.69%. ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ = 9.19 (dd, ^3J = 7.9 Hz, ^4J = 1.0 Hz, 1H, 3′-H^{Py}), 8.454 (dd, ^3J = 7.9 Hz, ^4J = 1.0 Hz, 1H, 5′-H^{Py}), 8.450 (dd, ^3J = 7.8 Hz, ^4J = 2.1 Hz, 1H, 3-H^{Py}), 8.01 (t, ^3J = 7.9 Hz, 1H, 4′-H^{Py}), 7.63 (dd, ^3J = 7.8 Hz, ^4J = 2.1 Hz, 1H, 5-H^{Py}), 7.49 (t, ^3J = 7.8 Hz, 1H, 4-H^{Py}), 7.16 (m, 2H, 3-H^{Ar}), 7.157 (m, 2H, 3′-H^{Ar}), 7.05 (ps t, 1H, 4-H^{Ar}), 7.045 (ps t, 1H, 4′-H^{Ar}), 3.03 (sept, ^3J = 6.9 Hz, 2H, C*H*(CH$_3$)$_2$), 2.80 (sept, ^3J = 6.9 Hz, 2H, C*H*(CH$_3$)$'_2$), 2.29 (s, 3H, =CC*H*$'_3$), 2.18 (s, 3H, =CC*H*$_3$), 1.26 (d, ^3J = 6.9 Hz, 6H, CH(C*H*$_3^A$CH$_3^B$)), 1.171 (d, ^3J = 6.9 Hz, 6H, CH(C*H*$_3^A$CH$_3^B$)′), 1.165 (d, ^3J = 6.9 Hz, 6H, CH(CH$_3^A$C*H*$_3^B$)), 1.14 (d, ^3J = 6.9 Hz, 6H, CH(CH$_3^A$C*H*$_3^B$)′). ^{13}C{^{1}H} NMR (126 MHz, THF-d_8, 298 K): δ = 167.4 (=*C*CH$'_3$), 165.6 (=*C*CH$_3$), 156.5 (C6′^{Py}), 151.7 (C6^{Py}), 149.5 (C2′^{Py}), 148.0 (C2^{Py}), 147.4 (C1′^{Ar}), 146.0 (C1^{Ar}), 137.3 (C4′^{Py}), 136.5 (C2^{Ar}), 136.2 (C2′^{Ar}), 128.5 (C3^{Py}), 127.4 (C3′^{Py}), 126.0 (C5^{Py}), 125.0 (C4^{Py}), 124.6, 124.3 (C4^{Ar}, C4′^{Ar}), 123.59, 123.56 (C3^{Ar}, C3′^{Ar}), 122.1 (C5′ ^{Py}), 29.1 (*C*H(CH$_3$)$'_2$), 28.7 (*C*H(CH$_3$)$_2$), 23.7 (CH(CH$_3^A$*C*H$_3^B$)), 23.5 (CH(CH$_3^A$*C*H$_3^B$)′), 23.0 (CH(*C*H$_3^A$CH$_3^B$)), 22.9 (CH(*C*H$_3^A$CH$_3^B$)′), 19.6 (=C*C*H$_3$), 17.2 (=CH*C*H$'_3$).

X-ray crystal structure analysis for ***12***: formula $C_{38}H_{46}N_4O$, M = 574.79, yellow crystal 0.50 × 0.30 × 0.03 mm, a = 11.2767(4), b = 10.4211(3), c = 29.1668(9) Å, β = 96.249(2)°, V = 3407.19(19) Å^3, ρ_{calc} = 1.121 g cm^{-3}, μ = 0.522 mm^{-1}, empirical absorption correction ($0.781 \leqslant T \leqslant 0.985$), Z = 4, monoclinic, space group $P2_1/n$, (No. 14), λ = 1.54178 Å, T = 223 K, ω and ϕ scans, 20 993 reflections collected (±*h*, ±*k*, ±*l*), $[(\sin\theta)/\lambda]$ = 0.60 Å^{-1}, 5794 independent (R_{int} = 0.054) and 4600 observed reflections [$I \geqslant 2\sigma(I)$], 398 refined parameters, R = 0.098, wR^2 = 0.260, max. residual electron density 0.37 (−0.24) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

