

Synthesis and Characterization of Neutral Technetium(III)-99 and -99m Complexes with O,P-Bidentate Phosphinocarboxylate Ligands. Crystal Structure of *mer*-[Tc(O₂CCH₂CH₂PPh₂)₃]·2Me₂SO†

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Reduction–substitution reactions of pertechnetate with a class of O,P-bidentate phosphinocarboxylic acid ligands HLⁿ [*n* = 1, 2-(diphenylphosphino)benzoic acid; *n* = 2, 3-(diphenylphosphino)propionic acid; *n* = 3, (diphenylphosphino)acetic acid; *n* = 4, 3-(diethylphosphino)propionic acid] afforded a series of neutral and paramagnetic [TcLⁿ₃] complexes. The products have been characterized by means of elemental analysis, IR, ¹H NMR, UV/VIS and FAB mass spectroscopy, and X-ray crystallography for [TcL²₃]. The latter crystallizes in the monoclinic space group *P*2₁/*n* with *Z* = 4, *a* = 21.718(10), *b* = 12.954(6), *c* = 18.038(9) Å and β = 106.59(4)°. The final *R* value was 0.061. Three deprotonated chelates surround the metal in a distorted-octahedral environment adopting a meridional configuration, and consequently there are two pairs of like donor atoms *trans* to one another with the remaining phosphorus atom *trans* to an oxygen atom. Similar reduction–substitution reactions have been performed utilizing the short-lived isotope ^{99m}Tc. The physicochemical properties of the resulting ^{99m}Tc-labelled species match very well those exhibited by the analogues prepared with the long-lived isotope ⁹⁹Tc. Thus the chemical structures of [^{99m}TcLⁿ₃] and [⁹⁹TcLⁿ₃] analogues are identical. Female Sprague–Dawley rats were injected with pre-purified [^{99m}TcLⁿ₃] (*n* = 1, 2 or 4) and the resulting biodistributions evaluated at different times post injection. All the complexes undergo very low, but significant, brain uptake which decreases with time.

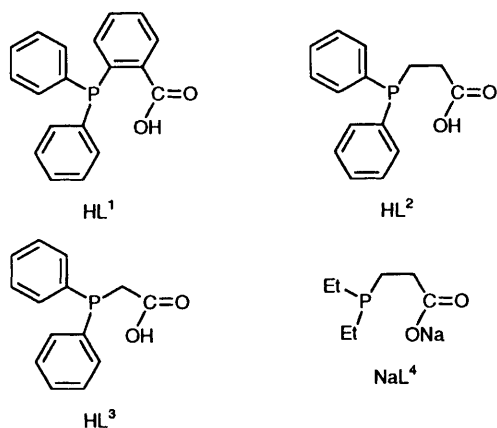
Tertiary phosphines are π-acid ligands¹ known to stabilize low oxidation states of transition metals.² A large variety of phosphine technetium complexes, containing the metal in oxidation states ranging from I to V, have been prepared.^{3–8} For instance, several mixed halide–phosphine compounds such as [Tc^{III}Cl₃(PMe₂Ph)₃] and [Tc^{IV}Cl₄(PPh₃)₂],⁷ obtained by reaction of pertechnetate with an excess of monotertiary phosphine and the appropriate hydrohalogenic acid, are precursors for the synthesis of low-valent technetium compounds. In addition, bidentate diphosphine (L–L) ligands are able to stabilize technetium-(V), -(III) and -(I) species [TcO(OH)(L–L)₂]²⁺, [TcX₂(L–L)₂]⁺ (X = Cl, Br, NCS or SR, R = alkyl or aryl) and [Tc(L–L)₃]⁺, respectively.⁹ The complex [TcO(OH)(L–L)₂]²⁺ is itself an excellent starting material for the synthesis of an extensive class of technetium-(III/II) compounds of the type [TcX₂(L–L)₂]^{+/0}, where X represents halide, thiocyanate^{10–15} or thiolate.^{16–20} Both mono- and bi-dentate tertiary phosphines have been used alone, or in conjunction with appropriate co-ligands, to label the short-lived metastable isomer ^{99m}Tc and some ^{99m}Tc-labelled radiopharmaceuticals containing phosphine ligands are now available: [^{99m}Tc-Q12]⁺ (TechnoCard®) {*trans*-[^{99m}TcL{P-((CH₂)₃OMe)₃}₂] where L = 1,2-bis(dihydro-2,2,5,5-tetramethyl 3(2*H*)-furanonato-4-methyleneimino)ethane}, a myo-

cardial imaging agent, contains two *trans*-axial monotertiary ether-substituted alkylphosphines which complete an octahedral array based on a tetradentate equatorial N₂O₂-Schiff-base ligand;^{21–24} [^{99m}TcO₂(P53)₂]⁺ {P53 = [EtO(CH₂)₃]-PCH₂CH₂P[(CH₂)₃OEt]} contains two bidentate ether-substituted alkyl diphosphines and is also under clinical evaluation as a myocardial imaging agent.²⁵ In addition, the bis(diphosphine) complex [^{99m}TcCl₂(dmpe)₂]⁺ [dmpe = 1,2-bis(dimethylphosphino)ethane] was historically the first cationic species to be evaluated as a myocardial perfusion imaging agent in humans.²⁶ It appears that phosphines are particularly well suited ligands for technetium since they form substitution-inert complexes with technetium centres in a variety of oxidation states. Moreover the use of phosphines minimizes the usual drawbacks which occur in the reduction of pertechnetate with Sn^{II}, since a phosphine ligand is able at once to reduce and co-ordinate to Tc, providing a radiolabelling procedure that is simplified and clean. For these reasons we have been studying the interaction of technetium and rhenium with a variety of derivatized phosphines of the type Ph₂PC₆H₄X-*o* (X = NH₂, SH or OH), which bear a conveniently positioned functional group. We have demonstrated that these bidentate ligands maintain the reducing properties typical of P^{III} and, at the same time, exhibit enhanced co-ordination abilities by virtue of the chelation effect.

The synthesis and physicochemical characterization of tris-substituted [Tc^{III}(Ph₂PC₆H₄X-*o*)₃] (X = O, S or NH) have been previously reported.^{27,28} In the present paper we describe the preparation and complete characterization of technetium(III)

† Supplementary data available (No. SUP 56960, 2 pp.): biodistributions in rats. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1993, Issue 1, pp. xxiii–xxviii.

