COMMUNICATION

The facile synthesis of a 1-alkyl-2-{[1-alkylpyridin-2(1*H*)-ylidene]-amino}pyridinium derived from 2-(chloromethyl)-6-formyl-4-methylphenol

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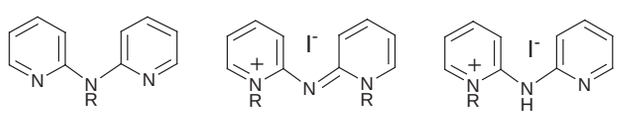
The reaction of 2-(chloromethyl)-6-formyl-4-methylphenol with 2,2′-dipyridylamine readily gave a 1-alkyl-2-{[1-alkylpyridin-2(1*H*)-ylidene]amino}pyridinium, the crystal structure of which was determined by X-ray crystallography.

N-Alkylation of 2,2′-dipyridylamine (**1**) to give **2** has been achieved by addition of a base, such as *n*-butyllithium or sodium hydride, followed by the requisite alkyl halide RX. Representative examples of this reaction involve R = benzyl,[1] trimethylsilyl,[2] and saturated alkyl chains having C_5 to C_{16}.[3,4]

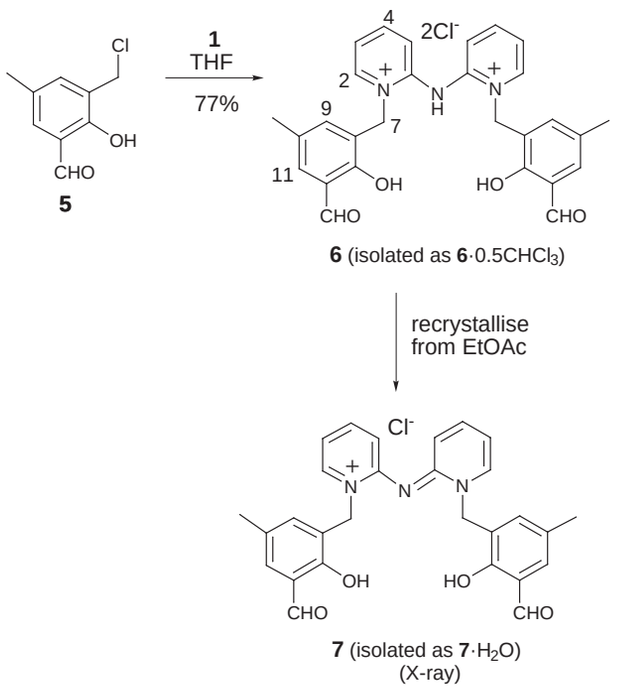


1 R = H
2 R = alkyl, $SiMe_3$ **3** **4**

When the base is omitted, as in the reaction of **1** with the simple alkyl iodides RI (R = CH_3, C_2H_5) at elevated temperatures, then the reduced nucleophilicity of the central nitrogen atom is such that 1-alkyl-2-{[1-alkylpyridin-2(1*H*)-ylidene]amino}pyridinium having the structure **3** are formed.[5–7] More recently a patent has disclosed that reaction of CH_3I with 2,2′-dipyridylamine in 1,2-dimethoxyethane in ethylene glycol–dimethyl ether for 24 hours at room temperature gives only the monoquaternised compound **4** (R = CH_3).[8]

We have investigated the reaction of 2-(chloromethyl)-6-formyl-4-methylphenol (**5**) with **1** and find that the product of the reaction is the corresponding 1-alkyl-2-{[1-alkylpyridin-2(1*H*)-ylidene]amino}pyridinium **6** (Scheme 1). The formation of the 1-alkyl-2-{[1-alkylpyridin-2(1*H*)-ylidene]amino}pyridinium is probably aided by the ready accessibility of the quinoidal form of **1**; the reaction is carried out in THF at 0 °C followed by an acid–base extraction using $CHCl_3$–H_2O and does not need the elevated temperatures reported for the synthesis of **3**. The reaction could, by analogy with the formation of 2,2′-pyridocyanines,[7,9] proceed by one of two routes (**A**→**B**→**C** and **D**→**E** in Fig. 1). It has been remarked that for the corresponding 2,2′-pyridocyanines the reaction path could not be predicted but may be influenced by steric factors as when R = CH_3 route **D**→**E** was followed whereas when R = C_2H_5 it was route **A**→**B**→**C** that was followed. It has not been possible to establish an exclusive reaction pathway in the current work. The bulk reaction product recovered prior to recrystallisation analysed as the doubly quaternised salt **6**·0.5$CHCl_3$ which on recrystallisation from ethyl acetate gave **7** as the monohydrate, **7**·H_2O.

