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Complexes of Trivalent Phosphorus Derivatives. XVI. Metal Complexes of Some Aziridinophosphines Related to Anticancer Drugs[1]

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Metal complexes of tris(aziridino)phosphine (I) and bis(aziridino)morpholinophosphine (II) have been prepared. Reactions of metal hexacarbonyls with the ligands in boiling dioxane give the complexes $LM(CO)_5$ (L = ligand I, M = Cr and Mo; L = ligand II, M = Mo). Reactions of the ligands with the benzonitrile complexes $(C_6H_5CN)_2MCl_2$ (M = Pd, Pt) in acetone solution give the corresponding L_2MCl_2 complexes (L = ligand I, II; M = Pd, Pt). The platinum chloride complexes can be converted to the corresponding iodides by metathesis with sodium iodide. The molecular ions in the mass spectra of the complexes $(C_2H_4N)_3PM(CO)_5$ (M = Cr, Mo) exhibit competitive losses of neutral CO and·C_2H_4N fragments. Infrared and nmr data on the new complexes are also presented and discussed. None of the new metal complexes of tris(aziridino)phosphine (I) has exhibited any evidence of useful activity against L-1210 lymphoid leukemia in BDF_1 mice. However, there are preliminary indications of limited activity against this leukemia for the bis(aziridino)morpholinophosphine (II) complexes.

Introduction

Among the alkylating agents of interest in cancer chemotherapy[3] are phosphorus derivatives containing a four-coordinate phosphorus atom bearing at least two aziridino rings. Such compounds include tris(aziridino)phosphine oxide [$(C_2H_4N)_3PO$ (TEPA)], tris(aziridino)phosphine sulfide [$(C_2H_4N)_3PS$ (TSPA or thio-TEPA)], and bis(aziridino)morpholinophosphine sulfide [$(C_2H_4N)_2P(NC_4H_8O)S$ (OPSPA)]. Analogous in structure to such antitumor agents would be metal complexes of the ligands tris(aziridino)phosphine (I) and bis(aziridino)morpholinophosphine (II), since such

I   II
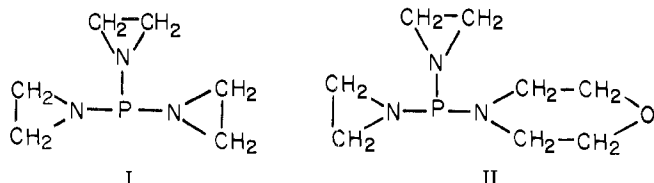
metal complexes would also contain a four-coordinate phosphorus atom bearing two or more aziridine rings and could be regarded as analogs of TEPA, thio-TEPA, or OPSPA with a metal atom in place of the oxygen or sulfur atom. Metal complexes of ligands I and II would also be closely related to reported metal complexes of tris(dimethylamino)phosphine.[1,4-6] This paper reports the reactions of the ligands I and II with various transition metal derivatives to give several new metal complexes of these ligands.

Experimental Section

Microanalyses (Tables I and II) were performed by the Pascher Mikroanalytisches Laboratorium, Bonn, Germany, and by the microanalytical laboratory of the University of Georgia under the supervision of Mr. W. Swanson. Infrared spectra (Tables III and IV) were taken in the indicated media and recorded on a Perkin-Elmer Model 621 spectrometer with grating optics. Nujol mulls between polyethylene plates were used for the far-infrared spectra in the

230-500-cm^{-1} region listed in Table IV. Proton nmr spectra (Tables I and II) were taken in $CDCl_3$ solutions and recorded at 60 MHz on a Perkin-Elmer Hitachi Model R-20 spectrometer. Melting and decomposition temperatures (Tables I and II) were taken in capillaries and are uncorrected. All operations involving organophosphorus derivatives were carried out under nitrogen, but the final complexes (Tables I and II) in the pure state can be handled in air for at least brief periods without decomposition.

The chemicals were obtained from the usual commercial sources. Reaction solvents (except for acetone and dichloromethane) were purified by distillation under nitrogen over sodium benzophenone ketyl.

Tris(aziridino)phosphine (I) was prepared from phosphorus trichloride, aziridine, and triethylamine according to the published procedure.[7] This ligand can be pyrophoric on exposure to air and appeared far more air sensitive than tris(dimethylamino)phosphine.

Preparation of Bis(aziridino)morpholinophosphine. A solution of 137 g (1 mol) of phosphorus trichloride and 105 g (1.1 mol) of triethylamine in 250 ml of dry benzene was cooled to −5° and then treated dropwise with a solution of 86 g (1 mol) of morpholine in 150 ml of dry benzene while stirring. After the addition of the morpholine was completed, the reaction mixture was stirred for 2 hr at room temperature. The precipitated triethylammonium chloride was then removed by filtration. Solvent was removed from the filtrate at ~35° (35 mm). Vacuum distillation of the residue gave a 40% yield of colorless liquid morpholinodichlorophosphine, bp 61-63° (1.25-1.5 mm). Proton nmr ($CDCl_3$): $\tau(OCH_2)$ 6.37 (multiplet), $\tau(NCH_2)$ 6.77 (multiplet).

