

Synthesis and Extraction Ability of Some Polyether Bisthioureas and Ureas

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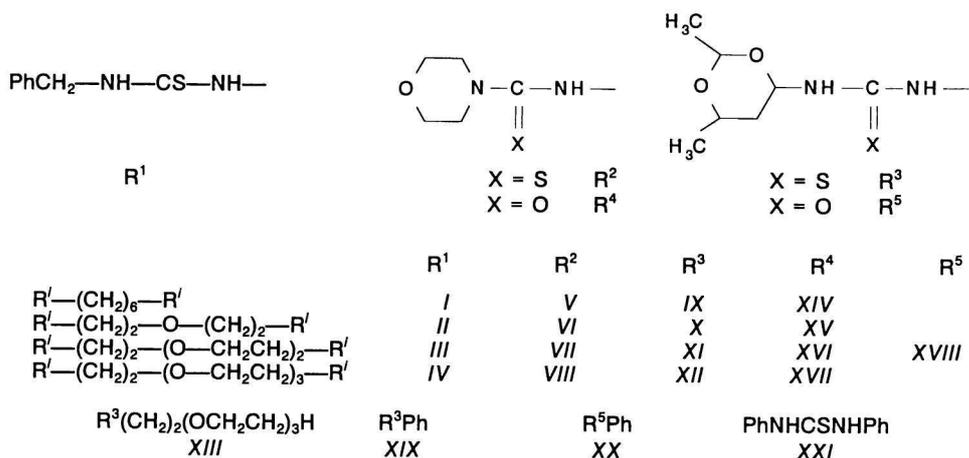
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For investigations of complexation properties, a series of bisthioureas in which the two thiourea groupings are linked with a polyether chain have been prepared by addition of amines to the corresponding isothiocyanates. The ability of the synthesized compounds to extract metal picrates from aqueous solutions was studied. It was found that, while all the thioureas extracted Ag^+ and Cu^{2+} ions, only some bisthioureas extracted Pb^{2+} and Cd^{2+} ions, and some other bisthioureas also relatively well extracted Ca^{2+} ions. On reaction with 2,4,6-trimethylbenzotriazole oxide, the thioureas were converted into urea derivatives which, however, exhibited practically no extraction ability.

The importance of ionophores, *i.e.* neutral organic molecules capable of forming stable complexes with metal ions, is well illustrated by the fact that extensive studies of their synthesis and properties were awarded by the Nobel prize in 1987. Principally, compounds of this type may be divided into three main groups: acyclic podands, cyclic coronands, and bicyclic cryptands [1, 2]. In general, podands have weaker complexing ability than cyclic ionophores (*i.e.* cryptands and coronands), however, the complexing abilities of some of them fully match those of cyclic derivatives, as evidenced by the example of 1,13-bis(8-quinolyl)-1,4,7,10,13-pentaoxatridecane (commercial name Kryptofix 5) [3]. Moreover, podands find an important use as ionophore components of liquid membranes in ion-selective electrodes where their high selectivity at relatively lower stability constant of the ligand may be of advantage [4]. The simpler structure of podands undoubtedly represents an advantage because they can be pre-

pared by less demanding and cheaper methods. From this viewpoint, it appears important to study complexing properties also of simple compounds promising in this respect.

We decided to synthesize a series of substituted thioureas and ureas $I-XX$ (see formulas) and study their complexing properties by the method of simple extraction of selected picrates [5–8]. The formation of complexes between the thiourea grouping and ions of heavy metals is generally known [9]. It was of interest whether linking two thiourea groups by a polyether chain would result in podand properties of the synthesized compounds (*i.e.* whether the compounds would extract ions of alkali or alkaline-earth metals). Moreover, the series of prepared compounds could give answers to other questions such as what is the effect of substituent on an *N'*-thiourea group, or of replacement of a thiourea by a urea group, *etc.* on the extraction ability of the compound. In the present paper we describe the synthesis of



bisthioureas and study of their ability to extract metal ions from aqueous solutions of the corresponding picrates.

