# Synthesis of Alkoxy-Substituted Pyridines from Mono- and Tricationic Pyridinium Salts

Andreas Schmidt,* Thorsten Mordhorst

Clausthal University of Technology, Institute of Organic Chemistry, Leibnizstrasse 6, 38678 Clausthal-Zellerfeld, Germany
Fax +49(5323)723861; E-mail: schmidt@ioc.tu-clausthal.de

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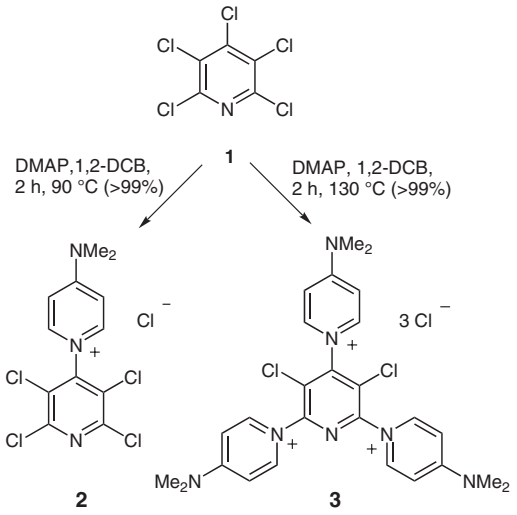
**Abstract:** Nucleophilic substitution reactions on 4-(4-dimethylamino)-pyridinium-substituted tetrachloropyridine with oxygen nucleophiles such as alkoxides and phenolates resulted in the formation of 4- or 2,4-alkoxy- or -phenoxy-substituted chloropyridines depending on the reaction conditions. Substitution on 2,4,6-tris(4-dimethylamino)pyridinium-substituted 3,5-dichloropyridine gave the corresponding 2,4,6-tris-alkoxy- or -phenoxy-substituted pyridines which are not available by other routes.

**Key words:** nucleophilic aromatic substitutions, pyridinium salts, pyridines, trication

Substitution reactions on halogenated heteroaromatics are well-known reactions in organic chemistry. In the case of pyridines, these reactions lead to numerous biologically, pharmaceutically or industrially interesting compounds.[1] Nucleophilic substitutions on halogen-substituted pyridines proceed via the *AE*-mechanism,[1] but $S_N$(*ANRORC*)-,[2] *EA*-[3] or $S_{RN1}$-mechanisms[4] are observed as well. A large number of reports prove that the 2- and 4-positions of chloropyridines smoothly react with a broad variety of nucleophiles in high yields,[5] whereas the 3-position is most often inert under these non-catalysed conditions.[6] 4-Nitro-substituted derivatives are exceptions from this observation.[7] However, substitution reactions on pentahalogenopyridines, although widely applied, suffer from considerable disadvantages. First, they are limited to the preparation of mono- or disubstituted chloropyridines and often give mixtures of 2- and 4-substituted tetrachloropyridines as well as 2,4-disubstituted trichloropyridines[1,8] on reaction with alkoxides and other nucleophiles.[9] It was described earlier that large nucleophiles attack partly or mainly the 2(6)-position of pentachloropyridine, whereas small nucleophiles substitute the 4-position.[9,10] An additional problematic issue is that some 4-alkoxy-substituted tetrachloropyridines decompose to tetrachloro-4-hydroxypyridine and alkenes under the reaction conditions applied,[10] so that their isolation is difficult. Consequently, a large number of simple substituted pyridines have never been described to date.

In continuation of our work on oligocationic heteroaromatics[11] and mesomeric betaines[12] we report here our results concerning substitution reactions on pyridinium-substituted pyridines **2** and **3** with oxygen nucleophiles. The (tetrachloropyridin-4-yl)pyridinium chloride **2** and the (3,5-dichloropyridine-2,4,6-triyl)-tris-pyridinium trichloride **3** are available in quantitative yields from pentachloropyridine (**1**) on reaction with DMAP (Scheme 1).[13]

We were interested in the synthetic potential of **2** and **3**, as they possess two distinct types of leaving groups with different leaving group tendencies.