A solution of 15.5 g (0.4 mol) of aziridine (ethylenimine) and 37.5 g (0.45 mol) of triethylamine in 150 ml of dry benzene was cooled to −5° and then treated dropwise with 33.8 g (0.2 mol) of the morpholinodichlorophosphine. After stirring of the mixture for an additional 2 hr at room temperature, the precipitated triethylammonium chloride was removed by filtration. Solvent was then removed from the filtrate at 35° (35 mm). Vacuum distillation of the residue gave 20.1 g (50% yield) of colorless hygroscopic airsensitive liquid bis(aziridino)morpholinophosphine (II), bp 103-113° (2-3 mm). Because of the sensitivity of this compound, completely satisfactory elemental analyses were not obtained. *Anal.* Calcd for $C_8H_{16}N_3OP$: C, 47.8; H, 8.0; N, 20.9; O, 8.0. Found: C, 46.3; H, 8.4; N, 20.6; O, 9.8.

Reactions of the Metal Hexacarbonyls with the Aziridinophosphines I and II. A mixture of 10 mmol of the metal hexacarbonyl, 11.3 mmol of the aziridinophosphine I or II, and 50 ml of dioxane was boiled under reflux with stirring until about 240 cm^3 of carbon monoxide had been evolved. The reactions with $Mo(CO)_6$ required only 30-60 min to reach this stage whereas the reaction with $Cr(CO)_6$ required about 24 hr. After the reaction was completed, the dioxane was removed under vacuum and the residue extracted with 40 ml of hexane. Filtration of the hexane extracts followed by concentration and cooling to −78° gave white crystals of the desired aziridinophosphinemetal pentacarbonyl, which were purified further by vacuum sublimation at 85-90° (0.1 mm) for the tris(aziridino)phosphine de-

(1) Part XV: R. B. King and T. F. Korenowski, *Inorg. Chem.*, 10, 1188 (1971).

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Table I. Metal Complexes of Tris(aziridino)phosphine

Compd	Color	Mp, °C	Yield, %	C Calcd	C Found	H Calcd	H Found	N Calcd	N Found	Other Calcd	Other Found	Proton nmr ^{a,b} τ	Aziridino NC_2H_4
$(C_2H_4N)_3PCr(CO)_5$	White	90–93	55	38.0	38.3	3.5	4.0	12.0	12.0	22.9 (O)	23.6 (O)	7.82 d (12)	7.98 d (13)
$(C_2H_4N)_3PMo(CO)_5$	White	108–110	49	33.6	33.5	3.1	3.0	10.7	10.8			7.85 d (12)	8.02 d (13)
$[(C_2H_4N)_3P]_2PdCl_2$	Yellow	143–144	71	29.4	29.5	4.9	5.1	17.1	17.0			7.57 (See text)	7.73 quintet
$[(C_2H_4N)_3P]_2PtCl_2$	Yellowish	170 dec	75	24.8	25.0	4.2	4.2	14.5	14.4	12.2 (Cl)	12.4 (Cl)	7.62 d (14)	7.70 septet
$[(C_2H_4N)_3P]_2PtI_2$	Yellow	139 dec	58	18.9	19.0	3.2	3.2	11.0	10.9	33.3 (I)	33.1 (I)	7.61 d (14)	7.67 quintet

^{a} d = doublet; coupling constants in hertz given in parentheses. ^{b} Proton nmr of the free ligand $(C_2H_4N)_3P$: τ 8.21 doublet (J = 9 Hz.).

Table II. Metal Complexes of Morpholinobis(aziridino)phosphine

Compd	Color	Mp. °C	Yield, %	C Calcd	C Found	H Calcd	H Found	N Calcd	N Found	Other Calcd	Other Found	Morpholino OCH_2	Morpholino NCH_2
$(C_2H_4N)_2P(NC_4H_8O)Mo(CO)_5$	White	102–103	28	35.7	36.2	3.7	4.1	9.6	9.4	22.0 (O)	22.5 (O)	6.42 t (4)	6.68 t (4)
$[(C_2H_4N)_2P(NC_4H_8O)]_2PdCl_2$	Pale yellow	145 dec	73	33.1	33.2	5.6	5.7	14.5	14.4	12.2 (Cl)	12.1 (Cl)	6.42	6.57
$[(C_2H_4N)_2P(NC_4H_8O)]_2PtCl_2$	Yellowish	186 dec	65	28.7	28.8	4.8	4.8	12.6	12.5	10.6 (Cl)	10.8 (Cl)	6.42	6.63
$[(C_2H_4N)_2P(NC_4H_8O)]_2PtI_2$	Yellow-orange	206 dec	46	22.6	22.5	3.8	3.8	9.9	9.7	29.8 (I)	29.9 (I)	6.39	6.66

^{a} d = doublet; t = triplet; coupling constants in hertz given in parentheses. ^{b} Proton nmr of the free ligand $(C_2H_4N)_2PNC_4H_8O$: morpholino, τ 6.43 t (5), τ 6.82 quartet (5); aziridino, τ 8.24 d (10).

rivatives and at 135° (0.1 mm) for the bis(aziridino)morpholinophosphine derivative.

