Synthesis, Stereochemistry and Ligating Properties of Tetraalkyl-Substituted Ethanedithioamides − Evidence for the Lowering of High-Energy Rotation Barriers under the trans Influence of Pt-σ-Bonded Aryl Groups

Santo Lanza,*[a] Francesco Nicolò,[a] and Giuseppe Tresoldi[a]

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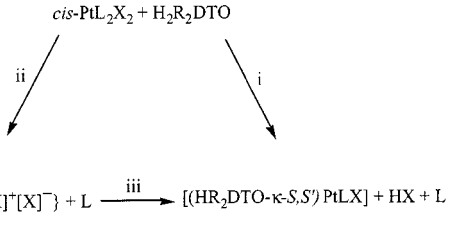
The structural and coordinating properties of five tetrasubstituted tetraalkyldithioxamides (R_4DTO) have been studied: tetraethyldithioxamide (Et_4DTO, **1**), tetrabenzyldithioxamide (Bz_4DTO, **2**), (*E*,*E*)-*N*,*N*′-dibenzyl-*N*,*N*′-diethyldithioxamide [(*E*,*E*)-Bz_2Et_2DTO, **3**], (*E*,*Z*)-*N*,*N*′-dibenzyl-*N*,*N*′-diethyldithioxamide [(*E*,*Z*)-Bz_2Et_2DTO, **4**], (*Z*,*Z*)-*N*,*N*′-dibenzyl-*N*,*N*′-diethyldithioxamide [(*Z*,*Z*)-Bz_2Et_2DTO, **5**]. The solid structure of **4**, determined by single-crystal X-ray diffraction, is characterised by two planar thioamide groups positioned almost orthogonally to each other, connected by a C–C single bond. Each of these dithioxamides showed high-energy barriers to rotation around both the C–N and the central C–C bond. This latter is a chiral torsion, so that R_4DTO species exist as pairs of enantiomers. Compounds **3**, **4** and **5** slowly isomerised in solution to give equimolar mixtures of the three isomers; the activation enthalpy of the process was 30.0 kcal mol^{-1}. The ligands **1**–**5** reacted with [$Pt(Me_2SO)_2X_2$] (X = Cl, Br, Me, Ph) to give chiral chelate complexes [(R_4DTO-κ-*S*,*S*′)PtX_2], but **3** (and also **4** and **5**) provided a mixture of three isomeric platinum chelates in which the *S*,*S*′-coordinated ligands showed the (*E*,*E*), (*E*,*Z*) and (*Z*,*Z*) conformations. Furthermore, the presence of small amounts of the platinum complexes *cis*-[$Pt(Me_2SO)_2Ph_2$] or [(Et_4DTO-κ-*S*,*S*′)$PtPh_2$] caused the fast isomerisation of large quantities of a given isomerically pure ligand. We have explained the collapse of the R_4DTO rotational barriers by assuming that a release of electrons from the metal atom to incoming ligands in the transition state twists these into a partially reduced, dithiolenic form.

Introduction

We have previously found that the reactions (Scheme 1) between H_2R_2DTO (*N*,*N*′-dialkyldithioxamides) and *cis*-[PtL_2X_2]-type complexes (L = Me_2SO, Me_2S; X = Cl, Me, Ph) give rise to (i) rubeanate compounds or (ii) tight ion pairs in high yield, depending on starting material and/or reaction medium.

In fact, when X = Me or Ph, methane or benzene leaves the coordination sphere of platinum(II),[1] while when X = Cl and the reaction is carried out in low-polar, noncoordinating solvents, hydrochloric acid (HCl) remains as a guest in the ion pair.[2] HCl can be easily removed from this ion pair by means either of Lewis nitrogen bases or of Brønsted basic solvents (iii).



Scheme 1

Furthermore, we have previously observed that the tetraethyldithioxamides (Et_4DTO) react with *cis*-[$Pt(Me_2SO)_2X_2$] similarly to other common neutral chelating ligands to give rise to [(Et_4DTO-κ-*S*,*S*′)PtX_2] complexes.[3]

Clearly, the different reaction course of *N*,*N*′-dialkyldithioxamides with respect to the tetraalkyl-substituted ones is due to the two amide hydrogen atoms allowing loss of Cl^- in the Werner substrates *cis*-[PtL_2Cl_2], and cleavage of the Pt−C bond in the corresponding organometallic complexes *cis*-[PtL_2R_2].

Another, perhaps more relevant, difference between the *N*,*N*′-dialkyl- and tetraalkyldithioxamides arises from their conformations in solution: the energy barrier around the C(=S)−C(=S) axis in the H_2R_2DTO species is low, while the same barrier is of high energy in R_4DTO molecules. Thus, tetraalkyldithioxamides, because of the tilted array of the two NCS moieties, exist as pairs of enantiomers.

Both classes of compounds display high-energy achiral torsion barriers around the C−N bonds, and the secondary dithioxamides are locked in the more favourable (*Z*) forms.[4]

[a] Dipartimento di Chimica Inorganica, Chimica Analitica e Chimica Fisica, Università di Messina,
Vill. S. Agata, Salita Sperone 31, 98166 Messina, Italy
Fax: (internat.) + 39-090/393756
E-mail: Lanza@chem.unime.it

The conformational differences seen in the free ligands are still evident in their platinum complexes [(HR_2DTO-κ-*S*,*S*′)PtLX] (**I**), {[(H_2R_2DTO-κ-*S*,*S*′)PtLX]$^+$,[Cl^-]} (**II**) and [(Et_4DTO-κ-*S*,*S*′)PtX_2] (**III**). In the rubeanate complexes **I**, the S−C−C−S skeleton is planar, owing to the loss of one of the two amide hydrogen atoms. In the ion pairs **II**, dithioxamides act as neutral ligands, and this implies that the two NCS moieties are twisted relative to one another, because of repulsion of amide hydrogen atoms.[5] The torsion angle between amide planes (about 40°), measured by X-ray diffraction in several metal complexes, seems to be independent of the metal centre (Zn, Cu, Sn and Bi) and coordination geometry (square-planar, tetrahedral, octahedral, bipyramidal),[6] and it is therefore probably a structural characteristic of neutral chelating secondary dithioxamides. In solution, however, the amide planes flip rapidly (on the NMR timescale) because of the low-energy torsion barrier around the C(=S)−C(=S) axis.