**Scheme 1**

First, we focused our interest on monocation **2** and found reaction conditions which allowed the straightforward syntheses of 4-alkoxy-substituted 2,3,5,6-tetrachloropyridines **5** and 2,4-dialkoxy-substituted 3,5,6-trichloropyridines **6** (Scheme 2). Furthermore, (hetero)aromatic ethers such as **7–9** were available starting from **2** (Scheme 3). The outcome of the reaction was dependent on the stoichiometric ratio of the starting materials, the reaction times, and temperatures, which are presented in Table 1.

Thus, treatment of pyridinium salt **2** with sodium methanolate yielded either tetrachloro-4-methoxypyridine **5a** or its 2,4-dimethoxy derivative **6a** depending on the reaction conditions. Pyridine **5a** is a known compound and had earlier been prepared by multi-step procedures (via tetrachloro-4-methylsulfonylpyridine[14] or 4-hydroxy-ethylsulfonamide[15]). Substitution on pentachloropyridine led to a mixture of isomers, from which **5a** was finally isolated after morefold recrystallizations.[16] The disubstituted

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**Table 1** Synthesis of Alkoxy- and Dialkoxy-Substituted Chloropyridines **5–9**

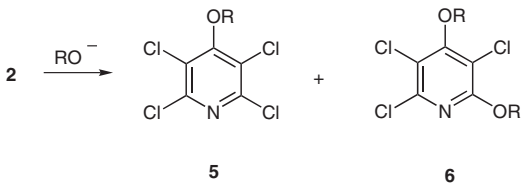
| Compound | R | Nucleophile (equiv) | Solvent | Reaction time (h), Temperature | Yield (%) |
|---|---|---|---|---|---|
| **5a** | Me | $MeO^-$ (1) | MeOH | 6, reflux | 51 |
| **6a** | Me | $MeO^-$ (5) | MeOH | 3, reflux | 55 |
| **5b** | Et | $EtO^-$ (1) | EtOH | 24, r.t. | 30 |
| **6b** | Et | $EtO^-$ (10) | EtOH | 6, reflux | 57 |
| **5c** | *i*-Pr | *i*-$PrO^-$ (5) | *i*-PrOH | 12, r.t. | 73 |
| **6c** | *i*-Pr | *i*-$PrO^-$ (10) | *i*-PrOH | 5, reflux | 87 |
| **5d** | *n*-Pr | *n*-$PrO^-$ (1) | *n*-PrOH | 24, r.t. | 28 |
| **6d** | *n*-Pr | *n*-$PrO^-$ (10) | *n*-PrOH | 6, reflux | 87 |
| **5e** | *t*-Bu | *t*-$BuO^-$ (8) | *t*-BuOH | 5, reflux | 33 |
| **5f** | *n*-Octyl | *n*-$OctO^-$ (1) | DMF[a] | 18, reflux | 23 |
| **5g** | Allyl | $C_3H_5O^-$ (5) | $C_3H_5OH$ | 12, r.t. | 28 |
| **7** | Ph | $PhO^-$ (1) | DMF[a] | 18, 100 °C | >99 |
| **8** | 4-$MeOC_6H_4$ | $C_7H_7O^-$ (10) | DMF[a] | 5, 100 °C | >99 |
| **9** | Pyridin-3-yl | $C_5H_4NO^-$ (1) | DMF[a] | 5, 100 °C | 31 |

[a] Equimolar amounts of $NaNH_2$ were added.

