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Derivatives of *cis*-$NPCl_2(NSOCl)_2$ and $(NPCl_2)_2$-NSOCl. Part XVI. The Preparation of some Aziridino (Ethylene-Imino) Derivatives of $(NPCl_2)_2NSOX$ (X = F, Az, Ph) with a Potential Anticancer Activity

J. C. VAN DE GRAMPEL*, A. A. VAN DER HUIZEN, A. P. JEKEL, D. WIEDIJK

Laboratorium voor Anorganische Chemie, Rijksuniversiteit Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands

J.-F. LABARRE and F. SOURNIES

Laboratoire Structure et Vie, Université Paul Sabatier, 205, Route de Narbonne, 31400 Toulouse, France

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Introduction

It is well-known that the replacement of chlorine atoms in $(NPCl_2)_3$ by secondary cyclic amines, like morpholine, piperidine and pyrolidine, predominantly procedes along a non-geminal pattern [1]. However, within this class of amines aziridine forms a remarkable exception, as here a geminal aminolysis is observed [1]. The aziridino derivatives formed are important from a physiological point of view as some of them possess a pronounced activity against animal tumors [2, 3].

For these reasons we started an investigation of the aziridino derivatives of the sulphur-containing six-membered ring systems $(NPCl_2)_2NSOX$ with X = F, Cl and Ph.

Experimental

All reactions were carried out in a dry nitrogen atmosphere. Aziridine was distilled from KOH prior to use. The ring compounds were prepared according to literature methods [4–6]. A solution of freshly distilled aziridine in dry diethylether was added dropwise to an ethereal solution of the ring compound $(NPCl_2)_2NSOX$ (X = F, Cl or Ph), cooled to −75 °C, under vigorous stirring. The reaction mixture was allowed to warm up slowly to room temperature and then stirred for an additional period of 17 hrs at that temperature. After filtration and extraction of the residue with diethylether, the filtrate and extracts were evaporated *in vacuo*. The crude reaction product was recrystallized from dry diethylether. Further experimental details:

*Author to whom correspondence should be addressed.

$(NPAz_2)_2NSOF$: molar ratio reactants 16:1; yield 62%, M.p. 111–112 °C.
Anal. C, 28.18 (28.32); H, 4.71 (4.75); N, 28.72 (28.90); S, 9.58 (9.45). $\delta^{31}P$ 35.7 ppm (85% H_3PO_4).

$(NPAz_2)_2NSOAz$ (I): molar ratio reactants 20:1; yield 57%, M.p. 86–87 °C.
Anal. C, 33.08 (33.15); H, 5.66 (5.56); N, 30.51 (30.93); S, 8.70 (8.85). $\delta^{31}P$ 35.4 ppm (85% H_3PO_4).

$(NPAz_2)_2NSOAz$ (II): under the same experimental conditions another isomer can be obtained, yield 42%, M.p. 104 °C.
Anal. C, 33.20 (33.15); H, 5.53 (5.56); N, 31.07 (30.93); S, 8.85 (8.85). $\delta^{31}P$ 35.4 ppm (85% H_3PO_4).

$(NPAz_2)_2NSOPh$: molar ratio reactants 16:1; yield 50%, M.p. 108–109 °C.
Anal. C, 42.61 (42.32); H, 5.39 (5.34); N, 24.64 (24.67); S, 8.17 (8.07). $\delta^{31}P$ 34.1 ppm (85% H_3PO_4).

