A Simple Metal-free Synthesis of 2,4,5-Trisubstituted Pyridines and Pyridine *N*-Oxides by [2+2] Cycloaddition of Enaminones to Propyne Iminium Salts

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Herein a simple one-pot metal-free synthesis of 2,4,5-trisubstituted pyridines and pyridine *N*-oxides by [2+2] cycloaddition of enaminones, which are prepared *in situ* from alkyl, aryl and heteroaryl methyl ketones using *N,N*-dimethylformamide dimethyl acetal (DMFDMA), and propyne iminium salts as electron-poor acetylenes, is described.

Key words: Enaminones, Propyne Iminium Salts, [2+2] Cycloadditions, 2,4,5-Trisubstituted Pyridines, 2,4,5-Trisubstituted Pyridine *N*-Oxides

Introduction

Pyridines and their *N*-oxides with aromatic or heteroaromatic substituents constitute an important class of compounds, which have found applications in medicinal chemistry [1]. Many of them are biologically active [2], such as streptonigrin [3], glivec [4] and rosuvastatin [5], and various natural products [6, 7]. They are also found in p38 mitogen-activated kinase inhibitors [8], and are *P*,*N*-ligands, used as catalysts in asymmetric reactions [9 – 11]. They are also convenient synthetic precursors of chiral dihydro- and tetrahydropyridines, which are of interest as intermediates in alkaloid synthesis, as agrochemicals, as well as in material sciences [12, 13]. Since the early days of synthetic organic chemistry chemists have searched for efficient methods to prepare functionalized pyridine derivatives [14 – 16].

Direct functionalization of pyridine remains a significant challenge. Electrophilic aromatic substitution is not effective without the inclusion of substituents to activate the pyridine ring. Additionally, pyridine derivatives that lack a good leaving group are generally unreactive toward nucleophilic aromatic substitution [17]. Organometallic nucleophiles can attack the heterocyclic ring directly, but this often leads to low yields in the absence of an external oxidant [18]. These factors have led to the use of pyridines functionalized at nitrogen to generate cationic pyridinium salts or neutral pyridinium ylides [19].

Palladium-catalyzed reactions are powerful and useful tools for the synthesis of heterocycles, especially for the formation of C–C bonds in aryl and heteroaryl substituted heterocycles [20 – 25]. In this context, the Suzuki reaction has a special significance [23 – 25]. An attractive alternative is a mild Negishi cross-coupling of 2-heterocyclic organozinc reagents with aryl and heteroaryl chlorides [26 – 28], which complements reactions with other 2-heteroaryl metal reagents [29]. Direct arylation and alkylation of nitropyridine *N*-oxides with Grignard reagents [30] and arylation of arenes and *N*-heteroarenes with diaryliodonium salts with-

out the use of transition metal catalysts [31] have recently been reported. Furthermore, the down side of using organometallic reagents in the pharmaceutical industry is their ever increasing cost, *i. e.* the progressive shortage of lithium, and the strict regulations relevant for pharmaceutical compounds regarding the residual traces of metals left in the final products. Recently, a flexible approach for the preparation of highly functionalized pyrid-4-ones *via* trimethylsilyl trifluoromethanesulfonate/base-promoted intramolecular condensation of β-ketoenamides has been developed [32, 33].

3-Dimethylaminopropenoates and related enaminones have been demonstrated to exhibit a broad applicability in heterocyclic synthesis [34–38], including the preparation of natural products and their analogs, such as aplysinopsins [39, 40], meridianines [41, 42] and dipodazines [43–45]. Recently, polysubstituted butadienes have been prepared by microwave-assisted [2+2] cycloadditions of enaminones to electron-poor acetylenes [46, 47].

Polysubstituted aminobutadienes prepared by this procedure are suitable for the preparation of polysubstituted pyridine derivatives. They also represent a group of isomeric intermediates in regard to the aminobutadienes prepared *via* the Michael addition in Bohlmann-Rahtz syntheses of pyridine derivatives [48, 49]. On this basis, a simple metal-free synthesis of 2-alkyl-, 2-cycloalkyl-, 2-aryl-, and 2-heteroaryl-substituted pyridine-3,4-dicarboxylates and their *N*-oxides has been developed [50].

The electron-poor propyne iminium triflates, prepared from 3-trifloxypropene iminium triflates by elimination of triflic acid, underwent [2+2] and [2+4] cycloadditions [51] with enamines. Their reactivity towards imines has also been reported [52]. *N*,*N*,*N*′,*N*′,*N*″,*N*″,*N*‴,*N*‴-Octamethyl-(but-2-yne)-bis(amidinium)-bis(tetrafluoroborate) as the first bis(amidinium) salt of an acetylenedicarboxylic acid and its reactivity in [4+2] cycloaddition reactions have been reported recently [53].

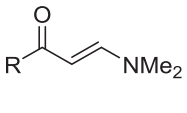
As an extension of the research recently developed in our laboratory, in this communication we report on a simple one-pot metal-free synthesis of 2,4,5-trisubstituted pyridine derivatives and their *N*-oxides by [2+2] cycloaddition of propyne iminium salts as electron-poor acetylenes to enaminones.

Results and Discussion

For our study we chose the (*E*)-3-(dimethylamino)-1-(substituted)prop-2-en-1-ones **1b**, **c** as substrates, and three propyne iminium salts **2a**, **b** and **3** as electron-poor acetylenes (Fig. 1).

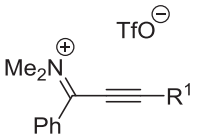
The cycloaddition was carried out in acetonitrile under microwave irradiation and was finished within 2 h to produce **6a**, **b**. Since the ^{1}H NMR spectra exhibited only broad signals even at lower temperature, the substitution pattern around the double bond could not be determined. Therefore, we decided to prepare single crystals of **6b** and **7**. Their structure has clearly shown that the configuration around the double bonds is 2*Z*,3*Z* (Figs. 2 and 3). This is in accordance with a regiospecific [2+2] cycloaddition.

The reaction can be explained by the following mechanism: The propyne iminium salts **2a** can be represented in various mesomeric forms, such as **2a**′ with a strong electrophilic position, which reacts with enaminones **1a**, **b** to form intermediates **4a**, **b** followed by cyclization to cyclobutene derivatives **5a**, **b** and conrotatory retro-electrocyclization to afford **6a**, **b** (Scheme 1). The propyne bis(amidinium) salt **3** reacts analogously to afford **7** (Scheme 2). The [2+2] cycloadditions of the propyne iminium salt **2a** is regio-



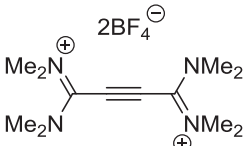
1

R: a) *n*-Pr
b) Ph
c) 3-$NO_2C_6H_4$
d) thienyl-3



2

R^1: a) Ph
b) cyclopropyl



3

Fig. 1. Enaminones **1a–d** and propyne iminium salts **2a**, **b** and **3**.

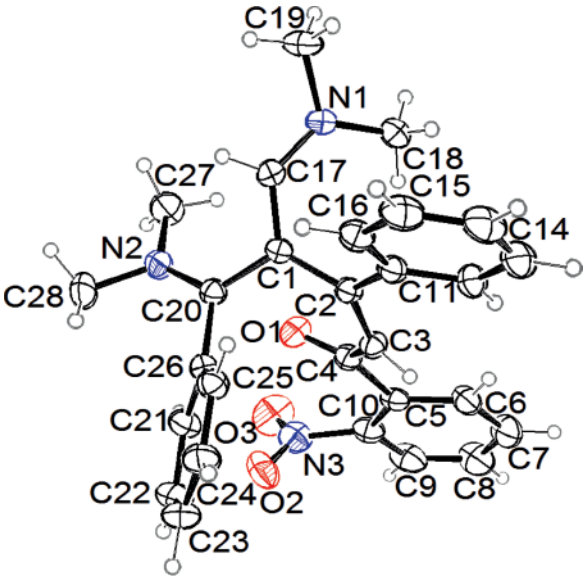


Fig. 2. ORTEP drawing of the cation of compound **6b** in the crystal and crystallographic numbering scheme adopted. Displacement ellipsoids at the 30 % probability level.