Non-SI unit employed: Ci = 3.7 × 10¹⁰ Bq.



complexes which incorporate a class of O,P-bidentate phosphino-carboxylic acid ligands HLⁿ [*n* = 1, 2-(diphenylphosphino)benzoic acid; *n* = 2, 3-(diphenylphosphino)propionic acid; *n* = 3, (diphenylphosphino)acetic acid; *n* = 4, 3-(diethylphosphino)propionic acid]. A comparative study of the same complexes prepared with the short-lived ^{99m}Tc isotope was conducted in order to ascertain both the *in vivo* stability and biodistribution of these uncharged radiopharmaceuticals. A preliminary report regarding these studies has appeared.²⁹

Experimental

Physical Measurements.—Elemental analyses were performed on a Carlo Erba model 1106 elemental analyzer. Infrared spectra were recorded on a Mattson 3030 Fourier-transform spectrometer (4000–400 cm^{−1}) using KBr pellets or Nujol mulls between CsI disks, ¹H and ³¹P NMR spectra and magnetic susceptibility measurements (Evans method³⁰) on a Bruker AC-200 instrument, using SiMe₄ (¹H) as internal reference and 85% aqueous H₃PO₄ (³¹P) as external reference. The UV/VIS spectra were recorded in CH₂Cl₂ using a Cary 17D spectrophotometer (700–220 nm). Conductivity measurements were made at 25 °C using a Metrohm Herison E518 conductometer. Fast-atom bombardment (FAB) mass spectra in the positive mode were recorded by using a glycerol matrix on a VG 30-250 spectrometer (VG Instrument) at the probe temperature. Xenon was used as the primary beam gas, and the ion gun was operated at 8 keV (*ca.* 1.28 × 10^{−15} J) and 100 μA. Data were collected over the range *m/z* 100–1000 at 0.7 s per scan. Cyclic voltammetry measurements were performed on a BAS (Bioanalytical System Inc.) CV-IB cyclic voltammograph at room temperature under an atmosphere of nitrogen by using a conventional three-electrode cell. A platinum-disk electrode (area *ca.* 10^{−3} cm²) was used as the working electrode, a platinum wire as the counter electrode and a saturated calomel reference electrode (SCE). Solely for CH₂Cl₂ solutions, a silver wire was used as a quasi-reference electrode. Controlled-potential coulometries were performed with an AMEL model 721 integrator and the following electrodes: platinum-spiral wire working electrode, platinum-auxiliary foil electrode isolated inside a salt bridge by a medium-glass frit, and an SCE. The measurements were done in dry and degassed MeCN or CH₂Cl₂ (Aldrich gold label solvent) with 0.1 mol dm^{−3} NEt₄ClO₄ (for MeCN solutions) or 0.2 mol dm^{−3} NBu₄ClO₄ (for CH₂Cl₂ solutions) as supporting electrolytes. Potentials were calculated at the midpoint between the anodic and cathodic peaks of the cyclic voltammetric waveform scanned at 0.2 V cm^{−1}, and were referenced internally to the ferrocenium-ferrocene couple.³¹ Low-temperature measurements were made in liquid-nitrogen-ethanol slurries. **CAUTION:** ⁹⁹Tc is a weak β-emitter (*E*_{max} = 0.292 MeV, *ca.* 4.67 × 10^{−14} J) with *t*_{1/2} = 2.12 × 10⁵ y. Handling of this material was carried out in laboratories approved for low-level radioactivity using glove-

boxes under moderate vacuum for the synthesis and recovery operations. Technetium-99m is a γ-emitter (*E*_γ = 0.142 MeV, *ca.* 2.27 × 10^{−14} J) with *t*_{1/2} = 6.02 h. Handling of this isotope requires adequate lead shielding when mCi amounts are utilized.

Materials.—Unless otherwise stated, all chemicals were of reagent grade. Technetium-99 as [NH₄][TcO₄] in 0.1 mol dm^{−3} ammonia solution, was obtained from the Radiochemical Centre, Amersham, while the tetrabutylammonium salt was prepared by addition of aqueous [NBu₄]Cl to a solution of [NH₄][⁹⁹TcO₄] in water; the white flocculent precipitate of the desired [NBu₄][⁹⁹TcO₄] salt was filtered off and washed with a few drops of Et₂O. The salts [NBu₄][⁹⁹TcOCl₄] and [NBu₄][⁹⁹TcO(eg)₂]² (H₂eg = ethylene glycol) were obtained according to literature methods.^{32,33} Technetium-99m was eluted as Na[^{99m}TcO₄] from a ⁹⁹Mo/^{99m}Tc commercial generator (Mallinckrodt Medical Inc.) in 0.9% aqueous NaCl solution. The salt NaL⁴ was supplied by Argus Chemicals, having been prepared according to the method described below. All solvents were stored over molecular sieves.

Synthesis of the Ligands.—2-(Diphenylphosphino)benzoic acid (HL¹). The procedure is a modification of that reported by Hoots *et al.*³⁴ A solution (70 cm³) of 15% butyllithium (108 mmol) in hexane was added slowly (over 15 min) to a solution of diphenylphosphine (PPh₂H) (10 g, 54 mmol) in tetrahydrofuran (thf) (200 cm³) at room temperature under a nitrogen atmosphere. The resulting red solution was stirred for 0.5 h. To this was added, dropwise over 1 h by means of a pressure-equalizing funnel, 2-chlorobenzoic acid (8.5 g, 54 mmol) in thf (50 cm³) at room temperature, under a nitrogen atmosphere. A golden yellow solution was obtained. After stirring for 3 h the mixture was poured into a separating funnel, mixed with water (250 cm³) and extracted with three portions (25 cm³) of Et₂O. The aqueous phase was acidified to pH 2 with concentrated HCl and extracted with three portions (35 cm³) of CH₂Cl₂. The combined CH₂Cl₂ fractions were finally washed with water (80 cm³) and reduced in volume to *ca.* 15 cm³. Methanol (*ca.* 8 cm³) was added to precipitate the pale yellow crystalline product which was subsequently collected after cooling the solution in a refrigerator. Yield: 85% based on PPh₂H (Found: C, 71.1; H, 5.9. C₁₉H₁₅O₂P·MeOH requires C, 71.00; H, 5.65%). ³¹P NMR (CDCl₃): δ −5.1.

3-(Diphenylphosphino)propionic acid (HL²) and (diphenylphosphino)acetic acid (HL³) were prepared according to the method reported by Podlahova and co-workers.³⁵ ³¹P NMR (CDCl₃): δ −17.9 (HL²); −17.4 (HL³). The ligands HL¹, HL² and HL³ are air-stable solids.

Sodium 3-(diethylphosphino)propionate (NaL⁴). A Schlenk flask (100 cm³) was charged with diethylphosphine (7.02 g, 78 mmol), ethyl 3-chloropropionate (10.65 g, 78 mmol), NaI (11.69 g, 78 mmol) and absolute EtOH (20 cm³). The mixture was refluxed for 15 h and after cooling NaOEt (78 mmol, 1.6 mol dm^{−3}) in EtOH (45 cm³) was added. The mixture was rotoevaporated and the residue extracted with ether (250 cm³). The oil, obtained after further rotoevaporation of the Et₂O, was distilled under reduced pressure at 55.0 °C (1 mmHg, *ca.* 133 Pa). The sodium salt was prepared by adding to the ester a NaOH solution (5%) in MeOH in 1:1 stoichiometric ratio. The mixture was stirred at room temperature for 2 d, the solvent was rotoevaporated and Et₂O (50 cm³) was added to the residue. Finally, the white solid was filtered off, washed with Et₂O and dried under vacuum. Yield: 41%. The salt NaL⁴ is air sensitive and must be stored under nitrogen. ³¹P NMR (D₂O): δ −20.5.

Synthesis of Technetium-99 Complexes.—The same general route was followed to prepare all the complexes. For [TcL₃][−] two different synthetic procedures are reported.