A similar reaction of $W(CO)_6$ with tris(aziridino)phosphine in 1:1 dioxane–dibutyl ether gave bright yellow crystals indicated by elemental analyses to be aziridinepentacarbonyltungsten, C_2H_4NH-$W(CO)_5$, in 27% yield. *Anal.* Calcd for $C_7H_5NO_5W$: C, 22.9; H, 1.4; N, 3.8; O, 21.8. Found: C, 23.6; H, 1.4; N, 3.8; O, 23.0.

A similar reaction of $Cr(CO)_6$ with bis(aziridino)morpholinophosphine in dioxane gave a mixture of crystals and a liquid; analyses of the crystals (Found: C, 48.1; H, 6.3; N, 13.8) were inconsistent with formulation as a simple bis(aziridino)morpholinophosphine-chromium carbonyl derivative.

Preparations of the Palladium and Platinum Chloride Complexes L_2MCl_2 (M = Pd, Pt) of Ligands I and II. A solution (M = Pd) or suspension (M = Pt) of 2.6 mmol of the bis(benzonitrile)metal dichloride $(C_6H_5CN)_2MCl_2$ (M = Pd, Pt) in 25–30 ml of absolute acetone was treated with 5.2–6.1 mmol of the aziridinophosphine. The reaction mixtures became yellow (M = Pd) or yellow-green (M = Pt) and a precipitate of the desired complex formed. Hexane was added to complete the precipitation of the product. The product was isolated by filtration and dried. The platinum derivatives were purified by dissolving in dichloromethane, filtering the dichloromethane solution, and reprecipitating with excess hexane.

Preparations of the Platinum Iodide Complexes L_2PtI_2 of Ligands I and II. A solution of the corresponding platinum chloride complex L_2PtCl_2 in dichloromethane (containing some acetone in the case of the bis(aziridino)morpholinophosphine derivative) was stirred with a large excess of sodium iodide at room temperature. The reaction mixture became more yellowish. Solvent was removed at ~25° (35 mm). The residue was extracted with benzene. Addition of hexane to the benzene extracts followed by slow cooling gave yellow to yellow-orange crystals of the L_2PtI_2 derivative.

A similar reaction of the palladium complex $[(C_2H_4N)_2P(NC_4-H_8O)]_2PdCl_2$ with excess sodium iodide in acetone solution gave an orange solid, dec pt ~ 135°. However, elemental analyses indicated the stoichiometry $[(C_2H_4N)_2P(NC_4H_8O)]_{1.5}PdI_2$. *Anal.* Calcd for $L_{1.5}PdI_2$: C, 21.8; H, 3.6; N, 9.5. Found: C, 22.2; H, 4.1; N, 8.5.

Reactions of Tris(aziridino)phosphine with Nickel(II) Chloride. Commercial $NiCl_2·6H_2O$ (5 mmol) was dehydrated with a 100% excess of 1,1-dimethoxypropane and then dried at 25° (0.1 mm). This dehydrated nickel(II) chloride was suspended in 50 ml of absolute acetone and treated at room temperature with 1.22 ml (1.78 g, 11.3 mmol) of tris(aziridino)phosphine dissolved in 10 ml of acetone. The reaction mixture became red-brown and a green precipitate formed. This precipitate was removed by filtration, washed with 22 ml of acetone in six portions, and dried. Analyses of this green solid indicated the stoichiometry $[(C_2H_4N)_3P]_2NiCl_2·2H_2O$. *Anal.* Calcd for $L_2NiCl_2·2H_2O$: C, 30.0; H, 5.8; N, 17.5. Found: C, 30.9; H, 6.5; N, 17.4.

A similar reaction of $(CH_3CN)_2NiCl_2$ with tris(aziridino)phosphine in acetone solution gave a green solid of approximate stoichiometry $(C_2H_4N)_3PNiCl_2·2H_2O$. *Anal.* Calcd for $LNiCl_2·2H_2O$: C, 22.3; H, 4.9; N, 13.0. Found: C, 22.5; H, 4.3; N, 12.8. The infrared spectrum of this product exhibited $\nu(CH)$ frequencies at 3119 (w), 3074 (w), 3030 (vw), and 2998 (w) cm^{-1} and a broad $\nu(OH)$ frequency at 3245 (m) cm^{-1}.

