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A caveat on the oxidation of 2,8-diphenyl-1,9,10-anthyridine to 2,8-diphenyl-5(10*H*)-1,9,10-anthyridone

N. N. Laxmi Madhavi, Paramasivam Senthivel and Ashwini Nangia*

School of Chemistry, University of Hyderabad, Hyderabad 500 046, India

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ABSTRACT: Crystallization of 2,8-diphenyl-1,9,10-anthyridine (**1a**) from various organic solvents afforded the corresponding anthyridone (**2a**). The conversion of anthyridine to anthyridone was monitored by ^{1}H NMR spectroscopy in deuterated solvents. It is found that the transformation is facile at ambient temperature and this could be relevant in triply hydrogen-bonded complexes of **1a** with neutral and cationic molecules. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: anthyridine; anthyridone; oxidation; ^{1}H NMR; supramolecular

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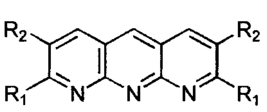
INTRODUCTION

Heterocycles with multiple hydrogen bonding groups have attracted attention recently because of their utility in the non-covalent self-assembly of supramolecular structures and in host–guest chemistry.[1] The arrays of complementary donor and acceptor hydrogen bonding sites in these molecules are useful building blocks for aggregation into well defined architectures.[2,3] Zimmerman and co-workers[4] have shown that 2,8-diphenyl-1,9,10-anthyridine (**1a**) forms complexes with complementary neutral molecules mediated through the DDD:AAA (D = donor, NH group; A = acceptor, pyridine N-atom) triple-point hydrogen bond recognition motif whereas 2,8-diphenyl-5(10*H*)-1,9,10-anthyridone (**2a**) binds through the DAD:ADA motif. Anslyn and co-workers[5] have carried out non-aqueous titrations on the DDD:AAA complexes of **1a** with cationic host molecules and found that recognition is mediated through hydrogen-bonded complex formation and not solely by proton transfer. Anthyridine and other heterocycles have gained importance as covalently bonded scaffolds in molecular recognition and crystal engineering.[1–3]



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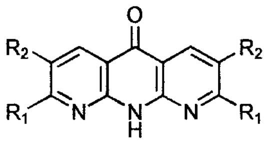

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a: R_1 = Ph, R_2 = H
b: R_1 = R_2 = Ph

We have recently examined the crystal structure of 2,3,7,8-tetraphenyl-1,9,10-anthyridine (**1b**), recrystallized from toluene and chlorobenzene.[6] The low-temperature structure of the PhMe and PhCl solvates of **1b** exhibit similarities in their packing features and their comparison shows that the moderately activated (Ph)C—H···π(Ph) interactions found in these structures (2.54 Å, $\theta = 151°$; 2.61 Å, $\theta = 143°$) have the characteristics of weak hydrogen bonds of the C—H···O [7] and C—H···N type. In continuation of this study, crystallization of **1a** from common organic solvents did not afford crystals of anthyridine but instead a new compound, anthyridone **2a**, was isolated. It was found that **1a** is partially or completely converted to **2a** during recrystallization over a period of 2–3 weeks at ambient temperature. While these experiments were in progress, we became aware that complexes of **1a** have been studied in acidic medium.[5b] In order to understand the factors that promote the **1a** → **2a** transformation, the reaction was monitored by ^{1}H NMR spectroscopy at 200 MHz in deuterated solvents ($CDCl_3$, CD_3OD and $CDCl_3$ filtered through basic alumina) at −10 and 25 °C. This study serves as a cautionary note about the instability of diphenylanthyridine and its derivatives.

EXPERIMENTAL AND RESULTS

Materials

2,8-Diphenyl-1,9,10-anthyridine (**1a**) was synthesized

**Correspondence to:* A. Nangia, School of Chemistry, University of Hyderabad, Hyderabad 500 046, India.
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Table 1. NMR spectra recorded for the reaction **1a** → **2a** in deuterated solvents

Solvent	Temperature (°C)	Time period (days)							
$CDCl_3$[a]	−10	1	3	5	8	15	22	40	100
$CDCl_3$[a]	25	6	21						
$CDCl_3$[b]	−10	4	7	25					
CD_3OD[c]	−10	2	4	7	14	21	39	100	

[a] $CDCl_3$ purchased from Aldrich and used as received.
[b] $CDCl_3$ filtered through basic alumina to remove HCl.
[c] CD_3OD purchased from Aldrich and used as received.

via the Friedländer condensation route of Caluwe and Majewicz[8] and characterized by its NMR spectrum. The compound failed to yield X-ray quality crystals from various organic solvents such as benzene, chlorobenzene, chloroform, dichloromethane, ethanol, nitromethane and toluene. Examination of the powders obtained after crystallization showed the compound to be largely or completely 2,8-diphenyl-5(10*H*)-1,9,10-anthyridone (**2a**), based on its IR and NMR spectra and comparison with an authentic sample.[8]

NMR spectroscopy

The NMR experiments were carried out by dissolving anthyridine **1a** in a suitable deuterated solvent ($CDCl_3$, CD_3OD) as a 0.15 M solution and maintaining the tube at the desired temperature (−10 or 25 °C). ^1H NMR (200 MHz) spectra were recorded at regular intervals (Table 1) and the transformation of **1a** to **2a** was monitored by integration of the well separated aromatic signals (Table 2). Experiments were conducted under four different conditions of solvent and temperature: (i) $CDCl_3$ at −10 °C; (ii) $CDCl_3$ at 25 °C; (iii) 'neutral' $CDCl_3$ at −10 °C ($CDCl_3$ filtered through basic alumina to remove traces of HCl); and (iv) CD_3OD at −10 °C. The progress of the reaction in $CDCl_3$ was monitored at regular intervals by integration of signals for **2a** at δ 8.05–8.20 (m, 4 H) and 7.76 (d, 2 H) against the signals for **1a** at δ 8.43–8.58 (m, 4 H) and 8.04 (d, 2 H). The NMR spectra for conditions (i) and (iv) are available from the epoc website at http//www.wiley.com/epoc.