[TcL₃][−]. **Method 1, from [NH₄][TcO₄].** Solid [NH₄][TcO₄] (25 mg, 0.14 mmol) was suspended in EtOH (5 cm³). To this

suspension was added solid HL¹ (340 mg, 0.65 mmol). After complete dissolution of the ligand, the solution was light yellow, while much of the [NH₄][TcO₄] had not dissolved. The mixture was refluxed for 1 h under a nitrogen atmosphere. When using [NBu₄][TcO₄], which is completely soluble in EtOH, the reaction occurs in 0.5 h. The initial yellow colour turned orange and at the end of the reaction an orange powder was filtered off. This solid [TcL¹₃] was washed three times with portions (2 cm³) of EtOH, followed by Et₂O (3 cm³) and dried over molecular sieves. Yield: 92% (Found: C, 65.6; H, 4.4. C₅₇H₄₂O₆P₃Tc·EtOH requires C, 66.7; H, 4.5%). The complex is soluble in CH₂Cl₂ and CHCl₃, slightly soluble in MeCN, EtOH, MeOH and Me₂CO, and insoluble in Et₂O, hydrocarbons, C₆H₆, CCl₄, dimethylformamide (dmf) and water.

Method 2, from [TcO(eg)₂]⁺. The salt [NBu₄][TcOCl₄] (50 mg, 0.1 mmol) was dissolved in the minimum amount of MeOH. Ethylene glycol (0.5 cm³) was added to the green solution, followed by dropwise addition of 0.75 mol dm⁻³ methanolic sodium acetate (1 cm³). Upon addition of solid HL¹ (153 mg, 0.5 mmol) the deep violet solution turned blue-green and then after 15 min became orange. At this stage no precipitate was present, but after evaporation of MeOH an orange precipitate of [TcL¹₃] formed. The solid was filtered off, washed with small volumes of EtOH and Et₂O, then dried over molecular sieves. Yield: 82% ¹H NMR (CDCl₃): 14 signals in the range δ 2.6–16.6. FAB mass spectrum: *m/z* 1015, [*M* + H]⁺. UV/VIS bands: 490 (ε = 800 dm³ mol⁻¹ cm⁻¹) and 395 nm (sh).

[TcL²₃]. Solid [NH₄][TcO₄] (25 mg, 0.14 mmol) and HL² (217 mg, 0.84 mmol) were dissolved in EtOH (5 cm³) to yield a light yellow solution. Upon reflux for 1 h the solution turned yellow-green, but even after cooling no precipitate formed. The solution was taken to dryness in a nitrogen stream to yield a yellow-green oil, which was washed five times with Et₂O (5 cm³) to eliminate phosphine oxide or unreacted ligand. The solid was taken to dryness in a nitrogen stream to yield a yellow-green oil, which was washed five times with Et₂O (5 cm³) to eliminate phosphine oxide or unreacted ligand. The solid was filtered off and treated with Me₂CO. A further amount of phosphine oxide remained on the filter, while crystals deposited from the acetone solution after a few minutes. The yellow crystals were filtered off and washed with Et₂O (2 cm³). Yield: 45%. Identical results can be obtained by using dimethyl sulfoxide (dmsO) instead of Me₂CO (Found: C, 56.6; H, 5.1. C₄₅H₄₂O₆P₃Tc·2dmsO requires C, 57.3; H, 5.3%). The complex [TcL²₃] is soluble in MeOH, EtOH, MeCN, CH₂Cl₂ and CHCl₃, slightly soluble in Me₂CO and dmsO and insoluble in hydrocarbons, Et₂O and H₂O. ¹H NMR (CDCl₃): 12 signals in the range δ 4.5–12.1. FAB mass spectrum: *m/z* 871, [*M* + H]⁺. UV/VIS bands: 455 (ε = 12 300 dm³ mol⁻¹ cm⁻¹) and 325 nm (sh).

[TcL³₃]. Solid [NH₄][TcO₄] (22 mg, 0.12 mmol) and HL³ (170 mg, 0.70 mmol) were suspended in EtOH (5 cm³). After complete dissolution of the ligand the solution turned yellow. The mixture, under a nitrogen atmosphere at room temperature, was stirred for 3 h until all the [NH₄][TcO₄] dissolved. The yellow-brown solution was concentrated in a nitrogen stream to yield an orange-brown oil. A solid was precipitated upon addition of Et₂O. This crude solid product could not be recrystallized from either Me₂CO or dmsO. Therefore, it was dissolved in Me₂CO (2 cm³) and the remaining white solid phosphine oxide was filtered off. The brown solution was loaded on the top of a Florisil® column (25 × 2.5 cm) prepared in Me₂CO. A yellow band was rapidly eluted, while the brown colour was fully retained on the top of the column. The acetone solution containing the yellow-orange band was taken to dryness and the resulting oil treated with Et₂O to yield a yellow powder of [TcL³₃]. Yield: 40% (Found: C, 60.1; H, 4.2. C₄₂H₃₆O₆P₃Tc requires C, 60.9; H, 4.4%). The complex is soluble in MeOH, EtOH, MeCN, Me₂CO, dmsO, CH₂Cl₂ and CHCl₃, and insoluble in Et₂O, hydrocarbons and water. FAB mass spectrum: *m/z* 829, [*M* + H]⁺. UV/VIS bands: 405 (6500) and 320 nm (ε = 10 400 dm³ mol⁻¹ cm⁻¹).

[TcL⁴₃]. All attempts at isolation always yielded intractable yellow oils soluble in any of the above-mentioned solvents. FAB mass spectrum: *m/z* 583, [*M* + H]⁺.

Synthesis of the Technetium-99m Complexes.—All these complexes were prepared by the same route, using solutions purged with argon. In a vial (5 cm³) containing Na[^{99m}TcO₄] (0.5 cm³) (usually about 5 mCi of [^{99m}TcO₄]⁻), which had been eluted from a commercial ⁹⁹Mo/^{99m}Tc generator with a saline solution, was added a 10⁻² mol dm⁻³ solution (0.5 cm³) of the ligand in ethanol–propane-1,2-diol (1:1). Finally, acetic acid (0.1 cm³) was added to bring the pH to 4.5–5.0. The vial was sealed under argon and heated in a paraffin oil-bath at 70 °C for 1 h. Radiochemical analyses, performed by HPLC with radio-metric detection, showed the yields of the three products to be consistently in the range 92–100%, and 85–90% of the injected activity was generally recovered in the eluate. The complexes can be purified from the excess of ligand, since the ligand and its corresponding phosphine oxide are insoluble in water in their acid forms. The crude preparation (1.1 cm³ of complex) was diluted with 0.1 mol dm⁻³ [NH₄][O₂CMe] (19 cm³) to yield a clear solution, pH 6.5. A Fisher C-18 column, previously prepared by washing with EtOH and then by 0.1 mol dm⁻³ aqueous [NH₄][O₂CMe], was loaded with the diluted preparation. Upon washing with 0.1 mol dm⁻³ [NH₄][O₂CMe] (4 cm³), 85% of the activity was retained on the column. The complex was then eluted with EtOH (0.5 cm³). To the resulting solution of the complex were added Tween 80 (Aldrich)–EtOH (1:1, 50 μl) and a volume of saline sufficient to provide a solution of 0.5 mCi cm⁻³ containing less than 10% EtOH. Before evaluation in animals, aliquots of the radiopharmaceutical solution were again tested by HPLC to monitor the stability of the complexes. The complex [^{99m}TcL³₃] was too unstable to allow evaluation of its biodistribution. The *n*-octanol–water partition coefficients (*K*_{oct/w}) measured for the complexes, according to a procedure reported elsewhere,³⁶ were 250 for [TcL¹₃], 32 for [TcL²₃] and 0.25 [TcL⁴₃].

