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LIQUID CHROMATOGRAPHY OF METAL COMPLEXES OF N-DISUBSTITUTED DITHIOCARBAMIC ACIDS

I. HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY OF NICKEL(II) BISDIALKYLDITHIOCARBAMATES*

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SUMMARY

The possibility of the separation and identification of nickel(II) bisdialkyl-dithiocarbamate (DTC) complexes by high-performance liquid-solid chromatography has been studied. Silica gel was used as the stationary phase and chloroform-cyclohexane mixtures as the mobile phase. The capacity factors (k') of dimethyl- up to dioctyl-DTC were measured as a function of the mobile phase composition. The influence of the branching of some N-dialkyl substituents was studied. The relationship between $\log k'$ and the number of carbon atoms in the alkyl substituents was investigated.

The separation of DTC complex mixtures is very complicated because exchange reactions have been observed to take place between every pair of complexes and, as a result of these reactions, new compounds are formed.

INTRODUCTION

Metal complexes of dithiocarbamic acid are a group of substances with very wide use in industry and especially in agriculture as active fungicides¹. As toxic activity of some dithiocarbamate (DTC) complexes has been observed in mammals and man², it is important to develop rapid and sensitive methods for their detection and determination for protection of the environment.

Chromatographic methods are very suitable for this purpose. Many workers

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have used column adsorption chromatography³⁻⁷, thin-layer chromatography⁸⁻²⁵ and gas-liquid chromatography²⁶⁻³⁴ for the study of metal DTC complexes. Recently studies have been published on the high-performance liquid chromatography (HPLC) of some of these complexes^{35,39,40}.

In our research we have been interested in the systematic study of metal complexes of DTC by HPLC. In this paper, we present results concerning the influence of N-alkyl substituents on the chromatographic properties of nickel(II) bisdialkyl-DTC complexes. These complexes exhibit a relatively high toxicity: the rat LD₅₀ for nickel(II) bisdimethyldithiocarbamate is 100 mg/kg (ref. 2).

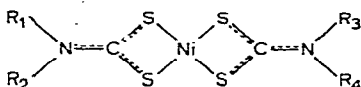
The second reason for our interest in nickel(II) DTC complexes was the fact that their formation is used in organic functional group analysis as a method for the detection and determination of the secondary amines³⁶. The combination of the chemical reaction with HPLC will improve the detection, identification and determination of secondary amines.

EXPERIMENTAL

The HPLC equipment consisted of a Waters Model 6000 pump (Waters Assoc., Milford, Mass., U.S.A.), a PM4 spectrophotometer (Zeiss, Oberkochen, G.F.R.) and a DuPont refractive index (RI) detector (DuPont Instruments, Wilmington, Del., U.S.A.). A stainless-steel column (200 × 4.5 mm I.D.) was packed with LiChrosorb SI 60 (10 μm) (Merck, Darmstadt, G.F.R.). The silica gel was dried for 6 h at 120° and the column was filled by a balanced-density slurry technique using tetrabromoethane and benzene as the suspending liquid. The initial packing pressure was 500 atm. After filling the column, the packing was washed with 300 ml of *n*-heptane. The column, when subsequently tested with benzene as solute and *n*-heptane as mobile phase with flow-rate of 0.83 ml·min⁻¹ (inlet pressure 19 atm), had a reduced plate height of 6.

Chemicals

Nickel(II) bisdialkylthiocarbamates with the general structure



were prepared by the usual procedure from dialkylamines, carbon disulphide and nickel(II) chloride in the absence of oxygen¹. The solid products were recrystallized three times from chloroform, analysed by elemental analysis and characterized by UV and IR spectroscopy and melting-point determination.

We investigated the chromatographic properties of the basic series of complexes from bisdimethyl- to bisdioctyl-DTC and of some derivatives with branched substituents, viz., bismethylisopropyl-, bisdiisopropyl- and bisdiisobutyl-DTC.

Solutions 0.005 M in chloroform were prepared except for the dimethyl-DTC, the solubility of which in all common solvents is very low and for which we used a saturated solution in chloroform.

All chemicals used for the synthesis of DTC complexes were of analytical-

reagent grade (Lachema, Brno, Czechoslovakia). All solvents were dried with magnesium perchlorate and distilled.