4.7. 2-[1-(2,6-Diisopropylphenylamino)methylethyl]pyridine-N-oxide (*15a*)

Trimethylaluminum (1.97 mL, 1.44 g, 20.0 mmol) was added carefully to a solution of **11a** (3.00 g, 10.1 mmol) in toluene (100 mL) at 0 °C and the reaction mixture was stirred over night at room temperature. After adding aqueous NaOH solution, the organic phase was separated and the aqueous phase was extracted with chloroform. The combined organic phases were dried over $MgSO_4$ and the solvent was removed in vacuo. Finally the product was obtained after column chromatography (SiO_2; pentane/triethylamine/chloroform/methanol 15:2:1:1) as a white solid (1.79 g, 57%). Crystallization from a chloroform/methanol/triethylamine mixture gave crystals suitable for X-ray diffraction. M.p. 88 °C (DSC). MS-ESI (*m*/*z*, ES+, in methanol): 313.2 $[M+H]^+$, 335.2 $[M+Na]^+$, 647.4 $[2M+Na]^+$. Anal. Calc. for $C_{20}H_{28}N_2O$: C, 76.88; H, 9.03; N, 8.97. Found: C, 76.89; H, 9.01; N, 8.88%. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ = 8.29 (dd, ^3J = 6.4 Hz, ^4J = 1.0 Hz, 1H, 6-H^{Py}), 7.33 (br d, 1H, 3-H^{Py}), 7.25 (br t, 1H, 4-H^{Py}), 7.19 (br t, 1H, 5-H^{Py}), 7.06 (m, 1H, 4-H^{Ar}), 7.02 (m, 2H, 3-H^{Ar}), 5.77 (br s, 1H, N*H*), 3.28 (sept, ^3J = 6.8 Hz, 2H, C*H*(CH$_3$)$_2$), 1.54 (s, 6H, NC(C*H*$_3$)$_2$), 1.02 (d, ^3J = 6.8 Hz, 12H, CH(C*H*$_3$)$_2$). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 298 K): δ = 156.3 (C2^{Py}), 148.4 (C2^{Ar}), 141.4 (C6^{Py}), 138.9 (C1^{Ar}), 126.3 (C4^{Py}), 125.1 (C4^{Ar}), 124.0 (C5^{Py}), 123.1 (C3^{Py}), 122.8 (C3^{Ar}), 58.0 (NC(CH$_3$)$_2$), 28.1 (*C*H(CH$_3$)$_2$), 26.1 (NC(*C*H$_3$)$_2$), 24.2 (CH(*C*H$_3$)$_2$).

X-ray crystal structure analysis for ***15a***: formula $C_{20}H_{28}N_2O$, M = 312.44, colorless crystal 0.35 × 0.30 × 0.15 mm, a = 17.666(1), b = 8.845(1), c = 36.415(1) Å, β = 100.21(1)°, V = 5599.9(7) Å^3, ρ_{calc} = 1.112 g cm^{-3}, μ = 0.529 mm^{-1}, empirical absorption correction ($0.837 \leqslant T \leqslant 0.925$), Z = 12, monoclinic, space group $P2_1/c$, (No. 14), λ = 1.54178 Å, T = 293 K, ω and ϕ scans, 50 552 reflections collected (±*h*, ±*k*, ±*l*), $[(\sin\theta)/\lambda]$ = 0.60 Å^{-1}, 9993 independent (R_{int} = 0.046) and 8034 observed reflections [$I \geqslant 2\sigma(I)$], 652 refined parameters, R = 0.050, wR^2 = 0.129, max. residual electron density 0.18 (−0.19) e Å^{-3}, hydrogen atom at N10 from difference fourier map, other calculated and refined as riding atoms.