In contrast, the compounds **III** display chiral torsion barriers as high in energy in solution as in the free ligand, and each of these complexes exists as a pair of potentially isolable enantiomers. We have already highlighted the significance of **III** as a new class of chiral chelate complexes,[3] in acknowledgment of the fact that this particular aspect in the chemistry of tetrasubstituted dithioxamide derivatives should be emphasised on account of the importance of metal complexes of chiral chelate ligands in asymmetric catalysis.[7]

Here we report a more extended series of R_4DTO platinum(II) coordination and organometallic complexes for achieving a better understanding of the chiral properties of such systems.

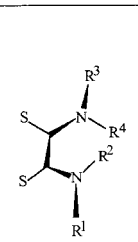
Results and Discussion

The synthetic route to the ligands started from dialkylamines and oxalyl chloride. The resulting oxamides were then treated with phosphorus pentasulfide to yield tetraalkyldithioxamides. Both oxamides and dithioxamides show barriers to rotation around both the amide bond and the central carbon−carbon (the pivot bond).[8] However, the barrier around the C−N bond is high in energy in both classes of compounds, while rotation around the pivot bond is hindered only in tetraalkyldithioxamides, the oxamide C(=O)−C(=O) barrier being of low energy (< 10 kcal/mol). As a consequence, the twisted dithioxamides are chiral molecules, as one can see from the resonances of the prochiral probes $-CH_2-C_6H_5$ and $-CH_2-CH_3$ in Table 1.

The barrier to rotation around the C−N bond means that both oxamides and dithioxamides with different substituents at each nitrogen atom display (*E*)/(*Z*) isomerism.

Actually, the synthesis of *N*,*N*′-dibenzyl-*N*,*N*′-diethyloxamide provides all possible geometrical isomers [(*E*,*E*), (*E*,*Z*), (*Z*,*Z*)] in equimolar ratio. The oxamide isomer mixture, on treatment with P_2S_5, is transformed into the corresponding isomers: (*E*,*E*)- (*E*,*Z*)- and (*Z*,*Z*)-*N*,*N*′-dibenzyl-*N*,*N*′-diethyldithioxamide. Each of these isomers exists as a pair of enantiomers, as a consequence of the twisting of the NCS fragments around the pivot bond.

Table 1. ^{1}H and ^{13}C NMR spectroscopic data (at 298 K, δ values relative to $SiMe_4$, *J* in Hz) for ligands **1**−**5**



	R^1	R^2	R^3	R^4
1	Et	Et	Et	Et
2	Bz	Bz	Bz	Bz
3	Et	Bz	Et	Bz
4	Et	Bz	Bz	Et
5	Bz	Et	Bz	Et

	^{1}H NMR[a]	^{13}C NMR[b]
1[c,d]	3.20[e] (dq, $^2J_{H,H}$ = 13.9, $^3J_{H,H}$ = 7.1, 2 H, CH_2) 3.30[e] (dq, 2 H, CH_2) 3.77[f](dq, $^2J_{H,H}$ = 13.2, $^3J_{H,H}$ = 7.1, 2 H, CH_2) 3.41[f] (dq, 2 H, CH_2) 0.86 (t, 6 H, Me) 0.99 (t, 6 H, Me)	40.60 (s, 2 C, CH_2) 44.10 (s, 2 C, CH_2) 10.65 (s, 2 C, Me) 12.69 (s, 2 C, Me) 192.97 (s, 2 C, CS)
2[d,g]	4.40[e] (d, $^2J_{H,H}$ = 13.2, 2 H, CH_2) 4.96[e] (d, 2 H, CH_2) 4.90[f] (d, $^2J_{H,H}$ = 15.1, 2 H, CH_2) 5.52[f] (d, 2 H, CH_2) 7.27 (m, 20 H, *o*,*m*,*p*-Ph)	51.10 (s, 2 C, CH_2) 55.11 (s, 2 C, CH_2) 127.87, (s, 2 C, *p*-Ph) 128.41, (s, 2 C, *p*-Ph) 128.30, 128.46, 128.80, 128.83 (s, 8 C, *o*,*m*-Ph) 133.73 (s, 2 C, *q*-Ph) 134.84 (s, 2 C, *q*-Ph) 195.66, (s, 2 C, CS)
3[g]	3.80[e] (dq, $^2J_{H,H}$ = 15.1, $^3J_{H,H}$ = 7.1, 2 H, CH_2) 4.03[f] (dq, 2 H, CH_2) 4.36[f] (d, $^2J_{H,H}$ = 15.1, 2 H, CH_2) 5.00[f] (d, 2 H, CH_2) 1.16 (t, 6 H, Me) 7.35 (m, 10 H, *o*,*m*,*p*-Ph)	44.60(s, 2 C, CH_2-Me) 55.78 (s, 2 C, CH_2-Ph) 10.21 (s, 2 C, Me) 128.00 (s, 2 C, *p*-Ph) 128.37 (s, 2 C, *m*-Ph) 128.80 (s, 2 C, *o*-Ph) 134.18 (s, 2 C, *q*-Ph) 194.28 (s, 2 C, CS)
4[g]	3.47[e] (dq, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 7.1, 2 H, CH_2) 3.52[e] (dq, 2 H, CH_2) 3.82[f] (dq, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 7.1, 2 H, CH_2) 4.11[f] (dq, 2 H, CH_2) 5.01[e] (d, $^2J_{H,H}$ = 15.1, 2 H, CH_2) 5.06[e] (d, 2 H, CH_2) 5.40[f] (d, $^2J_{H,H}$ = 14.3, 2 H, CH_2) 5.45[f] (d, 2 H) 1.21 (t, 6 H, Me) 1.26 (t, 6 H, Me) 7.33 (m, 10 H, *o*,*m*,*p*-Ph)	44.27(s, 1 C, CH_2-Me) 47.03(s, 1 C, CH_2-Me) 51.18(s, 1 C, CH_2-Ph) 55.75 (s, 1 C, CH_2-Ph) 10.04 (s, 1 C, Me) 12.35 (s, 1 C, Me) 127.87 (s, 1 C, *p*-Ph) 128.41 (s, 1 C, *p*-Ph) 128.83, 128.30, 127.96 (3s, 8 C, *o*,*m*-Ph) 134.09 (s, 1 C, q-Ph) 135.12 (s, 1 C, q-Ph) 193.94 (s, 1 C, CS) 195.93 (s, 1 C, CS)
5[g]	3.55[e,h] (m, $^3J_{H,H}$ = 7.1, 4 H) 5.12[f] (d, $^2J_{H,H}$ = 14.3, 2 H) 5.45[f] (d, 2 H) 1.26 (t, 6 H, Me) 7.37 (m, 10 H, *o*,*m*,*p*-Ph)	44.92(s,2 C,CH_2-Me) 51.07 (s, 2 C, CH_2-Ph) 12.33 (s, 2 C, Me) 127.96 (s, 2 C, *p*-Ph) 128.03 (s, 2 C, *m*-Ph) 128.82 (s, 2 C, *o*-Ph) 135.83 (s, 2 C, q-Ph) 194.65 (s, 2 C, CS)