Animal Biodistribution Studies.—Anaesthetized Sprague–Dawley rats (female, 180–200 g) were injected intravenously with the technetium-99m test solution (0.2 cm³). At various times after injection, groups of these rats were killed by cervical dislocation. Immediately after death a blood sample (1 cm³) was withdrawn from the heart. The organs of interest were excised, weighed and assayed for ^{99m}Tc content relative to appropriate blanks and standards. The resulting biodistribution data are available as SUP 56960.

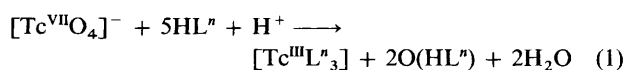
Crystal Structure Determination of [TcL²₃].2dmsO.—Suitable crystals of the complex were grown from dmsO upon slow evaporation. Characteristics of the data collection, processing and refinement are given in Table 1. Empirical absorption corrections, based on the ψ-scan method, were applied. The structure was solved by the heavy-atom method and refined by a full-matrix procedure. The hydrogens, apart from those of the dmsO molecules, were included in calculated positions with *U* = 0.07 Å², but were not refined. The final Fourier difference map showed fairly large peaks (up to 1.1 e Å⁻³) in the vicinity of the dmsO molecules. Final fractional atomic coordinates are given in Table 2, selected bond lengths and angles in Table 3. The programs used were those of the SHELX package.³⁷

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and remaining bond lengths and angles.

Results and Discussion

Synthesis of the Technetium-99 Complexes.—The preparation of all technetium-99 complexes was essentially the same, but the recovery procedures varied according to the different

solubilities of the compounds. The complex $[\text{TcL}^3_3]$ must be purified by chromatography, since its solubility is very similar to those of unreacted HL^3 and the corresponding phosphine oxide. The synthetic reactions are conducted with a five-fold excess of ligand; increasing the ligand:metal ratio beyond this does not improve the yield, but ratios less than this result in a drastic drop in yields. Equation (1) illustrates a probable stoichiometry for this reaction.



In these redox/substitution syntheses the phosphine functions both as a reductant (2 mol are consumed in the reduction of Tc^{VII} to Tc^{III} with the concomitant production of phosphine oxide) and a co-ordinating ligand; thus an extraneous reductant such as Sn^{II} is not required. The complex $[\text{TcL}^1_3]$ can also be prepared by redox/substitution starting from the technetium(v) complex $[\text{TcO}(\text{eg})_2]^-$.

The HL^n ligands can be considered to be derived from triphenylphosphine, where the carboxylic functional group is introduced into one of the three phenyl rings in an *ortho* position with respect to the aromatic carbon atom which is bonded to the P^{III} . It is this chelating carboxylate group which presumably promotes the efficient formation of $[\text{TcL}^1_3]$ rather than the analogue $[\text{Tc}^{\text{III}}\text{X}_3(\text{PPh}_3)_3]$ which is formed in the reaction of pertechnetate and HX with unsubstituted triphenylphosphine. The meridional configuration adopted by the bidentate ligands allows minimization of steric constraints among those six phenyl rings which are attached to the phosphorus atoms and are not directly involved in the co-ordination. Electronic factors would favour a facial arrangement in TcL^n_3 since this places all σ donors (oxygen) *trans* to a π acceptor (phosphorus). It appears that the steric demand of the bulky HL^n chelate determines the final configuration; thus the less favoured (from the electronic point of view) meridional configuration is obtained.

The complex $[\text{TcL}^3_3]$ is the only derivative which contains a five-membered chelate ring, and it is also the least stable of the series. It quickly decomposes in solution once the reducing medium is removed. This metastability of the 5/5/5 tris(chelate), relative to 6/6/6, for octahedral Tc^{III} is in contrast to that observed for bis(chelate) square-planar oxotechnetium(v) complexes wherein 5/5 is more stable than 6/6.³⁸ This difference

Table 1 Crystal data and data processing information for $[\text{TcL}^2_3]\cdot 2\text{dmso}$

Empirical formula	$\text{C}_{45}\text{H}_{42}\text{O}_6\text{P}_3\text{Tc}\cdot 2(\text{CH}_3)_2\text{SO}$
<i>M</i>	1026.9
Crystal dimensions (mm)	$0.12 \times 0.12 \times 0.18$
Crystal system	Monoclinic
Space group	$P2_1/n$
<i>a</i> /Å	21.718(10)
<i>b</i> /Å	12.954(6)
<i>c</i> /Å	18.038(9)
β /°	106.59(4)
<i>U</i> /Å ³	4863.4(4.1)
<i>Z</i>	4
<i>F</i> (000)	2128
<i>D</i> _c /g cm ⁻³	1.40
$\mu(\text{Mo-K}\alpha)/\text{mm}^{-1}$	0.52
Automatic diffractometer	Philips PW 1100
Radiation	$\text{Mo-K}\alpha$ ($\lambda = 0.7107$ Å)
Scanning range, scan width/°	$3.0 < 2\theta < 50.0$, 1.20
No. of unique reflections	8463
No. above three standard deviations	5595
Anisotropic thermal parameters	All non-H atoms (except dmso)
Final residual <i>R</i>	0.061
Function minimized ($w = 1$)	$\Sigma w(F_o - F_c)^2$
Data-to-parameter ratio	11:1
Largest difference peak/e Å ⁻³	1.1 [near S(1), S(2)]
Largest difference hole/e Å ⁻³	-0.8

Table 2 Fractional coordinates ($\times 10^4$) for $[\text{TcL}^2_3]\cdot 2\text{dmso}$