Procedures

The solutions of nickel(II) bisdialkyl-DTC were freshly prepared for each series of experiments and if kept overnight were stored in a refrigerator. Samples of 0.5–1 μ l were introduced by direct on-column injection using a 5- μ l Hamilton HP 305 syringe. The mixtures of complexes were prepared either directly in the syringe or by mixing the solutions in a small vessel before injection.

Capacity ratios (k') were calculated assuming that *n*-pentane is an unretained substance. Each value of k' given is the arithmetic mean of four measurements.

RESULTS AND DISCUSSION

Several solvents and their combinations (chloroform, carbon tetrachloride, dichloromethane, cyclohexane, *n*-hexane and *n*-heptane) were studied as the mobile phase. The best results were obtained with the system chloroform–cyclohexane.

Fig. 1 shows the dependence of the logarithm of the capacity ratios on the eluotropic strength (ϵ^0) of the mobile phase for the eleven bisdialkyl-DTC complexes of nickel(II).

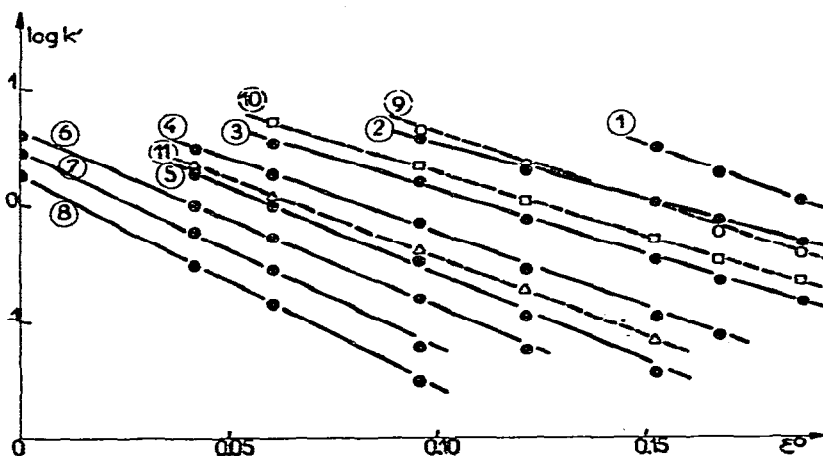


Fig. 1. Relationship between eluotropic strength (ϵ^0) of the mobile phase and $\log k'$ of Ni(II) bisdialkyl-DTC complexes. Dialkyl substituents: 1 = dimethyl; 2 = diethyl; 3 = dipropyl; 4 = dibutyl; 5 = dipentyl; 6 = dihexyl; 7 = diheptyl; 8 = dioctyl; 9 = methylisopropyl; 10 = diisopropyl; 11 = diisobutyl. Mobile phase: chloroform–cyclohexane mixtures.

The value of ϵ^0 for a mixture of two solvents A and B is calculated according to the following equation, derived by Snyder³⁷:

$$\epsilon^0 = \epsilon_A^0 + \frac{\log(N_B \cdot 10^{\alpha n_B (\epsilon_B^0 - \epsilon_A^0)} + 1 - N_B)}{\alpha n_B}$$

where N_B is the molar fraction of B, n_B the molecular size of solvent B and α the adsorbent activity function (= 1 in this case). The adsorption constants of di-*n*-alkyl-

substituted derivatives decrease with increasing eluotropic strength of the mobile phase and with increasing number of carbon atoms in the alkyl chains.

The branching of the alkyl chain increases the polarity of the diisopropyl derivative, which is more retained than the di-*n*-propyl-DTC complex. This increase in polarity (and consequently in k') can be related to the larger positive inductive effect of the isopropyl group. On the contrary, the diisobutyl complex is less retained than the di-*n*-butyl complex, which may be due to increased steric hindrance of the branched molecule.

The k' value of the nickel(II) bismethylisopropyl-DTC complex is very near that of nickel(II) bisdiethyl-DTC, but the order of elution depends on the composition of the mobile phase. When the concentration of chloroform in cyclohexane is less than 20% (v/v) ($\epsilon^0 < 0.15$), the influence of the methyl group is greater and k' is larger than for the latter complex. When a mobile phase with a higher chloroform concentration is used, the influence of the isopropyl group is evident; the k' values decrease owing to the high solubility of the isopropyl derivative in chloroform.

The dependence of the capacity ratios of symmetrical bisdialkyldithiocarbamates on the number of carbon atoms in the alkyl substituent is shown in Fig. 2 for different mobile phase compositions. The $\log k'$ versus carbon number graphs are linear.

