SYNTHESIS OF SOME SALICYLIC ACID DERIVATIVES AND STUDIES OF THEIR INTERACTION WITH URANYL ION

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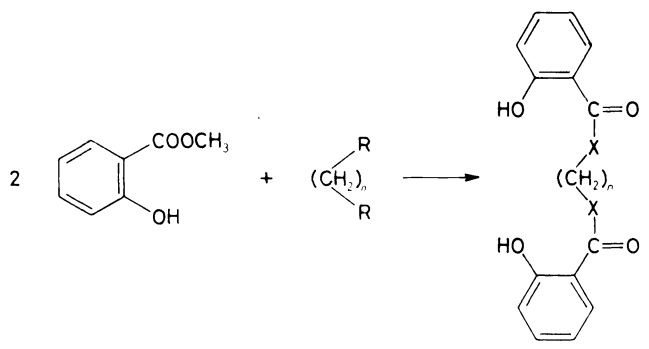
Some unsubstituted and substituted bis-derivatives of salicylic acid have been synthesized and their acidity constants determined spectrophotometrically in 61·10% aqueous ethanol. The stability constants of complexes these compounds form with UO_2^{2+}-ion were determined spectrophotometrically using the method of continuous variation under following conditions: pH 3·58 and 3·98, 61·10% aqueous ethanol, $\mu = 0{\cdot}5$ (LiCl), 25 ± 1°C.

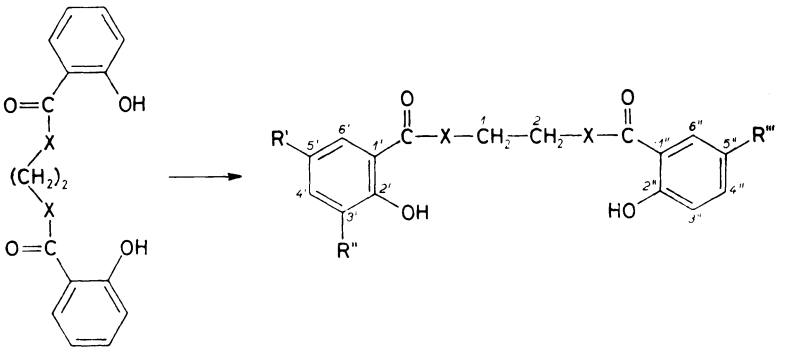
In our previous papers[1,2] the synthesis of some derivatives of salicylic acid (*I*–*IV*, *VIII* and *IX*) has been described. In the present paper we report the preparation of several new salicylic acid derivatives: 1,6-bis(salicyloyloxy)hexane (*V*), 1,7-bis(salicyloyloxy)heptane (*VI*), 1,8-bis(salicyloyloxy)octane (*VII*), and N,N'-disalicyloyl--1,4-butanediamine (*X*), according to Scheme 1. In addition, some nitro derivatives of salicylic acid such as 5'-nitro-1,2-bis(salicyloyloxy)ethane (*XI*), 5',5''-dinitro-1,2-



I, R = OH ; *n* = 2 ; X = O
II, R = OH ; *n* = 3 ; X = O
III, R = OH ; *n* = 4 ; X = O
IV, R = OH ; *n* = 5 ; X = O
V, R = OH ; *n* = 6 ; X = O
VI, R = OH ; *n* = 7 ; X = O
VII, R = OH ; *n* = 8 ; X = O
VIII, R = NH_2 ; *n* = 2 ; X = NH
IX, R = NH_2 ; *n* = 3 ; X = NH
X, R = NH_2 ; *n* = 4 ; X = NH

SCHEME 1

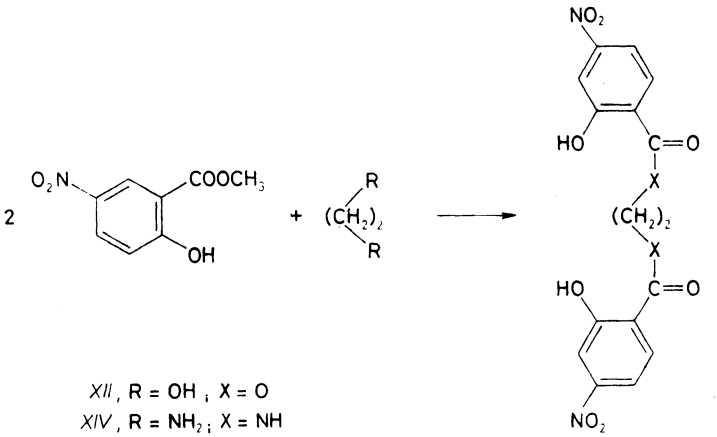
-bis(salicyloyloxy)ethane (*XII*), 3′,5″-dinitro-1,2-bis(salicyloyloxy)ethane (*XIII*) and 5′,5″-dinitro-N,N′-disalicyloyl-1,2-ethanediamine (*XIV*) are presented in Scheme 2. Alternatively, the synthesis of compounds *XII* and *XIV* is presented in Scheme 3.