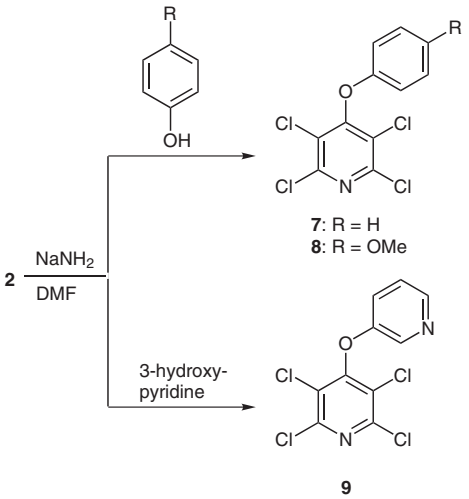
derivative **6a** was obtained earlier starting from pentachloropyridine and sodium methanolate after 22 hours at reflux temperature,[16] or by a five-step-procedure via tetrachloropyridine-4-sulfenyl chloride.[17] The method described here offers some advantages: First, mixtures of monosubstituted and disubstituted compounds are not formed, so that the separation of two species with very similar polarities and solubilities is not necessary. Moreover, polar by-products such as 2- or 2,6-dialkoxy-substituted pyridine-4-yl pyridinium salts as well as the leaving group DMAP can easily be removed by filtration over silica gel so that the work-up procedure is considerably facilitated.

Starting from **2**, we were therefore able to prepare the ethoxy, 1-propoxy, 2-propoxy, *t*-butoxy, *n*-octyloxy, and allyloxy derivatives **5b–g** and **6b–d** under the conditions presented in Table 1. From these, only **5b**,[18–20] **5d**[18] (alkylation of the pyridin-4-olate in low yields[18]) and **5e**[10] have been described before. The latter was obtained earlier in low yield on treatment of pentachloropyridine with potassium *tert*-butoxide as a mixture with its 2-isomer, and proved to be very sensitive towards the elimination of isobutene under formation of 4-hydroxypyridine.[10a] The instabilities of the 4-alkoxy-substituted chloropyridines, especially of the ethoxy-, *n*-propoxy-, *t*-butoxy- and *n*-octyloxy derivatives (**5b**, **5d**, **5e**, **5f**) is reflected in relatively low yields after purification.

Reaction of **2** with phenol, its 4-methoxy derivative, and 3-hydroxypyridine afforded the addition of a strong base to the DMF solution to generate the corresponding phenolates, which reacted to **7**, **8**, and **9** (Scheme 3). Sodium amide proved to give the best yields. Whereas **7** can also be prepared starting from pentachloropyridine followed by separation from its 2-isomer,[21] the ethers **8** and **9** are, to the best of our knowledge, new compounds.




**Scheme 2**




**Scheme 3**

**Table 2** Synthesis of 2,4,6-Trialkoxy-Substituted 3,5-Dichloro-pyridines

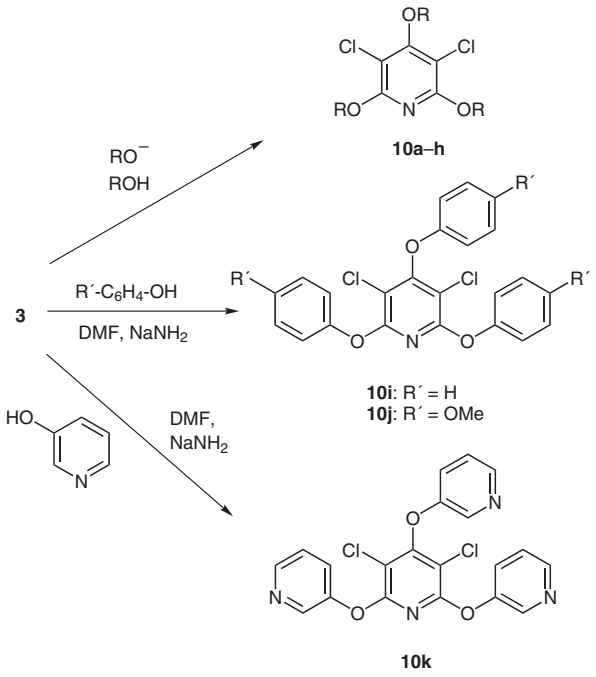
| Compound | R | Nucleophile | Solvent | Yield (%) |
|---|---|---|---|---|
| **10a** | Me | $MeO^-$ | MeOH[a] | >99 |
| **10b** | Et | $EtO^-$ | EtOH[a] | 55 |
| **10c** | *i*-Pr | *i*-$PrO^-$ | *i*-PrOH[a] | 87 |
| **10d** | *n*-Pr | *n*-$PrO^-$ | *n*-PrOH[a] | 59 |
| **10e** | *n*-Bu | *n*-$BuO^-$ | *n*-BuOH[a] | 55 |
| **10f** | *t*-Bu | *t*-$BuO^-$ | *t*-BuOH[a] | 20 |
| **10g** | Allyl | $CH_2$=$CHCH_2O^-$ | Allyl alcohol[a] | 95 |
| **10h** | *n*-Octyl | $CH_3(CH_2)_7O^-$ | $C_8H_{17}OH$[a] | 28 |
| **10i** | Ph | $PhO^-$ | DMF[b] | 71 |
| **10j** | 4-$MeOC_6H_4$ | 4-$MeOC_6H_4O^-$ | DMF[b] | 90 |
| **10k** | Pyridin-3-yl | Pyridin-3-olate | DMF[b] | 38 |