4.8. 2-[1-(2,6-Diisopropylphenylamino)methylethyl]-6-isopropylpyridine-N-oxide (*15b*) (according to the procedure described for the synthesis of *15a*)

Trimethylaluminum (113 μL, 85.0 mg, 1.18 mmol) was reacted with a solution of **11b** (0.20 g, 0.59 mmol) in toluene (15 mL). The described workup was carried out, to yield the product after column chromatography (SiO_2; pentane/triethylamine/chloroform/methanol 60:1:1:1) as a white solid (0.13 g, 63%). Crystallization from a *n*-heptane gave crystals suitable for X-ray diffraction. MS-ESI (*m*/*z*, ES+, in methanol): 355.3 $[M+H]^+$, 377.3 $[M+Na]^+$, 731.5 $[2M+Na]^+$. Anal. Calc. for $C_{23}H_{34}N_2O$: C, 77.92; H, 9.67; N, 7.90. Found: C, 77.67; H, 9.66; N, 7.65%. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.18 (m, 1H, 5-H^{Py}), 7.16 (m, 1H, 4-H^{Py}), 7.11 (dd, ^3J = 7.3 Hz, ^4J = 2.4 Hz, 1H, 3-H^{Py}), 7.04 (m, 1H, 4-H^{Ar}), 6.97 (m, 2H, 3-H^{Ar}), 5.99 (br s, 1H, N*H*), 3.87 (sept, ^3J = 6.9 Hz, 1H, C*H*(CH$_3$)$_2^{Py}$), 3.14 (br sept, ^3J = 6.9 Hz, 2H, C*H*(CH$_3$)$_2^{Ar}$), 1.54 (s, 6H, NC(C*H*$_3$)$_2$), 1.33 (d, ^3J = 6.9 Hz, 6H, CH(C*H*$_3$)$_2^{Py}$), 0.95 (d, ^3J = 6.9 Hz, 12H, CH(C*H*$_3$)$_2^{Ar}$). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$,

298 K): δ = 159.1 (C6^{Py}), 156.1 (C2^{Py}), 148.8 (C2^{Ar}), 139.6 (C1^{Ar}), 125.3 (C4^{Py}), 125.0 (C4^{Ar}), 122.7 (C3^{Ar}), 120.5 (C5^{Py}), 120.2 (C3^{Py}), 57.9 (NC(CH$_3$)$_2$), 28.0 (CH(CH$_3$)$_2^{Ar}$), 27.9 (CH(CH$_3$)$_2^{Py}$), 26.8 (NC(CH$_3$)$_2$), 24.1 (br, CH(CH$_3$)$_2^{Ar}$), 20.3 (CH(CH$_3$)$_2^{Py}$).

X-ray crystal structure analysis for ***15b***: formula $C_{23}H_{34}N_2O$, M = 354.52, colorless crystal 0.50 × 0.50 × 0.03 mm, a = 11.626(1), b = 18.960(1), c = 19.166(1) Å, V = 4224.7(5) Å^3, ρ_{calc} = 1.115 g cm^{-3}, μ = 0.068 mm^{-1}, empirical absorption correction (0.967 ⩽ T ⩽ 0.998), Z = 8, orthorhombic, space group *Pbca*, (No. 61), λ = 0.71073 Å, T = 198 K, ω and ϕ scans, 36160 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.62 Å^{-1}, 4287 independent (R_{int} = 0.072) and 2874 observed reflections [$I \geqslant 2\sigma(I)$], 262 refined parameters, R = 0.058, wR^2 = 0.141, max. residual electron density 0.31 (−0.30) e Å^{-3}, hydrogen atom at N10 from difference fourier map, other calculated and refined as riding atoms.

*4.9. 2-[1-(2,6-Diisopropylphenylamino)ethyl]pyridine-N-oxide (**16**) (according to the procedure described for the synthesis of **15a**)*