[a] At 300.13 MHz. [b] At 75.47 MHz. [c] C_6D_6. [d] The ligands **1** and **2** have already been published[22] but the NMR-spectroscopic data are completed for comparison. [e] Protons in *trans* position with respect to the sulfur atom. [f] Protons in *cis* position. [g] $CDCl_3$. [h] Overlapped signals, $^2J_{H,H}$ = not calculated.

By taking advantage of the different solubilities of the geometrical isomers in ethanol, we were able to obtain the pure (*E*,*E*) isomer **3** (insoluble in ethanol), as well as the (*E*,*Z*) isomer **4** (which crystallised from ethanol after ca. 1 h.) and the (*Z*,*Z*) isomer **5** (soluble in ethanol).

NMR spectroscopy provided useful information to establish the geometries of the isomers. Thus, compound **4**, the

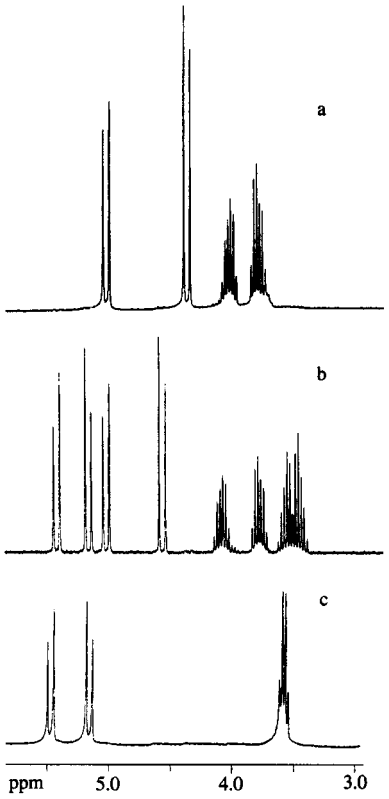


Figure 1. ^{1}H NMR spectra (methylene region) in $CDCl_3$ at 298 K of: a) (*E*,*E*)-Bz_2Et_2DTO (**3**), b) (*E*,*Z*)-Bz_2Et_2DTO (**4**) and c) (*Z*,*Z*)-Bz_2Et_2DTO (**5**)

enantiomeric couple in which the −CSNBzEt fragments have opposite (*E*,*Z*) geometries, showed in its ^{1}H NMR spectrum (Table 1 and Figure 1) two AB quadruplets, corresponding to the nonequivalent benzyl methylene protons, and two ABX_3 schemes featuring the ethyl hydrogen atoms as well.

Furthermore, studies of long-range coupling,[9] intramolecular nuclear Overhauser effects,[10] paramagnetic contact shifts[11] and benzene dilution[12] have shown that, in amides in which rotation about the N−CO bond is restricted, protons *cis* to the carbonyl groups are shielded more strongly than those in a "*trans*" arrangement, at least in the case of freely rotating alkyl substituents. In contrast, the corresponding thioamides display opposite magnetic anisotropies.[13] Thus, the (*E*,*E*) isomer **3**, insoluble in ethanol, showed the methylene proton signals of the ethyl group at lower fields in the ^{1}H NMR spectrum (and those of the benzyl group at higher field) than the corresponding resonances in **5**.

The preparative-scale separation of the above isomers offered an ideal opportunity to confirm the NMR assignment of their geometries by crystallographic analysis. For this reason, we grew a single crystal from a chloroform/ethanol (9:1, v/v) solution of **3**. Unfortunately, the crystal selected for the structural analysis was found to be (*E*,*Z*)-Bz_2Et_2DTO. This unexpected result indicated that spontaneous isomerisation of **3** had occurred in solution.

We observed afterwards that **3**, and also **4** and **5**, all became equimolar mixtures of the three enantiomeric couples within a few days when allowed to stand in chloroform at room temperature.

Kinetic monitoring of the above isomerisation process by ^{1}H NMR revealed a consecutive reversible process. This was a first-order reaction during the time in which the appearance of isomer **5** was negligible; we therefore measured the specific constants of the first-order process at 298, 310 and 323 K (Table 2). From these kinetic measurements, the activation enthalpy was estimated as 30.0 kcal mol^{-1}. This value agrees with the $\Delta H^{\ddagger}$ values for the (*Z*)/(*E*) isomerisation of several thioamides, determined by NMR spectroscopy, which have been found to be[14] in the range of 18−30 kcal mol^{-1}. Finally, the presence of **3**, **4** and **5** in equimolar quantities in the mixture indicated that the free-energy differences ΔG between the geometrical isomers were very small.