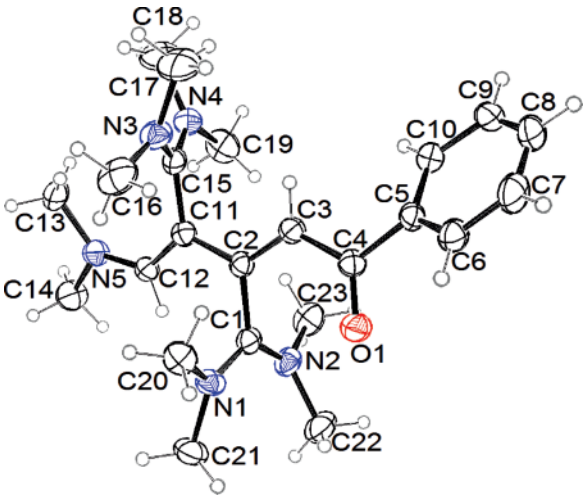


Fig. 3. ORTEP drawing of the cation of compound **7** in the crystal and crystallographic numbering scheme adopted. Displacement ellipsoids at the 30 % probability level.

selective due to the strong electrophilic character represented in their resonance structure **2a′**. The propyne iminium salts are more reactive than other electron-poor acetylenes, such as acetylenecarboxylates and acetylenedicarboxylates, and their reaction proceeds quantitatively at room temperature in a relatively short reaction time (0.5 – 2 h).

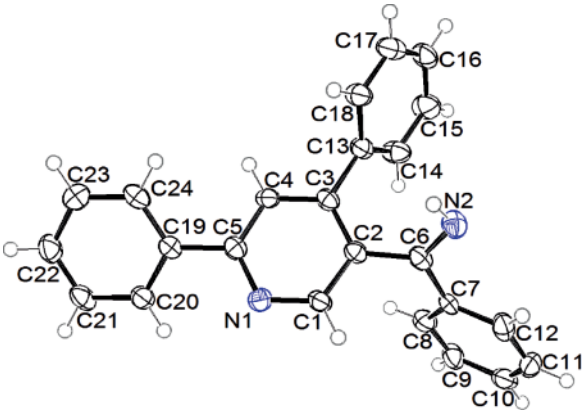


Fig. 4. ORTEP drawing of compound **11b** in the crystal and crystallographic numbering scheme adopted. Displacement ellipsoids at the 30 % probability level.

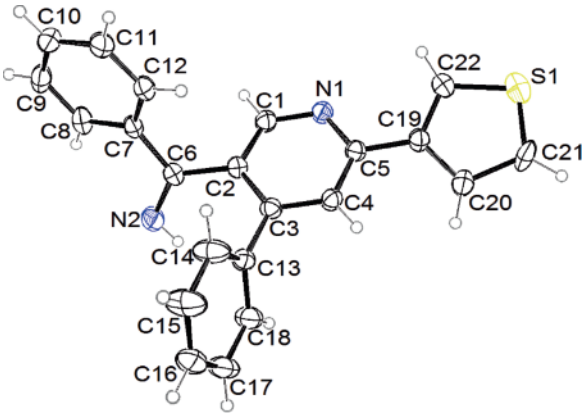
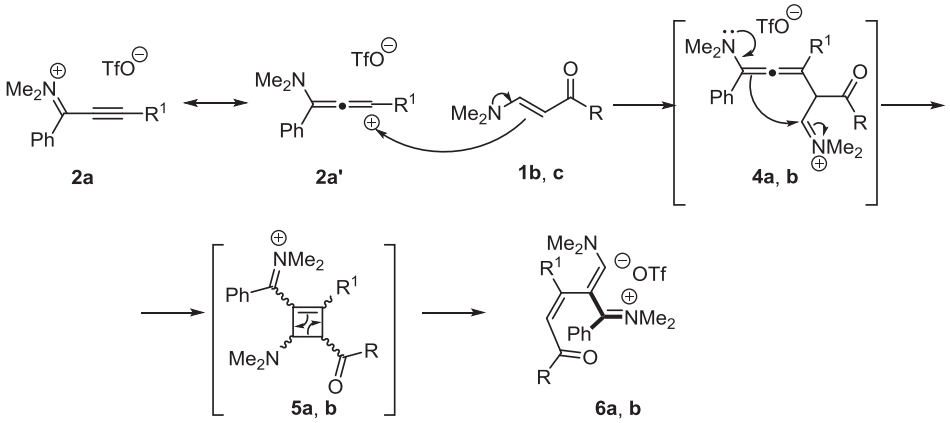


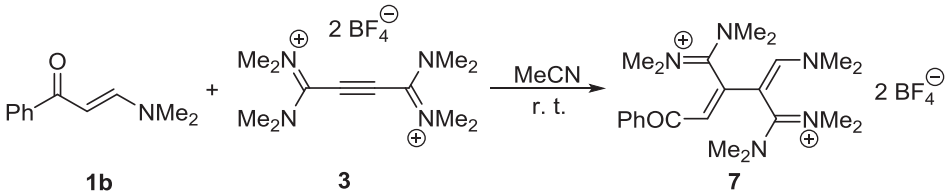
Fig. 5. ORTEP drawing of compound **11c** in the crystal and crystallographic numbering scheme adopted. Displacement ellipsoids at the 30 % probability level.

One-pot synthesis of 2,4,5-trisubstituted pyridine derivatives

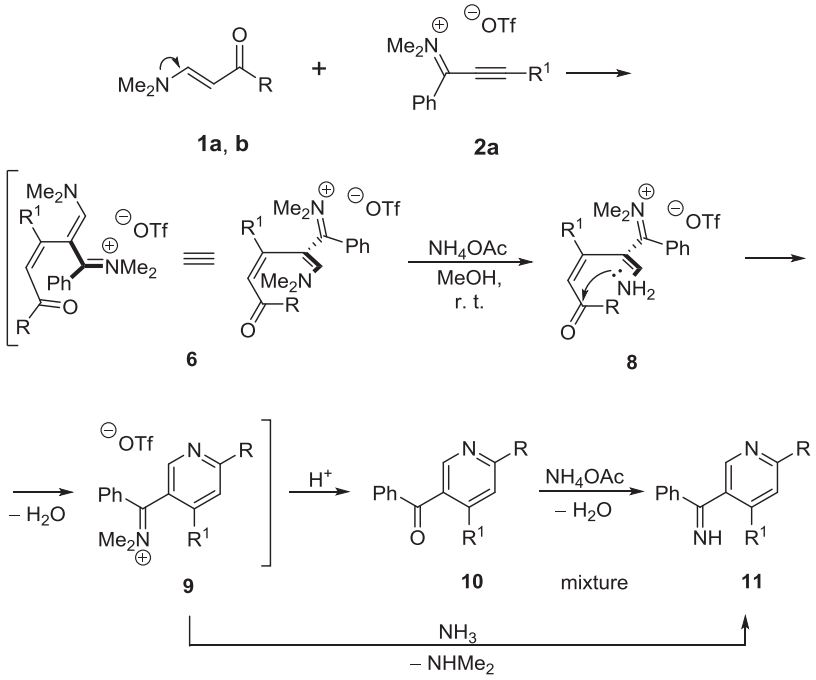
Because butadienes **6a**, **b** were extremely hygroscopic, we decided to prepare them *in situ* and use them in a one-pot synthesis of 2,4,5-trisubstituted pyridine derivatives. The reaction mixture was evaporated *in vacuo*, the oily residue was dissolved in methanol, and excess NH_4OAc was added to the solution. The mixture was stirred at room temperature for 2 – 48 h to give a mixture of ketone **10** and imine **11**, which were separated by column chromatography. The imine **11** could be easily hydrolyzed in dilute hydrochloric acid to give ketone **10** (Scheme 3, Table 1).