[a] Sodium salt.
[b] Stoichiometric amounts of sodium amide added.

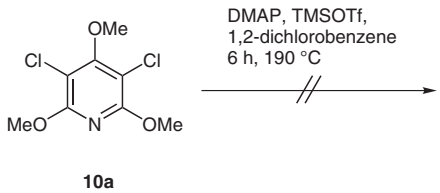
2,4,6-Trisubstitution on pentachloropyridine with nucleophiles have very scarcely been described in the literature. One example is the preparation of 2,4,6-trimethoxy-pyridine **10a** which was synthesized from pentachloropyridine at high temperature and pressure in an autoclave in 16% yield.[16a] By contrast, the trication **3** allows easy preparations of the hitherto inaccessible symmetrically substituted pyridines **10a–h** (Scheme 4, Tables 2 and 3), including the trimethoxy derivative, which is formed in quantitative yield by the method described here. Aliphatic alcohols can be used as solvents, whereas dimethylformamide proved to be the most suited solvent for substitutions with phenolates and pyridine-3-olate. The anionic species were generated by stoichiometric amounts of sodium amide. Thus, 2,4,6-triphenoxypyridine **10i**[22] and its *p*-methoxy derivate **10j**,[8] as well as the 2,4,6-tri-*O*-(3-hydroxypyridine) derivative **10k** were formed as colored solids.

It is apparent that the methoxy and the allyloxy derivate **10a** and **10g**, which cannot eliminate alkenes with concomitant formation of 4-hydroxypyridine, give the best yields. It has generally been supposed that the *tert*-butoxide ion is too large to penetrate to a ring carbon atom, and even if it does under vigorous conditions, immediate decomposition to *iso*-butene occurs.[10a] These observations explain the low yield of the 4-*t*-butoxy-pyridine **10f** which nonetheless could be completely characterized.

The substitutions are not reversible. Thus, no reaction was observable on treatment of **10a** with excess DMAP after heating at 190 °C in 1,2-dichlorobenzene over a period of six hours (Scheme 5). The addition of excess TMSOTf had no influence on the outcome of the reaction.