Atom	<i>X/a</i>	<i>Y/b</i>	<i>Z/c</i>	Atom	<i>X/a</i>	<i>Y/b</i>	<i>Z/c</i>
Tc	705(0)	369(1)	3062(0)	C(23)	2658(4)	1682(8)	4825(6)
P(1)	1548(1)	-966(1)	3196(1)	C(24)	3119(5)	1328(10)	5497(7)
P(2)	1437(1)	1653(1)	3756(1)	C(25)	2981(5)	535(11)	5924(6)
P(3)	-280(1)	1441(1)	2697(1)	C(26)	2383(5)	85(9)	5712(6)
O(1)	61(2)	-785(4)	2478(3)	C(27)	1920(4)	417(8)	5053(5)
O(2)	-423(4)	-2241(6)	2543(7)	C(28)	1142(3)	2786(6)	4147(4)
O(3)	948(2)	712(4)	2093(3)	C(29)	835(4)	2632(7)	4718(5)
O(4)	1262(3)	1400(5)	1155(3)	C(30)	642(4)	3467(8)	5064(5)
O(5)	464(2)	6(4)	4007(3)	C(31)	751(5)	4460(8)	4860(6)
O(6)	-44(3)	-1117(5)	4538(4)	C(32)	1028(5)	4618(7)	4274(6)
C(1)	1200(4)	-1815(6)	2368(5)	C(33)	1230(4)	3780(6)	3924(5)
C(2)	629(4)	-2405(6)	2488(5)	C(34)	-297(3)	2839(6)	2580(4)
C(3)	50(4)	-1763(7)	2515(5)	C(35)	-149(4)	3252(7)	1932(5)
C(4)	1886(3)	2146(6)	3121(5)	C(36)	-158(4)	4301(7)	1820(6)
C(5)	1456(4)	2389(6)	2305(5)	C(37)	-320(5)	4969(7)	2324(7)
C(6)	1215(4)	1455(6)	1814(5)	C(38)	-473(5)	4575(8)	2937(6)
C(7)	-666(3)	1204(7)	3456(5)	C(39)	-468(5)	3514(7)	3069(5)
C(8)	-697(4)	70(7)	3647(5)	C(40)	-868(4)	1048(6)	1791(4)
C(9)	-57(4)	-407(7)	4112(5)	C(41)	-1518(5)	1231(8)	1689(6)
C(10)	1779(4)	-1877(6)	3996(4)	C(42)	-1956(5)	1006(9)	960(7)
C(11)	2320(4)	-2500(7)	4096(5)	C(43)	-1747(5)	637(8)	399(6)
C(12)	2474(5)	-3217(7)	4675(6)	C(44)	-1115(5)	449(9)	467(6)
C(13)	2086(6)	-3344(8)	5151(6)	C(45)	-662(4)	658(7)	1185(5)
C(14)	1557(5)	-2750(8)	5055(6)	S(1)	5196(2)	1784(3)	4879(2)
C(15)	1392(4)	-2004(7)	4477(5)	O(7)	4718(5)	1211(8)	4256(6)
C(16)	2294(4)	-525(6)	3042(5)	C(46)	5040(8)	3085(13)	4685(9)
C(17)	2320(4)	-293(6)	2294(5)	C(47)	5917(8)	1691(14)	4646(10)
C(18)	2868(5)	143(7)	2176(7)	S(2)	7134(3)	2353(5)	2844(4)
C(19)	3396(5)	340(8)	2798(8)	O(8)	7819(7)	2092(10)	2957(8)
C(20)	3374(4)	127(7)	3541(7)	C(48)	6735(12)	2218(20)	1838(14)
C(21)	2830(4)	-300(7)	3664(5)	C(49)	7071(13)	3664(22)	2720(16)
C(22)	2056(3)	1213(6)	4619(4)				

Table 3 Selected bond lengths (Å) and angles (°) with estimated standard deviations (e.s.d.s) in parentheses

Tc–P(1)	2.479(2)	Tc–P(2)	2.393(2)	Tc–P(3)	2.478(2)
Tc–O(1)	2.112(5)	Tc–O(3)	2.014(6)	Tc–O(5)	1.978(6)
O(1)–C(3)	1.27(1)	O(3)–C(6)	1.30(1)	O(5)–C(9)	1.31(1)
C(3)–O(2)	1.21(1)	C(6)–O(4)	1.22(1)	C(9)–O(6)	1.19(1)
C(3)–C(2)	1.52(1)	C(6)–C(5)	1.50(1)	C(9)–C(8)	1.53(1)
C(2)–C(1)	1.52(1)	C(5)–C(4)	1.53(1)	C(8)–C(7)	1.51(1)
C(1)–P(1)	1.83(1)	C(4)–P(2)	1.82(1)	C(7)–P(3)	1.82(1)
P(1)–C(10)	1.82(1)	P(2)–C(22)	1.83(1)	P(3)–C(34)	1.82(1)
P(1)–C(16)	1.81(1)	P(2)–C(28)	1.82(1)	P(3)–C(40)	1.83(1)
S(1)–O(7)	1.49(1)	S(2)–O(8)	1.48(1)		
S(1)–C(46)	1.73(2)	S(2)–C(48)	1.78(3)		
S(1)–C(47)	1.74(2)	S(2)–C(49)	1.71(3)		
P(1)–Tc–P(2)	94.1(1)	P(1)–Tc–P(3)	167.1(1)	P(1)–Tc–O(1)	85.4(2)
P(1)–Tc–O(3)	82.5(2)	P(1)–Tc–O(5)	96.9(2)	P(2)–Tc–P(3)	98.3(1)
P(2)–Tc–O(1)	178.4(2)	P(2)–Tc–O(3)	90.1(2)	P(2)–Tc–O(5)	90.8(2)
P(3)–Tc–O(1)	82.3(2)	P(3)–Tc–O(3)	93.8(2)	P(3)–Tc–O(5)	86.6(2)
O(1)–Tc–O(3)	91.4(2)	O(1)–Tc–O(5)	87.8(2)	Tc–O(3)–C(6)	139.2(5)
O(3)–C(6)–C(5)	119.2(7)	O(3)–C(6)–O(4)	120.3(8)	C(6)–C(5)–C(4)	114.5(7)
C(5)–C(4)–P(2)	112.8(6)	C(4)–P(2)–Tc	108.0(3)	C(22)–P(2)–Tc	116.4(3)
C(28)–P(2)–Tc	120.5(3)	Tc–O(5)–C(9)	132.2(5)	O(5)–C(9)–C(8)	116.1(7)
O(5)–C(9)–O(6)	123.0(8)	C(9)–C(8)–C(7)	115.0(7)	C(8)–C(7)–P(3)	113.2(6)
C(7)–P(3)–Tc	104.7(3)	O(3)–Tc–O(5)	179.0(2)	Tc–O(1)–C(3)	134.4(6)
O(1)–C(3)–C(2)	121.1(8)	O(1)–C(3)–O(2)	122.7(9)	C(3)–C(2)–C(1)	116.4(7)
C(2)–C(1)–P(1)	110.3(6)	C(1)–P(1)–Tc	102.5(3)	C(10)–P(1)–Tc	123.9(3)
C(16)–P(1)–Tc	115.6(3)	C(34)–P(3)–Tc	125.1(3)	C(40)–P(3)–Tc	114.2(3)
O(7)–S(1)–C(46)	106.1(7)	O(7)–S(1)–C(47)	105.4(7)	C(46)–S(1)–C(47)	99.1(8)
O(8)–S(2)–C(48)	107.2(1.1)	O(8)–S(2)–C(49)	106.5(1.0)	C(48)–S(2)–C(49)	88.1(2.0)

Table 4 Redox potentials^a (in V) for the technetium couples

Complex	E°			ΔE° ^b
	Tc ^{III} –Tc ^{II}	Tc ^{II} –Tc ^I	Tc ^{III} –Tc ^{IV}	
[TcL ¹] ^c	–0.997	—	0.600	1.597
[TcL ²] ^c	–0.925	–1.778 ^d	0.638	1.567
[TcL ³] ^c	–0.731	–1.881	0.756	1.487 ^e
[TcCl ₂ (dppe) ₂] ⁺	–0.205			
[TcCl ₂ (dmpe) ₂] ⁺	–0.427 ^g			
[TcCl ₂ (depe) ₂] ⁺ ^h	–0.447 ^g			
[Tc(SMe) ₂ (dmpe) ₂] ⁺ ⁱ	–0.745	–1.915	0.730	1.475