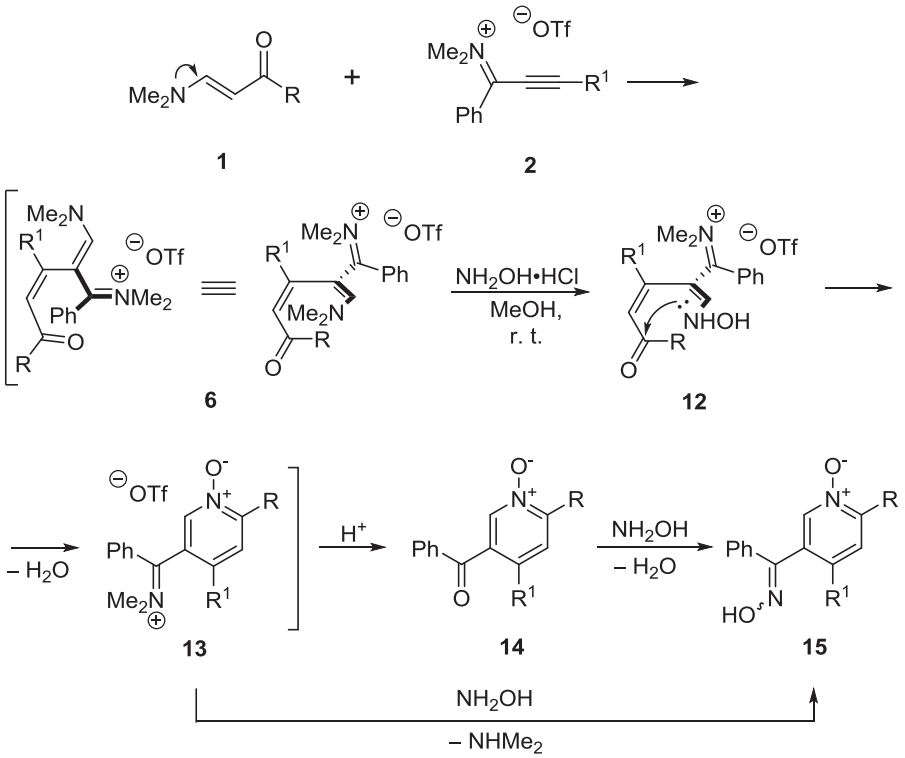
Scheme 1. Proposed mechanism for the formation of cycloadducts **6a**, **b** by [2+2] cycloaddition of enaminones **1b**, **c** to propyne iminium triflate **2a**.



Scheme 2. Formation of cycloadduct **7** by [2+2] cycloaddition of **1b** to **3**.



Scheme 3. Formation of 2,4,5-trisubstituted pyridines **10** and **11**.



Scheme 4. Formation of 2,4,5-trisubstituted pyridine *N*-oxides **14** and **15**.

Table 1. 2,4,5-Trisubstituted pyridines **10** and **11**.

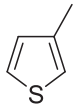
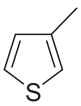
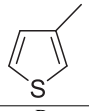
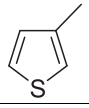
Products	R	R^1	Yield (%)	
10, **11**			**10**	**11**
a	*n*-Pr	Ph	45	45
b	Ph		22	67
c			–	50
d	*n*-Pr		23	15
e	Ph		49	25
f			43	26

Table 2. 2,4,5-Trisubstituted pyridine *N*-oxides **14** and **15**.

Products	R	R^1	Yield (%)	
14, **15**			**14**	**15**
a	Pr	Ph	46	–
b	Ph		21	10
c			39	14
d	Pr		22	14
e	Ph		10	30
f			13	24

One-pot synthesis of 2,4,5-trisubstituted pyridine N-oxides

The corresponding 2,4,5-trisubstituted pyridine *N*-oxides were prepared analogously. The cycloadducts **6a**, **b**, **c** and hydroxylamine hydrochloride were stirred in methanol at room temperature for 2 h. The dimethylamino group in **13** can be either hydrolyzed to give the ketone **14** or substituted by hydroxylamine to give the corresponding oxime **15** (Scheme 4, Table 2).

The structures of the new compounds were determined with ^{1}H and ^{13}C NMR spectroscopy, HRMS, IR spectroscopy, and microanalyses for C, H, and N. The structures of compounds **6b**, **7**, **11b**, and **11c** were confirmed by single-crystal X-ray diffraction analysis (Figs. 2 – 5 and Table 3).

Table 3. Crystal structure data for compounds **6b**, **7**, **11b**, and **11c**.

	6b	**7**	**11b**	**11c**
Empirical formula	$C_{29}H_{28}F_3N_3O_6S$	$C_{23}H_{37}B_2F_8N_5O$	$C_{24}H_{18}N_2$	$C_{22}H_{16}N_2S$
M_r	603.61	573.20	334.40	340.43
Crystal size, mm^3	$0.38 \times 0.35 \times 0.05$	$0.40 \times 0.28 \times 0.10$	$0.22 \times 0.15 \times 0.10$	$0.30 \times 0.25 \times 0.25$
Crystal system	monoclinic	monoclinic	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/a$	$P12_11$	$P12_11$
a, Å	10.6562(3)	15.1401(3)	8.2612(3)	5.9669(2)
b, Å	25.0568(6)	9.9531(4)	18.2270(11)	17.1251(5)
c, Å	11.0883(2)	19.4927(5)	5.9331(2)	8.522(5)
β, deg	96.960(1)	91.686(2)	90.012(3)	94.473(2)
V, Å^3	2938.87(12)	2936.10(15)	893.39(7)	868.1(5)
Z	4	4	2	2
$D_{calcd.}$, g cm^{-3}	1.36	1.30	1.24	1.30
$\mu(MoK_\alpha)$, cm^{-1}	0.2	0.1	0.1	0.2
$F(000)$, e	1256	1200	352	356
hkl range	$-13 \le h \le +13$	$-19 \le h \le +19$	$-10 \le h \le +11$	$-7 \le h \le +7$
	$-32 \le k \le +32$	$-12 \le k \le +12$	$-23 \le k \le +25$	$-22 \le k \le +22$
	$-14 \le l \le +14$	$-25 \le l \le +25$	$-5 \le l \le +7$	$-11 \le l \le +11$
$((\sin\theta)/\lambda)_{max}$, Å^{-1}	0.6508	0.6497	0.7081	0.6497
Refl. measured	24 543	43 759	15 793	13 771
Refl. unique	6660	6720	2399	3892
R_{int}	0.031	0.040	0.051	0.029
Param. refined	383	363	240	230
$R(F)/wR(F^2)$[a]	0.108/0.3838	0.118/0.3681	0.056/0.1364	0.0561/0.1689
x(Flack)	–	–	–[b]	0.04(12)
GoF (F^2)[a]	1.626	1.285	1.076	1.062
$\Delta\rho$(max/min), e Å^{-3}	1.33/−1.23	1.11/−0.67	0.28/−0.22	0.054/−0.44

[a] All reflections; [b] absolute structure cannot be determined reliably: $x(\text{Flack}) = -6(7)$.

Conclusion

In conclusion, we have described a simple, metal-free synthesis of 2-alkyl-, 2-aryl-, or 2-heteroaryl-, 4-phenyl- or 4-cyclopropyl-, 5-aroyl-substituted pyridines from the corresponding enaminones and propyne iminium salts. The method complements the current preparation of 2-substituted pyridine derivatives by coupling of organometallic reagents.

