Journal of Fluorine Chemistry, 44 (1989) 121–131

Received: October 13, 1988; accepted: March 14, 1989

COPPER CHLORIDE - CYANOPYRIDINE COMPLEXES AS CATALYSTS FOR THE DECOMPOSITION OF FLUOROPHOSPHONATE ESTERS

ALAN R. KATRITZKY, RICK J. OFFERMAN

Department of Chemistry, University of Florida, Gainesville, FL 32611 (U.S.A.)

H. D. DURST, J. R. WARD, J. W. HOVANEC and J. M. ALBIZO

Chemical Division, Research Directorate U. S. Army Chemical Research,
Development and Engineering Center, Aberdeen Proving Ground, MD 21010-5423
(U.S.A.)

SUMMARY

We have synthesized a number of copper complexes of O-alkylpyridine-2-carboximidates from the reaction of 2-cyanopyridine, copper(II) chloride dihydrate and various alcohols. These compounds have been tested as catalysts for the decomposition of the fluorophosphonates. The catalytic results show rate accelerations which approach 500-1000-fold over background (no metal catalysis).

0022-1139/89/$3.50

INTRODUCTION

Organophosphorus compounds with a P-F bond are potent inhibitors of the enzyme acetylcholinesterase [1]. The O-alkyl methylphosphonofluoridates such as sarin (O-isopropyl) or soman (O-pinacolyl) are known as "nerve agents" and have been the subject of considerable research to find ways to detoxify equipment or material contaminated with such compounds. The P-F bond is rapidly hydrolyzed in strong base [2], hence, the use of caustic is a common decontaminant of choice. The caustic, however, corrodes or degrades the contaminated material, so one would desire a decontaminant that retains the rapid reactivity of caustic at pH 14 near neutral pH.

It is well known that transition metal ions catalyze the hydrolysis of phosphorus-fluorine compounds such as sarin or O,O'-diisopropylphosphorfluoridate (DPF) [3-8]. Martell and coworkers made the most definitive study and showed that the active form of the metal ion was an aquo complex [3,4]. As the pH was increased or if the concentration of metal ion in solution became too high, the metal ions, e.g. copper(II), precipitated. Addition of chelating ligands such as tetramethylethylenediamine suppressed the formation of the precipitate; however, excess chelate binds all available coordination sites on the metal ion and halts catalysis [5].

The mechanism by which metal ions catalyze the hydrolysis of the P-F bond is uncertain. The rate law for the catalyzed path is first-order in phosphorus substrate, hydroxide and the aquometal ion. Hence, it is uncertain whether the catalyst is the hydroxometal ion or a complex between the metal ion and the phosphorus substrate followed by hydroxide ion attack. This ambiguity is common in metal ion catalysis as Breslow recently noted [9]. A combination of the two, i.e., a push-pull mechanism is also possible.

If a push-pull mechanism is indeed the correct one, this raises the possibility that the ligand on the metal can affect the rate of catalysis. To this end we have synthesized a number of copper complexes of O-alkyl-2-carboximidates from the reaction of 2-cyanopyridine **5**, copper(II) chloride, and various alcohols and tested their ability to catalyze the hydrolysis of the phosphonofluoridate, soman **4**. We felt that copper complexes of type 6 might be useful as catalysts for phosphate ester hydrolysis so we have also examined the ability of **6** (where R is a variety of alcohols and $M^{+2} = Cu^{+2}$) to hydrolyze the phosphonate ester GD **4**.

Several examples of alkyl pyridine-2-carboximidate complexes **1** have been prepared [10] where methyl, ethyl and n-butyl alcohol were employed (when $M^{+2} = Cu^{+2}$). The analogous cobalt, nickel and iron complexes have also been prepared where $R = CH_3$ [11]. Barnard and Watanabe and coworkers have prepared complexes such as **2** and **3** from the copper(II), methanol complex of **1** [10-14].