^a Potentials are reported with respect to ferrocenium–ferrocene; $E^\circ = (E_{pa} + E_{pc})/2$ values measured at 0.200 V s^{–1}; the supporting electrolyte is 0.1 mol dm^{–3} NEt₄ClO₄ unless otherwise noted. ^b $\Delta E^\circ = E^\circ(\text{Tc}^{\text{III}}\text{–Tc}^{\text{IV}}) - E^\circ(\text{Tc}^{\text{III}}\text{–Tc}^{\text{II}})$. ^c Recorded in CH₂Cl₂ and 0.2 mol dm^{–3} NBu₄ClO₄. ^d Peak separation ($E_{pa} + E_{pc}$) = 0.170 V; 0.090 ± 0.005 V for all other couples. ^e Calculated considering for $E^\circ(\text{Tc}^{\text{III}}\text{–Tc}^{\text{IV}})$ the potential value of peak E. ^f dppe = Ph₂PCH₂CH₂PPh₂. ^g From ref. 12; obtained by subtracting 0.195 V from the reported values. ^h depe = Et₂PCH₂CH₂PEt₂. ⁱ From ref. 9; listed values are obtained by subtracting 0.195 V from those reported.

presumably results from the greater steric demands of the six-coordinate, octahedral technetium(III) systems relative to the five-coordinate, square-planar oxotechnetium(V) systems. Interestingly the complex [TcL⁴], although evaluated only at tracer level (see below), is stable (at least throughout the duration of the study), indicating the versatility of this class of phosphinecarboxylate ligands with respect to phosphorus derivatization.

Characterization of the Technetium-99 Complexes.—Elemental analyses, as given in the Experimental section, are in agreement with the proposed formulation. In the IR spectra the C=O stretching vibrations of the phosphino carboxylate moieties are significantly lowered in energy (by ca. 60 cm^{–1}) with respect to those of the free ligands, indicating co-ordination of the chelates. Conductivity measurements carried out in MeCN show values below the normal range for 1:1 electrolytes,

indicating that the complexes are neutral. The FAB⁺ mass spectra exhibit peaks corresponding to the protonated molecular ion [M + H]⁺.

In the electronic spectra all compounds show a similar absorption pattern of two characteristic bands in the visible and near-UV region; these bands are less intense for [TcL¹]. The absorption spectrum in the near-UV region is well resolved only for [TcL³]. A similar pattern of bands in the visible region is exhibited by previously reported phosphinotechnetium(III) complexes of the type [TcX₂(L–L)₂]⁺,^{13–39} wherein the absorption in the near-UV region is assigned as arising from the phosphine-to-technetium charge-transfer (c.t.) transition, and that in the visible region as a ligand (S, halide, etc.)-to-technetium c.t. These assignments are directly derived from the dependencies of the absorption energy on the oxidation state of Tc and on the nature of the *trans*-axial sulfur or halide ligand. Despite the apparent similarity of the band patterns, the bands observed for the [TcLⁿ]₃ complexes are better attributed to a technetium-to-phosphorus c.t. transition on the basis of the following considerations: (i) the bands coherently move from the lowest energy for [TcL¹], in which the strongest π -acid character of L¹ renders the technetium(III) centre the hardest to reduce (see Table 4), to higher energy for [TcL²]₃ and [TcL³]₂, wherein the ligands are poorer π acids. The implication is that the bands arise from a technetium-to-phosphorus c.t. transition in which the Tc is formally oxidized and not reduced; indeed data of Table 4 indicate that the [TcL¹]₃ complex is the most easily oxidized to Tc^{IV}; (ii) the symmetry of the complex accounts for the splitting of the metal-to-phosphorus c.t. band into two components due to the presence in the molecule of two types of phosphorus (*trans*-P and *trans*-O).

The somewhat strained five-membered ring of L³ prevents good overlap and indeed the Tc→P c.t. bands are higher in energy than for L².

Cyclic voltammograms of the compounds [TcLⁿ]₃ exhibit an identical reduction pattern in the cathodic region. Two quasi-reversible electron transfers are present (all electron-transfer processes involve 1 equivalent, as established by controlled-potential coulometry carried out at potentials just beyond peaks A, C and E respectively). The voltammograms of Fig. 1

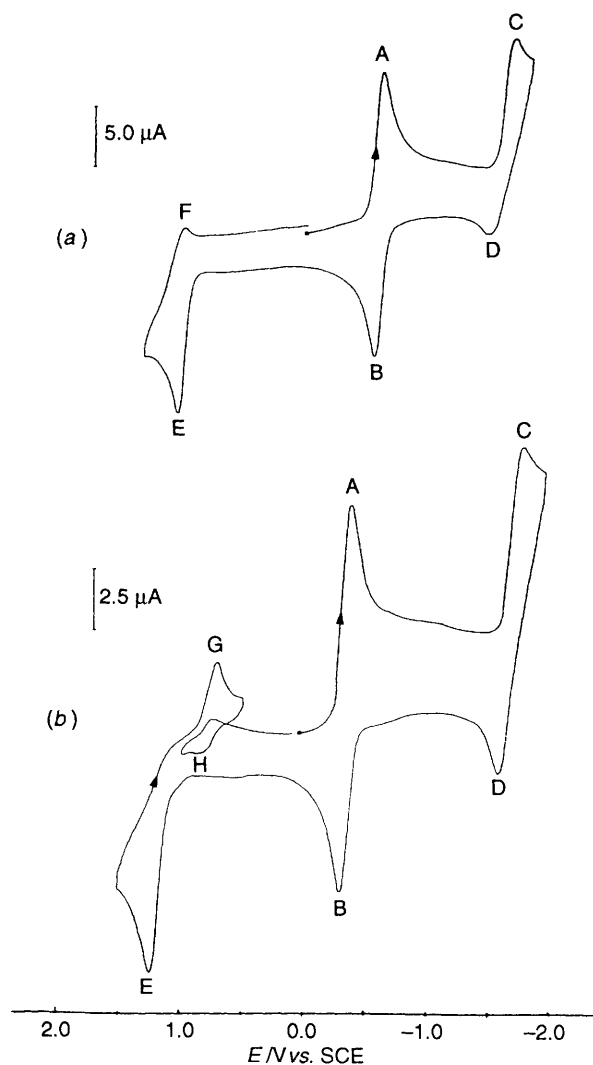


Fig. 1 Cyclic voltammograms of $10^{-3} \text{ mol dm}^{-3}$ $[\text{TcL}^2_3]$ (a) and $[\text{TcL}^3_3]$ (b). Conditions: 0.01 mol dm^{-3} NEt_4ClO_4 in MeCN, potentials measured vs. SCE

show the peaks A and B which are related to the couple $\text{Tc}^{\text{III}}-\text{Tc}^{\text{II}}$ and C and D which can be attributed to the one-electron reduction $\text{Tc}^{\text{II}}-\text{Tc}^{\text{I}}$. However, for the latter couple only the complex $[\text{TcL}^3_3]$ exhibits a peak separation ($E_a - E_c$) which meets quasi-reversible criteria (Table 4). In the anodic region both $[\text{TcL}^1_3]$ and $[\text{TcL}^2_3]$ show the peak system E/F which corresponds to the quasi-reversible $\text{Tc}^{\text{III}}-\text{Tc}^{\text{IV}}$ oxidation; upon oxidation the complex $[\text{TcL}^3_3]$ undergoes a chemical reaction as indicated by the persistence of the system G/H in voltammograms recorded at potential scan rates of $0.5-1 \text{ V s}^{-1}$, as well as at low temperature (-40°C) [Fig. 1(b)].