Experimental Section

Melting points were determined on a Stanford Research Systems MPA100 OptiMelt automated system. The NMR spectra were obtained on a Bruker Avance DPX 300 at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C and on a Bruker Avance III UltraShield 500 plus at 500 MHz for ^{1}H and 126 MHz for ^{13}C, using $CDCl_3$ and [D$_6$]DMSO with Me_4Si as the internal standard, as solvents. Mass spectra were recorded on an Agilent 6224 Accurate Mass TOF LC/MS spectrometer, IR spectra on a Perkin Elmer Spectrum BX FTIR spectrophotometer. Microanalyses were performed on a Perkin-Elmer CHN Analyzer 2400 II. Column chromatography (CC) was performed on silica gel (Fluka, Silica gel 60, particle size 35 – 70 μm). Starting compounds **1a**–**d** [50], **2a**, **b** [51], and **3** [53] were prepared according to the procedures reported in the literature.

*N-((2E,3Z)-2-((Dimethylamino)methylene)-5-oxo-1,3,5-triphenylpent-3-en-1-ylidene)-N-methylmethanaminium trifluoromethanesulfonate (**6a**)*

To a solution of (*E*)-3-(dimethylamino)-1-phenylprop-2-en-1-one (**1a**, 26.3 mg, 0.15 mmol) in MeCN (1 mL) was added *N*-(1,3-diphenylprop-2-yn-1-ylidene)-*N*-methylmethanaminium trifluoromethanesulfonate (**2a**, 71.2 mg, 0.186 mmol). The reaction mixture was stired for 30 min. Volatile components were evaporated *in vacuo,* and the product was isolated by column chromatography (EA-MeOH = 5 : 1) and crystallized from acetone-Et_2O. Yield: 79.5 mg (95 %) of yellow solid. M. p. 141.1 – 143.9 °C. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.64 (3H, br s, *Me*), 3.16 (3H, br s, *Me*), 3.26 (3H, br s, *Me*), 3.84 (3H, br s, *Me*), 6.97 – 7.23 (3H, m, Ph or/and C*H*), 7.32 – 7.88 (13H, m, Ph and C*H*), 8.18 (1H, br s, Ph or C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 102.3, 119.0, 122.9, 123.2, 128.2, 128.4, 128.8, 129.8, 131.2, 132.1, 133.1, 139.3, 140.4, 152.1, 190.4 ppm. – $C_{29}H_{29}F_3N_2O_4S$: calcd. C 62.35; H 5.23; N 5.01; found C 62.51; H 5.25; N 5.01. – HRMS ((+)-ESI): m/z = 409.2273 (calcd. 409.2280 for $C_{28}H_{29}N_2O$, $[M+H]^+$). – IR: ν_{max} (KBr) = 3057, 2928,

1643, 1618, 1579, 1555, 1450, 1395, 1371, 1277, 1262, 1214, 1145, 1032, 992, 764, 695, 638 cm^{-1}.

*N-((2E,3Z)-2-((Dimethylamino)methylene)-5-(2-nitrophenyl)-5-oxo-1,3-diphenylpent-3-en-1-ylidene)-N-methylmethanaminium trifluoromethanesulfonate (**6b**)*

To a solution of (*E*)-3-(dimethylamino)-1-(2-nitrophenyl)prop-2-en-1-one (**1b**, 49.0 mg, 0.22 mmol) in MeCN (1 mL) was added *N*-(1,3-diphenylprop-2-yn-1-ylidene)-*N*-methylmethanaminium trifluoromethanesulfonate (**2a**, 85.4 mg, 0.22 mmol). The reaction mixture was stirred for 2 h. Volatile components were evaporated *in vacuo*, and the product was isolated by column chromatography (EA-MeOH = 5 : 1) and crystallized from acetone-Et_2O. Yield: 122.0 mg (92 %) of a red solid. M. p. 147.1 – 148.7 °C. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ =2.71 (3H, br s, *Me*), 3.21 (6H, br s, 2*Me*), 3.78 (3H, br s, *Me*), 6.68 (1H, br s, C*H*), 7.31 – 7.80 (13H, m, Ph and C*H*), 8.06 (1H, d, J = 8.1 Hz, Ph), 8.23 (1H, br s, C*H*) ppm. – ^{19}F NMR ($CDCl_3$): δ = –78.2 ppm. – ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ =41.8, 46.0, 47.6, 119.8, 122.4, 124.8, 128.2, 128.9, 129.3, 129.8, 130.4, 130.9, 131.7, 132.5, 134.2, 138.6, 139.8, 146.7, 189.3 ppm. – $C_{29}H_{28}F_3N_3O_6S$: calcd. C 57.70; H 4.68; N 6.96; found C 57.76; H 4.58; N 6.87. – HRMS ((+)-ESI): m/z = 454.2141 (calcd. 454.2131 for $C_{28}H_{28}N_3O_3$, $[M+H]^+$). – IR: ν_{max} (KBr) = 1618, 1523, 1488, 1448, 1392, 1365, 1305, 1262, 1223, 1152, 1106, 1049, 1030, 979, 858, 767 cm^{-1}.

*N,N′-((2Z,3Z)-1,4-bis(dimethylamino)-2-((dimethylamino)-methylene)-3-(2-oxo-2-phenylethylidene)butane-1,4-diylidene)-bis(N-methylmethanaminium) tetrafluoroborate (**7**)*

To a solution of (*E*)-3-(dimethylamino)-1-phenylprop-2-en-1-one (**1a**, 43.75 mg, 0.25 mmol) in MeCN (2 mL) was added *N,N,N′,N′,N″,N″,N‴,N‴*-octamethylacetylene-bis(carboxamidinium) bis(tetrafluoroborate) (**3**, 99.25 mg, 0.25 mmol). The reaction mixture was stirred for 3 h. Volatile components were evaporated *in vacuo* and the residue crystallized from PhMe. Yield: 104.5 mg (72.9 %) of a yellow solid. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.13 (H, br s, NMe_2), 3.30 (12H, br s, 2 × NMe_2), 3.40 (6H, br s, NMe_2), 6.33 (1H, s, C*H*), 6.84 (1H, s, C*H*), 7.53 – 7.58 (2H, m, Ph), 7.64 – 7.69 (1H, m, Ph), 7.94 – 7.97 (2H, m, Ph) ppm. – HRMS ((+)-ESI): m/z = 486.3017 (calcd. 486.3027 for $C_{23}H_{37}N_5OBF_4$, $[M–BF_4]^+$). – IR: ν_{max} (NaCl) = 3447, 1628, 1560, 1522, 1507, 1496, 1457, 1402, 1301, 1269, 1231, 1198, 1123, 1083, 884, 855 cm^{-1}.

*General procedure for the preparation of substituted (pyridin-3-yl)methanones **10** and substituted (pyridine-3-yl)methanimines **11***

To a solution of enaminone **1** (0.20 – 0.24 mmol) in MeCN (1 mL) was added propyne iminum salt **2** (0.20 – 024 mmol). The reaction mixture was stirred at r. t. for 2 h. Volatile components were evaporated *in vacuo*. The oily residue was dissolved in MeOH (1 mL), NH_4OAc (154 mg, 2.0 mmol) was added, and the mixture was stirred at r. t. for 2 d. Volatile components were evaporated *in vacuo*, and the products were separated by column chromatography (EA-PE 1 : 1).

The following compounds were prepared in this manner:

*Phenyl(4-phenyl-6-propylpyridin-3-yl)methanone (**10a**) and phenyl(4-phenyl-6-propylpyridin-3-yl)methanimine (**11a**)*

Prepared from **1a** (34.0 mg, 0.24 mmol) and **2a** (77.0 mg, 0.20 mmol).

10a: Yield: 27.0 mg (45 %) of a colorless oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.04 (3H, t, J = 7.0 Hz, CH_3), 1.86 (2H, h, J = 7.0 Hz, CH_2), 2.90 (2H, t, J = 7.0 Hz, CH_2), 7.19 – 7.32 (8H, m, Ph+C*H*), 7.44 (1H, dd, J_1 = 7.0 Hz, J_2 = 1.5 Hz, Ph), 7.66 (2H, dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, Ph), 8.65 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 14.2, 23.2, 40.6, 123.4, 128.5, 128.7, 128.8, 130.0, 132.0, 133.4, 137.3, 138.1, 149.3, 149.4, 164.7, 197.0 ppm. – HRMS ((+)-ESI): m/z = 302.1537 (calcd. 302.1539 for $C_{21}H_{20}NO$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 2958, 2925, 2863, 1662, 1588, 1532, 1447, 1378, 1315, 1286, 1225, 1176, 1139, 1072, 1044, 943, 922, 891, 804 cm^{-1}.