EXPERIMENTAL

Described procedures were used for preparation of the α,ω -diamines [10], α,ω -diisothiocyanates [11, 12], *rel*-(2*S*,4*R*,6*S*)-2,6-dimethyl-4-isothiocyanato-1,3-dioxane (DID) [13], *rel*-(2*S*,4*R*,6*S*)-2,6-dimethyl-4-*N'*-phenylthioureido-1,3-dioxane (XIX) [13], and 2,4,6-trimethylbenzotrile oxide [14]. The remaining amines used and *N,N'*-diphenylthiourea (XXI) were commercial products which were distilled or crystallized prior to use.

Melting points of the compounds were determined on a Kofler block. Infrared spectra were measured on a Specord IR 75 instrument, ^1H NMR spectra on a Tesla BS 487A (at 80 MHz) or Varian XL 200 (at 200 MHz) instrument, ^{13}C NMR spectra on a Tesla BS 567 spectrometer at 23.15 MHz. The absorbance of picrate solutions was measured on a UV-VIS Varian DMS 200 spectrometer.

Thioureas I—XIII

An ethereal solution of the corresponding amine (for I—IV benzylamine, V—VIII morpholine, IXa—IXc 1,6-diaminohexane, X 1,5-diamino-3-oxapentane, XI 1,8-diamino-3,6-dioxaoctane, XII 1,11-diamino-3,6,9-trioxaundecane, XIII 3,6,9-trioxaundecylamine) was added at -10°C to an ethereal solution of the isothiocyanate (for I, V 1,6-diisothiocyanatohexane, II, VI 1,5-diisothiocyanato-3-oxapentane, III, VII 1,8-diisothiocyanato-3,6-dioxaoctane, IV, VIII 1,11-diisothiocyanato-3,6,9-trioxaundecane, IXa—IXc, X—XIII DID) in the amount of substances ratio 2.2 : 1 for I—VIII, 1 : 1.9 for IX—XII, 1.3 : 1 for XIII. After stirring at room temperature for 1 h, the solvent was evaporated and the residue chromatographed on a column of silica gel. Crystalline products were purified by crystallization. Using this procedure, the following thioureas were prepared:

1,6-Bis(N'-benzylthioureido)hexane (I), yield = 1.5 g (72 %), m.p. = $157\text{--}159^\circ\text{C}$ (acetone—light petroleum). For $\text{C}_{22}\text{H}_{30}\text{N}_4\text{S}_2$ ($M_r = 414.63$) $w_i(\text{calc.})$: 63.73 % C, 7.29 % H, 13.51 % N; $w_i(\text{found})$: 63.42 % C, 7.03 % H, 13.62 % N. ^1H NMR spectrum ($\text{DMSO-}d_6$), δ : 1.55 (br s, 4H, CH_2), 1.70 (m, 4H, CH_2), 3.60 (m, 4H, CH_2), 4.91 (d, 4H, CH_2), 7.56 (s, 10H, H_{arom}), 7.75 (t, 2H, NH), 8.05 (t, 2H, NH). ^{13}C NMR spectrum ($\text{DMSO-}d_6$), δ : 26.1, 28.6, 43.4, 46.8, 126.7, 127.2, 128.1, 138.3, 182.2.

1,5-Bis(N'-benzylthioureido)-3-oxapentane (II), yield = 1.43 g (68 %), m.p. = $110\text{--}112^\circ\text{C}$ (ethanol). For $\text{C}_{20}\text{H}_{26}\text{N}_4\text{OS}_2$ ($M_r = 402.57$) $w_i(\text{calc.})$: 59.67 % C,

6.51 % H, 13.92 % N; $w_i(\text{found})$: 59.88 % C, 6.65 % H, 13.72 % N. ^1H NMR spectrum (CDCl_3), δ : 3.45—3.95 (m, 8H, CH_2), 4.75 (s, 4H, CH_2), 7.35 (s, 10H, H_{arom}), 6.90—7.50 (m, 4H, NH). ^{13}C NMR spectrum (CD_3COCD_3), δ : 44.8, 48.5, 70.1, 127.8, 128.3, 129.1, 139.8, 184.3.