Table 2. First-order rate constants for uncatalysed and catalysed isomerisation process of **3**

T [K][a]	k_1 [s^{-1}]	Catalyst
323	1.89×10^{-3}	–
310	2.12×10^{-4}	–
298	3.24×10^{-5}	–
298	3.15×10^{-4}	$[Pt(Me_2SO)_2(C_6H_5)_2]$[b]
298	3.02×10^{-4}	$[Pt(Et_4DTO)(C_6H_5)_2]$[b]
298	3.58×10^{-5}	$[Pt(Et_4DTO)_2Cl_2]$[b]
298	2.73×10^{-5}	$[Pt(Et_4DTO)Br_2]$[b]
298	3.90×10^{-5}	$[Pt(Me_2SO)Cl_2]$[b]

[a] $CHCl_3$. [b] [(*E*,*E*)-Bz_2Et_2DTO]/[complex] = 30.

X-ray Structure of 4

The crystal structure of compound **4** consists of discrete molecules of the ligand $[(C_2H_5)(C_6H_5{-}CH_2)NCS{-}]_2$, packed together by van der Waals interactions. The crystallographic asymmetric unit is represented by one molecule, shown with the corresponding atom-labelling scheme in Figure 2. It was not possible to determine the absolute con-

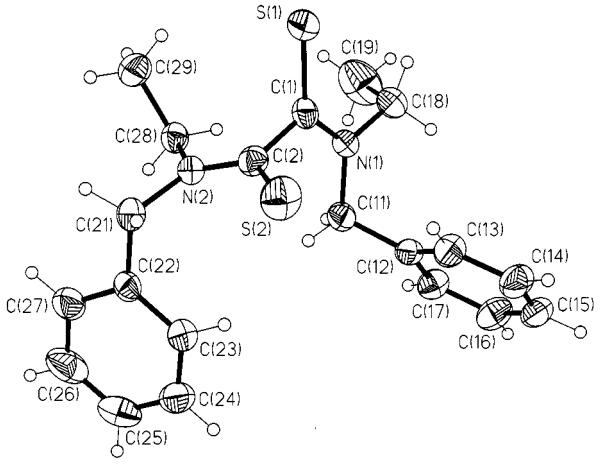


Figure 2. Molecular structure of **4** with the numbering scheme

figuration, expected from the crystallographic space group and spectroscopic evidence, despite the good quality of diffraction data and the structure model definition. In fact, the enantiomorph parameter of Flack,[15] included in the last cycle of the model refinement, converged stably to 0.55(9), a value in the middle of the theoretical extremes of 0.0 for the correct and 1.0 for the incorrect absolute configuration, respectively. This ambiguous situation has already been investigated[16] and the corresponding crystal sample was described as "inversion twin": a solid packing that is a perfect twin formed by the co-crystallisation of both enantiomers.

The ligand scheme comprises a central bulk made up of a dithionic fragment that carries an *N*-benzyl-*N*-ethylamine unit bonded to each carbon atom. On comparison of the geometric data of the two thioamides, the two $(C_2H_5)(C_6H_5{-}CH_2)NCS$ fragments appear to be very similar. The ethyl groups show some difference, which may be related to the disorder of the terminal methyl group [C(19)], as clearly evidenced by its significantly larger displacement parameters, when compared with the corresponding values for C(29). Electronic delocalisation inside each thioamide fragment is limited, as evidenced by the bond data for the almost flat geometry observed for each nitrogen atom. Both the C(1)C(2) bond length of 1.500(4) Å, denoting a single σ-bond, and the S=C−C=S torsion angle of 87.8(3)°, indicating the orthogonal disposition of the dithionic groups, point to the total absence of conjugation between the two thioamide fragments. This staggered arrangement is largely due both to steric and to electronic effects, as we have already pointed out in our previous work on an *N*,*N*,*N*′,*N*′-tetraethyl derivative,[3] in which the geometric parameters of the central N(=S)C−C(=S)N moiety are comparable. Hindrance effects play an important role in determining the disposition of substituents on both thioamide nitrogen atoms.

Metal Complexes of R_4DTO Ligands

S,*S*′−Pt chelation is postulated for all the complexes, since *N*,*N*′−Pt coordination is an unfavourable coordination mode both for steric and for electronic reasons. In fact, the nitrogen lone pairs are barely available for the coordination, because of their involvement in the CN partial double bond, especially since they are protected by bulky alkyl groups. Furthermore, *N*,*N*′−Pt coordination should be a disfavoured hard chelate ligand−soft metal interaction.

$(R^1_2R^2_2DTO)PtX_2$ compounds have been obtained as pure microcrystalline powders if $R^1 = R^2 =$ Et or Bz, X = Ph, Cl, Br.

In solution, all these complexes displayed well-resolved double ABX_3 (Et_4DTO derivatives) and AB (Bz_4DTO compounds) spectral schemes (Table 3). This means that the chiral torsion barriers around the pivot bonds, as well as the achiral torsion barriers around amide bonds, were of high energy even when tetraalkyldithioxamides were linked to platinum(II) fragments.

The Me derivative **11** was unstable and was characterised only in solution.

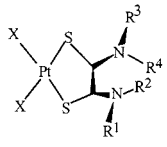
The three Bz_2Et_2DTO isomers displayed unexpected behaviour when they were treated with *cis*-$[Pt(Me_2SO)_2Ph_2]$ species; when one of the isomers (any one of the three) was treated with an equimolar quantity of the platinum complex, there was a mixture obtained containing the isomeric metal complexes [(*E*,*E*)-, (*E*,*Z*)-, (*Z*,*Z*)-Bz_2Et_2DTO)$PtPh_2$] in an equimolar ratio, together with the three isomers of the free ligand and the starting *cis*-$[Pt(Me_2SO)_2Ph_2]$. In other words, the equilibrium according to Scheme 2 took place and caused the isomerisation of the given pure isomer of Bz_2Et_2DTO.

Actually, the presence of catalytic amounts of *cis*-$[Pt(Me_2SO)_2Ph_2]$ complexes produced fast isomerisation of large amounts of a pure isomer (Table 2).