11a: Yield: 27.0 mg (45 %) of a colorless oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.04 (3H, t, J = 7.0 Hz, CH_3), 1.85 (2H, h, J = 7.0 Hz, CH_2), 2.90 (2H, t, J = 7.0 Hz, CH_2), 7.20 – 7.31 (9H, m, Ph+C*H*), 7.44 (2H, br s, Ph), 8.58 (1H, s, C*H*), 9.81 (1H, br s, N*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 14.2, 23.2, 40.5, 123.5, 128.0, 128.3, 128.5, 128.6, 128.7, 130.8, 132.7, 138.1, 138.5, 148.4, 149.3, 163.7, 176.6 ppm. – HRMS ((+)-ESI): m/z = 301.1698 (calcd. 301.1699 for $C_{21}H_{21}N_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 3194, 3058, 2959, 2870, 1589, 1572, 1532, 1495, 1478, 1446, 1357, 1258, 1187, 1145, 1090, 1045, 1026, 1000, 928, 886, 853, 777 cm^{-1}.

*(4,6-Diphenylpyridin-3-yl)(phenyl)methanone (**10b**) and (4,6-diphenylpyridin-3-yl)(phenyl)methanimine (**11b**)*

Prepared from **1b** (35.0 mg, 0.20 mmol) and **2a** (75.0 mg, 0.196 mmol).

10b: Yield: 15.0 mg (21.5 %) of a colorless oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.27 – 7.35 (7H, m, Ph), 7.44 – 7.50 (2H, m, Ph), 7.51 – 7.54 (2H, m, Ph), 7.70 – 7.72 (2H, m, Ph), 7.86 (1H, s, C*H*), 8.10 – 8.12 (2H, m, Ph), 8.82 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 121.2, 127.4, 128.6, 128.8, 128.88, 128.94, 129.1, 130.0, 130.1, 132.8, 133.5, 137.3, 138.1, 138.7, 149.9, 150.0, 159.2, 196.8 ppm. – HRMS ((+)-ESI): m/z = 336.1383 (calcd. 336.1383 for $C_{24}H_{18}NO$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1661, 1587,

1531, 1493, 1465, 1445, 1367, 1316, 1292, 1279, 1229, 1178, 1147, 1075, 1041, 1026, 943, 889, 783 cm^{-1}.

11b: Yield: 44.0 mg (67 %) of a colorless solid. M. p. 126.2 – 127.8 °C. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.20 – 7.26 (5H, m, Ph+N*H*), 7.28 – 7.33 (4H, m, Ph), 7.45 – 7.54 (5H, m, Ph), 7.78 (1H, d, J = 0.6 Hz, C*H*), 8.07 – 8.11 (2H, m, Ph), 8.74 (1H, d, J = 0.6 Hz, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 121.3, 127.3, 128.0, 128.4, 128.6, 128.7, 129.1, 129.7, 130.9, 133.6, 138.1, 138.4, 138.8, 149.0, 149.8, 158.5, 176.5 ppm. – HRMS ((+)-ESI): m/z = 335.1542 (calcd. 335.1548 for $C_{24}H_{19}N_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 3483, 1664, 1637, 1617, 1584, 1530, 1495, 1474, 1445, 1358, 1281, 1238, 1187, 1150, 1076, 1021, 935, 884, 824, 793, 782 cm^{-1}.

*Phenyl(4-phenyl-6-(thiophen-3-yl)pyridin-3-yl)methanimine (**11c**)*

Prepared from **1d** (43.4 mg, 0.24 mmol) and **2a** (77.0 mg, 0.20 mmol).

10c: Yield: 34.0 mg (50 %) of a colorless solid. M. p. 153.7.1 – 156.4 °C. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.18 – 7.25 (5H, m, Ph), 7.26 – 7.33 (3H, m, Ph), 7.42 (1H, dd, J_1 = 3.0 Hz, J_2 = 5.1 Hz, thiophene), 7.44 – 7.47 (2H, m, Ph), 7.66 (1H, d, J = 0.6 Hz, C*H*), 7.73 (1H, dd, J_1 = 1.5 Hz, J_2 = 5.1 Hz, thiophene), 7.78 (1H, br s, N*H*); 8.02 (1H, dd, J_1 = 1.5 Hz, J_2 = 3.0 Hz, thiophene), 8.68 (1H, d, J = 0.6 Hz, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 121.0, 124.8, 126.4, 126.8, 128.0, 128.4, 128.6, 128.70, 128.72, 130.9, 133.2, 138.0, 138.4, 141.6, 149.1, 149.8, 154.5, 176.5 ppm. – HRMS ((+)-ESI): m/z = 341.1124 (calcd. 341.1112 for $C_{22}H_{17}N_2S$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1599, 1586, 1515, 1495, 1445, 1420, 1360, 1292, 1240, 1186, 1152, 1094, 1072, 1044, 1021, 938, 887, 862, 830, 803, 788 cm^{-1}.

*(4-Cyclopropyl-6-propylpyridin-3-yl)(phenyl)methanone (**10d**) and (4-cyclopropyl-6-propylpyridin-3-yl)(phenyl)-methanimine (**11d**)*

Prepared from **1a** (34.0 mg, 0.24 mmol) and **2b** (69.4 mg, 0.20 mmol).

10d: Yield: 12.0 mg (23 %) of a colorless oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.58 (2H, dt, J_1 = 4.8 Hz, J_2 = 7.0 Hz, cyclopropyl), 0.76 (5H, m, cyclopropyl+CH_3), 1.54 (2H, h, J = 7.0 Hz, CH_2), 1.78 (1H, tt, J_1 = 5.1 Hz, J_2 = 8.4 Hz, cyclopropyl), 2.54 (2H, t, J = 7.0 Hz, CH_2), 6.46 (1H, s, C*H*), 7.26 (2H, t, J = 7.8 Hz, Ph), 7.34 (1H, d, J = 7.4 Hz, Ph), 7.63 (2H,d, J = 7.1 Hz, Ph), 8.20 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 11.1, 13.1, 14.1, 23.2, 40.5, 117.6, 128.8, 130.4, 132.8, 137.8, 148.41, 148.42, 153.5, 164.3, 196.9 ppm. – HRMS ((+)-ESI): m/z = 266.1537 (calcd. 266.1539 for $C_{18}H_{20}NO$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 2956, 2925, 2863, 1661, 1594, 1538, 1448, 1374, 1315, 1281, 1165, 1070, 1026, 946, 913, 889, 760 cm^{-1}.

11d: Yield: 8.0 mg (15 %) of a colorless oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.67 (2H, dt, J_1 = 4.7 Hz, J_2 = 7.0 Hz, cyclopropyl), 0.79 – 0.83 (2H, m, cyclopropyl), 0.92 (3H, t, J = 7.4 Hz, CH_3), 1.58 (1H, tt, J_1 = 5.1 Hz, J_2 = 8.3 Hz, cyclopropyl), 1.69 (2H, h, J = 7.4 Hz, CH_2), 2.68 (2H, t, J = 7.4 Hz, CH_2), 6.55 (1H, s, C*H*), 7.32 – 7.35 (2H, m, Ph), 7.39 – 7.43 (1H, m, Ph), 7.61 – 7.63 (2H,m, Ph), 8.25 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 10.7, 13.2, 14.2, 23.3, 40.6, 117.0, 128.2, 128.7, 131.3, 134.4, 138.5, 147.6, 151.1, 163.2, 176.4 ppm. – HRMS ((+)-ESI): m/z = 266.1537 (calcd. 266.1539 for $C_{18}H_{20}NO$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 2958, 2925, 2863, 1594, 1571, 1539, 1488, 1447, 1367, 1356, 1274, 1227, 1191, 1157, 1023, 942, 887, 782 cm^{-1}.