Reaction of Tris(aziridino)phosphine with Zinc Chloride. A suspension of 0.75 g (5.5 mmol) of anhydrous zinc chloride in 50 ml of dichloromethane was treated with 1.2 ml (1.8 g, 11 mmol) of tris(aziridino)phosphine. After stirring for several hours at room temperature, the dichloromethane solution was filtered and product precipitated from the filtrate by adding excess hexane. The crude product was purified by redissolving in dichloromethane and reprecipitating with excess hexane to give, after drying under vacuum, 1.81 g (68% yield) of a white solid of stoichiometry $[(C_2H_4N)_3P]_2$-$ZnCl_2·2H_2O$. *Anal.* Calcd for $L_2ZnCl_2·2H_2O$: C, 29.6; H, 5.8; N, 17.2. Found: C, 29.7; H, 5.5; N, 15.9. The proton nmr spectrum of this complex in $(CD_3)_2SO$ solution was of poor quality but exhibited a resonance at τ 7.18 assigned to the aziridine protons.

Reaction of Bis(aziridino)morpholinophosphine with Zinc Chloride. Reaction of anhydrous zinc chloride with bis(aziridino)morpholinophosphine in dichloromethane solution by a procedure completely analogous to that given above for the reaction of anhydrous zinc chloride with tris(aziridino)phosphine gave a 74% yield of a white solid of stoichiometry $(C_2H_4N)_2P(NC_4H_8O)ZnCl_2·2H_2O$. *Anal.* Calcd for $LZnCl_2·2H_2O$: C, 27.0; H, 5.1; N, 11.8; Cl, 19.9. Found: C, 27.3; H, 5.6; N, 11.5; Cl, 19.2.

Mass Spectra. The mass spectra listed below were taken on the University of Georgia Perkin-Elmer Hitachi RMU-6 mass spectrometer at 70 eV with a chamber temperature of 110° and a sample tempera-

Table III. Infrared Spectra of Metal Complexes of Aziridinophosphines

Compd	ν(CH),[a] cm^{-1} Aziridino ring ν_{asym}	ν_{sym}	Morpholino ring ν_{asym}	ν_{sym}	ν(CO),[b] cm^{-1} A$_1$	B$_1$	E	A$_1$
$(C_2H_4N)_3P$	3060 m	2985 s						
$(C_2H_4N)_3PCr(CO)_5$	3061 w	2987 w			2068 w	?	1946 s	1954 m
$(C_2H_4N)_3PMo(CO)_5$	3073 w	2995 m			2079 w	?	1950 s	1957 m
$[(C_2H_4N)_3P]_2PdCl_2$	3084 vw	2997 w						
	3070 vw	2985 w						
$[(C_2H_4N)_3P]_2PtCl_2$	3084 vw	2992 w						
	3066 vw	2986 w						
$[(C_2H_4N)_3P]_2PtI_2$	3065 vw	2974 w						
		2929 w						
$(C_2H_4N)_2P(NC_4H_8O)$	3047 w	2976 m	2956 w	2847 m				
$(C_2H_4N)_2P(NC_4H_8O)Mo(CO)_5$	3059 w	2977 m	2947 w	2889 w	2080 m	1990 w	1949 s	1961 m
			2910 w	2848 w				
$[(C_2H_4N)_2P(NC_4H_8O)]_2PdCl_2$	3051 vw	2979 w	2948 w	2894 vw, br				
			2922 vw, br	2846 w				
$[(C_2H_4N)_2P(NC_4H_8O)]_2PtCl_2$	3056 vw	2987 w	2951 w	2883 vw, br				
			2925 vw, br	2851 w				
$[(C_2H_4N)_2P(NC_4H_8O)]_2PtI_2$	3055 vw	2973 vw	2949 vw	2840 w				

[a] Fluorolube mulls. [b] Cyclohexane solutions.

Table IV. Far-Infrared Spectra (500–230 cm^{-1}) of Palladium and Platinum Halide Complexes of Aziridinophosphines

Compd	ν(M–Cl), cm^{-1}	Other bands, cm^{-1}
$[(C_2H_4N)_3P]_2PtCl_2$	298 m, 276 m	497 m, 481 m, 424 m, 396 w, 371 w, 305 m
$[(C_2H_4N)_3P]_2PtI_2$		491 m, 432 w, 382 vw, 320 w
$[(C_2H_4N)_2PNC_4H_8O]_2PdCl_2$	296 m, 274 m	487 s, 440 w, 426 w, 388 m, 348 w, 243 m
$[(C_2H_4N)_2PNC_4H_8O]_2PtCl_2$	292 m, 270 m	490 s, 451 w, 442 w, 429 w, 395 m, 347 m, 242 m
$[(C_2H_4N)_2PNC_4H_8O]_2PtI_2$		495 m, 471 s, 444 m, 379 w, 345 vw, 239 vw

ture of 110–120°. Relative intensities (based on the ions with ^{52}Cr and ^{98}Mo isotopes) are given in parentheses after the ion formula.