Trimethylaluminum (14.2 mL, 28.4 mmol) was reacted with a solution of **5a** (4.00 g, 14.2 mmol) in toluene (100 mL). The described workup was carried out, to yield the product after column chromatography (SiO_2; pentane/chloroform/methanol 10:3:1) as a white solid (3.18 g, 75%). Crystallization from a chloroform/methanol/triethylamine mixture gave crystals suitable for X-ray diffraction. M.p. 93 °C (DSC). MS-ESI (*m*/*z*, ES+, in methanol): 299.2 [M+H]$^+$, 321.2 [M+Na]$^+$. Anal. Calc. for $C_{19}H_{26}N_2O$: C, 76.47; H, 8.78; N, 9.39. Found: C, 76.33; H, 8.80; N, 9.40%. ^{1}H NMR (600 MHz, C_7D_8, 298 K): δ = 7.71 (dd, ^3J = 6.1 Hz, ^4J = 1.4 Hz, 1H, 6-H^{Py}), 6.97 (m, 2H, 3-H^{Ar}), 6.94 (m, 1H, 4-H^{Ar}), 6.32 (dd, ^3J = 7.4 Hz, ^4J = 2.2 Hz, 1H, 3-H^{Py}), 6.14 (td, ^3J = 7.4 Hz, ^4J = 1.4 Hz, 1H, 4-H^{Py}), 6.11 (ddd, ^3J = 7.4 Hz, ^3J = 6.1 Hz, ^4J = 2.2 Hz, 1H, 5-H^{Py}), 5.64 (br s, 1H, N*H*), 4.00 (m, 1H, NC*H*(CH$_3$)), 3.47 (sept, ^3J = 6.8 Hz, 2H, C*H*(CH$_3$)$_2$), 1.69 (d, ^3J = 6.9 Hz, 3H, NCH(C*H*$_3$)), 1.18 (d, ^3J = 6.8 Hz, 6H, CH(C*H*$_3^A$CH$_3^B$)), 1.03 (d, ^3J = 6.8 Hz, 6H, CH(CH$_3^A$C*H*$_3^B$)). ^{13}C{^{1}H} NMR (151 MHz, C_7D_8, 298 K): δ = 152.3 (C2^{Py}), 143.0 (C1^{Ar}), 142.9 (C2^{Ar}), 140.5 (C6^{Py}), 125.1 (C3^{Py}), 123.93 (C4^{Ar}), 123.86 (C3^{Ar}), 123.79, 123.77 (C4^{Py}, C5^{Py}), 61.1 (NCH(CH$_3$)), 27.8 (*C*H(CH$_3$)$_2$), 24.6 (CH(*C*H$_3^A$CH$_3^B$)), 24.4 (CH(CH$_3^A$*C*H$_3^B$)), 17.7 (NCH(*C*H$_3$)).

X-ray crystal structure analysis for **16**: formula $C_{19}H_{26}N_2O$, M = 298.42, colorless crystal 0.15 × 0.10 × 0.10 mm, a = 13.240(1), b = 10.673(1), c = 13.257(1) Å, β = 112.16(1)°, V = 1735.0(2) Å^3, ρ_{calc} = 1.142 g cm^{-3}, μ = 0.071 mm^{-1}, empirical absorption correction (0.990 ⩽ T ⩽ 0.993), Z = 4, monoclinic, space group $P2_1/c$, (No. 14), λ = 0.71073 Å, T = 198 K, ω and ϕ scans, 14030 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.66 Å^{-1}, 4121 independent (R_{int} = 0.062) and 2511 observed reflections [$I \geqslant 2\sigma(I)$], 208 refined parameters, R = 0.051, wR^2 = 0.131, max. residual electron density 0.14 (−0.21) e Å^{-3}, hydrogen atom at N9 from difference fourier map, other calculated and refined as riding atoms.

*4.10. κN,O-{2-[1-(2,6-Diisopropylphenylamido)ethyl]pyridine-N-oxide}dimethylaluminum (**22**)*