*(4-Cyclopropyl-6-phenylpyridin-3-yl)(phenyl)methanone (**10e**) and (4-cyclopropyl-6-phenylpyridin-3-yl)(phenyl)-methanimine (**11e**)*

Prepared from **1b** (42.0 mg, 0.24 mmol) and **2b** (69.4 mg, 0.20 mmol).

10e: Yield: 29.0 mg (49 %) of a yellow oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.88 (2H, m, cyclopropyl), 1.02 (2H, m, cyclopropyl), 2.07 (1H, m, cyclopropyl), 7.25 (1H, s, C*H*), 7.46 – 7.50 (5H, m, Ph), 7.59 – 7.63 (1H, m, Ph), 7.88 – 7.90 (2H, m, Ph), 7.97 – 7.99 (2H, m, Ph), 8.57 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 11.1, 13.4, 115.5, 127.3, 128.9, 129.0, 129.7, 130.4, 133.6, 133.9, 137.8, 139.0, 149.2, 153.7, 159.2, 196.8 ppm. – HRMS ((+)-ESI): m/z = 300.1382 (calcd. 300.1383 for $C_{21}H_{18}NO$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1660, 1590, 1535, 1478, 1446, 1363, 1315, 1283, 1213, 1168, 1071, 1023, 927, 903, 780 cm^{-1}.

11e: Yield: 15.0 mg (25 %) of a yellow oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.82 (2H, m, cyclopropyl), 1.91 (2H, m, cyclopropyl), 2.07 (1H, tt, J_1 = 5.2 Hz, J_2 = 8.4 Hz, cyclopropyl), 7.18 (1H, s, C*H*), 7.40 – 7.43 (3H, m, Ph), 7.46 – 7.49 (3H, m, Ph), 7.71 – 7.73 (2H, m, Ph), 7.95 – 7.96 (2H, m, Ph), 8.47 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 10.7, 13.5, 115.0, 127.2, 128.2, 128.8, 129.0, 129.4, 131.4, 135.4, 138.4, 139.3, 148.2, 151.5, 158.4, 176.2 ppm. – HRMS ((+)-ESI): m/z = 299.1556 (calcd. 299.1543 for $C_{21}H_{19}N_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1590, 1535, 1480, 1446, 1354, 1195, 1023, 918, 888, 780 cm^{-1}.

*(4-Cyclopropyl-6-(thiophen-3-yl)pyridin-3-yl)(phenyl)-methanone (**10f**) and (4-cyclopropyl-6-(thiophen-3-yl)pyridin-3-yl)(phenyl)methanimine (**11f**)*

Prepared from **1d** (43.0 mg, 0.24 mmol) and **2b** (69.4 mg, 0.20 mmol).

10f: Yield: 26.0 mg (43 %) of a yellow oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.87 (2H, m, cyclopropyl), 1.03 (2H, m, cyclopropyl), 2.09 (1H, tt, J_1 = 5.2 Hz, J_2 = 8.4 Hz, cyclopropyl), 7.15 (1H, s, C*H*), 7.41 (1H, dd, J_1 = 3.0 Hz, J_2 = 5.1 Hz, thiophene), 7.49 (2H, t, J = 7.8 Hz, Ph), 7.60 – 7.64 (1H, m, Ph), 7.66 (1H dd, J_1 = 1.2 Hz, J_2 = 5.1 Hz, thiophene), 7.87 – 7.89 (2H, m, Ph), 7.96 (1H, dd, J_1 = 1.2 Hz, J_2 = 3.0 Hz, thiophene), 8.52 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 11.0, 13.3, 115.1, 124.8, 126.4, 126.8, 128.8, 130.4, 133.3, 133.8, 137.9, 141.8, 149.4, 153.8, 155.1, 196.7 ppm. – HRMS ((+)-ESI): m/z = 306.0949 (calcd. 306.0947 for $C_{19}H_{16}NOS$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1658, 1590, 1532, 1447, 1424, 1315, 1281, 1214, 1167, 1070, 1025, 943, 912, 866, 834, 797 cm^{-1}.

11f: Yield: 16.0 mg (26 %) of a yellow oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.82 (2H, m, cyclopropyl), 0.92 (2H, m, cyclopropyl), 1.72 (1H, tt, J_1 = 5.2 Hz, J_2 = 8.4 Hz, cyclopropyl), 7.09 (1H, s, C*H*), 7.40 – 7.43 (3H, m, Ph+thiophene), 7.47 – 7.50 (1H, m, Ph), 7.65 (1H dd, J_1 = 1.2 Hz, J_2 = 5.1 Hz, thiophene), 7.70 – 7.73 (2H, m, Ph), 7.92 (1H, dd, J_1 = 1.2 Hz, J_2 = 3.0 Hz, thiophene), 8.42 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 10.6, 13.5, 114.7, 124.2, 126.3, 126.7, 128.2, 128.8, 131.4, 135.1, 138.4, 141.9, 148.2, 151.5, 154.3, 176.2 ppm. – HRMS ((+)-ESI): m/z = 305.1106 (calcd. 305.1107 for $C_{19}H_{17}N_2S$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1519, 1533, 1486, 1447, 1424, 1366, 1333, 1289, 1224, 1194, 1154, 1070, 1040, 1026, 935, 890, 799 cm^{-1}.

*General procedure for the preparation of substituted pyridine N-oxides **14** and **15***

To a solution of enaminone **1** (0.20 – 0.24 mmol) in MeCN (1 mL) was added propyne iminum salt **2** (0.20 – 024 mmol). The reaction mixture was stirred at r. t. for 2 h. Volatile components were evaporated *in vacuo*. The oily residue was dissolved in MeOH (1 mL),

$NH_2OH \times HCl$ (35 mg, 0.5 mmol) was added, and the mixture was stirred at r. t. for 2 d. Volatile components were evaporated *in vacuo*, and the products were separated by medium- pressure liquid chromatography (MPLC) (EA-PE 1 : 1).

The following compounds were prepared in this manner:

*5-Benzoyl-4-phenyl-2-propylpyridine 1-oxide (**14a**)*

Prepared from **1a** (34.0 mg, 0.24 mmol) and **2a** (77.0 mg, 0.20 mmol).

14a: Yield: 29.0 mg (46 %) of a colorless oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.10 (3H, t, J = 7.0 Hz, CH_3), 1.86 (2H, h, J = 7.0 Hz, CH_2), 3.01 (2H, t, J = 7.0 Hz, CH_2), 7.20 – 7.25 (5H, m, Ph), 7.33 (2H, d, J = 8.0 Hz, Ph), 7.35 (1H, s, C*H*), 7.49 (1H, t, J = 8.0 Hz, Ph), 7.69 (2H, dd, J_1 = 1.0 Hz, J_2 = 8.0 Hz, Ph) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 14.2, 19.6, 32.6, 126.3, 128.5, 128.7, 128.87, 129.92, 130.0, 134.1, 134.5, 136.1, 136.5, 138.2, 139.0, 153.8, 193.5 ppm. – HRMS ((+)-ESI): m/z = 318.1489 (calcd. 318.1489 for $C_{21}H_2NO_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 3054, 2960, 2868, 1668, 1612, 1595, 1516, 1481, 1448, 1399, 1317, 1290, 1233, 1173, 1119, 1076, 1034, 1006, 900, 871, 823, 770 cm^{-1}.

*5-Benzoyl-2,4-diphenylpyridine 1-oxide (**14b**) and 5-(imino(phenyl)methyl)-2,4-diphenylpyridine 1-oxide (**15b**)*

Prepared from **1b** (42.0 mg, 0.24 mmol) and **2a** (77.0 mg, 0.20 mmol).

