Indium Chelate Complexes. II*. Synthesis and Characterization of Neutral Indium Chelates with Dithio Ligands

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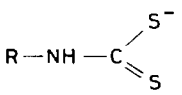
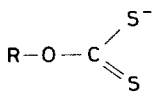
Neutral lipophilic indium chelates with the radioactive indium isotopes ^{111}In and ^{113m}In are used as blood cell labelling agents in diagnostic nuclear medicine [2–4]. The compounds used up to now, $^{111}In(oxine)_3$ and $^{111}In(tropolone)_3$, are not fully satisfactory due to considerable cell toxicity of the ligands. This situation has initiated studies on the complex formation of In^{3+} with other ligands which are expected to form neutral lipophilic indium complexes. Recently, we reported on the synthesis and characterization of dialkyldithiocarbamato chelates as well as some *in vitro* data of the compounds [1].

Here, a report is given which deals with the formation of indium(III) complexes with monoalkyldithiocarbamates (**I**), alkylxanthates (**II**), dialkyldithiophosphates (**III**) and diphenyldithiophosphinate (**IV**).



I



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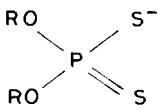
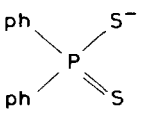


III



IV

Experimental

The ligands were prepared by standard literature methods and used as their sodium salts. $InCl_3$ was purchased from Merck.

$InCl_3$ (200 mg, 1 mmol) was dissolved in 5 ml 0.05 N HCl and under stirring an aqueous solution of the ligand (about 5 mmol in 50 ml) was added dropwise. The resulting mixture containing a colourless solid was stirred for 30 min and the product was extracted with methylene chloride. The extracts were dried over sodium sulphate and the solvent was removed *in vacuo* to yield a colourless powder.

Pure products can be obtained by recrystallization from methylene chloride/ethanol. Typical yields are in the range between 70 and 90%. Analytical data are reported in Table I.

Infrared spectra (in KBr) were recorded on a UR 20 spectrometer (Carl-Zeiss-Jena) and NMR spectra on a WX 90 DS (Bruker spectrospin). Chemical shifts are relative to TMS and H_3PO_4, respectively.

TABLE I. Melting Points and Analytical Data of InL_3 Chelates

Complex	Melting point (°C)	Elemental analysis (%)[a]			
		C	H	N	S
$In(benzHdtc)_3$	>163 dec.	43.6 (41.6)	3.7 (3.6)	6.3 (6.0)	29.1 (29.1)
$In(cyclohexHdtc)_3$	>170 dec.	39.3 (38.4)	6.1 (5.6)	6.6 (5.9)	30.0 (29.5)
$In(dodecHdtc)_3$	52–8	52.2 (51.2)	8.8 (10.0)	4.7 (4.5)	21.5 (22.0)
$In(Etxan)_3$	>300 dec.	22.6 (22.6)	3.1 (3.2)		40.2 (39.2)
$In(i\text{-}propxan)_3$	152–7	27.7 (26.9)	4.0 (4.0)		36.9 (35.9)
$In(sec\text{-}butxan)_3$	119–20	32.0 (32.1)	4.8 (4.9)		34.2 (33.9)
$In(cyclohexxan)_3$	>200 dec.	39.5 (39.1)	5.2 (5.0)		30.1 (29.1)
$In(Me_2dtp)_3$	124–5	12.3 (13.1)	3.1 (3.0)		32.8 (31.3)
$In(Et_2dtp)_3$	66–8	21.5 (21.6)	4.5 (4.5)		28.7 (27.9)
$In(i\text{-}prop_2dtp)_3$	96–9	28.6 (29.1)	5.6 (5.6)		25.5 (24.8)
$In(Ph_2dtpi)_2$	235–6	50.1 (50.2)	3.4 (3.5)		22.3 (22.7)

[a]Calculated(found).

Results and Discussion

The reaction of $InCl_3$ with aqueous solutions of dithio ligands (dialkyldithiophosphates (R_2dtp^-), diphenyldithiophosphinate (Ph_2dtpi), monoalkyldithiocarbamates ($RHdtc^-$) and alkylxanthates ($Rxan^-$)) results in the formation of crystalline substances which have been proved to be neutral tris-chelates of indium(III). The preparation route follows that for a series of tris(dialkyldithiocarbamato)-indium(III) complexes [1] and is in contrast to earlier reports in which similar complexes were reported to be obtained in anhydrous media only [5–7]. To our

*For Part I see ref. 1.

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TABLE II. NMR Results

Complex	Spectral results (nucleus, chem. shift (ppm), mult., int.)
$In(benzHdtc)_3$	^1H: NH 11.02t(1H); phenyl 7.32m(5H); CH_2 4.59s(2H)
$In(cyclohexHdtc)_3$	^1H: NH 10.42t(1H); CH 3.45m(1H); CH_2 0.9–2.05m(10H)
$In(dodecHdtc)_3$	^1H: NH 7.47t(1H); N–CH_2 3.39m(2H); CH_2 1.22m(20H); CH_3 0.84t(7H)
$In(Etxan)_3$	^1H: CH_2 4.50q(2H); CH_3 1.47t(3H)
$In(i\text{-}propxan)_3$	^1H: CH 5.09m(1H); CH_3 1.42d(6H)
$In(sec\text{-}butxan)_3$	^1H: CH 4.93m(1H); CH_2 1.78m(2H); CH–CH_3 1.40d(3H); CH_2–CH_3 0.96t(3H)
$In(cyclohexxan)_3$	^1H: CH 4.8m(1H); CH_2 1.08–2.28m-(10H)
$In(Me_2dtp)_3$	^1H: CH_3 1.40 ^{31}P: 99.6
$In(Et_2dtp)_3$	^1H: CH_2 3.55q(2H); CH_3 1.17t(3H) ^{31}P: 99.8
$In(i\text{-}prop_2dtp)_3$	^1H: CH 4.99m(1H); CH_3 1.42d(6H) ^{31}P: 96.0
$In(Ph_2dtpi)_3$	^{31}P: 58.4

knowledge, this is the first report on isolated crystalline indium chelates with monoalkyldithiocarbamates and alkylxanthates. Some of the latter ones have only been studied in solution by Sutton [8].

The compounds are easily soluble in chloroform, soluble in benzene, and insoluble in hydrocarbons. They are stable in air.

Infrared spectra of the dithiocarbamato complexes show NH frequencies in the 3200 cm^{-1} region, indicating the expected S⌒S coordination. The C···N frequencies are hypsochromically shifted by about 40 cm^{-1} with respect to those for the uncoordinated ligands.

Further support for the stated structure is given by the ^1H and ^{31}P NMR results (Table II) which suggest that the donor atoms are coordinated in an octahedral arrangement. The ^{31}P chemical shifts agree well with those found for the corresponding planar nickel(II) dithiophosphates [9]. The differences observed are probably mainly caused by the influence of the alkyl substitution. A general chemical shift sequence dependent on the coordination geometry may be derived including the values for tetrahedral zinc(II) dithiophosphates [10]: octahedral ≈ tetrahedral > planar.

The marked high-field value for $In(Ph_2dtpi)_3$ in comparison to the dithiophosphato complexes also agrees with Ni(II) and Zn(II) chelates and may be explained by the lack of a negative inductive effect of the oxygen atoms neighbouring the phosphorus atom.

Summarizing, it should be mentioned that anhydrous conditions are not necessary for the preparation of In(III) chelates if dithio ligands participate. This fact underlines the possibility of introducing lipophilic neutral indium compounds of the described type into nuclear medical research. *In vitro* studies are in progress.

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