Trimethylaluminum (0.49 mL, 0.37 g, 5.10 mmol) was added to a solution of **5a** (0.72 g, 2.55 mmol) in toluene (25 mL) at 0 °C and stirred over night. Then the volatiles were removed in vacuo and the residue was washed with less pentane, to get the product as a yellow solid (0.61 g, 67%). ^{1}H NMR (600 MHz, C_7D_8, 333 K): δ = 7.80 (br d, ^3J = 6.6 Hz, 1H, 6-H^{Py}), 7.02 (m, 3H, 3-/4-H^{Ar}), 6.62 (br t, ^3J = 7.8 Hz, 1H, 4-H^{Py}), 6.54 (br d, ^3J = 7.8 Hz, 1H, 3-H^{Py}), 6.13 (br dd, ^3J = 7.8 Hz, ^3J = 6.6 Hz, 1H, 5-H^{Py}), 4.18 (q, ^3J = 6.9 Hz, 1H, NC*H*(CH$_3$)), 3.86 (sept, ^3J = 6.8 Hz, 1H, C*H*(CH$_3$)$_2$), 3.09 (sept, ^3J = 6.8 Hz, 1H, C*H*(CH$_3$)$'_2$), 1.28 (d, ^3J = 6.9 Hz, 3H, NCH(C*H*$_3$)), 1.18 (d, ^3J = 6.8 Hz, 3H, CH(C*H*$_3^A$CH$_3^B$)), 1.17 (d, ^3J = 6.8 Hz, 3H, CH(CH$_3^A$C*H*$_3^B$)), 1.10 (d, ^3J = 6.8 Hz, 3H, CH(C*H*$_3^A$CH$_3^B$)′), 1.04 (d, ^3J = 6.8 Hz, 3H, CH(CH$_3^A$C*H*$_3^B$)′), −0.54 (br. s, 3H, Al(C*H*$_3$)$_2$), −0.77 (br s, 3H, Al(C*H*$_3$)$_2$). ^{13}C{^{1}H} NMR (151 MHz, C_7D_8, 333 K): δ = 158.9 (C2^{Py}), 149.7 (C2^{Ar}), 148.8 (C2′^{Ar}), 145.9 (C1^{Ar}), 141.7 (C6^{Py}), 138.3 (C4^{Py}), 125.1 (C4^{Ar}), 124.6 (C3^{Py}), 124.3 (C3′^{Ar}), 123.9 (C3^{Ar}), 123.7 (C5^{Py}), 60.9 (NCH(CH$_3$)), 28.1 (*C*H(CH$_3$)$'_2$), 27.4 (*C*H(CH$_3$)$_2$), 26.0 (CH(*C*H$_3^A$CH$_3^B$)), 25.7 (CH(*C*H$_3^A$CH$_3^B$)′), 25.57 (CH(CH$_3^A$*C*H$_3^B$)′), 25.55 (CH(CH$_3^A$*C*H$_3^B$)), 20.1 (NCH(*C*H$_3$)), −7.2, −9.4 (br, Al(*C*H$_3$)$_2$).

*4.11. κN,O-{2-[1-(2,6-Diisopropylphenylamido)methylethyl]pyridine-N-oxide}dimethylaluminum (**23**)*

Trimethylaluminum (1.97 mL, 1.44 g, 20.0 mmol) was added to a solution of **11a** (3.00 g, 10.1 mmol) in toluene (50 mL) at 0 °C and stirred over night. Then the volatiles were removed in vacuo and the residue was washed with pentane, to get the product as a light yellow solid. Crystallization from a pentane solution at −20 °C gave crystals suitable for X-ray diffraction. M.p. 160 °C (DSC, Decomp.). ^{1}H NMR (600 MHz, C_6D_6, 298 K): δ = 7.43 (d, ^3J = 6.2 Hz, 1H, 6-H^{Py}), 7.16 (m, 1H, 4-H^{Ar}), 7.13 (m, 2H, 3-H^{Ar}), 6.53 (dd, ^3J = 7.9 Hz, ^4J = 1.7 Hz, 1H, 3-H^{Py}), 6.43 (td, ^3J = 7.9 Hz, ^4J = 1.3 Hz, 1H, 4-H^{Py}), 5.95 (ddd, ^3J = 7.9 Hz, ^3J = 6.2 Hz, ^4J = 1.7 Hz, 1H, 5-H^{Py}), 3.37 (sept, ^3J = 6.8 Hz, 2H, C*H*(CH$_3$)$_2$), 1.45 (s, 6H, NC(C*H*$_3$)$_2$), 1.27 (d, ^3J = 6.8 Hz, 6H, CH(C*H*$_3^A$CH$_3^B$)), 1.10 (d, ^3J = 6.8 Hz, 6H, CH(CH$_3^A$C*H*$_3^B$)), −0.23 (s, 6H, Al(C*H*$_3$)$_2$). ^{13}C{^{1}H} NMR (151 MHz, C_6D_6, 298 K): δ = 161.6 (C2^{Py}), 150.0 (C2^{Ar}), 145.1 (C1^{Ar}), 140.4 (C6^{Py}), 133.9 (C4^{Py}), 124.7 (C4^{Ar}), 123.5 (C3^{Ar}), 122.9 (C5^{Py}), 121.8 (C3^{Py}), 58.6 (NC(CH$_3$)$_2$), 28.0 (NC(*C*H$_3$)$_2$), 27.8 (*C*H(CH$_3$)$_2$), 26.2 (CH(*C*H$_3^A$CH$_3^B$)), 25.1 (CH(CH$_3^A$*C*H$_3^B$)), −6.9 (br, Al(*C*H$_3$)$_2$).