14b: Yield: 21.0 mg (30 %) of a colorless solid. M. p. 141.1 – 143.3 °C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.24 – 7.27 (3H, m, Ph), 7.28 – 7.30 (2H, m, Ph), 7.36 (2H, t, J = 8.0 Hz, Ph), 7.48 – 7.54 (4H, m, Ph), 7.57 (1H, s, C*H*), 7.75 – 7.76 (2H, m, Ph), 7.93 (2H, dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, Ph), 8.44 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 128.3, 128.5, 128.6, 128.8, 129.0, 129.1, 129.5, 130.1, 130.3, 132.0, 134.3, 135.4, 136.0, 136.3, 138.4, 140.0, 150.2, 193.3 ppm. – HRMS ((+)-ESI): m/z = 352.1328 (calcd. 352.1332 for $C_{24}H_{18}NO_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1668, 1609, 1595, 1578, 1516, 1497, 1474, 1448, 1393, 1316, 1292, 1228, 1180, 1131, 1074, 1005, 910, 888, 865, 764 cm^{-1}.

15b: Yield: 7.0 mg (10 %) of a colorless solid. M. p. 234.1 – 237.4 °C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.10 – 7.13 (2H, m, Ph), 7.16 – 7.19 (1H, m, Ph), 7.22 – 7.23 (3H, m, Ph), 7.29 – 7.30 (2H, m, Ph), 7.34 – 7.36 (2H, m, Ph), 7.51 – 7.55 (3H, m, Ph), 7.60 (1H, s, C*H*), 7.96 – 7.98 (2H, m, Ph), 8.45(1H, s, C*H*), 12.00 (1H, s, N*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 126.7, 128.0, 128.1, 128.3, 128.6, 128.8, 129.1, 129.4, 129.9, 130.2, 130.4, 132.2, 134.3, 136.3, 141.1, 141.6, 149.1, 152.5 ppm. – HRMS ((+)-ESI): m/z = 351.1487 (calcd. 351.1492 for $C_{24}H_{19}N_2O$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1736, 1607, 1571, 1475, 1443, 1391, 1321, 1302, 1260, 1218, 1136, 1039, 1023, 962, 912, 771 cm^{-1}.

*5-Benzoyl-4-phenyl-2-(thiophen-3-yl)pyridine 1-oxide (**14c**) and 5-((hydroxyimino)(phenyl)methyl)-4-phenyl-2-(thiophen-3-yl)pyridine 1-oxide (**15c**)*

Prepared from **1d** (43.4 mg, 0.24 mmol) and **2a** (77.0 mg, 0.20 mmol).

14c: Yield: 28.0 mg (39 %) of a colorless solid. M. p. 154.6 – 158.9 °C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.26 – 7.31 (5H, m, Ph), 7.33 – 7.36 (2H, m, Ph), 7.44 (1H, dd, J_1 = 3.0 Hz, J_2 = 5.0 Hz, thiophene), 7.48 – 7.51 (1H, m, Ph), 7.71 – 7.73 (3H, m, Ph+thiophene), 7.80 (1H, s, C*H*), 8.45 (1H, s, C*H*), 9.02 (1H, dd, J_1 = 1.0 Hz, J_2 = 3.0 Hz, thiophene) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 125.7, 126.2, 127.2, 128.5, 128.8, 128.97, 128.99, 130.1, 130.7, 131.3, 134.0, 134.2 136.1, 136.5, 138.4, 140.5,

145.0, 193.2 ppm. – HRMS ((+)-ESI): m/z = 358.0899 (calcd. 358.0896 for $C_{22}H_{16}NO_2S$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1666, 1596, 1576, 1512, 1478, 1448, 1380, 1355, 1290, 1228, 1154, 1075, 1005, 905, 874, 804, 770 cm^{-1}.

15c: Yield: 10.0 mg (14 %) of a colorless solid. M. p. 249.1 – 253.0 °C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.17 – 7.20 (2H, m, Ph), 7.23 – 7.24 (1H, m, Ph), 7.26 – 7.28 (3H, m, Ph), 7.33 – 7.35 (4H, m, Ph), 7.43 (1H, dd, J_1 = 5.0 Hz J_2 = 3.0 Hz, C*H*), 7.72 (1H, dd, J_1 = 1.0 Hz, J_2 = 5.0 Hz, thiophene),7.79 (1H, s, C*H*), 8.38 (1H, s, C*H*), 8.94 (1H, dd, J_1 = 1.0 Hz, J_2 = 3.0 Hz, thiophene), 9.68 (1H, br s, O*H*) ppm. – ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 125.6, 126.1, 126.9, 127.5, 128.0, 128.5, 128.6, 128.8, 129.0, 129.8, 130.4, 131.6, 134.3, 136.8, 140.2, 141.0, 144.1, 153.2 ppm. – HRMS ((+)-ESI): m/z = 373.1007 (calcd. 373.1005 for $C_{22}H_{17}N_2O_2S$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1635, 1616, 1522, 1492, 1416, 1379, 1353, 1315, 1302, 1245, 1220, 1136, 1090, 1035, 969, 923, 891, 874, 806, 766 cm^{-1}.

*5-Benzoyl-4-cyclopropyl-2-propylpyridine 1-oxide (**14d**) and 4-cyclopropyl-5-((hydroxyimino)(phenyl)methyl)-2-propylpyridine 1-oxide (**15d**)*

Prepared from **1d** (34.0 mg, 0.24 mmol) and **2b** (69.4 mg, 0.20 mmol).

14d: Yield: 12.0 mg (22 %) of a yellow oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.72 (2H, m, cyclopropyl), 0.95 (2H, m, cyclopropyl), 1.03 (3H, t, J = 7.4 Hz, CH_3), 1.76 (2H, h, J = 7.4 Hz, CH_2), 1.90 (1H, tt, J_1 = 5.1 Hz, J_2 = 8.5 Hz, cyclopropyl), 2.89 (2H, t, J = 7.4 Hz, CH_2), 6.77 (1H, s, C*H*), 7.48 (2H, t, J = 7.8 Hz, Ph), 7.62 (1H, d, J = 7.4 Hz, Ph), 7.80 (2H, d, J = 7.1 Hz, Ph), 8.16 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 10.2, 12.8, 14.2, 19.8, 32.8, 121.4, 129.1, 130.3, 134.5, 135.4, 136.7, 138.3, 141.9, 153.8, 193.5 ppm. – HRMS ((+)-ESI): m/z = 282.1483 (calcd. 282.1489 for $C_{18}H_{20}NO_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 2969, 2929, 1666, 1595, 1491, 1449, 1408, 1312, 1282, 1232, 1154, 1088, 1030, 912, 886 cm^{-1}.

15d: Yield: 8.0 mg (14 %) of a yellow oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.66 (2H, br s, cyclopropyl), 0.84 (2H, br s, cyclopropyl), 1.04 (3H, t, J = 7.4 Hz, CH_3), 1.62 (1H, ddd, J_1 = 5.2 Hz, J_2 = 8.4 Hz, J_3 = 13.6 Hz, cyclopropyl), 1.77 (2H, h, J = 7.4 Hz, CH_2), 2.92 (2H, t, J = 7.4 Hz, CH_2), 6.75 (1H, s, C*H*), 7.26 – 7.32 (3H, m, Ph), 7.43 – 7.45 (2H, m, Ph), 8.05 (1H, s, C*H*), 11.16 (1H, br s, O*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 9.9, 13.0, 14.3, 19.9, 32.8, 120.7, 126.7, 128.7, 129.7, 130.3, 135.0, 138.8, 144.0, 151.8, 152.2 ppm. – HRMS ((+)-ESI): m/z = 297.1669 (calcd. 297.1598 for $C_{18}H_{21}N_2O_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 2958, 2925, 2863, 1594, 1571, 1539, 1488, 1447, 1367, 1356, 1274, 1227, 1191, 1157, 1023, 942, 887, 782 cm^{-1}.