A

XI, R′ = NO_2 ; R″, R‴ = H ; X = O
XII, R′, R‴ = NO_2 ; R″ = H ; X = O
XIII, R′ = H ; R″, R‴ = NO_2 ; X = O
XIV, R′, R‴ = NO_2 ; R″ = H ; X = NH

SCHEME 2



XII, R = OH ; X = O
XIV, R = NH_2 ; X = NH

SCHEME 3

In formulae *XII* and *XIV* correct substituent position on benzene rings are: 2-HO, 5-NO_2.

Determination of the acidity constants of newly synthesized compounds, being diprotic acids, and of the stability constants of complexes these compounds form with UO_2^{2+}-ion was carried out by spectrophotometric methods[3,4].

At pH 4 the compounds are in H_2L form. Thus, the apparent stability constant (β') of the complex UO_2L can be expressed as

$$\beta' = \frac{|UO_2L|\,|H_3O^+|^2}{|UO_2^{2+}|\,|H_2L|} = \frac{A/A_{ex}}{c_x(1 - A/A_{ex})^2},$$

where A is the measured absorbance (corrected for the absorbance of UO_2^{2+}-ion and ligand if they absorb at the same analytical wavelength); A_{ex} is extrapolated (calculated) absorbance and c_x is the concentration of complex. The stability constant (β) of the complex was calculated by equation

$$\beta = \beta'\alpha(L(H)),$$

where $\alpha(L(H))$ is given as

$$\alpha(L(H)) = 1 + \frac{|H_3O^+|}{K_2} + \frac{|H_3O^+|^2}{K_1K_2}.$$

Here, K_1 and K_2 are the acidity constants of synthesized ligands.

EXPERIMENTAL

The IR spectra (in cm^{-1}) were recorded with a Perkin–Elmer 457 spectrometer. The chemical shifts are given in ppm; symbols s, d, dd, t, q and m denote singlet, doublet, double doublet, triplet, quartet, and multiplet, respectively. The ^1H NMR spectra were recorded with a Varian 60A instrument. The mass spectra were measured with a Varian CH-5 spectrometer (the first number denotes the m/z value, and the ion abundances are given in parentheses). The melting points were determined with a Büchi SMP-20 apparatus and are not corrected. The spectrophotometric measurements were carried out on a UV-VIS Specord, Zeiss-Jena at room temperature 25 ± 1°C in a matched quartz cells having a 1 cm pathlength.

All chemicals used were of at least analytical-reagent grade. The purified synthesized compounds were kept protected from light and their stock solutions in concentration of $2{\cdot}5 \cdot 10^{-4}$ to $1 \cdot 10^{-2}$ mol dm^{-3} (depending on their solubility) in 61·10% aqueous ethanol were prepared from the vacuum dried preparations by accurate weighing. Solutions for the determination of acidity constants were obtained from stock solutions by dilution in buffer systems in 61·10% ethanol of known pH (pH 1·60—11·30; ΔpH 0·2, $\mu = 0{\cdot}5$ (LiCl)). The absorbances of the solutions were measured at analytical wavelength 250 nm for the compound *V*; 325 nm for the compound *X*; 333 nm for the compounds *III*, *VI*, *VII* and *XII*, and 385 nm for the compound *XIV*.

