# Zinc(II) complexes of sulfinamides—I. N-Phenyl 2-propane sulfinamide, t-butyl N-phenyl and t-butyl N-cyclohexyl sulfinamoyl acetates

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Abstract—The zinc(II) complexes of the title sulfinamoyl compounds  $L_2 ZnX_2 (X = Cl, Br)$  were prepared and studied by NMR and ir methods All the complexes have a tetrahedral  $[O_2X_2]$  coordination and NH X hydrogen bonding

# **1** INTRODUCTION

The zinc(II) complexes are of interest for many reasons such as (i) the variety of coordinating geometries around the metal atom and (ii) their use as chemical models of the active site of zinc metalloproteins. In this second way, we now focus our attention on the possibility of determining the affinity of potential inhibitors for the catalytic site of alcohol dehydrogenases. These inhibitor enzyme interactions are roughly approximated to zinc halide complexation [1]

The ligands under investigation are three sulfinamides with or without a carboxylic ester group at the  $\beta$ position

> $\langle \odot \rangle$ - NHSOCH(CH<sub>3</sub>)<sub>2</sub> I  $\langle \odot \rangle$ - NHSOCH<sub>2</sub>COOtBu II  $\langle \odot \rangle$ - NHSOCH<sub>2</sub>COOtBu III

The compound II and other related compounds [2] in this series display inhibiting properties on cinnamoyl alcohol dehydrogenase, a zinc-containing metalloprotein involved in the lignification process

The complexing properties of this type of ligand are unknown to date This first study considers  $ZnBr_2$  and  $ZnCl_2$  complexes of the above-mentioned three compounds

The stoichiometry of the complexes will be established by  ${}^{1}HNMR$  spectroscopy and their geometrical structure, including the chelating atoms assignment, will be developed by the 1r techniques

# 2 EXPERIMENTAL

### 2.1 Synthesis of sulfinamides

Typical procedures and physical properties for II and III are described in Ref [3]

Isopropyl N-phenyl sulfinamoyl ester iPrMgCl Grignard reagent is obtained by adding excess of isopropyl chloride (80 mmol) to a stirred solution of 16g magnesium chips (66 mmol) in dry ether (40 cm<sup>3</sup>) The N-thionyl aniline PhNSO (4 g, 29 mmol) in dry ether (20 cm<sup>3</sup>) is then slowly added A rapid reaction occurs The mixture is then stirred for 5 min, hydrolysed with 5% aqueous ammonium chloride and extracted with ether This solvent is removed, and petroleum ether added A white solid ( $F = 85^{\circ}$ ) precipitates after 30 min in 91% yield Purification is achieved by washing with ether several times

<sup>1</sup>H NMR (ppm, CDCl<sub>3</sub>) 6 9–7 3 (m, 5H), 6 4 (s, 1H), 3 05 (sept, 1H), 1 4(d, 3H), 1 3(d, 3H)

#### 2.2 Preparation of zinc complexes

To a 0.05 M chloroform solution of the ligand was added  $ZnX_2$  in excess (two or three times the stoichiometric amount) After centrifuging  $ZnX_2$ , the solvent is removed by bubbling a flow of dry nitrogen. The gummy product was analysed without further purification. Its chloroform solution shows, by 1 r spectroscopy, no trace of water [4] or residual  $ZnX_2$ 

#### 23 Spectra

<sup>1</sup>H NMR spectra were performed in the FT on a Bruker WH-90 apparatus at 90 MHz for CDCl<sub>3</sub> solutions with Me<sub>4</sub>Si as internal reference Infrared spectra were recorded on Beckman IR 9 and Perkin-Elmer 683 spectrometers in KBr pellets for solids and in 005 M CHCl<sub>3</sub> solution by using NaCl 05 mm cells in the 4000–400 cm<sup>-1</sup> frequency range, or polyethylene cells in the 600–200 cm<sup>-1</sup> range

#### **3 RESULTS AND DISCUSSION**

# 3.1 Stoichiometry of the complexes

When increased quantities of pure ligand (L) are added to a chloroform solution of ligand + ZnX<sub>2</sub>  $(\rho = [Zn^{2+}]/[L] > 2)$  a chemical shift variation  $(\Delta \delta_i)$ is observed for the neighboring protons of the sulfinamoyl groups The plot  $\Delta \delta_i = f(\rho)$  for the different protons exhibits a breaking point defining two straight lines (see Fig 1 for the CH protons) The slope of the first one at low  $\rho$  values is the most important while for the second it is much weaker or even zero This point defines the stoichiometry of the complex