1,8-Bis(N'-benzylthioureido)-3,6-dioxaoctane (III), yield = 1.17 g (61 %), m.p. = $87\text{--}89^\circ\text{C}$ (ethanol—water). For $\text{C}_{22}\text{H}_{30}\text{N}_4\text{O}_2\text{S}_2$ ($M_r = 446.63$) $w_i(\text{calc.})$: 59.16 % C, 6.77 % H, 12.55 % N; $w_i(\text{found})$: 58.89 % C, 6.53 % H, 12.21 % N. ^1H NMR spectrum (CDCl_3), δ : 3.45 (s, 4H, CH_2), 3.54 (br s, 8H, CH_2), 4.70 (d, 4H, CH_2), 6.73 (m, 2H, NH), 7.18 (m, 2H, NH), 7.35 (s, 10H, H_{arom}). ^{13}C NMR spectrum (CDCl_3), δ : 44.4, 48.6, 69.9, 70.1, 127.6, 127.7, 128.7, 137.6, 182.4.

1,11-Bis(N'-benzylthioureido)-3,6,9-trioxaundecane (IV), yield = 1.37 g (70 %), oil. For $\text{C}_{24}\text{H}_{34}\text{N}_4\text{O}_3\text{S}_2$ ($M_r = 490.68$) $w_i(\text{calc.})$: 58.75 % C, 6.99 % H, 11.42 % N; $w_i(\text{found})$: 58.43 % C, 6.58 % H, 11.24 % N. ^1H NMR spectrum (CDCl_3), δ : 3.49 (s, 8H, CH_2), 3.57 (br s, 8H, CH_2), 4.71 (d, 4H, CH_2), 6.75 (m, 2H, NH), 7.13 (m, 2H, NH), 7.35 (s, 10H, H_{arom}). ^{13}C NMR spectrum (CDCl_3), δ : 44.4, 48.6, 69.9, 70.0, 127.6, 128.7, 137.8, 182.8.

1,6-Bis(morpholinothioureido)hexane (V), yield = 1.55 g (56 %), m.p. = $120\text{--}122^\circ\text{C}$ (acetone—light petroleum). For $\text{C}_{16}\text{H}_{30}\text{N}_4\text{O}_2\text{S}_2$ ($M_r = 374.56$) $w_i(\text{calc.})$: 51.31 % C, 8.07 % H, 14.96 % N; $w_i(\text{found})$: 51.14 % C, 8.32 % H, 14.73 % N. ^1H NMR spectrum (CDCl_3), δ : 1.48 (br s, 4H, CH_2), 1.65 (m, 4H, CH_2), 3.68 (m, 4H, CH_2), 3.81 (br s, 16H, CH_2), 5.88 (t, 2H, NH). ^{13}C NMR spectrum (CDCl_3), δ : 26.4, 29.2, 46.1, 47.9, 66.5, 183.2.

1,5-Bis(morpholinothioureido)-3-oxapentane (VI), yield = 2.35 g (81 %), m.p. = $113\text{--}115^\circ\text{C}$ (acetone—light petroleum). For $\text{C}_{14}\text{H}_{26}\text{N}_4\text{O}_3\text{S}_2$ ($M_r = 362.51$) $w_i(\text{calc.})$: 46.39 % C, 7.23 % H, 15.43 % N; $w_i(\text{found})$: 46.72 % C, 7.38 % H, 15.12 % N. ^1H NMR spectrum (CDCl_3), δ : 3.72 (t, 4H, CH_2), 3.80 (br s, 16H, CH_2), 3.90 (m, 4H, CH_2), 6.10 (t, 2H, NH). ^{13}C NMR spectrum (CDCl_3), δ : 45.7, 47.7, 66.1, 69.3, 182.6.

1,8-Bis(morpholinothioureido)-3,6-dioxaoctane (VII), yield = 2.33 g (90 %), m.p. = $103\text{--}105^\circ\text{C}$ (acetone—light petroleum). For $\text{C}_{16}\text{H}_{30}\text{N}_4\text{O}_4\text{S}_2$ ($M_r = 406.56$) $w_i(\text{calc.})$: 47.27 % C, 7.44 % H, 13.78 % N; $w_i(\text{found})$: 47.01 % C, 7.53 % H, 13.91 % N. ^1H NMR spectrum (CDCl_3), δ : 3.67 (m, 8H, CH_2), 3.82 (br s, 16H, CH_2), 3.91 (m, 4H, CH_2), 6.17 (t, 2H, NH). ^{13}C NMR spectrum (CDCl_3), δ : 45.7, 47.6, 66.1, 69.3, 70.1, 182.7.