In turn, starting complex *cis*-$Pt(Me_2SO)_2Cl_2$, when treated with a stoichiometric amount of an isomerically pure ligand, quantitatively gave the three isomeric complexes [(*E*,*E*)-, (*E*,*Z*)-, (*Z*,*Z*)-Bz_2Et_2DTO)$PtCl_2$]. However, an excess of isomerically pure ligand, if present, isomerises at a similar rate of the spontaneous isomerisation process.

These findings supported the idea that chelation of a tertiary dithioxamide to a PtX_2 fragment lowered the energy of the barriers to rotation around CN and (S)C−C(S) bonds.

Table 3. ^{1}H and ^{13}C NMR spectroscopic data (at 300.13 and 75.47 MHz, δ values relative to $SiMe_4$, *J* in Hz) for complexes **6**−**13**



	R^1 R^2 R^3 R^4 X
6	Et Et Et Et Cl
7	Et Et Et Et Br
8	Et Et Et Et Ph
9	Bz Bz Bz Bz Cl
10	Bz Bz Bz Bz Ph
11	Bz Bz Bz Bz Me
12	Bz Et Bz Et Cl (*ZZ* isomer)
	Et Bz Et Bz Cl (*EE* isomer)
	Et Bz Bz Et Cl (*EZ* isomer)
13	Bz Et Bz Et Ph (*ZZ* isomer)
	Et Bz Et Bz Ph (*EE* isomer)
	Et Bz Bz Et Ph (*EZ* isomer)

	^{1}H NMR	^{13}C NMR
6[a,b]	3.80[c] (dq, $^2J_{H,H}$ = 13.8, $^3J_{H,H}$ = 7.2, 2 H, CH_2) 3.97[c] (dq, 2 H, CH_2) 4.10[d] (dq, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 7.2, 2 H, CH_2) 4.31[d] (dq, 2 H, CH_2) 1.43 (t, 6 H, Me) 1.46 (t, 6 H, Me)	16.72 (s, 4 C, Me) 54.12, 56.53 (2s, 4 C, CH_2) 195.94 (s, 2 C, CS)
7[a]	3.80[c] (dq, $^2J_{H,H}$ = 13.8, $^3J_{H,H}$ = 7.2, 2 H, CH_2) 3.97[c] (dq, 2 H, CH_2) 4.10[d] (dq, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 7.2, 2 H, CH_2) 4.31[d] (dq, 2 H, CH_2) 1.43 (t, 6 H, Me) 1.45 (t, 6 H, Me)	
8[b,e]	3.51[f] ($^3J_{H,H}$ = 7.2, m, 6 H, CH_2) 4.43[d] ($^2J_{H,H}$ = 13.5, $^3J_{H,H}$ = 7.2, dq, 2 H, CH_2) 1.38 (t, 6 H, Me) 1.48 (t, 6 H, Me) 6.94 (m, 6 H, *m*,*p*-Ph) 7.39 ($^3J_{PtH}$ = 83.5, *m*, 4 H, *o*-Ph)	11.49, 12.56 (2s, 4 C, Me); 46.31, 48.08 (2s, 4 C, CH_2); 121.00 ($^4J_{PtC}$ = 14.0, s, 2 C, *p*-Ph); 126.50 ($^2J_{PtC}$ = 86.8, s, 4 C, *o*-Ph); 138.10 ($^3J_{PtC}$ = 46.4, s, 4 C, *m*-Ph); 144.40 (s, 2 C, q-Ph); 186.91 (s, 2 C, CS)

Table 3. *(Continued)*

9[a]	5.06[c,d] (d, 4 H, CH_2) 5.20[c] (d, $^2J_{H,H}$ = 15.1, 2 H, CH_2) 5.42[d] (d, $^2J_{H,H}$ = 14.8, 2 H, CH_2) 7.30 (m, 20 H, *o,m,p*-bz)	57.73, 60.82 (2s, 4 C, CH_2); 128.88–129.71 (20C, *o,m,p*-bz); 131.99, 133.17 (2s, 4 C, q-bz); 196.15 (s, 2 C, CS)
10[g]	4.12[c,d] (m, 4 H, CH_2) 4.86[d] (d, $^2J_{H,H}$ = 14.3, 2 H, CH_2) 4.69[c] (d, $^2J_{H,H}$ = 14.3, 2 H, CH_2) 7.31 (m, 30 H, *o,m,p*-bz and *o,m,p*-Ph)	52.59, 54.40 (2s, 4 C, CH_2); 122.22 ($^4J_{PtC}$ = 14.0, s, 2 C, *p*-Ph); 126.77 ($^3J_{PtC}$ = 86.8, s, 2 C, *o*-Ph); 128.62–129.53 (m, 12 C, *m,p*-bz); 131.23, 133.08 (2s, 4 C, quat-bz); 137.95 ($^3J_{PtC}$ = 46.4, s, 2 C, *m*-Ph); 144.25 (s, 2 C, q-Ph); 183.72 (s, 2 C, CS)
11[g]	3.70[c] (d, $^2J_{H,H}$ = 14.1, 2 H, CH_2) 3.85[c] (d, 2 H, CH_2) 4.77[d] (m, 2 H, CH_2) 5.31[d] (d, $^2J_{H,H}$ = 14.1, 2 H, CH_2) 2.12 (s, $^2J_{PtH}$ = 93.4, 6 H, Pt-Me) 7.35 (m, 20 H, *o,m,p*-bz)	
12[g]	3.91[h] ($^3J_{H,H}$ = 7.14, m, 4 H, CH_2-Et) 4.88–5.64[h] (8d, $^2J_{H,H}$ = 14.3, 4 H, CH_2-bz) 1.23, 1.34, 1.46, (3t, 6 H, Me) 7.46 (m, 10 H, *o,m,p*-bz)	11.69, 13.00, 13.17 (4s, 6 C, Me); 50.02, 50.59, 52.98, 53.11 (2s, 2 C, CH_2-Et); 57.85, 58.09, 60.12, 60.73, (4s, 2 C, CH_2-bz); 129.13, 129.22 (2s, 2 C, *p*-bz); 129.54 – 129.89 (br, 8 C, *o,m*-bz); 130.59, 132.50, 132.73, 133.73 (4s, 2 C, q-bz); 93.21, 193.65, 194.03, 194.36 (4s, 2 C, CS)
13[g]	4.24, 3.46, 3.27 h (m, $^3J_{H,H}$ = 7.14, 4 H, CH_2-Et) 5.70–4.20 h (8d, $^2J_{H,H}$ = 14.3, 4 H, CH_2-bz) 1.23, 1.34, 1.47 (3t, 6 H, Me) 7.25 (m, 20 H, *o,m,p*-bz and *o,m,p*-Ph)	10.79, 10.91, 11.99, 12.11, (4s, 6 C, Me); 45.46, 45.55, 46.84 (3s, 2 C, CH_2-Et); 53.59, 55.63, 55.69 (3s, 2 C, CH_2-bz); 122.10 ($^4J_{PtC}$ = 14.1, s, 2 C, *p*-Ph); 122.44–128.57 (m, 10C, *o,m,p*-bz); 126.69 ($^3J_{PtC}$ = 88.6, s, 4 C, *o*-Ph); 131.37, 131.51, 133.17, 133.25 (4s, 2 C, q-bz);138.03, 138.06 ($^3J_{PtC}$ = 44.6, 2s, 4 C, *m*-Ph); 144.37, 144.40, 144.46, 144.53 (4s,2 C, q-Ph); 184.85, 185.01.185.57, 186.07 (4s, 2 C, CS).