A. $(C_2H_4N)_3PCr(CO)_5$: $(C_2H_4N)_3PCr(CO)_5^+$ (35), $(C_2H_4N)_3$-$PCr(CO)_4^+$ (0.6), $(C_2H_4N)_2PCr(CO)_5^+$ (4.2), $(C_2H_4N)_3PCr(CO)_3^+$ (10), $(C_2H_4N)_2PCr(CO)_4^+$ (0.8), $(C_2H_4N)_3PCr(CO)_2^+$ (6.0), $(C_2H_4$-$N)_2PCr(CO)_3^+$ (4.4), $(C_2H_4N)_3PCrCO^+$ (88), $(C_2H_4N)_2PCr(CO)_2^+$ (6.9), $(C_2H_4N)_3PCr^+$ (96), $(C_2H_4N)_2PCrCO^+$ (4.2), $(C_2H_4N)_2PNCr^+$ and/or $C_2H_4NPCr(CO)_2^+$ (100), $(C_2H_4N)_2PCr^+$ (2.9), $C_2H_4NPN_2Cr^+$ and/or $C_2H_4NPCrCO^+$ (30), $C_2H_4NPNCr^+$ and/or $PCr(CO)_2^+$ (40), $(C_2H_4N)_2Cr^+$ and/or $Cr(CO)_3^+$ (25), $C_2H_4NPCrH^+$ (11), $C_2H_4NPCr^+$ (3.8), $C_2H_3NPCr^+$ (4.6), CrN_2P^+ and/or $PCrCO^+$ (11), $C_2H_4NCH_2Cr^+$ and/or $Cr(CO)_2^+$ (9.6), $(C_2H_4N)_3PCr^{2+}$ (6.2), $NPCrH^+$ (15), $NPCr^+$ (49), $C_2H_5NCr^+$ (10), $C_2H_4NCr^+$ (50), $CrNCH_3^+$ (15), $CrNCH_2^+$ and/or $CrCO^+$ (16), $CrNCH^+$ (28), CrN^+ (10), Cr^+ (~40), and C_2-H_4N^+ (9.6). Metastable ions at m/e 184.3 (s) [$(C_2H_4N)_3PCrCO^+ \rightarrow (C_2H_4N)_3PCr^+ + CO$], m/e 157 (vs) [$(C_2H_4N)_3PCr^+ \rightarrow (C_2H_4N)_2PN$-$Cr^+ + C_2H_4$], and m/e 129.3 (vs) [$(C_2H_4N)_2PNCr^+ \rightarrow C_2H_4NPN_2$-$Cr^+ + C_2H_4$].

B. $(C_2H_4N)_3PMo(CO)_5$: $(C_2H_4N)_3PMo(CO)_5^+$ (25), $(C_2H_4$-$N)_3PMo(CO)_4^+$ (2.1), $(C_2H_4N)_2PMo(CO)_5^+$ (3.8), $(C_2H_4N)_3PMo$-$(CO)_3^+$ (60), $(C_2H_4N)_2PMo(CO)_4^+$ (2.1), $(C_2H_4N)_3PMo(CO)_2^+$ (3.0), $(C_2H_4N)_2PMo(CO)_3^+$ (6.6), $(C_2H_4N)_3PMoCO^+$ (1.7), $(C_2H_4N)_2P$-$Mo(CO)_2^+$ (0.4), $(C_2H_4N)_3PMo^+$ (21), $(C_2H_4N)_2PMoCO^+$ (6.2), $(C_2$-$H_4N)_2PNMo^+$ and/or $C_2H_4NPMo(CO)_2^+$ (100), $(C_2H_4N)_2PMo^+$ (14), $C_2H_4NPN_2Mo^+$ and/or $C_2H_4NPMoCO^+$ (62), $C_2H_4NPNMo^+$ and/or $PMo(CO)_2^+$ (21), $C_2H_4NPMoH^+$ (21), MoN_2P^+ and/or $PMoCO^+$ (43), $MoPN^+$ (21), $MoNCH_3^+$ (11), MoN^+ (19), Mo^+ (9.4), $(C_2H_4N)_2P^+$ (21), $C_2H_5NP^+$ (3.6), $C_2H_4NP^+$ (3.8), $C_2H_3NP^+$ (5.1), and $C_2H_4N^+$ (36).