1,11-Bis(morpholinothioureido)-3,6,9-trioxaundecane (VIII), yield = 1.34 g (55 %), m.p. = $101\text{--}103^\circ\text{C}$ (acetone—light petroleum). For $\text{C}_{18}\text{H}_{34}\text{N}_4\text{O}_5\text{S}_2$ ($M_r = 450.61$) $w_i(\text{calc.})$: 47.98 % C, 7.61 % H, 12.43 % N; $w_i(\text{found})$: 48.22 % C, 7.42 % H, 12.56 % N. ^1H NMR spectrum (CDCl_3), δ : 3.67 (m, 12H,

CH₂), 3.82 (br s, 16H, CH₂), 3.91 (m, 4H, CH₂), 6.33 (t, 2H, NH). ¹³C NMR spectrum (CDCl₃), δ: 45.7, 47.6, 66.2, 69.3, 69.9, 70.4, 182.6.

1,6-Bis[N'-(2,6-dimethyl-1,3-dioxan-4-yl)thioureido]hexane (IXa–IXc), yield = 4.57 g (80 %) of a mixture of diastereoisomers which after chromatography in chloroform–acetone ($\varphi_r = 5 : 1$) afforded: *1,6-bis[N'-(rel-(2S,4R,6S)-2,6-dimethyl-1,3-dioxan-4-yl)thioureido]hexane (IXa)*, yield = 3 g (53 %), m.p. = 173–175 °C (acetonitrile–light petroleum). For C₂₀H₃₈N₄O₄S₂ ($M_r = 462.68$) $w_i(\text{calc.})$: 51.92 % C, 8.28 % H, 12.10 % N; $w_i(\text{found})$: 51.79 % C, 8.30 % H, 11.72 % N. ¹H NMR spectrum (CD₃COCD₃), δ: 1.13 (d, 6H, CH₃), 1.19 (d, 6H, CH₃), 1.37 (m, 4H, CH₂), 1.62 (m, 4H, CH₂), 1.76 (m, 4H, CH₂), 3.58 (m, 4H, CH₂), 4.10 (m, 2H, CH), 5.08 (q, 2H, CH), 5.58 (m, 2H, CH), 7.14 (br m, 2H, NH), 7.47 (br m, 2H, NH). ¹³C NMR spectrum (DMSO-*d*₆), δ: 20.7, 21.1, 25.9, 28.3, 35.1, 48.5, 67.1, 76.2, 90.8, 182.1; *1-[N'-(rel-(2S,4R,6S)-2,6-dimethyl-1,3-dioxan-4-yl)thioureido]-6-[N'-(rel-(2S,4S,6S)-2,6-dimethyl-1,3-dioxan-4-yl)thioureido]hexane (IXb)*, yield = 0.2 g (4 %), m.p. = 158–160 °C (acetonitrile–light petroleum); $w_i(\text{found})$: 51.73 % C, 8.25 % H, 11.76 % N. ¹H NMR spectrum (CD₃COCD₃), δ: 1.13 (d, 3H, CH₃), 1.17 (d, 3H, CH₃), 1.19 (d, 3H, CH₃), 1.22 (d, 3H, CH₃), 1.37 (m, 4H, CH₂), 1.60 (m, 4H, CH₂), 1.76 (m, 2H, CH₂), 1.78 (m, 2H, CH₂), 3.55 (m, 4H, CH₂), 3.81 (m, 1H, CH), 4.11 (m, 1H, CH), 4.80 (q, 1H, CH), 5.08 (q, 1H, CH), 5.58 (m, 1H, CH), 5.69 (m, 1H, CH), 7.16 (br m, 2H, NH), 7.23 (br m, 1H, NH), 7.52 (br m, 1H, NH). ¹³C NMR spectrum (DMSO-*d*₆), δ: 20.6, 21.0, 25.9, 28.3, 35.1, 37.1, 43.8, 48.5, 67.1, 70.8, 76.2, 79.9, 90.8, 96.0, 182.0; *1,6-bis[N'-(rel-(2S,4S,6S)-2,6-dimethyl-1,3-dioxan-4-yl)thioureido]hexane (IXc)*, yield = 0.8 g (14 %), m.p. = 178–180 °C (acetone–light petroleum); $w_i(\text{found})$: 51.63 % C, 8.20 % H, 11.79 % N. ¹H NMR spectrum (CD₃COCD₃), δ: 1.17 (d, 6H, CH₃), 1.21 (d, 6H, CH₃), 1.36 (m, 4H, CH₂), 1.59 (m, 4H, CH₂), 1.78 (m, 4H, CH₂), 3.54 (m, 4H, CH₂), 3.81 (m, 2H, CH), 4.80 (q, 2H, CH), 5.66 (m, 2H, CH), 7.16 (br m, 2H, NH), 7.22 (br m, 2H, NH). ¹³C NMR spectrum (DMSO-*d*₆), δ: 20.6, 21.0, 25.9, 28.3, 37.1, 43.8, 70.8, 79.9, 96.0, 181.9.