[a] $[D_7]$DMF. [b] The complexes **6** and **8** have already been published,[3] but the NMR-spectroscopic data are included for comparison. [c] Protons *trans* to the sulfur atom. [d] Protons *cis* to the sulfur atom. [e] C_6D_6. [f] Three overlapped ABX_3 systems, $^2J_{H,H}$, for protons *trans* to sulfur, not calculated. [g] $CDCl_3$. [h] Overlapped signals.

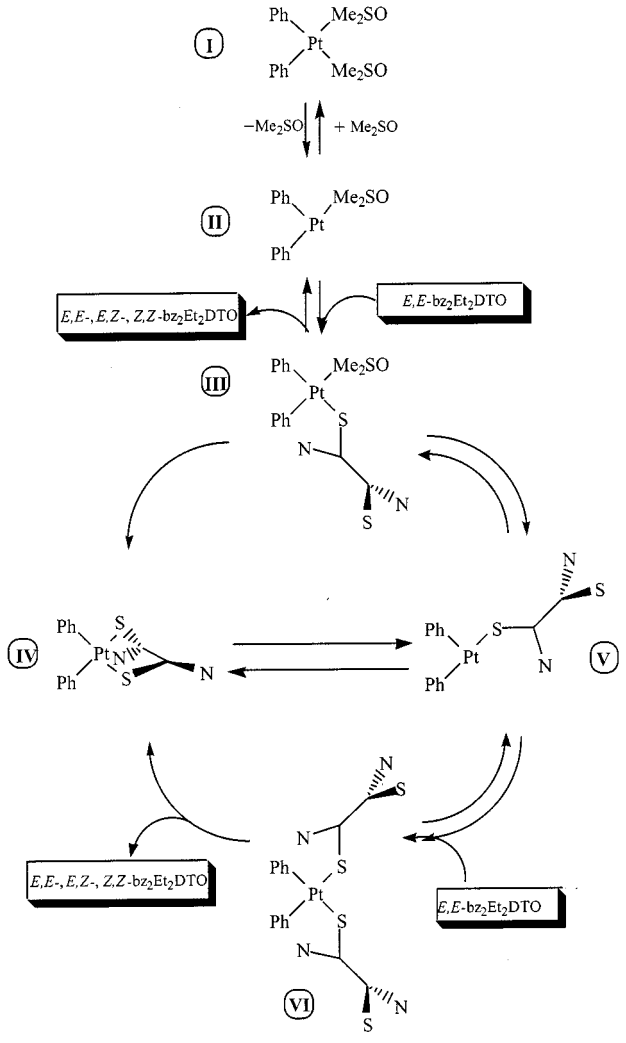
$$bz_2Et_2DTO + cis\text{-}[Pt(Me_2SO)_2Ph_2] \rightleftharpoons (EE\text{-},EZ\text{-},ZZ\text{-}\ bz_2Et_2DTO)PtPh_2 + 2Me_2SO$$

Scheme 2

We assumed that, when the dithioxamide molecule approached the platinum atom in the transition state, a transfer of electron density from the metal centre to the ligand was able to occur, and the ligand was consequently able, in the transition state, to approach the planar dithiolenic form, this obviously bringing about the collapse of both CN and central C−C barriers. The subsequent evolution of the transition state toward the products, or also toward the reagents, restored the dithioxamides, free or coordinated, in all the possible isomeric forms.

The organometallic complexes *cis*-$[Pt(Me_2SO)_2Ph_2]$ and $[Pt(R_4DTO)Ph_2]$, but not the classical Werner compounds *cis*-$[Pt(Me_2SO)_2Cl_2]$ and $[Pt(R_4DTO)Cl_2]$, were able to catalyse the isomerisation of isomerically pure ligand (Table 2). The difference in the behaviour of the two classes of compound can be attributed to the great *trans* influence of the phenyl groups in **I** (Scheme 3), which favours the dissociation of one sulfoxide molecule and gives rise to an intermediate of reduced coordination number. The chemistry of such kinds of intermediate is well understood.[17]

In the absence of external sulfoxide, the proposed intermediate **II** can be saturated by one sulfur "tooth" of an isomerically pure dithioxamide molecule; the subsequent ring-closure process to give the chelate **IV** requires the collapse of both C−C and C−N rotational barriers, as evidenced by the spectral analysis of **IV** (Table 3). Further dissociation of **IV** produces **V** as a three-coordinated intermediate, which takes a new isomerically pure molecule and



Scheme 3. Catalytic cycle for the isomerisation of (*E,E*)-Bz_2Et_2DTO ligand; the ligand input occurs in the steps II → III and V → VI, the output in the steps III → II and VI → IV

forms **VI** as a saturated intermediate. This, upon chelation, restores **IV** together with the equivalent quantity of (*E*,*E*)-, (*E*,*Z*)- and (*Z*,*Z*)-Bz_2Et_2DTO isomers. The alternative paths − **V** → **III** → **II** or **V** → **III** → **IV** − appear unlikely under the actual experimental conditions because of the exceedingly high [(*E*,*E*)-Bz_2Et_2DTO]/[Me_2SO] ratio. As evidence, the isomerisation rate of the (*E*,*E*) isomer when *cis*-[$Pt(Me_2SO)_2Ph_2$] was the catalyst ([DTO]/[Pt] = 30) was similar to that observed when [$Pt(Et_4DTO)Ph_2$] was used as catalyst ([DTO]/[Pt] = 30) and the sulfoxide path did not exist.