**Scheme 4**




**Scheme 5**

**Table 3** Characterization of New Compounds[a]

| Compound | Mp (°C) | $^1$H NMR (DMSO-$d_6$) δ [ppm], $J$ [Hz] | $^{13}$C NMR (DMSO-$d_6$)[b] δ [ppm] | EIMS $m/z$ (%) |
|---|---|---|---|---|
| **5c** | 63 | 4.84 (m, 1 H, CH), 1.33 (d, $^3J$ = 6.1 Hz, 6 H, $CH_3$) | 160.5 (C-4), 145.7 (C-2/6), 124.9 (C-3/5), 79.9 (CH), 22.3 ($CH_3$) | 274 (24) [$M^+$], 232 (100) |
| **5f**[c] | Oil | 4.19 (t, $^3J$ = 6.4 Hz, 2 H, $OCH_2$), 1.85 (m, overlapped, 2 H, 2-$CH_2$), 1.48 (m, overlapped, 2H, 7-$CH_2$), 1.30 (m, overlapped, 8 H, 3-$CH_2$, 4-$CH_2$, 5-$CH_2$, 6-$CH_2$), 0.89 (s, 3 H, $CH_3$) | 161.7 (C-4), 146.7 (C-2/6), 125.0 (C-3/5), 70.5 ($OCH_2$), 31.8 ($CH_2$), 30.0 ($CH_2$), 29.2 ($CH_2$), 29.1 ($CH_2$), 25.6 ($CH_2$), 22.6 ($CH_2$), 14.1 ($CH_3$) | 346 (31) [$M^+$], 42 (100) |
| **5g** | 44 | 5.81 (m, 1 H, CH), 5.23 (m, 1 H, =$CH_2$), 5.05 (m, 1 H, =$CH_2$), 4.52 (m, 2 H, $CH_2$) | 156.8 (C-4), 145.6 (C-2/6), 132.3 (=CH), 119.6 (C-3/5), 118.2 (=$CH_2$), 75.1 ($CH_2$) | 273 (22) [$M^+$], 41 (100) |
| **6b** | Oil | 4.36 (q, $^3J$ = 7.1 Hz, 2 H, $CH_2$), 4.22 (q, $^3J$ = 7.1 Hz, 2 H, $CH_2$), 1.39 (t, $^3J$ = 7.1 Hz, 3 H, $CH_3$), 1.35 (t, $^3J$ = 7.1 Hz, 3 H, $CH_3$) | 160.8 (C-4), 157.2 (C-2), 143.1 (C-6), 117.0 (C-3), 111.0 (C-5), 70.4 ($CH_2$), 63.9 ($CH_2$), 15.3 ($CH_3$), 14.1 ($CH_3$) | 271 (58) [$M^+$], 254 (100) |
| **6c** | Oil | 5.20 (h, $^3J$ = 6.2 Hz, 1 H, OCH), 4.78 (h, $^3J$ = 6.2 Hz, 1 H, OCH), 1.35 (d, $^3J$ = 6.2 Hz, 6 H, $CH_3$), 1.32 (d, $^3J$ = 6.2 Hz, 6 H, $CH_3$) | 159.9 (C-4), 156.8 (C-2), 143.2 (C-6), 116.9 (C-3), 111.5 (C-5), 78.7 (CH), 71.1 (CH), 22.3 ($CH_3$), 21.5 ($CH_3$) | 299 (74) [$M^+$], 213 (100) |
| **6d** | Oil | 4.26 (t, $^3J$ = 6.6 Hz, 2 H, $OCH_2$), 4.12 (t, $^3J$ = 6.6 Hz, 2 H, $OCH_2$), 1.77 (m, 4 H, $CH_2$), 1.02 (t, $^3J$ = 6.6 Hz, 3 H, $CH_3$), 0.98 (t, $^3J$ = 6.6 Hz, 3 H, $CH_3$) | 160.9 (C-4), 157.4 (C-2), 143.1 (C-6), 116.8 (C-3), 110.8 (C-5), 75.8 (O$CH_2$), 69.3 ($OCH_2$), 22.9 ($CH_2$), 21.5 ($CH_2$), 10.1 (2 × $CH_3$) | 298 (72) [$M^+$], 255 (100) |
| **8** | 61 | 6.81 (m, 4 H, PhH), 3.79 (s, 3 H, $CH_3$) | 157.9 (C-4), 156.0 (C-4′), 149.3 (C-2/6), 147.2 (C-1′), 125.5 (C-3/5), 116.6 (C-2′/4′), 115.0 (C-3′/5′), 55.7 ($CH_3$) | 329 (100) [$M^+$] |
| **9**[c] | 109 | 8.36 (d, $^5J$ = 4.8 Hz, 1 H, 2-H), 8.25 (d, $^3J$ = 2.9 Hz, 1 H, 6-H), 7.23 (dd, $^4J$ = 8.4 Hz, $^5J$ = 4.8 Hz, 1 H, 5-H), 7.07 (dd, $^4J$ = 8.4 Hz, $^4J$ = 2.9 Hz, 1 H, 4-H) | 155.5 (C-4), 150.8 (C-3), 146.4 (C-6′), 144.4 (C-2/6), 137.4 (C-2′), 124.2 (C-5′), 123.3 (C-4′), 121.4 (C-3/5) | 311 (70) [$M^+$], 273 (100) |