1,5-Bis[N'-(2,6-dimethyl-1,3-dioxan-4-yl)thioureido]-3-oxa-pentane (X), chromatography in chloroform–acetone ($\varphi_r = 1 : 1$) afforded 4.48 g (64 %) of oily mixture of diastereoisomers. For C₁₈H₃₄N₄O₅S₂ ($M_r = 450.62$) $w_i(\text{calc.})$: 47.98 % C, 7.61 % H, 12.43 % N; $w_i(\text{found})$: 47.73 % C, 7.49 % H, 12.51 % N. ¹³C NMR spectrum (CD₃COCD₃) of dominant stereoisomer, δ: 21.2, 21.7, 38.4, 45.1, 70.9, 72.2, 81.7, 97.4, 184.1.

1,8-Bis[N'-(2,6-dimethyl-1,3-dioxan-4-yl)thioureido]-3,6-dioxaoctane (XI), chromatography in chloroform–acetone ($\varphi_r = 1 : 1$) afforded 3.7 g (51 %) of oily

mixture of diastereoisomers. For C₂₀H₃₈N₄O₆S₂ ($M_r = 494.68$) $w_i(\text{calc.})$: 48.56 % C, 7.74 % H, 11.33 % N; $w_i(\text{found})$: 48.79 % C, 7.63 % H, 11.52 % N. ¹³C NMR spectrum (CD₃COCD₃) of dominant stereoisomer, δ: 21.3, 21.7, 38.4, 48.1, 70.8, 70.9, 72.2, 81.7, 97.6, 184.1.

1,11-Bis[N'-(2,6-dimethyl-1,3-dioxan-4-yl)thioureido]-3,6,9-trioxaundecane (XII), chromatography in benzene–acetone ($\varphi_r = 1 : 1$) afforded 3 g (54 %) of oily mixture of diastereoisomers. For C₂₂H₄₂N₄O₇S₂ ($M_r = 538.73$) $w_i(\text{calc.})$: 49.05 % C, 7.86 % H, 10.40 % N; $w_i(\text{found})$: 49.30 % C, 7.61 % H, 10.58 % N. ¹³C NMR spectrum (CD₃COCD₃) of dominant stereoisomer, δ: 21.7, 21.8, 36.1, 45.4, 68.5, 70.0, 71.0, 71.8, 78.8, 92.1, 184.7.

N-(rel-(2S,4R,6S)-2,6-Dimethyl-1,3-dioxan-4-yl)-N'-3,6,9-trioxaundecylthiourea (XIII), yield = 3.2 g (78 %), m.p. = 91–93 °C. For C₁₅H₃₀N₂O₅S ($M_r = 350.48$) $w_i(\text{calc.})$: 51.41 % C, 8.63 % H, 7.99 % N; $w_i(\text{found})$: 51.32 % C, 8.42 % H, 8.11 % N. ¹³C NMR spectrum (CD₃COCD₃), δ: 15.5, 21.3, 21.8, 36.1, 42.3, 66.8, 68.5, 69.9, 70.5, 70.9, 71.1, 78.7, 92.0, 184.6.