It is therefore possible to envisage a catalytic cycle in which the three-coordinate intermediates (**II** and **V** in Scheme 3) produce the input of isomerically pure dithioxamide, while the saturated intermediates (**VI** and **III**) produce the output of the isomerised mixture of ligands.

Studies on coordination of tetraalkyldithioxamides with various $Mo(CO)_{4-x}(PR_3)_x$ led tom Dieck to make the interesting assertion that dithioxamide links the metal atom as dithione−Mo^0 or dithiolene−Mo^{II}, depending on the electronic disposal at the metal centre.[18]

This proposal was supported by Wedd et al., who provided X-ray and NMR evidence for the dithiolenic coordination of Et_4DTO in *trans*-[$Mo(CO)_2(PR_3)_2$-(Et_4DTO)].[19]

These literature references support our hypothesis of a dithiolenic transition state as the key step in the isomerisation process of Bz_2Et_2DTO.

Unfortunately, the easy isomerisation of R_4DTO ligands as a consequence of their linkage with PtX_2 fragments indicates that the resolution of optically pure R_4DTO species through metal complexation is probably impracticable, in spite of the fact that the barrier around the pivot bond is of an energy high enough to allow, in principle, the separation of the two enantiomers.

Experimental Section

General Remarks: The precursors *cis*-$Pt(Me_2SO)_2Cl_2$,[20] *cis*-$Pt(Me_2SO)_2Br_2$,[20] *cis*-$Pt(Me_2SO)_2Ph_2$,[21] *cis*-$Pt(Me_2SO)_2Me_2$,[21] the ligands tetraethyldithioxamide (Et_4DTO) (**1**)[22] and tetrabenzyldithioxamide (Bz_4DTO) (**2**)[22] and the complexes [(Et_4DTO)$PtCl_2$] (**6**)[3] and [(Et_4DTO)$PtPh_2$] (**8**)[3] were prepared according to literature procedures. Solvents and other chemicals were of the highest purity grade commercially available and were used as purchased. ^1H and ^{13}C NMR spectra were recorded at 298 K unless stated otherwise, with a Bruker AMX-R 300 spectrometer at 300.13 and 75.47 MHz, respectively (δ in ppm relative to TMS, *J* in Hz). ^1H- and ^{13}C-NMR-spectroscopic data for the new ligands are given in Table 1 and for the complexes in Table 3. Compound **11** was not isolated in the solid state, and its characterisation was restricted to solution only.

Synthesis of (*E*,*E*)-*N*,*N*′-Dibenzyl-*N*,*N*′-diethyldithioxamide [(*E*,*E*)-Bz_2Et_2DTO, 3], (*E*,*Z*)-*N*,*N*′-Dibenzyl-*N*,*N*′-diethyldithioxamide [(*E*,*Z*)-Bz_2Et_2DTO, 4] and (*Z*,*Z*)-*N*,*N*′-Dibenzyl-*N*,*N*′-diethyldithioxamide [(*Z*,*Z*)-Bz_2Et_2DTO, 5]: Oxalyl chloride (6.346 g, 0.05 mol) and *N*-benzyl-*N*-ethylamine (27.042 g, 0.2 mol) were dissolved in benzene (120 mL). After the reaction mixture has stood overnight, diethylamine hydrochloride was filtered off, and benzene was distilled in vacuum from the filtrate to leave the crude *N*,*N*′-dibenzyl-*N*,*N*′-diethyloxamide as a mixture of (*E*,*E*), (*E*,*Z*) and (*Z*,*Z*) isomers. Phosphorus pentasulfide (3.825 g, 0.02 mmol) was added in small increments to a refluxing xylene solution (80 mL) of the crude oxamide. After the reaction mixture had been refluxed for 4 h, it was cooled and filtered from a black residue. Xylene was removed from the filtrate in vacuo, and a dithioxamide isomer mixture was obtained. This product was dissolved in ethanol (60 mL); the white, microcrystalline compound that remained undissolved provided the pure isomer **3**. The ethanolic filtrate, when allowed to stand, gave pure crystals of the isomer **4**. Finally, the pure isomer **5** was obtained when the solvent was removed from the ethanolic solution in vacuo.

Isomer 3: Yield 4.99 g (28%). $C_{20}H_{24}N_2S_2$ (356.55): calcd. C 67.37, H 6.78, N 7.86; found C 67.30, H 6.80, N 7.90.

Isomer 4: Yield 4.63 g (26%). $C_{20}H_{24}N_2S_2$ (356.55): calcd. C 67.37, H 6.78, N 7.86; found C 67.40, H 6.80, N 7.80.

Isomer 5: Yield 3.92 g (22%). $C_{20}H_{24}N_2S_2$ (356.55): calcd. C 67.37, H 6.78, N 7.86; found C 67.20, H 6.90, N 7.80.

Synthesis of [(Et_4DTO-κ-*S*,*S*′)$PtBr_2$] (7): Et_4DTO (0.232 g, 1 mmol) was added as solid to a stirred suspension of *cis*-$Pt(Me_2SO)_2Br_2$ (0.511 g, 1 mmol) in chloroform (60 mL) at ambient temperature. A deep red solution was obtained, and within a few minutes a red solid precipitated in high yield. The compound was washed with dichloromethane/diethyl ether (1:1) and dried in vacuo. Yield 0.499 g (85%). $C_{10}H_{20}Br_2N_2PtS_2$ (587.30): calcd. C 20.45, H 3.43, N 4.77; found C 20.40, H 3.50, N 4.70.