| **10a**[c] | 86 | 3.81 (s, 3 H, $CH_3$), 3.80 (s, 6 H, $CH_3$) | 157.2 (C-4), 153.0 (C-2/6), 108.5 (C-3/5), 55.3 ($CH_3$), 54.5 (2 × $CH_3$) | 237 (100) [$M^+$] |
| **10b**[c] | Oil | 4.39 (q, $^3J$ = 7.0 Hz, 4 H, $CH_2$), 4.19 (q, $^3J$ = 7.0 Hz, 2 H, $CH_2$), 1.43 (m, 9 H, $CH_3$) | 161.2 (C-4), 156.3 (C-2/6), 103.3 (C-3/5), 69.8 ($CH_2$), 63.0 (2 × $CH_2$), 15.5 ($CH_3$), 14.5 (2 × $CH_3$) | 279 (100) [$M^+$] |
| **10c** | 32 | 5.19 (m, 2 H, CH), 4.71 (m, 1 H, CH), 1.36 (s, 6 H, $CH_3$), 1.33 (s, 12 H, $CH_3$) | 159.9 (C-4), 155.5 (C-2/6), 102.6 (C-3/5), 77.4 (CH), 70.0 (2 × CH), 22.2 (2 × $CH_3$), 21.7 (4 × $CH_3$) | 321 (100) [$M^+$] |
| **10d** | Oil | 4.25 (t, $^3J$ = 6.6 Hz, 4 H, $OCH_2$), 4.02 (t, $^3J$ = 6.6 Hz, 2 H, $OCH_2$), 1.74 (m, 6 H, $CH_2$), 1.04 (t, $^3J$ = 6.6 Hz, 6 H, $CH_3$), 0.99 (t, $^3J$ = 6.6 Hz, 3 H, $CH_3$) | 160.8 (C-4), 156.0 (C-2/6), 102.1 (C-3/5), 75.2 ($OCH_2$), 68.3 (2 × $OCH_2$), 22.9 ($CH_2$), 21.7 (2 × $CH_2$), 10.2 (3 $CH_3$) | 322 ($M^+$, 100) |
| **10e** | Oil | 4.33 (t, $^3J$ = 6.5 Hz, 4 H, $OCH_2$), 4.08 (t, $^3J$ = 6.5 Hz, 2 H, $OCH_2$), 1.71 (m, 6 H, $CH_2$), 1.43 (m, 6 H, $CH_2$), 0.93 (t, $^3J$ = 6.5 Hz, 9 H, $CH_3$) | 160.8 (C-4), 156.0 (C-2/6), 102.2 (C-3/5), 73.4 ($OCH_2$), 66.6 (2 × $OCH_2$), 31.5 ($CH_2$), 30.3 (2 × $CH_2$), 18.6 (2 × $CH_2$), 18.5 ($CH_2$), 13.6 (2 × $CH_3$), 13.5 ($CH_3$) | 364 (100) [$M^+$] |
| **10f** | 41 | 1.57 (s, 9 H, $CH_3$), 1.50 (s, 18 H, $CH_3$) | 164.9 (C-4), 153.9 (C-2/6), 101.1 (C-3/5), 81.9 ($CMe_3$), 75.6 (2 $CMe_3$), 29.3 (3 × $CH_3$), 27.9 (6 × $CH_3$) | 252 (100) [$M^+ - 2 \times C_4H_8$] |
| **10g** | Oil | 6.10 (3 H, =CH), 5.30 (m, 6 H, =$CH_2$), 4.88 (dt, $^3J$ = 5.7 Hz, $^5J$ = 1.4 Hz, 4 H, $OCH_2$), 4.67 (dt, $^3J$ = 5.7 Hz, $^5J$ = 1.4 Hz, 2 H, $OCH_2$) | 160.5 (C-4), 155.4 (C-2/6), 132.9 (2 $CH$=$CH_2$), 132.6 ($CH$=$CH_2$), 119.2 (2 × =$CH_2$), 118.0 (=$CH_2$), 102.7 (C-3/5), 74.2 (2 × $OCH_2$), 67.5 ($OCH_2$) | 317 (84) [$M^+$], 275 (100) |
| **10h** | Oil | 4.32 (t, $^3J$ = 5.7 Hz, 6 H, $OCH_2$), 3.38 (m, 6 H; $CH_2$), 1.71 (m, 6 H, $CH_2$), 1.25 (m, 24 H, $CH_2$), 0.86 (t, $^3J$ = 6.5 Hz, 9 H, $CH_3$) | 158.8 (C-4), 145.8 (C-2/6), 111.2 (C-3/5), 60.6 (3 × $OCH_2$), 32.5 (3 × $CH_2$), 31.2 (3 × $CH_2$), 28.9 (3 × $CH_2$), 28.7 (3 × $CH_2$), 25.5 (3 × $CH_2$), 22.1 (3 × $CH_2$), 13.9 (3 × $CH_3$) | 532 (100) [$M^+$] |