RESULTS AND DISCUSSION

Synthesis of Copper (II) Complexes of O-Alkylpyridine-2-carboximidates

Table 1 illustrates the copper complexes synthesized. These compounds are easily prepared by the route shown in Scheme 1. In general the alcohol is employed as the solvent and solutions of $CuCl_2 \cdot 2H_2O$ and 2-cyanopyridine **5** are mixed and stirred at room temperature. The highly-colored product **6** precipitates from solution, is filtered, washed with ether and dried. Compounds derived from volatile alcohols could be recrystallized from the alcohol while those derived from non-volatile alcohols were washed with ether. In one instance a copper complex of type **2** was prepared in 78% yield from **6a** and benzylamine by the method of Suzuki and coworkers [11].

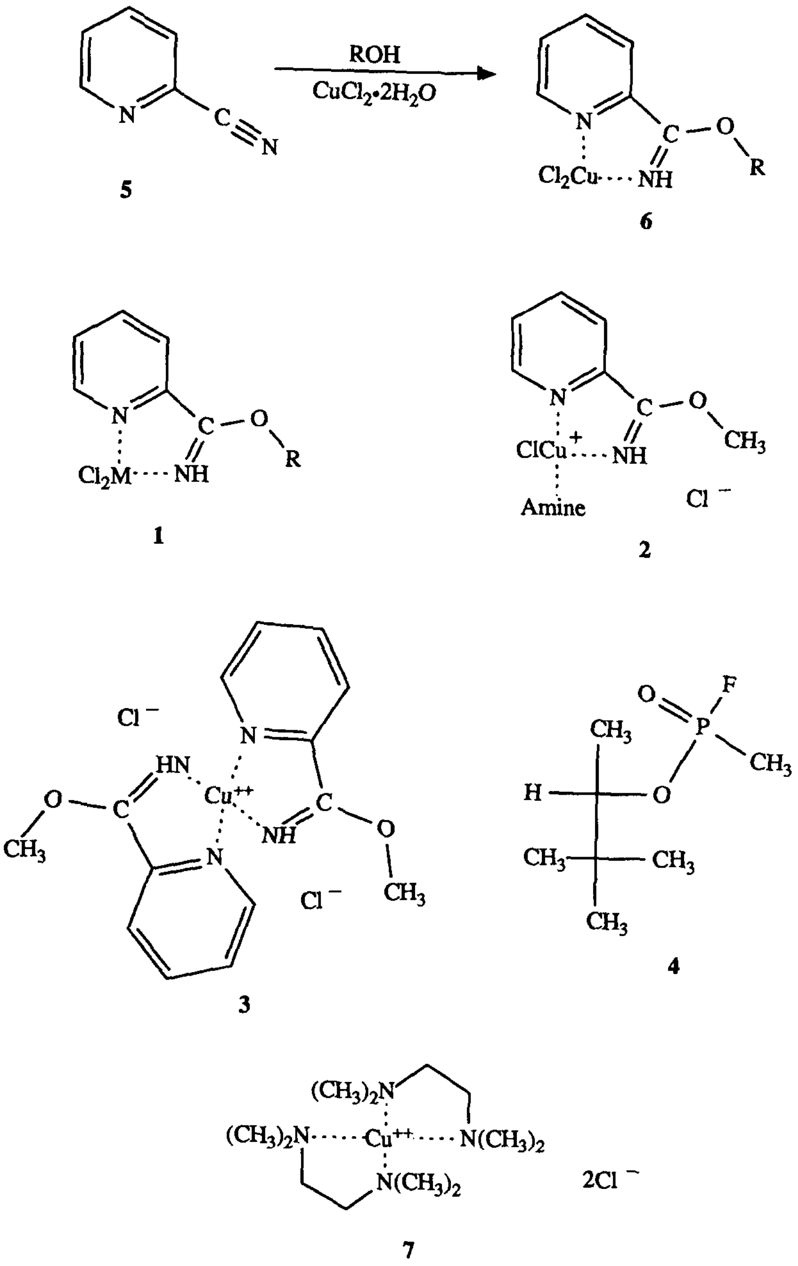
Characterization of these compounds is carried out by C, H, N analysis and melting point. Attempts at obtaining ^1H and ^{13}C NMR were unsuccessful, resulting only in broad peaks in the specta, presumably because of the paramagnetism of Cu^{+2}.

TABLE 1

Preparation of Metal Complexes of O-Alkylpyridine-2-carboximidates 2 and 6.