Discussion

Tris(dimethylamino)phosphine is now well-known[4–6] to bond to transition metals through its phosphorus atom rather than one of its three nitrogen atoms. The available spectroscopic data on the well-characterized complexes of both tris(aziridino)phosphine (I) and bis(aziridino)morpholinophosphine (II) also support coordination of the phosphorus atoms rather than the nitrogen atoms of these ligands. The infrared ν(CO) frequencies of the metal pentacarbonyl complexes of I and II (Table III) are close to those[1] reported for analogous metal pentacarbonyl complexes of tris(dimethylamino)phosphine rather than at the lower values to be expected[8] if a nitrogen atom of the aziridinophosphines

I and II were bonded to the metal atom. The proton nmr spectra of all of the well-characterized complexes of tris-(aziridino)phosphine (Table I) except for the palladium complex $[(C_2H_4N)_3P]_2PdCl_2$ (see below) exhibited single doublets consistent with equivalence of all of the aziridine protons and splitting of the resonance by the single phosphorus atom. Such equivalence of the aziridine rings in tris(aziridino)phosphine metal complexes requires the phosphorus atom rather than one of the nitrogen atoms to be coordinated to the metal atom.

Reactions of metal halides with aminophosphines containing phosphorus–nitrogen bonds to give aminophosphine metal halide complexes have as potential complications the cleavage of the phosphorus–nitrogen bond by the metal halide possibly to give metal complexes of the amino fragment. This is presumably why ligands like tris(dimethylamino)phosphine, unlike trialkyl- and triarylphosphines, form relatively few complexes with simple metal halides despite their extensive metal carbonyl chemistry. In order to minimize the risk of cleavage of the phosphorus–nitrogen bond in the preparations of palladium and platinum chloride complexes of the aziridinophosphines I and II, the reactions of the free ligands with the benzonitrile complexes $(C_6H_5$-$CN)_2MCl_2$ (M = Pd, Pt) in an inert solvent were used to prepare the complexes of type L_2MCl_2 (L = ligand I, II; M = Pd, Pt). That cleavage of the phosphorus–nitrogen bond can be a difficulty in the preparation of metal complexes of aziridinophosphines is shown by the isolation of a 27% yield of yellow crystals analyzing for aziridine(pentacarbonyl)tungsten, $C_2H_4NHW(CO)_5$, from the reaction of tris-(aziridino)phosphine with hexacarbonyltungsten in a boiling 1:1 mixture of dioxane and di-n-butyl ether.

For evaluation as antitumor agents we wanted simple metal chloride complexes of some of the first-row transition metals with the aziridinophosphines I and II. Products were

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isolated from reactions of the aziridinophosphines I and II with nickel and zinc chloride derivatives; despite our efforts to maintain anhydrous conditions these products contained some water possibly because the starting metal chlorides were not completely anhydrous. The stoichiometries of these products were simple but some were peculiar by having too little ligand for reasonable coordination numbers if only the phosphorus atoms of the aziridinophosphines are complexed with the nickel or zinc atoms. We feel that these complexes involving first-row transition metals in "normal" +2 oxidation states with π-bonding ligands may represent examples of coordination through nitrogen (or possibly even oxygen in ligand II) of the aziridinophosphines I and II.

The proton nmr spectra of the tris(aziridino)phosphine metal complexes except for the palladium(II) chloride derivatives exhibited the expected doublets (see above) from equivalent aziridine protons split by the phosphorus atom. The proton nmr spectrum of the palladium complex $[(C_2H_4N)_3P]_2PdCl_2$ exhibited a symmetrical five-line pattern containing an outer doublet (separation 14 Hz) and an inner triplet (separations 4.5 Hz) with identical midpoints of the doublet and triplet. This appears to arise through "virtual coupling"[9] with a phosphorus–phosphorus coupling constant in $[(C_2H_4N)_3P]_2PdCl_2$ intermediate between the small to negligible values required for a simple doublet (such as that found in the platinum compounds $[(C_2H_4N)_3P]_2PtX_2$ (X = Cl, I)) and the very large values required for a 1:2:1 triplet.

The identical nmr chemical shifts of all of the ligand protons in the proton nmr spectrum of each of the tris(aziridino)phosphine (I)–metal complexes requires that the following three processes occur at rates rapid relative to the nmr time scale: (1) inversion at the aziridine nitrogen atoms;[10,11] (2) rotation around the phosphorus–nitrogen bonds; (3) rotation around the metal–phosphorus bond. In the corresponding metal complexes of bis(aziridino)morpholinophosphine (II) even these three processes occurring at rapid rates are insufficient to make all of the aziridine protons equivalent. Two resonances of equal relative intensities are thus expected for the aziridino protons in the metal complexes of bis(aziridino)morpholinophosphine. These expected two resonances are clearly observed as two overlapping doublets in the proton nmr spectrum of the molybdenum carbonyl complex $(C_2H_4N)_2P(NC_4H_8O)Mo(CO)_5$ (Table II). The situation in the palladium and platinum complexes of the type L_2MX_2 is still more complex because of the presence of two ligands and the possibility for cis–trans isomers; we feel that the present data are insufficient for an unambiguous interpretation of the apparent quintets and septets observed for the aziridine protons in the palladium and platinum(II) halide complexes of bis(aziridino)morpholinophosphine(II).