**Table 3** Characterization of New Compounds[a] (continued)

| Compound | Mp (°C) | $^1$H NMR (DMSO-$d_6$) δ [ppm], *J* [Hz] | $^{13}$C NMR (DMSO-$d_6$)[b] δ [ppm] | EIMS *m/z* (%) |
|---|---|---|---|---|
| **10k** | 149 | 8.52 (d, $^4J$ = 2.8 Hz, 1 H, 2′-H), 8.37 (d, $^4J$ = 2.8 Hz, 3 H, 6′-H), 8.52 (dd, $^4J$ = 2.8 Hz, $^3J$ = 4.7 Hz, 2 H, 2′-H), 7.63 (dd, $^4J$ = 2.8 Hz, $^3J$ = 4.7 Hz, 1 H; 5′-H), 7.58 (dd, $^5J$ = 2.8 Hz, $^3J$ = 4.7 Hz, 2 H, 5′-H), 7.48 (d, $^3J$ = 4.7 Hz, 1 H; 4′-H), 7.32 (d, $^3J$ = 4.7 Hz, 2 H, 4´-H) | 156.8 (C-4), 155.0 (C-2/6), 152.1 (C-3′), 149.1 (2 × C-3′), 146.2 (2 × C-4′), 144.8 (C-4′), 142.4 (2 × C-2′), 137.7 (C-2′), 128.8 (2 × C-5′), 124.8 (C-5′), 124.0 (2 × C-6′), 122.5 (C-6′), 106.5 (C-3/5) | 428 (100) [M$^+$] |

[a] Satisfactory microanalyses were obtained for all new compounds, except for **5f, 10c, 10f, 10h** which is presumably due to their easy thermal decomposition.
[b] Numbering: C-4 corresponds to the 4-position of the pyridine ring; C-4′ and 4′-H refers to the 4-positions of phenyl (**10i**, **j**) or pyridine rings (**10k**), respectively.
[c] NMR spectra were taken in $CDCl_3$.