Cmpd.	R	Cryst. Form.	Yield (%)	m.p. °C	Analysis						
					Required			Molecular Formula	Found		
					C	H	N		C	H	N
6a	CH_3	Blue Powder	92	230 (d)	31.07	2.98	10.36	$C_7H_8N_2OCuCl_2$	30.78	2.64	10.06
6b	CH_2CH_2OH	Blue Powder	79	207-208	31.96	3.35	9.32	$C_8H_{10}N_2O_2CuCl_2$	31.60	2.97	9.03
6c[a]	CH_2CH_2OH	Blue Powder	48	207-208	31.96	3.35	9.32	$C_8H_{10}N_2O_2CuCl_2$	31.73	2.86	9.05
6d	$(CH_2)_3OH$	Blue Powder	85	202-203	34.36	3.84	8.90	$C_9H_{12}N_2O_2CuCl_2$	34.07	3.60	8.59
6e	$CH_2CH_2OCH_3$	Blue/green Pow.	94	183-185	32.49	4.24	8.42	$C_9H_{12}N_2O_2CuCl_2$[b]	32.96	3.81	8.32
6f	$CH_2CH_2OC_4H_9$	Blue Powder	40	173-174	40.40	5.09	7.85	$C_{12}H_{18}N_2O_2CuCl_2$	40.25	5.02	7.80
6g	$(CH_2CH_2O)_2C_2H_5$	Blue/green Pow.	38	131-132	36.89	5.16	7.17	$C_{12}H_{18}N_2O_3CuCl_2$[d]	37.26	4.77	7.48
6h	$(CH_2CH_2O)_2C_4H_9$	Blue/green Pow.	88	141-142	41.03	5.66	6.84	$C_{14}H_{22}N_2O_3CuCl_2$[b]	40.65	5.38	e
6i	$CH(CH_3)CO_2H$	Blue/green Pow.	48	240 (d)	32.89	3.07	8.52	$C_9H_{10}N_2O_3CuCl_2$	33.28	2.73	e
6j	$C_{16}H_{33}$	Green Powder	87	62-64	49.39	8.29	5.23	$C_{22}H_{38}N_2OCuCl_2$[c]	50.14	7.99	5.39
2	f	Blue Plates	78	168-169	44.51	4.54	11.12	$C_{14}H_{17}N_3OCuCl_2$	44.30	4.55	11.05

[a] Ethylene glycol/water (50/50) used as solvent. [b] Calculated for 1/2 H_2O. [c] As trihydrate. [d] As monohydrate. [e] Carbon and hydrogen analysis obtained only. [f] Amine employed was benzyl amine.



Scheme 1. Synthesis of 2-Cyanopyridine-Copper Complexes

Kinetics of the Decomposition of Fluorophosphonates

In the decomposition of fluorophosphonates by metal (e.g., Cu^{+2}) ions two basic strategies have been employed; i. reaction in bulk solvent and ii. reaction at a phase boundary (e.g. the Menger metallo-micelle [15]). As discussed in the introduction, the copper chloride-cyanopyridine complexes appeared attractive as a catalytic species for bulk hydrolysis. Thus if a system could be designed whereby a water soluble hydrotrope catalyst could be employed in the bulk phase at neutral pH (without necessitating the use of a high-surfactant additive) then the fluorophosphonate hydrolysis would be greatly simplified. To this end we have synthesized compounds which were designed to show increased water solubility (i.e., **6b-i**). The testing method employed a catalyzed decomposition of soman (**4**) using various concentrations of **6a-i**, following the kinetics of decomposition by fluoride release using an ion selective electrode.

One particularly interesting compound for study in this series was the copper chloride-cyanopyridine complex derived from ethylene glycol, **6b**. This species forms readily by mixing ethylene glycol, 2-cyanopyridine and $CuCl_2$ and crystallized analytically pure (after washing with ether) from the reactive solution in a short time (less than 5 min). Equally pure **6c** can also be prepared from a mixture of ethylene glycol and water (50:50) just as quickly. Thus this species was potentially useful as a component of a low temperature hydrolysis medium where ethylene glycol/water mixtures may be required to prevent freezing.

An additional derivative, the copper chloride-cyanopyridine complex **6j**, was synthesized as a potentially useful self-aggregating interface catalyst. When tested against soman the material decomposed upon dissolution. Thus the material was not further tested because of this solution instability.