Detailed assignments of the infrared spectra of aziridine (ethylenimine) have been made.[12] Similar infrared bands (for brevity not listed in detail) are found in the 800–1300-cm^{-1} region of the metal complexes of the aziridinophosphines prepared during this work providing additional evidence that the aziridine ring remains intact in these complexes.

Previous workers[13] have shown that in complexes of the type $XM(CO)_5$ (M = Mn and Re in the cited work) the nor-

mally infrared-inactive B_1 $\nu(CO)$ mode can gain appreciable infrared intensity if the X ligand is sufficiently asymmetrical. In the metal pentacarbonyl complexes of the symmetrical tris(aziridino)phosphine (I), $(C_2H_4N)_3PM(CO)_5$ (M = Cr, Mo), the infrared B_1 $\nu(CO)$ mode is too weak to be unequivocally observed whereas in the molybdenum pentacarbonyl complex of the less symmetrical bis(aziridino)morpholinophosphine (II), $(C_2H_4N)_2P(NC_4H_8O)Mo(CO)_5$, the infrared B_1 $\nu(CO)$ mode is clearly observable as a weak but sharp and well-defined band at 1990 (w) cm^{-1} (Table III).

The square-planar palladium and platinum complexes $[(C_2H_4N)_3P]_2MX_2$ and $[(C_2H_4N)_2PNC_4H_8O]_2MX_2$ (M = Pd, X = Cl; M = Pt, X = Cl, I) can exist as either cis or trans isomers. Comparisons of the far-infrared spectra of corresponding platinum chloride and iodide complexes (Table IV) reveal medium-intensity bands at 295 ± 3 and 272 ± 3 cm^{-1} which are present in the platinum chloride but not the platinum iodide derivatives. These bands are therefore assigned to the $\nu(Pt-Cl)$ frequencies. The presence of two infrared-active $\nu(Pt-Cl)$ frequencies in the derivatives $[(C_2H_4N)_3P]_2PtCl_2$ and $[(C_2H_4N)_2PNC_4H_8O]_2PtCl_2$ indicate them to be cis rather than trans isomers. A similar pair of far-infrared bands in the palladium complex $[(C_2H_4N)_2PNC_4H_8O]_2PdCl_2$ at 296 and 274 cm^{-1} can be tentatively assigned to the $\nu(Pd-Cl)$ frequencies suggesting that this palladium chloride complex is also the cis isomer.

The molecular ions in the mass spectra of metal carbonyl complexes of the ligands $[(CH_3)_2N]_3E$ (E = P, As)[14-16] exhibit competitive losses of carbonyl groups involving rupture of the metal–carbon bonds and losses of neutral dimethylamino fragments involving rupture of the phosphorus–nitrogen bonds. The ratio $[M - 44]/([M - 44] + [M - 28])$, where M is the molecular ion, has been used as a semiquantitative estimate of the relative strengths of the phosphorus–nitrogen bonds and metal–carbon bonds in $[(CH_3)_2N]_3E$ (E = P, As) complexes. The molecular ions in the mass spectra of the tris(aziridino)phosphine complexes $(C_2H_4M)_3PM(CO)_5$ (M = Cr, Mo) analogously undergo competitive losses of carbonyl groups and C_2H_4N (*i.e.*, 42 mass units) fragments. Combination of these two processes gives a long series of ions separated by 14 mass units. Unfortunately, some of the ion assignments are ambiguous because of the similarity in the nominal-mass values of different fragments (*i.e.*, $2C_2H_4N = 3CO$ and $C_2H_4 = CO$). The ratio $[M - 42]/([M - 42] + [M - 28])$ for the tris(aziridino)phosphine complexes corresponds to the ratio $[M - 44]/([M - 44] + [M - 28])$ for the tris(dimethylamino)phosphine and tris(dimethylamino)arsine complexes. The values for the ratio $[M - 42]/([M - 42] + [M - 28])$ for the tris(aziridino)phosphine complexes $(C_2H_4N)_3PM(CO)_5$ are 0.88 (M = Cr) and 0.64 (M = Mo) suggesting that the strengths of the phosphorus–nitrogen bonds relative to the metal–carbonyl bonds in the tris(aziridino)phosphinemetal carbonyl complexes are similar to the strengths of the arsenic–nitrogen bonds relative to the metal–carbonyl bonds in tris(dimethylamino)arsine complexes where the corresponding ratios for the complexes $[(CH_3)_2N]_3AsM(CO)_5$ are 1.00 (M = Cr) and 0.52 (M = Mo). The phosphorus–nitrogen bonds appear to be more readily broken in the tris(aziridino)phosphine complexes $(C_2H_4N)_3PM(CO)_5$ than in the corresponding tris(dimethylamino)phosphine complexes $[(CH_3)_2N]_3PM(CO)_5$.