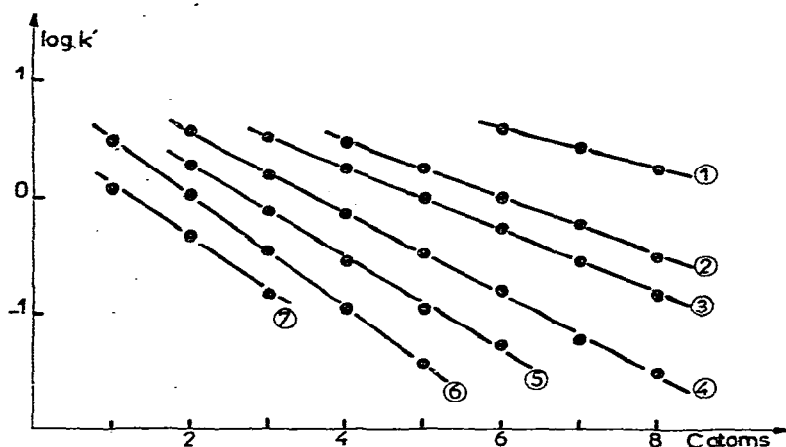


Fig. 2. Dependence of $\log k'$ on the number of carbon atoms in the alkyl chain of Ni(II) bisdialkyl-DTC complexes in cyclohexane-chloroform mixtures containing $x\%$ (v/v) of chloroform. Curves: 1, $x = 0$; 2, $x = 2$; 3, $x = 4$; 4, $x = 8$; 5, $x = 12,5$; 6, $x = 20$; 7, $x = 33,3$.

On the basis of these results, we tried to separate mixtures of nickel(II) bisdialkyl-DTC complexes. We noticed an interesting fact: when two complexes with different alkyl substituents were injected simultaneously on the column, three peaks were always obtained. The systematic occurrence of a third peak means that some reaction readily takes place between the two original symmetrical complexes. It is probable that it is the exchange of ligands, according to the equation



We determined the k' values of the third peaks for most combinations from diethyl- to dioctyldithiocarbamates of nickel(II). We omitted the dimethyl complex because of its very low solubility in the solvents used and its very low reactivity (which may be due, at least partly, to the low concentration). The relationship between the $\log k'$ values of nickel(II) DTC complexes with branched alkyl groups and their mixed-ligand complexes and the mobile phase eluotropic strength is shown in Fig. 3 as an example.

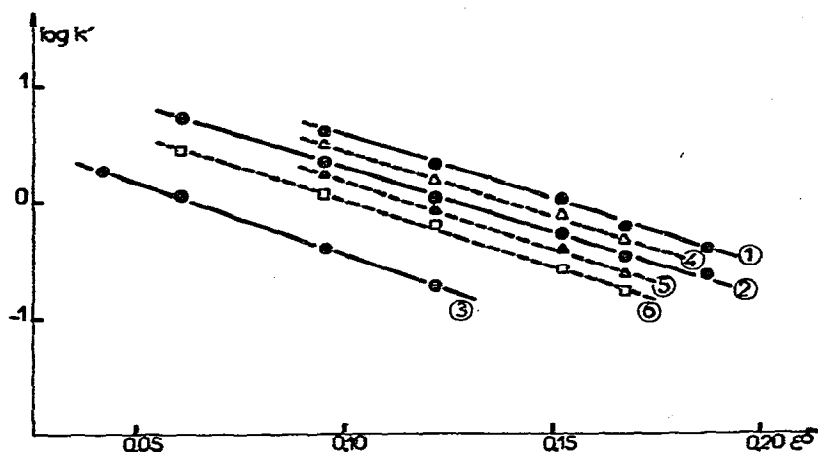


Fig. 3. Relationship between eluotropic strength (ϵ^0) of the mobile phase and $\log k'$ of Ni(II) bisdialkyl-DTC with branched alkyl substituents. Curves 1, 2 and 3, symmetrical complexes: 1 = bis-methylisopropyl; 2 = bisdiisopropyl; 3 = bisdiisobutyl. Curves 4, 5 and 6, mixed-ligand complexes: 4 = methylisopropyl and diisopropyl; 5 = methylisopropyl and diisobutyl; 6 = diisopropyl and diisobutyl.