For all the complexes the observed stoichiometry Zn L is 1.2 Its analysis was confirmed by atomic absorption for the  $ZnBr_2$  complex



Fig 1 <sup>1</sup>H Chemical shift variation  $(\Delta \delta_{CH})$  in CDCl<sub>3</sub> as a function of  $\rho = [Zn^{2+}]/[L]$  for the sulfinamoul compounds

# 32 Infrared specta (Table 1)

The bands at highest wavenumbers  $(3350-3280 \text{ cm}^{-1})$  recorded for  $0.05 \text{ M CHCl}_3$  solutions are assigned to v (bonded NH) For acetanilide [5] these stretching vibrations were observed at 3324 and 3286 cm<sup>-1</sup>, while the *trans* and *cis* v (free NH) are, respectively, 3447 and 3400 cm<sup>-1</sup> On the other hand, in 0.005 M solutions, those bands do not disappear for the three compounds, which implies a strong association

In the solid state there is only one broad band v(NH) at 3100–3180 cm<sup>-1</sup> typical of polymeric associations

For the zinc complexes one v(NH) broad band is observed at low wavenumbers, the  $\Delta v(NH)$  values are 82 (ZnBr<sub>2</sub>) and 92 cm<sup>-1</sup> (ZnCl<sub>2</sub>) for I, 85 and 50 cm<sup>-1</sup> (ZnBr<sub>2</sub>) and 95 and 60 cm<sup>-1</sup> (ZnCl<sub>2</sub>) for II, 110 cm<sup>-1</sup> (ZnBr<sub>2</sub> and ZnCl<sub>2</sub>) for III Larger lowering values are reported for Zn(II)-amine complexes such as 143 and 115 cm<sup>-1</sup> for 4-aminobenzophenone [6]

The v(C=O) and v(C-O) frequencies of the ester molety are not perturbed by zinc complexation On the other hand, the very intense v(S=O) band is shifted down from 1065–1084 cm<sup>-1</sup> in CHCl<sub>3</sub> towards 1040–1060 cm<sup>-1</sup> ( $\Delta v = 5$ –30 cm<sup>-1</sup>) in the solid state and even more, i e 985–1005 cm<sup>-1</sup> ( $\Delta v = 78$ –84 cm<sup>-1</sup>) in 0.05 M CHCl<sub>3</sub> solution by zinc complexation

The v(S-N) vibration is assigned to the band at

859–900 cm<sup>-1</sup> following the literature values  $(800-920 \text{ cm}^{-1} \text{ for sulfonamides [7]}, 839 \text{ cm}^{-1} \text{ for } \text{MeSO}_2\text{NHMe}[8]$  and  $840 \text{ cm}^{-1} \text{ for } N$ -sulfonylammonium salts [9]) This band of medium intensity becomes weaker after zinc complexation but its frequency is increased up to  $40 \text{ cm}^{-1}$  for compound I

In the far 1r region a number of bands are encountered, among them the possible Zn-halide and Zn-O vibrations with ZnBr<sub>2</sub> 252 cm<sup>-1</sup> for I and III, 265 cm<sup>-1</sup> for II, with ZnCl<sub>2</sub> 295 and 337 cm<sup>-1</sup> for I, 290 and 340 cm<sup>-1</sup> for II and 285 and 335 cm<sup>-1</sup> for III

These assignments are made on the basis of some results from the literature (1) for the *pseudotetrahedral* ZnX<sub>2</sub> L complex of 2,2-dimethyl-1,3-diaminopropane [10] v(ZnBr as) was found at 226 cm<sup>-1</sup>, v(ZnBrs) at 213 cm<sup>-1</sup>, v(ZnCl as) at 276 cm<sup>-1</sup> and v(ZnCls) at 320 cm<sup>-1</sup>, (11) for the *tetrahedral* complexes ZnX<sub>2</sub> L<sub>2</sub> of  $\beta$ -picoline [11] v(ZnBr) = 244 cm<sup>-1</sup> and v(ZnCl) = 327 and 284 cm<sup>-1</sup> while (11) for the *hexacoordinated* ZnX<sub>2</sub> 2L complexes of 4,6-dimethylpyridine 2(1H) thione [12] v(ZnBr) is at 168 and 228 cm<sup>-1</sup> and v(ZnCl) at 252 and 271 cm<sup>-1</sup>