In order to gain insight into the structure of the quaternised product the crystal structure of **7**·H_2O was solved; an ORTEP diagram of the cation therein is given in Fig. 2. Selected bond lengths are given in the caption. The bond lengths at the central N atom, N(1)–C(1) 1.330(3) and N(1)–C(13) 1.336(3) Å, differ considerably from those found for the corresponding atoms in 2,2′-dipyridylamine[10] [1.388, 1.391 Å]. These short bond lengths and the symmetry of the molecule do not permit identification of a resonance extreme structure as written above for **7** and suggest that the charge is delocalised throughout the molecule. The pyridine rings are not coplanar being inclined at 45.5° to each other. Furthermore the pyridine N atoms are aligned in a "*cis*" configuration in **7**·H_2O in contrast to a "*trans*" configuration in 2,2′-dipyridylamine and in the monoquaternised product **8** (R = CH_3).[2] The benzene rings in **7**·H_2O are not parallel with each other but inclined at 20.4°. This, and the inter-centroid separation of 4.025 Å, suggests that there is no π–π interaction between the rings. The water molecule is not intramolecularly associated with **7** but is hydrogen-bonded to the chloride anion [O(1w_a)–Cl 3.074 Å] with a short contact to a CH in a symmetry related phenol [O(1w_a)–C(22) 3.368; O(1w_a)–H(22) 2.454 Å].



5 **6** (isolated as **6**·0.5$CHCl_3$) **7** (isolated as **7**·H_2O) (X-ray)

Scheme 1

The generality of the reaction is being explored with regard to the construction of macrocyclic ligands bearing cationic spacers and capable of selective anion complexation.

Experimental

The synthesis of 6·0.5$CHCl_3$

2-(Chloromethyl)-6-formyl-4-methylphenol (1.85 g, 0.01 mol)

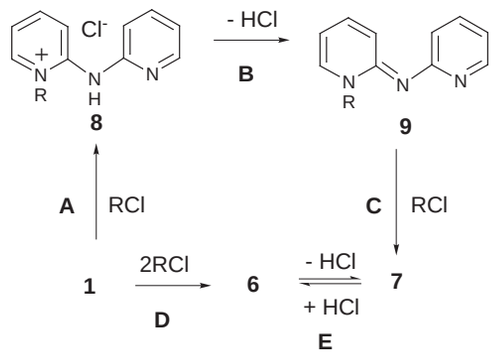


Fig. 1 The proposed reaction pathways.

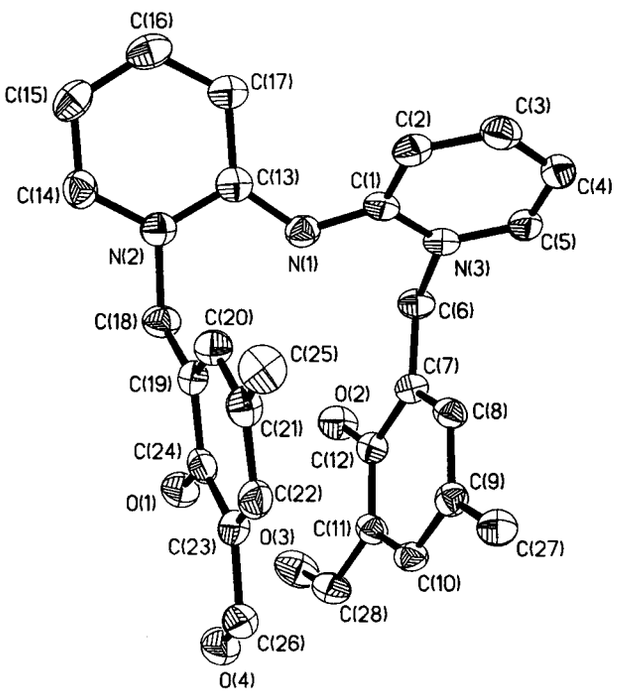


Fig. 2 An ORTEP view of the cation present in **7**·H_2O. Selected bond distances and angles: N(1)–C(1) 1.330(3), N(1)–C(13) 1.336(3), N(3)–C(1) 1.377(3), N(3)–C(5) 1.362(4), C(1)–C(2) 1.418(4), C(2)–C(3) 1.363(4), C(3)–C(4) 1.403(4), C(4)–C(5) 1.357(4), N(2)–C(13) 1.376(4), N(2)–C(14) 1.362(4), C(13)–C(17) 1.419(4), C(17)–C(16) 1.356(4), C(16)–C(15) 1.395(4), C(15)–C(14) 1.360(4), N(2)–C(18) 1.473(3), N(3)–C(6) 1.472(3) Å, C(1)–N(1)–C(13) 123.3(2)°.