The electrochemistry of the $[\text{TcL}^n_3]$ complexes is dominated by the reversible $\text{Tc}^{\text{III}}-\text{Tc}^{\text{II}}$ couple, which may be accompanied by the $\text{Tc}^{\text{II}}-\text{Tc}^{\text{I}}$ and $\text{Tc}^{\text{III}}-\text{Tc}^{\text{IV}}$ processes of variable degree of chemical reversibility depending on the nature of L^n . For both $\text{Tc}^{\text{III}}-\text{Tc}^{\text{II}}$ and $\text{Tc}^{\text{II}}-\text{Tc}^{\text{I}}$ electron transfers, the data of Table 4 show that the phosphinocarboxylate complexes are consistently several hundred millivolts more difficult to reduce than $[\text{Tc}^{\text{III}}\text{X}_2(\text{L}-\text{L})_2]^+$ compounds ($\text{L}-\text{L}$ = diphosphine, X = halide or thiolate). This gross effect reflects the change in the co-ordination sphere of the former complexes to three phosphorus atoms rather than four, as in the latter, plus the introduction of the strong σ -donating carboxylate ligands. The reduction in the number of P donors in the co-ordination sphere

reduces the net π -back bonding and stabilizes Tc^{III} relative to Tc^{II} , while the carboxylate groups have the same effect through σ donation of electron density.

Within the $[\text{TcL}^n_3]$ series the comparison of E° values indicates that $[\text{TcL}^1_3]$, which contains the ligand with the highest π -acid character, is the hardest to reduce and, conversely, the easiest to oxidize. This result is somewhat surprising when compared to data from the $[\text{TcX}_2(\text{L}-\text{L})_2]^+$ systems, in which it is clearly established that increasing the π -acid character of the ligand(s) favours delocalization of charge density from the metal which in turn preferentially stabilizes the lower oxidation state. Therefore, the reduction from Tc^{III} to Tc^{II} in $[\text{TcL}^n_3]$ species does not merely reflect the π -acid properties of the ligand but must also reflect the steric factors inherent in the co-ordinating ability of those ligands (see above). The small variation in E° values for the couple $\text{Tc}^{\text{III}}-\text{Tc}^{\text{II}}$ in $[\text{TcL}^1_3]$ and $[\text{TcL}^2_3]$ complexes (-0.997 vs. -0.925 V , respectively) indicates that the nature of the two-atom carbon chain between the co-ordinating phosphorus and the carboxylic group is not a prime determinant of E° , or, in other words, that the phosphine and carboxylate moieties are relatively independent in their effect on the redox properties of the complexes. The complex $[\text{TcL}^3_3]$ is easier to reduce than $[\text{TcL}^2_3]$ by 0.194 V , presumably because of the different metal chelate ring (five- vs. six-membered) in the co-ordination sphere. The lower stability of $[\text{TcL}^3_3]$ relative to the L^2 and L^1 analogues is also confirmed by the ΔE° value which is the lowest of the series (Table 4).

For all complexes, the ^1H NMR signals are broad and spread over a large range indicating their paramagnetic character. Consequently, no ^{31}P NMR signals are observed. The paramagnetism of these complexes is also confirmed by magnetic susceptibility measurements in solution. The average value of $\mu_{\text{eff}} = 2.8$ is in agreement with two unpaired electrons, which corresponds to a technetium(III) $d^4(t_{2g})^4$ configuration in an octahedral environment.

Structure of $[\text{TcL}^2_3]\cdot 2\text{dmso}$.—It is well known⁴⁰ that in $[\text{M}(\text{bidentate ligand})_3]$ complexes with large six-membered chelate rings, where the angle about the metal atom subtended by the bidentate ring is close to 90° , the expected stereochemistry is close to octahedral. Indeed, in $[\text{TcL}^2_3]$ within the TcPCCCO six-membered rings the bite distance averages 3.1 \AA , the angles about Tc are 85.4 , 90.1 and 86.6° and, consequently, the co-ordination environment about technetium is the expected distorted octahedron (Figs. 2 and 3). Because of the meridional arrangement of the three ligands, there are two pairs of like-donor atoms *trans* to each other, leaving the remaining phosphorus atom *trans* to an oxygen atom. The metal lies slightly out (0.05 \AA) of the best plane through the equatorial P(1), P(2), P(3), O(1) plane, toward the apical O(5) atom. The $\text{Tc}-\text{P}(2)$ bond length *trans* to O(1) is considerably shorter (0.08 \AA) than the mutually *trans* $\text{Tc}-\text{P}$ bonds, since a P atom is better able to accept π -electron density from Tc^{III} when it is *trans* to oxygen than when it is *trans* to another π -accepting P atom. Likewise, the mutually *trans* $\text{Tc}-\text{O}$ bonds are *ca.* 0.11 \AA shorter than the one which is *trans* to P(2). In the analogous compound $[\text{TcL}^5_3]$,²⁸ $[\text{HL}^5 = 2\text{-(diphenylphosphino)phenol}]$, which contains three TcPCCO five-membered rings, the $\text{Tc}-\text{P}$ bond length *trans* to O is shorter by 0.03 \AA and the mutually *trans* $\text{Tc}-\text{O}$ bonds are shorter by *ca.* 0.07 \AA .

A comparison of the $\text{Tc}-\text{P}$ and $\text{Tc}-\text{O}$ bond lengths in the present complex with those in related compounds⁴¹ confirms that the values are in the expected range and the remainder of the distances and angles within the three ligand systems are normal. The presence of some disorder or partial occupancy of the two dmso molecules, together with a considerable thermal motion, yields a solvent molecule which is not well resolved and results in two different S-C bonds (1.78 and 1.71 \AA) with an unrealistic C-S-C angle (88.1°). There are no observed close contacts in the structure.