Table 2 reports the pseudo-first order rate constants, measured as fluoride release, from the catalyzed hydrolysis of **4** in this study. In addition the 2:1 complex between tetramethylenediamine (TMEDA) and copper, **7**, is included for comparison. We found that **2**, **6a**, **6b**, **6d** and **6g** were all quite similar in their aqueous hydrolysis rate at comparable concentrations, with **6d** (the best) being about twice as effective as **6a** (the poorest). This data shows that these complexes were about a factor of 10 less effective in their catalytic activity than the TMEDA/Cu species **7**.

EXPERIMENTAL

Melting points were determined with a hot-stage microscope and are uncorrected. 2-Cyanopyridine, copper(II) chloride and all of the alcohols were purchased from Aldrich Chemical Co. and were used without further purification. Microanalyses were performed under the supervision of Dr. R. W. King (University of Florida).

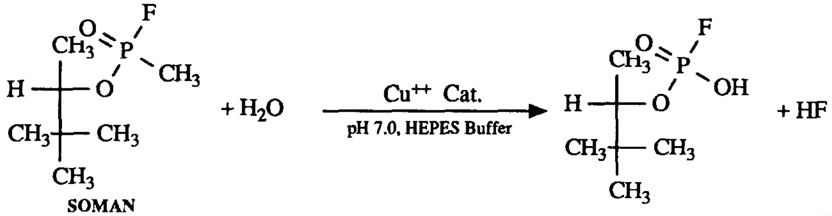
A brief experimental procedure for the preparation of the copper complexes is as follows: 2-cyanopyridine (1 eq.) in 10 mL of the alcohol was added to a solution of $CuCl_2 \cdot 2H_2O$ (1 eq.) in 20 mL of the alcohol. The mixture was allowed to stir until precipitation appeared to be complete. The crystals were filtered, washed with ether and dried *in vacuo* to yield the product.

Equipment: an Orion Model 96-09 combination fluoride electrode was fitted to a Fisher model 825 MP pH meter. The meter has an ASCII output *via* an RS232C port. This was connected to the serial port of an Apple Macintosh Plus computer using the standard Macintosh-to-Hayes modem cable. Reactions were carried out in a 5.00 mL jacketed glass vessel (Pierce cat # 20013) fitted with a magnetic stirrer.

Software: Data acquisition was accomplished using a program called 'CONC vs TIME' which was written by the authors in Microsoft BASIC*. First-order kinetics calculations were performed by the KORE method of Swain [16] using a translation of

TABLE 2

Pseudo-First-Order Rate Constants for Soman Hydrolysis in Aqueous Buffer at 25 °C, pH 7.0



SOMAN

Compound	Concentration 10^3 [M]	$k_{obs.}$ min^{-1}
2	5.89	0.1370
2	4.71	0.1239
2	3.54	0.1042
2	2.36	0.0849
2	1.18	00563
6a	5.76	0.1198
6a	4.61	0.1042
6a	3.46	0.0905
6a	2.30	0.0759
6a	1.80	0.0503
6b	6.06	0.1123
6b	4.85	0.1124
6b	3.63	0.0986
6b	2.42	0.0814
6d	7.30	0.1819
6d	5.84	0.1891
6d	4.38	0.1594
6d	2.92	0.1146
6d	1.46	0.0732
6e	----[a]	--------
6f	----[a]	--------
6g	5.61	0.1060
6g	4.49	0.1168
6g	3.37	0.1104
6g	2.24	0.0664
6g	1.12	0.0524
6h	----[a]	--------
6i	----[b]	--------
6j	----[b]	--------
7	6.00	2.266
7	2.40	1.435
7	1.20	0.799

[a] Decomposed on dissolution in buffer.

[b] Not sufficiently soluble in buffer.

the original FORTRAN program into Microsoft BASIC for the Macintosh. "KORE",* in turn, produces direct output on the Apple Imagewriter printer with options to store the output report on disc and to create a file which can be used to produce a graph of the data. Graphs were produced by Cricket Graph^{TM}, a commercial graphing program for the Macintosh. The output report on disk can be read, edited and printed using any of the word processing programs available for the Macintosh.