1a is stable for 1 day at −10 °C but new peaks begin to appear by the third day which are clearly visible by the fifth day and intensify by the eighth day. From then onwards, the anthyridone concentration builds up steadily and **2a** is the major component of the mixture by day 40. The conversion to **2a** is complete and clean by day 100, that is, a solution of **1a** in $CDCl_3$ is completely converted to **2a** in 3 months at sub-zero temperature. Since recrystallization and complexation experiments were also carried out at ambient temperature, the reaction was examined at 25 °C (condition (ii)). The transformation to **2a** was found to be over four times faster, showing 50% conversion in 6 days and complete transformation to **2a** in 21 days.

Traces of HCl were removed from $CDCl_3$ by filtration through basic alumina prior to use (neutral $CDCl_3$, condition (iii)).[9] The removal of acid from $CDCl_3$ was found to slow the reaction 2–3-fold based on comparison with the spectra for condition (i). Thus, the transformation of **1a** to **2a** may be suppressed at sub-zero temperature under neutral conditions. Although the data are qualitative and reaction kinetics were not measured, the results clearly show the progress of the reaction and the acceleration due to heat and acid.

Table 2. ^1H NMR chemical shifts (δ, 200 MHz) of **1a** and **2a** recorded in $CDCl_3$ and CD_3OD

δ (ppm)[a]	
1a	**2a**
8.78 (9.22) (s, 1 H, C5-H)	9.50[b] (9.32)[b] (br s, 1 H, N10-H)
8.58–8.43 (8.55–8.40) (m, 4 H, *o*-H of Ph ring)	8.79 (8.75) (d, J = 8 Hz, 2 H, C4- and C6-H)
8.40 (8.60) (d, J = 8 Hz, 2 H, C4- and C6-H)	8.20–8.05 (8.50–8.35) (m, 4 H, *o*-H of Ph ring)
8.04 (8.26) (d, J = 8 Hz, 2 H, C3- and C7-H)	7.76 (8.25) (d, J = 8 Hz, 2 H, C3- and C7-H)
7.65–7.50 (7.65–7.50) (m, 6 H, *m*/*p*-Ph H)	7.70–7.50 (7.65–7.45) (m, 6 H, *m*/*p*-Ph H)

[a] Values in parentheses are those recorded in CD_3OD.
[b] Small variation in δ value of NH proton.

The effect of a protic solvent was examined next in CD_3OD (condition (iv)). The study in this case, however, was complicated by the low solubility of **1a** in CD_3OD and because the NMR signals for the two compounds do not appear as well separated, non-overlapping signals. Moreover, the transformation in $CDCl_3$ was found to be clean whereas in CD_3OD new unidentified peaks appeared around δ 7.90. Despite the broadened signals, the baseline noise and the impurity signals, it can be inferred that the progress in CD_3OD is analogous to that recorded in $CDCl_3$.

The above experiments were performed with diphenylanthyridine **1a** and it should be mentioned that tetraphenylanthyridine **1b** behaves similarly, except that the transformation to **2b** is slower. The difference between the two rates is sufficiently significant that we were able to obtain single crystals of **1b** from toluene and chlorobenzene[6] in less than 2 weeks without appreciable decomposition to **2b** whereas such a procedure was not successful with **1a**. Even in the case of **1b**, solvents in which crystallization takes a longer time proved to be problematic. It is likely that the additional phenyl rings in **1b** slow the conversion to anthyridone **2b** compared with **1a** → **2a**. Further, it was noted that the NMR signals in **1b** and also in the *p*-tolyl derivative of **1a** do not show much variation in chemical shift values. The NMR traces displayed on the epoc website could therefore be used as a guide to monitor the transformation in related systems.

The mechanistic details of the above oxidation were not investigated, but a parallel may be drawn with the formation of 1-methyl-2-pyridone from 1-methylpyridinium salts by hydrolysis and oxidation.[10] This example, however, is a simple precedent and the mechanism of the reaction **1a** → **2a** will have to be confirmed independently.

CONCLUSION

This NMR study of the transformation of 2,8-diphenyl-1,9,10-anthyridine (**1a**) to 2,8-diphenyl-5(10*H*)-1,9,10-anthyridone (**2a**) shows that the reaction is facile at ambient temperature and atmospheric conditions. Based on these results, tetraphenylanthyridine (**1b**) is less susceptible to spontaneous oxidation than **1a**. Further, the reaction may be suppressed by exclusion of moisture and acid and by conducting the experiments at low temperature. These results should be of great interest to supramolecular chemists using 1,9,10-anthyridines for molecular recognition because the oxidation of anthyridine to anthyridone changes the AAA hydrogen bonding array to an ADA motif.

Additional material

NMR spectra of the conversion of **1a** to **2a** in $CDCl_3$ and CD_3OD (conditions (i) and (iv)) are available from the epoc website at http://www.wiley.com/epoc.

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