X-ray crystal structure analysis for **23**: formula $C_{22}H_{33}AlN_2O$, M = 368.48, yellow crystal 0.30 × 0.25 × 0.10 mm, a = 14.9530(6), b = 10.2917(3), c = 28.8857(12) Å, β = 94.139(1)°, V = 4433.7(3) Å^3, ρ_{calc} = 1.104 g cm^{-3}, μ = 0.104 mm^{-1}, empirical absorption correction (0.970 ⩽ T ⩽ 0.990), Z = 8, monoclinic, space group *C*2/c, (No. 15), λ = 0.71073 Å, T = 198 K, ω and ϕ scans, 13025 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.59 Å^{-1}, 3911 independent (R_{int} = 0.094) and 1932 observed reflections [$I \geqslant 2\sigma(I)$], 243 refined parameters, R = 0.060, wR^2 = 0.155, max. residual electron density 0.21 (−0.25) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Acknowledgements

Financial support from the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged. We thank the BASF for a generous gift of solvents.

Appendix A. Supplementary material

CCDC 658474, 658475, 658476, 658477, 658478, 658479, 658480, 658481, 658482 and 658483 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. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2008.05.032.

References

[1] R. Furuyama, J. Saito, S. Ishii, H. Makio, M. Mitani, H. Tanaka, T. Fujita, J. Organomet. Chem. 690 (2005) 4398–4413;
H. Makio, N. Kashiwa, T. Fujita, Adv. Synth. Catal. 344 (2002) 477–493;
Review: G.W. Coates, P.D. Hustad, S. Reinartz, Angew. Chem. 114 (2002) 2340–2361;