Discussion

Although not studied in detail it can be assumed that the aziridinolysis of the cyclic compound $(NPCl_2)_2NSOX$ (X = F, Cl, Ph) follows a geminal pathway. This is underlined by a spectroscopic (mass, ^{31}P NMR) investigation during aziridinolysis of $(NPCl_2)_2NSOPh$ which confirmed the formation of $NPCl_2NPAz_2NSOPh$ (Az = aziridino) while $(NPClAz)_2$-NSOPh was absent [7]. The presence of an aziridino group in PClAm (Am = amino) results in a shift of the ^{31}P resonance signal to much lower field than observed for other cyclic amines (Table I). Introducing a second amine a shielding effect is observed, but the influence of morpholine (or piperidine) is twice as large as that of aziridine. Related to this difference in behaviour is the relatively low Mullikan charge (−0.852) on N in aziridine compared with that in dimethylamine (−0.780), as was found by a preliminary *ab initio* calculation [12]. Probably the small deactivation of the phosphorus centre combined with the small size of the aziridino group promotes S_N2 substitution at PClAz rather than at PCl_2.

It is noteworthy that $(NPAz_2)_2NSOAz$ can be obtained in two isomeric forms, which can be recrystallized from boiling diethylether solution without isomerization. The IR spectra of the two compounds show minor differences. As indicated in the DTA diagram (Fig. 1) isomer II (M.p. 104 °C) undergoes during melting a phase transition to isomer I, which is obviously the most stable form. A structure determination by X-rays shows that apart from space group symmetry the molecules in the two isomers differ by

TABLE I. ^{31}P NMR Data of some Amino-substituted Triazatriphosphorines and Thiatriazadiphosphorines; Chemical Shifts (in ppm *versus* 85% H_3PO_4) are Defined as Positive in Low Field Direction.

Compound	Chemical shift (solvent $CDCl_3$)			$\|J_{P-P}\|$ (Hz)	Ref.
	PCl_2	PClAm	PAm_2		
$(NPCl_2)_3$	19.9				[8]
$NPClAz(NPAz_2)_2$		42.6	37.2	29.4	[9]
$NPClMorph(NPMorph_2)_2$		29.5	19.0	41.6	[9]
$NPClPip(NPPip_2)_2$		30.4	19.6	40.7	[9]
$(NPCl_2)_2NSOCl$	26.3				[8]
$(NPAz_2)_2NSOAz$			35.4		This study
$(NPMorph_2)_2NSOMorph$			16.9		[8]
$(NPPip_2)_2NSOPip$			17.6		[10]
$(NPPyr_2)_2NSOPyr$			14.2		[8]
$(NPCl_2)_2NSOF$	26.1				[8]
$(NPAz_2)_2NSOF$			35.7		This study
$(NPMorph_2)_2NSOF$			16.9		[11]
$(NPPyr_2)_2NSOF$			14.3		[11]
$(NPCl_2)_2NSOPh$	20.7				[6]
$(NPAz_2)_2NSOPh$			34.1		This study

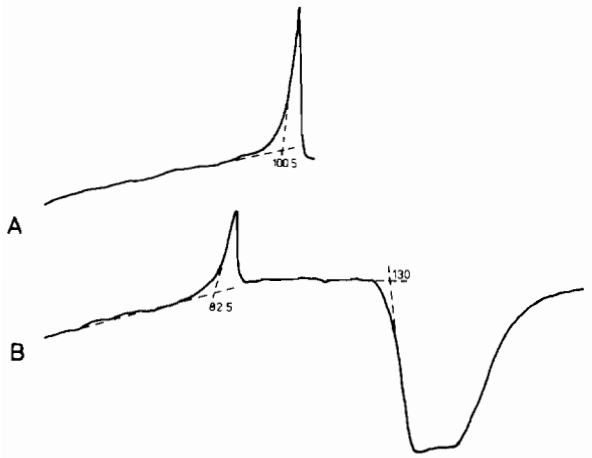

Fig. 1. A. DTA diagram of $(NPAz_2)_2NSOAz$ II (M.p. 104 °C) to 110 °C. B. DTA diagram of the same sample after cooling to room temperature. In both cases decomposition is observed at about 130 °C.

the position of the aziridino groups with respect to the PNS-ring [13].

The derivatives prepared possess a pronounced activity against P388 and P1210 leukemias and B16 sarcoma in mice. In this respect the compound $(NPAz_2)_2NSOAz$ is the most promising one because of its relatively low toxicity [14].

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