Ureas XIV–XVIII and XX

A solution of 2,4,6-trimethylbenzotrile oxide in acetonitrile was added dropwise to stirred solutions of the corresponding thioureas V–VIII, XI, and XIX in acetonitrile (15 cm³) in the amount of substances ratio 2.2 : 1 for XIV, 2.1 : 1 for XV–XVII, 2.5 : 1 for XVIII, and 1.2 : 1 for XX at room temperature under nitrogen. The reaction was followed by TLC and was usually complete in 4–5 h at room temperature. After evaporation of the solvent, the product was separated from mesityl isothiocyanate by chromatography on silica gel and purified by crystallization from acetone–hexane. The following ureas were prepared by the above-described procedure:

1,6-Bis(morpholinoureido)hexane (XIV), yield = 0.87 g (79 %), m.p. = 184–185 °C. For C₁₆H₃₀N₄O₄ ($M_r = 342.44$) $w_i(\text{calc.})$: 56.12 % C, 8.83 % H, 16.36 % N; $w_i(\text{found})$: 55.85 % C, 8.56 % H, 16.21 % N. IR spectrum (CHCl₃), $\tilde{\nu}/\text{cm}^{-1}$: 1635 $\nu(\text{C}=\text{O})$. ¹H NMR spectrum (DMSO-*d*₆), δ: 1.65 (br s, 8H, CH₂), 3.40 (dt, 4H, CH₂), 3.62 (t, 8H, CH₂), 3.93 (t, 8H, CH₂), 6.79 (t, 2H, NH). ¹³C NMR spectrum (CDCl₃), δ: 25.8, 29.5, 39.7, 43.5, 65.8, 157.6.

1,5-Bis(morpholinoureido)-3-oxapentane (XV), yield = 0.87 g (96 %), m.p. = 116–118 °C. For C₁₄H₂₆N₄O₅ ($M_r = 330.39$) $w_i(\text{calc.})$: 50.89 % C, 7.39 % H, 16.96 % N; $w_i(\text{found})$: 51.05 % C, 8.12 % H, 16.85 % N. IR spectrum (CHCl₃), $\tilde{\nu}/\text{cm}^{-1}$: 1635 $\nu(\text{C}=\text{O})$. ¹H NMR spectrum (CDCl₃), δ: 3.25–3.90 (m, 24H, CH₂), 5.17 (m, 2H, NH). ¹³C NMR spectrum (CDCl₃), δ: 40.7, 44.0, 66.5, 70.3, 158.0.

1,8-Bis(morpholinoureido)-3,6-dioxaoctane (XVI), yield = 0.68 g (75 %), m.p. = 191–193 °C. For

$C_{16}H_{30}N_4O_6$ ($M_r = 374.44$) w_i (calc.): 51.32 % C, 8.08 % H, 14.96 % N; w_i (found): 51.43 % C, 7.89 % H, 14.73 % N. IR spectrum ($CHCl_3$), $\tilde{\nu}/cm^{-1}$: 1635 $\nu(C=O)$. 1H NMR spectrum ($CDCl_3$), δ : 3.25–3.95 (m, 28H, CH_2), 5.15 (m, 2H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ : 40.6, 44.0, 66.5, 70.2, 70.3, 157.9.

1,11-Bis(morpholinoureido)-3,6,9-trioxaundecane (XVII), yield = 0.7 g (75 %), m.p. = 109–111 °C. For $C_{18}H_{34}N_4O_7$ ($M_r = 418.49$) w_i (calc.): 51.66 % C, 8.19 % H, 13.39 % N; w_i (found): 51.53 % C, 7.93 % H, 13.24 % N. IR spectrum ($CHCl_3$), $\tilde{\nu}/cm^{-1}$: 1640 $\nu(C=O)$. 1H NMR spectrum ($CDCl_3$), δ : 3.25–4.00 (m, 32H, CH_2), 5.22 (m, 2H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ : 40.6, 44.0, 66.5, 70.1, 70.3, 70.4, 157.9.