The ratio of v(ZnBr)/v(ZnCl) is 0.75–0.77 for compounds I, II and III in good agreement with 0.75 as for the  $\beta$ -picoline complexes and the value of 0.76 reported by CLARK [136] for a *tetrahedral* arrangement around the zinc atom

Some structural implications are drawn from the previous results

In the solid state all the sulfinamoyl compounds show polymeric associations related to their low v (NH) and v (S=O) frequencies As a matter of fact the v (S=O) frequency is lowered to the extent of 10–15 cm<sup>-1</sup> for solid cyclic sulfites [15] and the phenomenon occurs generally for the v (NH) of amino and amido compounds [16]

In the dilute chloroform solution the ligands can be self-associated in three ways



			_				=					
	<b>t</b>	Г	ZnBr <sub>2</sub> 2L	ZnCl <sub>2</sub> 2L	<b>*</b> 1	Ľ	ZnBr <sub>2</sub> 2L	ZnCl <sub>2</sub> 2L	<b>*</b>	L	ZnBr <sub>2</sub> 2L	ZnCl <sub>2</sub> 2L
								3425 br				
		3300 m				3315 br				3350 w		
(INH)			3218 br	3208 br		3280	3230 br	3220 br			3240 hr	3240 hr
•	3100 br				3143 vs				3180 m			
·(C=0)					1735 vs	1725 vs	1728 vs	1728 vs	1730 vs	1725 vs	1725 vs	1730 vs
(C = C)	1600s	1600 s	1600 m	1600 m	1600 s	1600 m	1600 m	1600 m				•
·(C-N)		1175 w	1145 br	1150 br	1155 vs	1162 vs	1157s	1155 s	1160s	1160 s	1155s	1155 s
,(C-O),					1130s	1130s	1130s	1130sh	1135s	1120 m	1123 m	1125 m
(S=O)	1040 vs	1070 vs	990 vs	992 vs	1060 vs	1084 vs	1005 vs	1000s	1060 vs	1065 vs	985 vs	987 vs
·(S-N)	865 m	860 m	900 m	900 m	885s	870 m	895 m	893 m	863 m	859 w	875 w	877 w
ngand		502 m	508 m	508 m		504 s	500s	502 s	545 w	550 w	550 w	550 w
und other		482 w	472 w	472 w		496 s						
ands		418 w				462 m	463 w	465 w	450 w	463 w	465 w	465 w
						432 w	431 w	432 w				
		330 w				388 w	390 w		390 w		360 w	360 w
(Zn Cl)				337 m				340 ш				335 m
(ZnO)			252 m	295 ш			265 m	290 w			252 m	285 m

-. Table 1 Principal  $\Gamma$  bands (cm<sup>-1</sup>) of ligands and their zi Zinc(II) complexes of sulfinamides-I

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---a cyclic (CCD) or acyclic (ACD) dimer with a cis conformation of the NH and S =O bonds explained by the lower v(NH) frequency (3280-3300 cm<sup>-1</sup>) The occurrence of an acyclic dimer was found for acetanilide[17]

—an acyclic dimer (ATD) with a trans NH/S=O conformation according to the higher v(NH) frequency (3315-3350 cm<sup>-1</sup>)

When the zinc complex is formed it is concluded that (i) the C=O and C-O stretching vibrations are not perturbed, (ii) there is a strong lowering of the v(NH) and v(S=O) frequencies, (iii) there is an important increase in v(S-N), (iv) the stoichiometry of the complex is 2L ZnX<sub>2</sub>, (v)  $v(ZnBr)/v(ZnCl) \sim 0.75$ is characteristic of a tetrahedral structure [13]

These results lead to the following tetracoordinated complex



Two H X bonds have been considered as a consequence of the great variation of frequency noticed for the three S=O, S-N and N-H vibrators This interpretation is supported by (i) the observation of similar hydrogen bonds for the N-methyl aniline complexed with the tetrabutyl ammonium bromide where the variation reaches  $170 \text{ cm}^{-1}$  [18] and (ii) occurrence of a charge transfer between the six atoms constituting the three bonds N-H, S=O and Zn-Br as indicated by the arrows (see scheme)

As a matter of fact, in this hypothesis, the force constant of S=O and NH bonds are decreased and that of the S-N bond is increased as observed



No significant modification appears in the spectra when substituting  $ZnBr_2$  by  $ZnCl_2$  for the three compounds so that the same structural feature is expected in both cases

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