Synthesis of [(Bz_4DTO-κ-*S*,*S*′)$PtCl_2$] (9): The synthetic procedure was essentially the same as described above for **7**, from Bz_4DTO (0.481 g, 1 mmol), *cis*-$Pt(Me_2SO)_2Cl_2$ (0.422 g, 1 mmol) and chloroform (80 mL). The compound was obtained as red solid. Yield 0.597 g (80%). $C_{30}H_{28}Cl_2N_2PtS_2$ (746.69): calcd. C 48.26, H 3.78, N 3.75; found C 48.20, H 3.80, N 3.75.

Synthesis of [(Bz_4DTO-κ-*S*,*S*′)$Pt(C_6H_5)_2$] (10): Bz_4DTO (0.481 g, 1 mmol) and *cis*-[$Pt(Me_2SO)_2(C_6H_5)_2$] (505 mg, 1 mmol) were stirred in chloroform (60 mL). The resulting red solution was concentrated in vacuo (ca 20 mL), and hexane (40 mL) was then added. The compound precipitated as a red powder. Yield 0.564 g (68%). $C_{42}H_{38}N_2PtS_2$ (829.99): calcd. C 60.78, H 4.61, N 3.38; found C 60.40, H 6.70, N 3.30.

In situ Preparation of [(Bz_4DTO-κ-*S*,*S*′)$PtMe_2$] (11): Bz_4DTO (0.0252 g, 0.05 mmol) and *cis*-$Pt(Me_2SO)_2(CH_3)_2$ (0.0190 g, 0.05 mmol) were stirred in $CDCl_3$ (2 mL) for 1 h. The ^1H NMR spectrum of the solution was then recorded.

Synthesis of [Bz_2Et_2DTO-κ-*S*,*S*′)$PtCl_2$] (12) [Equimolar Mixture of the (*E*,*E*), (*E*,*Z*) and (*Z*,*Z*) Isomers]: The pure isomer (*E*,*E*)-Et_2Bz_2DTO (0.356 g, 1 mmol) and *cis*-$Pt(Me_2SO)_2Cl_2$ (0.422 g, 1 mmol) were stirred in chloroform (60 mL). The solution became red, and the compound, which was a mixture of three isomers, precipitated as deep red microcrystals. Yield 0.404 g (65%). $C_{20}H_{24}Cl_2N_2PtS_2$ (622.54): calcd. C 38.59, H 3.89, N 4.50; found C 38.40, H 3.90, N 4.40.

Synthesis of [(Bz_2Et_2DTO-κ-*S*.S′)$PtPh_2$] (13) [Equimolar Mixture of (*E*,*E*), (*E*,*Z*) and (*Z*,*Z*) Isomers]: *cis*-$Pt(Me_2SO)_2Ph_2$ (0.505 g,

1 mmol) and the pure isomer (*E*,*E*)-Bz_2Et_2DTO (1.068 g, 3 mmol) were stirred in chloroform (60 mL). The solution became red and the compound precipitated as red solid. Satisfactory analytical data were not obtained, due to the presence of the free ligand.

X-ray Data Collection and Structure Refinement of 4: Suitable crystals of compound **4** were obtained by slow concentration of a chloroform/ethanol (90:10, v/v) solution of **3**, which underwent spontaneous isomerisation during the crystallisation (see Discussion). Diffraction data were collected at room temperature with a Siemens P4 automatic four-circle diffractometer, by use of graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). Lattice parameters were obtained from least-squares refinement of the setting angles of 40 reflections with $11° \leq 2\theta \leq 30°$. No sign of crystal deterioration was found during the data collection up to $2\theta = 50°$ with variable-speed 2θ-ω scan type. The intensities of the 2340 measurements were evaluated by a 2θ profile procedure[23] and then corrected for Lorentz dispersion effects. An absorption correction was applied by fitting a pseudo-ellipsoid to the azimuthal scan data of 12 high c reflections[24] (R_{int} = 0.9%). The systematic absences unambiguously indicated the space group $P2_12_12_1$ of the orthorhombic system [a = 7.978(2), b = 12.777(2), c = 19.075(3) Å, Z = 4, D_c = 1.218 g/cm^3, μ = 22.77 cm^{-1}]. The structure was solved by Direct Methods with the SHELXTL-PLUS system[25] (also used to perform data reduction) and subsequently completed by a combination of least-squares techniques and Fourier syntheses. Whereas several hydrogen atoms were located on the final ΔF map, the H atoms were included in the refinement according to the "riding model" method with the X−H bond geometry depending on the parent atom X and with a unique common fixed isotropic displacement parameter (0.070 Å^2). The refinement, with all non-hydrogen atoms anisotropic and the function $w(F_o^2 - F_c^2)^2$ minimised for all the 2229 unique reflections, was carried out by the full-matrix, least-squares technique, based on F^2, with SHELXL93.[26] The model converged to the final residual $R(F_o) = [\Sigma||F_o| - |F_c||]/\Sigma|F_o| = 0.0279$, $wR(F_o^2) = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2} = 0.0525$ and $GoF = [\Sigma w(|F_o| - |F_c|)^2/(N_{obsd.} - N_{var})]^{1/2} = 1.022$ with the final weighting scheme $w = \exp(\sin\theta/l)^2/[\sigma^2(F_o)^2 + \{0.0090 \times [\max(F_o^2,0) + 2F_c^2]\}^2]$ for 1546 reflections with $F \geq 4\sigma(F)$. A parameter for extinction correction was included in the last refinement cycles and assumed the final value $53(8)\cdot10^{-4}$. In the last difference Fourier map, the density residuals were not significant [range −0.11, 0.09 eÅ^{-3}]. The enantiomorph parameter[15] was included in the last refinement cycles of the structure model, and quickly converged to 0.55(9). Neutral atom scattering factors and anomalous dispersion correction were from ref.[27] Final geometrical calculations and drawings were carried out with the PARST program[28] and the XP utility of the Siemens package, respectively. CCDC-170711 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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