1,8-Bis[N'-(2,6-dimethyl-1,3-dioxan-4-yl)ureido]-3,6-dioxaoctane (XVIII), yield = 0.61 g (84 %), m.p. = 147–150 °C. For $C_{20}H_{38}N_4O_8$ ($M_r = 462.54$) w_i (calc.): 51.94 % C, 8.28 % H, 12.11 % N; w_i (found): 51.73 % C, 8.32 % H, 11.94 % N. IR spectrum ($CHCl_3$), $\tilde{\nu}/cm^{-1}$: 1660 $\nu(C=O)$. ^{13}C NMR spectrum ($DMSO-d_6$) of dominant stereoisomer, δ : 20.6, 21.0, 38.9, 40.5, 69.4, 69.7, 70.8, 77.2, 95.7, 156.3.

rel-(2S,4S,6S)-2,6-Dimethyl-4-N'-phenylureido-1,3-dioxane (XX), yield = 0.22 g (87 %), m.p. = 194–195 °C. For $C_{13}H_{18}N_2O_3$ ($M_r = 250.30$) w_i (calc.): 62.38 % C, 7.25 % H, 11.19 % N; w_i (found): 62.48 % C, 7.13 % H, 11.24 % N. IR spectrum ($CHCl_3$), $\tilde{\nu}/cm^{-1}$: 1680 $\nu(C=O)$. 1H NMR spectrum ($CDCl_3$), δ : 1.25 (m, 6H, CH_3), 1.80 (m, 2H, CH_2), 3.92 (m, 1H, CH), 4.75 (q, 1H, CH), 5.67 (m, 1H, CH), 6.90 (m, 1H, NH), 7.25 (m, 5H, H_{arom}), 8.20 (m, 1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ : 21.0, 21.3, 39.3, 71.7, 78.9, 96.9, 118.7, 122.3, 134.4, 139.7, 154.8.

Extraction Experiments

A 5×10^{-3} M aqueous solution of the given metal picrate (3 cm^3) was extracted for 5 min with 10^{-2} M dichloromethane solution (3 cm^3) of the studied organic ligand I–XXI. An aliquot (1 cm^3) was taken from the aqueous layer, adjusted to 50 cm^3 with distilled water and absorbance at $\lambda = 354\text{ nm}$ of this solution was determined. The same procedure was applied to a blank experiment (an aqueous solution of the corresponding picrate was extracted with pure dichloromethane). From the obtained values of A and A_0 the percentages of the extraction were calculated; these are averages of four measurements and are given in Table 1.

RESULTS AND DISCUSSION

The bithioureas I–VIII were prepared from the known diisothiocyanates [11, 12] which were treated with benzylamine or morpholine. In the preparation

of bithioureas IX–XII as well as thioureas XIII and XIX we started from DID [13] which was treated with the appropriate amine. The ureas XIV–XVIII and XX were prepared from the corresponding thioureas (i.e. V–VIII, XI, and XIX) by reaction with 2,4,6-trimethylbenzoyl isocyanide [15].

Since the obtained 1,3-dioxane derivatives contain three chiral carbon atoms, compounds IX–XIII and XVIII–XX can exist in several diastereoisomeric forms. As we had already shown earlier [13, 16], in the addition of amines to DID (in which the methyl groups are equatorial and the isothiocyanate group axial) the arising thiourea group can undergo spontaneous epimerization (particularly in the presence of traces of acids) to give a 1,3-dioxane derivative with all the three groups in the equatorial position. This epimerization can be well observed by ^{13}C NMR spectroscopy because the axial-equatorial change of the substituent at C-4 is accompanied by characteristic downfield shift of the C-2 and C-6 signals of 1,3-dioxane ring resulting from the absence of the known γ -gauche effect [16].

In the case of bithioureas IX–XII, the reaction can lead to three diastereoisomers. In the first, the thiourea groups on both the 1,3-dioxane rings are axial, in the second the thiourea group on one dioxane ring is axial and on the other equatorial, and in the third one the thiourea groups on both dioxane rings are equatorial. In the case of bithiourea IX, we indeed isolated chromatographically all the three diastereoisomers mentioned and identified them. Originally, we intended also to follow the effect of stereochemistry on the complexing properties (i.e. whether there will be any difference in the extraction ability between the mentioned three diastereoisomers of compound IX). However, as we already mentioned, in solvents containing traces of acids the thiourea group undergoes spontaneous epimerization, in some solvents faster (e.g. in chloroform), in some slower (e.g. in acetone or dichloromethane). Also during formation of thiourea complexes with heavy metal ions the thiourea group may epimerize as we had proved for the reaction of *rel*-(2S,4R,5S,6S)-2,6-diethyl-4-isothiocyanato-5-methyl-1,3-dioxane with $NiCl_2$ [16]. This means that in extraction experiments with pure stereoisomer of substituted 1,3-dioxane already after its dissolution, and particularly during the extraction, an equilibrium between the individual diastereoisomers could be established and the experiment would be then performed with their mixture. For this reason, we did not separate compounds X–XII into pure diastereoisomers and carried out the extraction experiments with the obtained diastereoisomeric mixtures.