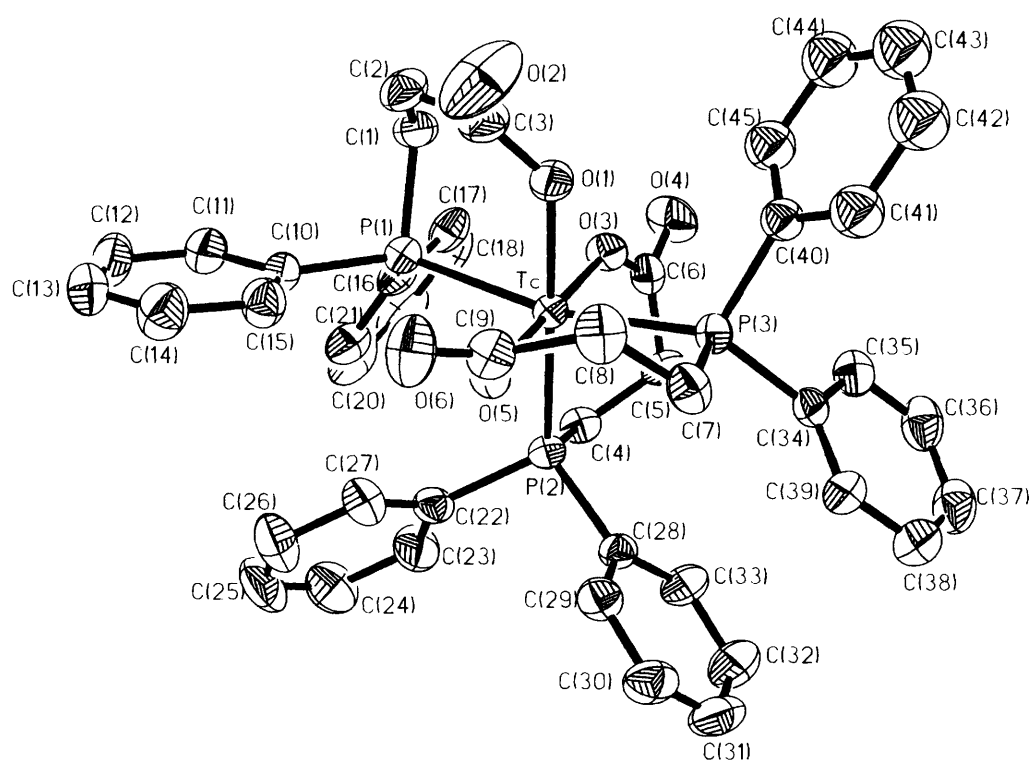


Fig. 2 Perspective view of the complex $[\text{TcL}_3] \cdot 2\text{dmsO}$ showing the atomic numbering scheme. The two dmsO molecules are omitted for clarity. The thermal ellipsoids are drawn at 40% probability level

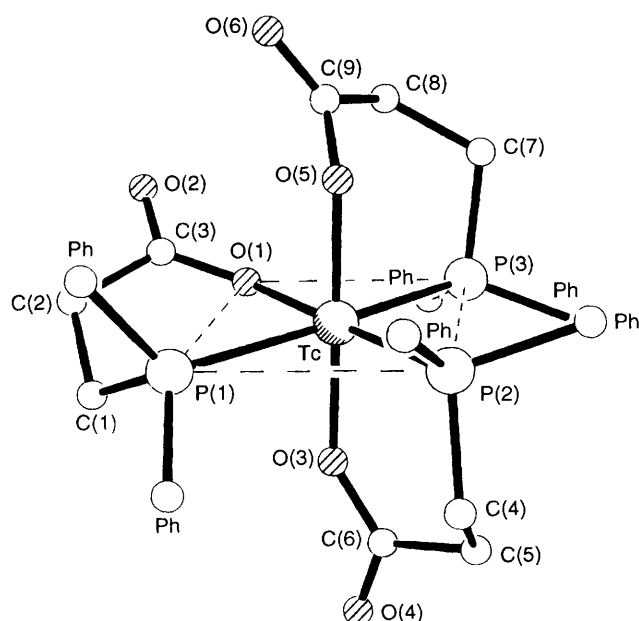


Fig. 3 Stereochemistry of the complex. The two dmsO molecules and the six C_6H_5 groups are omitted for clarity

Synthesis, Characterization and Biodistribution of the Technetium-99m Complexes.—The technetium-99m complexes are easily and readily obtained in very high radiochemical yields from $[\text{}^{99\text{m}}\text{TcO}_4]^-$. No purification procedures are necessary in order to enhance the radiochemical purity of the product. For both $[\text{}^{99}\text{TcO}_4]^-$ and $[\text{}^{99\text{m}}\text{TcO}_4]^-$ starting materials, the synthetic reaction proceeds much more efficiently and cleanly in the presence of a proton source such as acetic acid. In the absence of such a source, HPLC analysis shows that a mixture of different compounds is obtained. This proton requirement possibly results from the stoichiometric necessity of converting the oxo groups of pertechnetate into water. All the complexes

were characterized by means of HPLC analysis coupled with radiometric detection. The retention times exhibited by the 'no carrier added' $^{99\text{m}}\text{Tc}$ reaction mixtures were compared to those exhibited by the technetium-99 complexes prepared using mg amounts of ^{99}Tc and found to be identical. In addition, 'carrier added' $^{99\text{m}}\text{Tc}$ experiments were performed to confirm the identity of the molecular structure complexes from both ^{99}Tc and $^{99\text{m}}\text{Tc}$. In these experiments the chromatographic traces from both the radiometric (for $^{99\text{m}}\text{Tc}$) and electronic (for ^{99}Tc) detectors show a peak corresponding to the $[\text{TcL}_3]$ species at the same retention time. This peak was collected from the eluate, reduced in volume by rotary evaporation, and submitted to positive-ion FAB. The resulting molecular ion peaks correspond to those shown by the technetium complexes produced at the macroscopic level. These experiments confirm the identities of $[\text{}^{99\text{m}}\text{TcL}_3]$ to be the same as those established for the $[\text{}^{99}\text{TcL}_3]$ complexes.

In rats, $[\text{}^{99\text{m}}\text{TcL}_3]$ and $[\text{}^{99\text{m}}\text{TcL}_2]$ exhibit a very low, but significant [0.13 and 0.09% injected dose per g at 30 s post injection (p.i.), respectively] brain uptake which decreases with time (0.02 and 0.004% injected dose per g at 30 min p.i.). The more lipophilic complex, $[\text{}^{99\text{m}}\text{TcL}_3]$, shows the greater brain and greater liver uptake and, presumably owing to the high number of benzene rings, higher retention in the blood pool. Interestingly, for this complex the brain: blood ratio is constant (0.02:1) with time, indicating that it is always in equilibrium between the blood and brain tissues; this suggests that it freely crosses the blood-brain barrier. The biodistribution data for the compound $[\text{}^{99\text{m}}\text{TcL}_4]$ reflect its decreased lipophilicity, in agreement with the physicochemical results (HPLC retention time, $K_{\text{oc}/\text{w}}$, solubility). The replacement of phenyl by ethyl groups in the phosphinocarboxylate backbone dramatically reduces the blood binding and the liver uptake. Nevertheless, the brain uptake remains unchanged with respect to the more lipophilic $[\text{TcL}_3]$ and $[\text{TcL}_2]$ species, even though an improved blood:brain ratio (0.05:1) is obtained. The higher kidney uptake observed for the complex $[\text{TcL}_3]$ indicates that its reduced lipophilicity favours renal excretion, but this occurs without improved brain uptake.

Conclusion

Phosphine ligands which contain a pendant carboxylic group react directly with pertechnetate to generate a series of neutral, paramagnetic technetium(III) complexes of general formula $[\text{TcL}^n_3]$, in which three deprotonated chelates surround the metal in a meridional configuration. The stability of the resulting complexes is highly dependent on the size of the chelate ring, a six- being more favoured than a five-membered ring. Substitution of phenyl by alkyl in the ligand backbone only enhances the reducing ability of the ligand toward $[\text{TcO}_4]^-$. The $\text{Tc}^{\text{III}}-\text{Tc}^{\text{II}}$ redox potentials of the $[\text{TcL}^n_3]$ series, relative to those found for $[\text{TcX}_2(\text{L}-\text{L})_2]^+$ complexes, can be understood on the basis of the different number of π -acid phosphino groups in the co-ordination sphere. The simplicity of the synthesis of these stable complexes in high radiochemical purity from 'no carrier added' $^{99\text{m}}\text{TcO}_4^-$ prompted us to evaluate their biodistribution in rats. However, no interesting biological results were obtained.

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