Assuming that the third peaks correspond to the mixed-ligand complexes L_1 -Ni- L_2 , we compared the experimental k' values with values calculated according to the equation

$$\log k'_{L_1-Ni-L_2} = \frac{1}{2} (\log k'_{L_1-Ni-L_1} + \log k'_{L_2-Ni-L_2})$$

which assumes the independence of the contributions of the different groups of the molecule to the free energy of adsorption³⁸. The results obtained with the mobile phase of optimal composition (8% chloroform in cyclohexane) are illustrated in Fig. 4.

We observed a systematic discrepancy between the measured and calculated values. The larger the difference between the number of carbon atoms in ligands L_1 and L_2 , the larger was the deviation between the experimental and theoretical values of $\log k'$ of the mixed-ligand complexes formed. Owing to the influence of an asymmetrical structure, the mixed-ligand complex molecule acquires a dipole moment and its adsorption is stronger.

The velocity of the formation of the mixed-ligand complexes and their stability in solution are depending on the type of substituents on the nitrogen atom, on the solvent and naturally on the temperature.

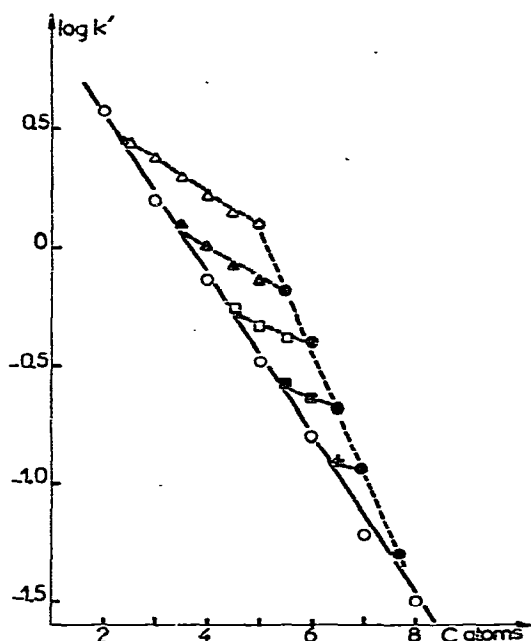


Fig. 4. Dependence of $\log k'$ on the number of carbon atoms in the alkyl chain of Ni(II) bisdialkyl-DTC and Ni(II) mixed-ligand DTC complexes. Mobile phase: 8% (v/v) chloroform in cyclohexane. \circ , Ni(II) bisdialkyl-DTC (alkyl = ethyl, propyl, ..., octyl). Ni(II) mixed-ligand complexes: \triangle , combinations of diethyl- with dipropyl-, dibutyl-, dipentyl-, dihexyl-, diheptyl- and dioctyl-DTC; \blacktriangle , combinations of dipropyl- with dibutyl-, dipentyl-, dihexyl- and diheptyl-DTC; \square , combinations of dibutyl- with dipentyl-, dihexyl- and diheptyl-DTC; \blacksquare , combinations of dipentyl- with dihexyl- and diheptyl-DTC; $+$, combination of dihexyl- with diheptyl-DTC; \bullet , combinations of dioctyl- with diethyl-, dipropyl-, dibutyl-, dipentyl-, dihexyl- and diheptyl-DTC.

According to our current results concerning the kinetics of ligand-exchange reactions, the stability of the mixed-ligand complexes is low at temperatures higher than 35° . Under such conditions, the peaks corresponding to these complexes cannot be detected. That is most probably the reason, why the existence of mixed-ligand complexes was not observed in the analysis of mixtures of nickel(III) bisdialkyl-DTC complexes by gas chromatography at temperatures of 240° or more²¹.

CONCLUSION

The results obtained for the series of nickel(II) bisdialkyl-DTC complexes indicate a substantial influence of the N-alkyl substituent and the mobile phase composition on the capacity ratios, which permits the choice of suitable conditions for the separation, identification and possible determination of individual complexes. The limit of detection using a UV detector is in the range 10^{-9} – 10^{-10} M of nickel (at a wavelength of 325 nm).

As primary and tertiary amines do not react during the formation of nickel(II) DTC complexes, the combination of this reaction and analysis by the HPLC makes the identification of secondary amines possible.

The separation and quantitation of a mixture of different nickel(II) DTC com-

plexes, however, is severely complicated by the formation of new complexes by ligand exchange reactions between each pair of original DTC derivatives. The verification of the assumption that the new compounds formed are mixed-ligand complexes, the investigation of their kinetics of formation and the study of the possible formation of mixed complexes with other metal ions and ligands will be reported in further papers.

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