*5-Benzoyl-4-cyclopropyl-2-phenylpyridine 1-oxide (**14e**) and 4-cyclopropyl-5-((hydroxyimino)(phenyl)methyl)-2-phenylpyridine 1-oxide (**15e**)*

Prepared from **1b** (42.0 mg, 0.24 mmol) and **2b** (69.4 mg, 0.20 mmol).

14e: Yield: 6.0 mg (10 %) of a yellow oil. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.76 (2H, m, cyclopropyl), 0.97 (2H, m, cyclopropyl), 1.93 (1H, tt, J_1 = 5.2 Hz, J_2 = 8.4 Hz, cyclopropyl), 6.97 (1H, s, C*H*), 7.47 – 7.53 (5H, m, Ph), 7.65 (1H, t, J = 7.4 Hz, Ph), 7.79 – 7.81 (2H, m, Ph), 7.88 – 7.90 (2H, m, Ph), 8.25 (1H, s, C*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 10.5, 12.9, 123.5, 128.6, 129.2, 129.5, 130.2, 130.4, 132.4, 134.6, 136.4, 136.5, 139.1, 142.0, 150.2, 193.3 ppm. – HRMS ((+)-ESI): m/z = 316.1330 (calcd. 316.1332 for $C_{21}H_{18}NO_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1666, 1595, 1482, 1448, 1404, 1288, 1221, 1006, 907, 810, 763 cm^{-1}.

15e: Yield: 19.0 mg (30 %) of a yellow solid. M. p. 215.9 – 219.4 °C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.65 (2H, br s, cyclopropyl), 0.82 (2H, br. s, cyclopropyl), 2.07 (1H, ddd, J_1 = 5.2 Hz, J_2 = 8.4 Hz, J_3 = 13.5 Hz, cyclopropyl), 6.89 (1H, s, C*H*), 7.22 – 7.28 (3H, m, Ph), 7.40 – 7.45 (5H, m, Ph), 7.77 – 7.79 (2H, m, Ph), 8.12 (1H, s, C*H*), 11.68 (1H, br s, N*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 10.1, 13.1, 122.8, 126.7, 128.5, 128.7, 129.7, 129.8, 130.0, 132.0, 132.6, 134.9, 139.6, 144.9, 149.0, 151.3 ppm. – HRMS ((+)-ESI): m/z = 331.1446 (calcd. 331.1441 for $C_{21}H_{19}N_2O_2$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1617, 1485, 1438, 1406, 1321, 1263, 1219, 1198, 1158, 1121, 1019, 1000, 968, 896, 802, 773 cm^{-1}.

*5-Benzoyl-4-cyclopropyl-2-(thiophen-3-yl)pyridine 1-oxide (**14f**) and 4-cyclopropyl-5-((hydroxyimino)(phenyl)methyl)-2-(thiophen-3-yl)pyridine 1-oxide (**15f**)*

Prepared from **1d** (43.0 mg, 0.24 mmol) and **2b** (69.4 mg, 0.20 mmol).

14f: Yield: 8.0 mg (13 %) of a colorless solid. M. p. 106.7 – 110.9 °C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.78 (2H, m, cyclopropyl), 1.00 (2H, m, cyclopropyl), 1.98 (1H, tt, J_1 = 5.2 Hz, J_2 = 8.4 Hz, cyclopropyl), 7.26 (1H, s, C*H*), 7.43 (1H, dd, J_1 = 3.1 Hz, J_2 = 5.2 Hz, thiophene), 7.50 – 7.53 (2H, m, Ph), 7.64 – 7.67 (2H, m, thiophene+Ph), 7.88 – 7.89 (2H, m, Ph), 8.30 (1H, s, C*H*), 8.90 (1H dd, J_1 = 1.2 Hz, J_2 = 3.1 Hz, thiophene) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 10.3, 13.0, 121.6, 125.6, 127.3, 129.1, 130.3, 130.5, 131.5, 134.5, 135.2, 136.6, 139.7, 141.8, 145.1, 193.2 ppm. – HRMS ((+)-ESI): m/z = 322.0898 (calcd. 322.0896 for $C_{19}H_{16}NO_2S$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1664, 1609, 1595, 1520, 1485, 1449, 1381, 1349, 1315, 1285, 1221, 1153, 1116, 1072, 1024, 912, 873, 822, 801 cm^{-1}.

15f: Yield: 15.0 mg (24 %) of a colorless solid. M. p. 197.2 – 200.3 °C. – ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 0.72$ (2H, m, cyclopropyl), 0.88 (2H, br s, cyclopropyl), 1.69 (1H, tt, $J_1 = 5.3$ Hz, $J_2 = 8.4$ Hz, cyclopropyl), 7.18 (1H, s, C*H*), 7.27 – 7.30 (2H, m, Ph), 7.31 – 7.34 (1H, m, Ph), 7.44 (1H, dd, $J_1 = 3.1$ Hz, $J_2 = 5.1$ Hz, thiophene), 7.47 – 7.49 (2H, m, Ph), 7.65 (1H, dd, $J_1 = 1.2$ Hz, $J_2 = 5.1$ Hz, thiophene), 8.17 (1H, s, C*H*), 11.83 (1H, br s, O*H*) ppm. – ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta = 9.8$, 13.1, 121.0, 125.4, 126.7, 127.7, 128.7, 129.7, 130.2, 131.1, 131.8, 135.0, 139.8, 144.0, 144.5, 151.3 ppm. – HRMS ((+)-ESI): $m/z = 337.1004$ (calcd. 337.1005 for $C_{19}H_{17}N_2O_2S$, $[M+H]^+$). – IR: ν_{max} (NaCl) = 1616, 1529, 1494, 1434, 1383, 1348, 1320, 1304, 1217, 1200, 1159, 1120, 1058, 1026, 976, 934, 896, 860, 802, 770 cm^{-1}.

*Phenyl(4-phenyl-6-propylpyridin-3-yl)methanone (**10a**)*

To a solution of phenyl(4-phenyl-6-propylpyridin-3-yl)methanimine (**11a**, 19.0 mg, 0.0633 mmol) in CH_2Cl_2 (2 mL)-H_2O (0.5 mL) was added concentrated HCl (2 drops). The solution was stirred overnight at room temperature. Water was decanted, first $NaHCO_3$ and then Na_2SO_4 were added. The suspension was filtered, and volatile components were evaporated *in vacuo*. Yield: 12.4 mg (65 %) of a colorless oil. The ^{1}H NMR spectrum was consistent with **10a**.

*(4,6-Diphenylpyridin-3-yl)(phenyl)methanone (**10b**)*

To a solution of (4,6-diphenylpyridin-3-yl)(phenyl)-methanimine (**11b**, 10.9 mg, 0.0326 mmol) CH_2Cl_2 (2 mL)-H_2O (0.5 mL) was added concentrated HCl (2 drops). The solution was stirred overnight at room temperature. Water was decanted, first $NaHCO_3$ and then Na_2SO_4 were added. The suspension was filtered, and volatile components were evaporated *in vacuo*. Yield: 10.2 mg (93 %) of colorless oil. The ^{1}H NMR spectrum was consistent with **10b**.

X-Ray structure determinations

Single crystal diffraction data for compounds **6b**, **7** and **11c** (Fig. 2 – 5, Table 3) have been collected on a Nonius Kappa CCD diffractometer at r. t. with MoK_α radiation (λ = 0.71073 Å, graphite monochromator) using the Nonius COLLECT Software [54]. The data were processed using DENZO [55]. For compound **11b** diffraction data were collected on an Agilent SuperNova dual source diffractometer with an Atlas detector at 150(2) K. These data were processed using CRYSALIS PRO [56]. All structures were solved with Direct Methods, using SIR 97 [57]. Full-matrix least-squares refinements on F^2 were employed with anisotropic displacement parameters for all non-hydrogen atoms. H atoms were placed at calculated positions and treated as riding; SHELXL-97 [58] was used for structure refinement and interpretation. Drawings of the structures were produced using ORTEP-III [59, 60]. Crystal structure data for all four compounds are summarized in Table 3.

CCDC 984532 – 984535 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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