The extraction ability of the compounds was estimated by the known picrate test [5–8] in which an aqueous solution of the corresponding metal picrate

Table 1. Percents of Extraction of Metal Picrates from Aqueous Solutions by the Prepared Thioureas and Ureas

Compound	Li ⁺	Na ⁺	K ⁺	Rb ⁺	Cs ⁺	NH ₄ ⁺	Ca ²⁺	Ba ²⁺	Ag ⁺	Cu ²⁺	Pb ²⁺	Cd ²⁺
I	0	0	0	1	0	0	21	0	34	14	0	7
II	7	3	6	7	7	5	46	5	96	77	38	64
III	5	3	3	6	1	4	35	5	97	75	37	56
IV	7	4	8	10	4	9	9	6	92	59	52	54
V	5	4	7	9	4	0	6	4	98	65	2	9
VI	5	6	5	13	2	6	9	9	97	60	8	13
VII	1	1	0	3	1	0	5	1	94	39	0	4
VIII	4	2	3	5	3	0	6	6	96	46	11	8
IX	2	0	0	3	0	0	2	0	95	69	54	35
X	0	0	2	1	0	0	2	0	94	67	13	18
XI	0	0	0	1	0	0	2	0	94	72	20	24
XII	0	0	0	4	0	0	2	0	94	70	23	20
XIII	2	0	1	0	1	4	2	0	92	26	3	0
XIX	4	0	0	0	0	1	4	2	93	62	3	3
XXI	1	1	1	0	0	0	2	1	94	71	6	0
XIV	0	0	3	4	0	0	3	2	9	3	0	0
XV	0	0	0	0	0	0	2	3	5	1	0	0
XVI	0	0	0	0	0	0	2	2	8	0	1	4
XVII	0	0	0	0	0	0	1	0	4	1	0	3
XVIII	6	6	8	5	6	7	5	2	6	7	9	2
XX	4	0	0	0	0	0	2	3	0	0	1	1

* Owing to the low solubility the saturated solution of organic ligand in dichloromethane was used.

was extracted with a solution of the studied organic ligand in dichloromethane. The decrease in the concentration of the picrate in the aqueous phase after extraction was followed spectrophotometrically at $\lambda = 354$ nm. The thus obtained absorbance values were compared with those of a blank and the extraction ability of the corresponding ligand was expressed in percents

$$\text{extraction/\%} = 100(A_b - A)/A_b$$

where A_b is the absorbance in the blank experiment (*i.e.* after extraction with dichloromethane without the organic ligand) and A is the absorbance of the sample (*i.e.* after extraction with dichloromethane solution of the organic ligand). The obtained results are listed in Table 1. As seen, all the compounds with thiourea group (*i.e.* I–XIII, XIX, and XXI) markedly extract heavy metal ions such as Ag^+ and Cu^{2+} . Accordingly, the thiourea group as such is responsible for complexation of these ions. On the other hand, compounds with only one thiourea group (XIII, XIX, and XXI), as well as the bismorpholine compounds V–VIII, do not extract ions Cd^{2+} and Pb^{2+} from aqueous solutions. However, these ions are relatively well extracted with the bithioureas II–IV and IX–XII, respectively. Of all the ligands studied, only compounds I–III exhibited relatively good complexing properties for the Ca^{2+} cation; all other compounds extracted from aqueous solutions neither alkali metal ions nor NH_4^+ , Ca^{2+} , and Ba^{2+} ions.

From the data in Table 1 we can further see that in all the cases studied only the sulfur atom in the thiourea grouping participated in the complexation because the studied urea derivatives XIV–XVIII and XX exhibited practically no extraction power. The

obtained results thus indicate that in the studied compounds neither oxygen atoms of the polyether chain nor oxygen and nitrogen atoms of the urea group or the heterocycle participate in the complexation. Consequently, we cannot expect typical podand properties from the compounds under investigation.

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