was dissolved in tetrahydrofuran (75 ml) and 2,2′-dipyridylamine (3.44 g, 0.02 mol), predissolved in tetrahydrofuran (50 ml) was added dropwise at 0 °C over 1.5 hours. The reaction mixture was stirred for a further hour to give a bright yellow solution from which the solvent was removed *in vacuo*. Distilled water (100 ml) was added to the viscous residue, and the resulting solution made basic (pH 11) by addition of 4 M NaOH. The resulting solution was washed with chloroform (6 × 25 ml). The aqueous layer was then neutralised with 2 M HCl and the product recovered by extraction with chloroform (5 × 25 ml). The chloroform was removed *in vacuo* to give **6**·0.5$CHCl_3$ as a white solid (yield = 77%). Found: C, 56.93; H, 4.44; N, 6.77%. Reqd. for $C_{28}H_{27}Cl_2N_3O_4$·0.5$CHCl_3$: C, 57.04; H, 4.62; N, 7.00%. FAB MS *m*/*z* = 468 $[C_{28}H_{26}N_3O_4]^+$; IR (KBr disc)/cm^{-1} 3488 (*ν*OH), 1656 (*ν*C=O); ^{1}H NMR ($CDCl_3$) *δ* 9.80 (s, 1 H, CHO), 8.30 (dd, *J* 6.7, 1.2, 1 H, H-2), 7.76 (ddd, *J* 7.0, 6.7, 1.8, 1 H, H-3), 7.31 (d, *J* 1.5, 1 H, H-11), 7.23 (d, *J* 1.5, 1 H, H-9), 7.05 (d(br d), 1 H, H-5), 6.85 (ddd, *J* 7.0, 7.0, 1.2, 1 H, H-4), 5.50 (s, 2 H, H-7) and 2.15 (s, 3 H, CH_3). Recrystallisation of the white solid from ethyl acetate gave colourless blocks of **7**·H_2O suitable for X-ray analysis.

X-Ray structure

Crystal data for $C_{28}H_{28}ClN_3O_5$; $M = 521.98$. Crystallises from ethyl acetate as colourless blocks; crystal dimensions 0.43 × 0.22 × 0.22 mm. Triclinic, $a = 10.0958(11)$, $b = 11.6777(12)$, $c = 12.6726(13)$ Å, $\alpha = 102.926(2)°$, $\beta = 107.872(2)°$, $\gamma = 108.421(2)°$, $U = 1261.2(2)$ Å^3, $Z = 2$, $D_c = 1.375$ g cm^{-3}, space group $P\bar{1}$ (C_i^1, no. 2), Mo-Kα radiation ($\bar{\lambda} = 0.71073$ Å), μ(Mo-Kα) = 0.196 mm^{-1}, $F(000) = 548$.

Data collected were measured on a Bruker Smart CCD area detector with an Oxford Cryosystems low temperature system held at 150 K. Cell parameters were refined from the setting angles of 156 reflections (θ range 1.81° to 28.28°). Reflections were measured from a hemisphere of data collected of frames each covering 0.3 degrees in omega. Of the 8380 reflections measured, all of which were corrected for Lorentz and polarisation effects and for absorption by semi-empirical methods based on symmetry-equivalent and repeated reflections (minimum and maximum transmission coefficients 0.9203 and 0.9581), 3396 independent reflections exceeded the significance level $|F|/\sigma(|F|) > 4.0$ The structure was solved by direct methods and refined by full matrix least squares methods on F^2. Hydrogen atoms were placed geometrically and refined with a riding model (including torsional freedom for methyl groups) and with U_{iso} constrained to be 1.2 (1.5 for methyl groups) times U_{eq} of the carrier atom. Refinement converged at a final $R = 0.0707$ ($wR_2 = 0.2082$ for all 5759 unique data, 334 parameters, mean and maximum δ/σ 0.000, 0.000), with allowance for the thermal anisotropy of all non-hydrogen atoms. Minimum and maximum final electron density −0.356 and 0.977 e A^{-3}. A weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.1409P)^2 + 0.0000P]$ where $P = (F_o^2 + 2F_c^2)/3$ was used in the latter stages of refinement. Complex scattering factors were taken from the program package SHELXL97[11] as implemented on the Viglen Pentium computer.†

Acknowledgements

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Notes and references

† Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/281.

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