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The metal complexes of the aziridinophosphines I and II described in this paper were prepared in order to evaluate their potential as alkylating agents in cancer chemotherapy. Alkylating properties for the selected aziridinophosphine complexes $(C_2H_4N)_3PM(CO)_5$ (M = Cr, Mo) and $[(C_2H_4N)_3P]_2PdCl_2$ were demonstrated by positive γ-(4-nitrobenzyl)-pyridine (NBP) tests.[17] The compounds described in this paper were screened for activity against L-1210 lymphoid leukemia in BDF$_1$ mice. The metal complexes of tris(aziridino)phosphine (Table I) were found to be ineffective. The metal carbonyl complexes $(C_2H_4N)_3PM(CO)_5$ (M = Cr, Mo) were ineffective at doses below 100–200 mg/kg. At larger doses (e.g., 400 mg/kg) these compounds were toxic such that the mean survival time was drastically reduced. The compounds $[(C_2H_4N)_3P]_2MX_2$ (M = Pd, X = Cl; M = Pt, X = Cl, I) exhibited similar behavior, but their toxic doses were somewhat lower (<100 mg/kg).

Preliminary antileukemia screening of the metal complexes of bis(aziridino)morpholinophosphine (II) has been more encouraging. The molybdenum carbonyl complex $(C_2H_4N)_2P$-$(NC_4H_8O)Mo(CO)_5$ was nontoxic even in doses of 400 mg/kg and lengthened the mean survival time by 9–48% at such doses. The metal(II) halide complexes $[(C_2H_4N)_2P$-$(NC_4H_8O)]_2MX_2$ (M = Pd, X = Cl; M = Pt, X = Cl, I) were somewhat more toxic (lethal doses below 100 mg/kg) but lengthened the mean survival time by up to 21% at doses appreciably below the lethal doses. These results, although

(17) J. Epstein, R. W. Rosenthal, and R. J. Ess, *Anal. Chem.*, **27**, 1435 (1955).

still too fragmentary to draw any definite conclusions, suggest that appropriate metal complexes of bis(aziridino)morpholinophosphine (II) could be of value in cancer chemotherapy. Considerably more work is needed in order to establish any relationships between structure and antileukemia activity in bis(aziridino)morpholinophosphine (II)–metal complexes.

Isocyanide–Metal Complexes. IV. Reactions of Allylbis(acetonitrile)chlorodicarbonylmolybdenum with Various Isocyanides[1,2]

R. B. KING* and MOHAN SINGH SARAN[3]

Alkyl isocyanides rapidly replace at room temperature the two acetonitrile ligands in $C_3H_5Mo(CO)_2(CH_3CN)_2Cl$ to form $C_3H_5Mo(CO)_2(RNC)_2Cl$ (R = methyl, ethyl, isopropyl, *tert*-butyl, neopentyl, cyclohexyl). The course of further reaction depends upon the specific alkyl isocyanide. Thus *tert*-butyl isocyanide forms successively $C_3H_5Mo(CO)(Me_3CNC)_3Cl$ and $[(Me_3CNC)_4MoCl]_2$ whereas methyl and ethyl isocyanides form ultimately cis-$(RNC)_4Mo(CO)_2$ (R = CH_3, C_2H_5). Proton nmr spectra on alkyl isocyanide complexes of the types cis-$(RNC)_4Mo(CO)_2$ and $C_3H_5Mo(CO)(RNC)_3Cl$ indicate that the chemical shifts of the protons on the β-carbon atom of the alkyl isocyanide ligand are much more sensitive to changes in the environment of the alkyl isocyanide ligand than the chemical shifts of the protons on either the α- or γ-carbon atoms.

Introduction

Recently we reported[4] a spectroscopic study of *tert*-butyl isocyanide derivatives of the octahedral metal carbonyls. For this work as many as possible of the octahedral metal carbonyl derivatives with various numbers of carbonyl groups replaced by *tert*-butyl isocyanide ligands were required. The octahedral *tert*-butyl isocyanide–metal

(1) Part III: R. B. King and M. S. Saran, *Inorg. Chem.*, **13**, 364 (1974).
(2) A portion of this work was presented at the 25th Southeastern Regional Meeting of the American Chemical Society, Charleston, S. C., Nov 1973; see Abstracts, No. 286.
(3) Postdoctoral research associate.
(4) R. B. King and M. S. Saran, *Inorg. Chem.*, **13**, 74 (1974).

carbonyl complexes obtained from *tert*-butyl isocyanide and the octahedral metal carbonyls, their acetonitrile complexes, and their olefin complexes were successfully used for this spectroscopic study.

The work of tom Dieck, Friedel, and Renk[5,6] suggested that reductive elimination of allyl chloride from the complex[7] $C_3H_5Mo(CO)_2(CH_3CN)_2Cl$ on treatment with *tert*-butyl isocyanide might provide an alternate route to some of the required octahedral metal carbonyl complexes. How-

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