G.W. Coates, P.D. Hustad, S. Reinartz, Angew. Chem., Int. Ed. 41 (2002) 2236–2257.
[2] J. Strauch, T.H. Warren, G. Erker, R. Fröhlich, P. Saarenketo, Inorg. Chim. Acta 300 (2000) 810–821.
[3] A. Mori, H. Abe, S. Inoue, Appl. Organomet. Chem. 9 (1995) 189–197;
K.D. Shimizu, B.M. Cole, C.A. Krueger, K.W. Kuntz, M.L. Snapper, A.H. Hoveyda, Angew. Chem. 109 (1997) 1782–1785;
K.D. Shimizu, B.M. Cole, C.A. Krueger, K.W. Kuntz, M.L. Snapper, A.H. Hoveyda, Angew. Chem., Int. Ed. 36 (1997) 1704–1707;
A.H. Hoveyda, A.W. Hird, M.A. Kacprzynski, Chem. Commun. (2004) 1779–1785;
L.C. Wieland, H. Deng, M.L. Snapper, A.H. Hoveyda, J. Am. Chem. Soc. 127 (2005) 15453–15456.
[4] K. Nienkemper, V.V. Kotov, G. Kehr, G. Erker, R. Fröhlich, Eur. J. Inorg. Chem. (2006) 366–379. and references cited therein.
[5] N. Hata, Bull. Chem. Soc. Jpn. 31 (1958) 224–228.
[6] W. Mathes, W. Sauermilch, Liebigs Ann. Chem. 618 (1958) 152–158.
[7] See for a comparison F.H. Allen, O. Kennard, D.G. Watson, J. Chem. Soc., Perkin Trans. 2 (1987) S1–S19;
B.B. Small, M. Brookhart, Macromolecules 32 (1999) 2120–2130.
[8] I.J. Pachter, J. Am. Chem. Soc. 75 (1953) 3026–3027.
[9] V. Boekelheide, W.J. Linn, J. Am. Chem. Soc. 76 (1954) 1286–1291;
C. Fontenas, E. Bejan, H. Ait Haddou, G.G.A. Balavoine, Synth. Commun. 25 (1995) 629–633.
[10] C.A. Buehler, L.A. Walker, P. Garcia, J. Org. Chem. 26 (1961) 1410–1413.
[11] See also: E. Pasquinet, P. Rocca, F. Marsais, A. Godard, G. Quéguiner, Tetrahedron 54 (1998) 8771–8782.
[12] W.K. Fife, J. Org. Chem. 48 (1983) 1375–1377.
[13] For an organometallic example see e.g.: K. Kunz, G. Erker, S. Döring, S. Bredeau, G. Kehr, R. Fröhlich, Organometallics 21 (2002) 1031–1041.
[14] See for example: Y. Tagawa, K. Hama, Y. Goto, M. Hamana, Heterocycles 40 (1995) 809–816;
O. Mongin, P. Rocca, L. Thomas-dit-Dumont, F. Trecourt, F. Marsais, A. Godard, G. Queguiner, J. Chem. Soc., Perkin Trans. 1 (1995) 2503–2508;
A. Couture, E. Huguerre, P. Grandclaudon, Tetrahedron Lett. 30 (1989) 183–184;
S.L. Taylor, D.Y. Lee, J.C. Martin, J. Org. Chem. 48 (1983) 4156–4158.
[15] R.A. Abramovitch, R.T. Coutts, E.M. Smith, J. Org. Chem. 37 (1972) 3584–3587.
[16] S.E. Denmark, Y. Fu, Tetrahedron: Asymmetry 17 (2006) 687–707.
[17] For a Pd-catalyzed example see: R.-A. Fallahpour, M. Neuburger, Eur. J. Org. Chem. (2001) 1853–1856;
Y. Yamamoto, T. Tanaka, M. Yagi, M. Inamoto, Heterocycles 42 (1996) 189–194.
[18] T.V. Laine, M. Klinga, M. Leskelä, Eur. J. Inorg. Chem. (1999) 959–964;
C. Bianchini, H.M. Lee, G. Mantovani, A. Meli, W. Oberhauser, New J. Chem. 26 (2002) 387–397;
V.C. Gibson, R.K. O'Reilly, D.F. Wass, A.J.P. White, D.J. Williams, Dalton Trans. (2003) 2824–2830;
N. Saino, F. Amemiya, E. Tanabe, K. Kase, S. Okamoto, Org. Lett. 8 (2006) 1439–1442.
[19] A. Koppl, H.G. Alt, J. Mol. Catal. A: Chem. 154 (2000) 45–53;
G.J.P. Britovsek, S.P.D. Baugh, O. Hoarau, V.C. Gibson, D.F. Wass, A.J.P. White, W.D.J. Williams, Inorg. Chim. Acta 345 (2003) 279–291;
T. Tagata, M. Nishida, Adv. Synth. Catal. 346 (2004) 1655–1660;
K. Yliheikkilae, K. Axenov, M.T. Raeisaenen, M. Klinga, M.P. Lankinen, M. Kettunen, M. Leskelä, T. Repo, Organometallics 26 (2007) 980–987.
[20] See for a comparison: M. Bruce, V.C. Gibson, C. Redshaw, G.A. Solan, A.J.P. White, D.J. Williams, J. Chem. Soc., Chem. Commun. (1998) 2523–2524;
V.C. Gibson, C. Redshaw, A.J.P. White, D.J. Williams, J. Organomet. Chem. 550 (1998) 453–456;
K. Nienkemper, G. Kehr, S. Kehr, R. Fröhlich, G. Erker, J. Organomet. Chem. 693 (2008) 1572–1589.
[21] P.A. Cameron, V.C. Gibson, C. Redshaw, J.A. Segal, M.D. Bruce, A.J.P. White, D.J. Williams, J. Chem. Soc., Chem. Commun. (1999) 1883–1884.
[22] P. Hormnirun, E.L. Marshall, V.C. Gibson, R.I. Pugh, A.J.P. White, Proc. Natl. Acad. Sci. USA 103 (2006) 15343–15348.