The $^1$H and $^{13}$C NMR spectra were recorded on Bruker ARX-400 and DPX-200 spectrometers and were taken in DMSO-$d_6$ at 200 MHz and 400 MHz, respectively, at 20 °C. The chemical shifts are reported in ppm relative to internal TMS (δ = 0.00). Multiplicities are described by using the following abbreviations: s = singlet, d = doublet, t = triplet, h = heptet, m = multiplet, br = broad. The mass spectra (ESIMS) were measured with a Hewlett-Packard HP 5989B or a Varian SAT2100T with GC3900. Melting points are uncorrected.

**Synthesis of the 4-Alkoxy-2,3,5,6-tetrachloro-pyridines 5a–g and the 2,4-Dialkoxy-3,4,6-trichloropyridines 6a–d**

A solution of 1-(4-dimethylamino)-[2,3,5,6-tetrachloro-pyridin-4-yl]-pyridinium chloride (**2**; 10.0 mmol, 3.74 g) in alcohol (30 mL) was treated with a solution of the sodium alkoxide in the corresponding alcohol (50 mL). The solvents, reaction times and temperatures are presented in Table 1. After completion of the reaction the alcohols were distilled off in vacuo and the residues were chromatographed in a short column on silica gel with EtOAc–petroleum ether (1:1).

**5a**

Mp 114 °C (114–115 °C,[16] 117–119 °C,[16a] 113.5 °C[16b]).

**5b**

Mp 54 °C (54–56 °C,[19] 56–58 °C[20]).

**5d**

The reported mp for **5d** is incorrect; mp 83–85 °C (28–29 °C[18]).

**5e**

Mp 70 °C (70–72 °C[10a]).

**6a**

Mp. 117 °C (116.5–117.5 °C[16b]).

**Synthesis of the 4-(Hetero)aryl-Substituted Tetrachloropyridines 7–9**

Sodium amide (0.43 g, 11.0 mmol) was suspended in anhyd DMF (80 mL) and was treated with 1-(4-dimethylamino)-[2,3,5,6-tetrachloropyridin-4-yl]pyridi-nium chloride (**2**; 3.74 g, 10.0 mmol) and phenol (0.94 g, 10.0 mmol), 4-methoxyphenol (1.24 g, 10.0 mmol), 3-hydroxypyridine (0.95 g, 10.0 mmol), and 1-octanol (1.3 g, 10.0 mmol). The reaction mixture was heated as indicated in Table 1. DMF was then distilled off and the residue was chromatographed on silica gel (EtOAc–petroleum ether, 1:2; short column).

**Synthesis of the 2,4,6-Trialkoxy-Substituted 3,5-Dichloropyridines 10a–h**

A solution of the trication **3** [6.15 g, 10.0 mmol in alcohol (50 mL) (cf. Table 2)] was treated with a solution of the sodium alkoxide (0.2 mol) in the corresponding alcohol (100 mL). Except for the synthesis of **10g** (stirring at r.t. for 24 h), the mixtures were heated for 6 h at reflux temperature. After completion of the reaction the alcohols were distilled off in vacuo and the residues were chromatographed on silica gel with EtOAc–petroleum ether (1:1; short column).

**10a**

Mp 86 °C.

**Synthesis of the 2,4,6-Triphenoxy-Substituted 3,5-Dichloropyridines 10i,j and the 2,4,6-Tri(pyridin-3yl)-oxy-Substituted 3,5-Dichloropyridine (10k)**

Sodium amide (1.30 g, 33 mmol) and trication **3** (6.15 g, 10 mmol) were suspended in DMF (100 mL). Then, phenol (2.82 g, 30 mmol), 4-methoxyphenol (3.72 g, 30 mmol), or 3-hydroxypyridine (2.85 g, 30 mmol) was added. After the reaction time and temperature as described in Table 2, DMF was distilled off in vacuo and the residue was chromatographed on silica gel with EtOAc–petroleum ether (1:1).

**10i**

Mp 102 (105–107 °C[22]).

**10j**

Mp 145 °C.

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