The methodology used to obtain sample data was that of Hovanec, *et al.* [17] and Durst, *et al.* [15,18]. Procedure: All sample runs were done at 25.0 °C. The fluoride electrode was standardized using 0.001 M and 0.0001M sodium fluoride in the buffer of choice. Standardization was performed in accordance with the instructions provide by the manufacturers of the electrode and meter. The reaction vessel was then charged with 5.00 mL of the reaction medium and the stirrer started. The fluoride electrode was inserted with care to avoid the entrapment of air bubbles on the sensing surface. The meter reading was allowed to stabilize. The program "CONC vs TIME" was then started and the header information typed in. The reaction was initiated by adding 50 µL of 0.1 M soman in isopropanol. Simultaneously, the "PRINT" button on the pH meter was pressed. As quickly as practical, the "PRINT INTERVAL" button on the meter was pressed and the time interval, in seconds, was entered. Thereafter, the information transfer to the computer occurs automatically at that interval. The values are listed on the computer screen as they are logged. At any time during the run, a different print interval may be entered by first pressing "PRINT" on the meter and then typing "command-." on the computer keyboard.

REFERENCES

1 B. C. Saunders, 'Phosphorous and Fluorine. The Chemistry and Toxic Action of Their Organic Compounds.' Cambridge University Press, New York/London, 1957.

---

*Available from authors

2 J. R. Ward, Y. Yang, R. B. Wilson, W. D. Burrows and L. L. Ackerman. Bioinorg. Chem. 16 (1988) 12.

3 R. L. Gustafson and A. E. Martell. J. Am. Chem. Soc. 84 (1962) 2309.

4 R. L. Gustafson, S. Chabarek, Jr., and A. E. Martell. J. Am. Chem. Soc. 85 (1963) 598.

5 R. L. Gustafson and A. E. Martell. J. Am. Chem. Soc. 81 (1959) 525.

6 T. Wagner-Juragg, B. E. Hackley, Jr., T. A. Lies, O. O. Owens, and R. Proper. J. Am. Chem. Soc. 77 (1955) 922.

7 J. Epstein and D. H. Rosenblatt. J. Am. Chem. Soc. 80 (1958) 3596.

8 R. C. Courtney, R. L. Gustafson, S. J. Westerback, H. Hyytiainen, S. C. Chaberek, Jr., and A. E. Martell. J. Am. Chem. Soc. 79 (1957) 3030.

9 S. H. Gellman, R. Petter and R. Breslow. J. Am. Chem. Soc. 108 (1986) 2388 and references therein.

10 P. F. B. Barnard. J. Chem. Soc. (A) (1969) 2140.

11 S. Suzuki, M. Nakahara and K. Watanabe. Bull. Chem. Soc. Jpn. 44 (1971) 1441.

12 S. Suzuki, M. Nakahara and K. Watanabe. Bull. Chem. Soc. Jpn. 47 (1974) 645.

13 K. Watanabe and K. Kidokoro. Chem. Lett. (1975) 67.

14 K. Sakai, T. Ito and K. Watanabe. Bull. Chem. Soc. Jpn. 40 (1967) 1660.

15 F. M. Menger, L. H. Gan, E. Johnson and H. D. Durst. J. Am. Chem. Soc. 109 (1987) 2800.

16 C. G. Swain, M. S. Swain and L. F. Berg. J. of Chemical Information and Computer Science 20 (1980) 47.

17 a) J. W. Hovanec, J. M. Albizo and J. R. Ward. 'Decontamination of Organophosphorous Esters by Hydrolysis Catalyzed by Transition-Metal Ions,' U. S. Army Chemical Research, Development and Engineering Center Technical Report, CRDEC-TR-88061, March 1988. b) J. W. Hovanec, H. D. Durst and G. L. Cooper. 'A Facile Method for the Acquisition, Reduction and Reporting of Kinetic Data from Ion-Specific Electrodes', U. S. Army Chemical Research, Development and Engineering Center Technical Report CRDEC-SP-890000, in press.

18 R. A. Moss, D. Bolikal, H. D. Durst and J. W. Hovanec. Tetrahedron Lett. 29 (1988) 2433.