The solutions for the determination of stability constants of complexes of UO_2^{2+}-ion and the derivatives of salicylic acid were prepared in 61·10% ethanol ($\mu = 0{\cdot}5$ (LiCl) at pH 3·58 and 3·98). Absorbances of these solutions were measured at the wavelengths of 240 and 308 nm for compounds *I*—*VII* (Scheme 1); at 240 and 303 nm for compounds *VIII*—*X*; at 303 and 312 nm for compound *XII* and at 308 and 317 nm for compound *XIV*. The stock solution of uranyl nitrate in a concentration of 0·05 mol dm^{-3} in 61·10% ethanol was standardised gravimetrically with 8-hydroxyquinoline as precipitating reagent[5]. Buffer solutions of suitable pH values were

prepared by adding the proper volumes of glycine (HA of concentration 0·1027 mol dm^{-3} or citric acid of concentration $2·124 . 10^{-2}$ mol dm^{-3}) to a $9·396 . 10^{-2}$ mol dm^{-3} lithium hydroxide, all solutions having $\mu = 0·5$ (LiCl) in 61·10% aqueous ethanol. The pH values for various ratios of HA/A^- in 61·10% aqueous ethanol, $\mu = 0·5$ were calculated previously from the measured potentials and obtained values of E^0 for the glass electrode in the same solution[6].

The 61·10% aqueous ethanol was prepared by weight (±0·01%) from ethanol of reagent grade purified by distillation (the 78°C fraction, having 6·2% of water was used) with demineralized and boiled water (specific electric resistance $> 10^6$ Ω cm).

Preparation of α,ω-bis(salicyloyloxy)alkanes *V*– *VII*

Methyl salicylate (30·40 g, 0·20 mol); α,ω-alkanediol (0·11 mol) and sodium (0·25 g, 0·011 mol) were mixed in a distillation flask. The reaction mixture was heated gradually in an oil bath at atmospheric pressure, while methanol and the excess of α,ω-alkanediol were slowly removed by vacuum distillation. The total reaction time was 2 h. After the distillation was completed, distilled water (150 cm^3) and hydrochloric acid (1 : 1, to pH 6–7) were added to the distillation residue. Reaction product was extracted by ether and the obtained extract was dried with anhydrous sodium sulfate. After removal of Na_2SO_4 and ether 30·70 g (86%); 33·47 g (90%); 30·50 g (79%) of crude product *V*, *VI* or *VII* were obtained, respectively. Recrystallisations from 95% ethanol (150 cm^3) gave finally 13·70 g (38%) of pure compound *V*, m.p. 78°C; 19·66 g (53%) of pure compound *VI*, m.p. 68°C and 7·80 g (20%) of pure compound *VII*, m.p. 69–70°C, respectively.

1,6-*Bis(salicyloyloxy)hexane* (V). IR spectrum (KBr, ν_{max}): 3 450 (O—H), 3 140 (C—H, arom.), 2 940, 2 840 (C—H), aliph.), 1 670 (C=O, ester.), 1 615, 1 590 (C=C, arom.), 1 490, 1 470 (C=C, C—H). ^{1}H NMR spectrum ($CDCl_3$): 1·60 m, 8 H; 4·30 t, 4 H; 6·85 m, 4 H; 7·40 m, 2 H; 7·80 dd, 2 H. Mass spectrum (*m/z*, rel. %): 358 (M^+ 11), 139 (13), 121 (100), 120 (39), 92 (13), 83 (13), 82 (34), 55 (22). For $C_{20}H_{22}O_6$ (358·4) calculated: 67·02% C, 6·19% H; found: 67·26% C, 6·38% H.

1,7-*Bis(salicyloyloxy)heptane* (VI). IR spectrum (KBr, ν_{max}) 3 400 (O—H), 3 150 (C—H, arom.), 2 940, 2 860 (C—H, aliph.), 1 675 (C=O), 1 615, 1 595 (C=C, arom.) 1 490, 1 470 (C=C, C—H). ^{1}H NMR spectrum ($CDCl_3$): 1·25–2·00 m, 10 H; 4·20–4·50 t, 4 H; 6·70–7·15 m, 4 H; 7·30–7·60 m, 2 H; 7·90 dd, 2 H; 8·30 s, 2 H. Mass spectrum (*m/z*, rel. %): 372 (M^+, 9), 139 (29), 138 (26), 121 (100), 120 (40), 96 (24), 55 (31). For $C_{21}H_{24}O_6$ (372·4) calculated: 67·73% C, 6·50% H; found: 67·61% C, 6·53% H.

1,8-*Bis(salicyloyloxy)octane* (VII). IR spectrum (KBr, ν_{max}): 3 420 (O—H), 3 120 (C—H, arom.), 2 925, 2 850 (C—H, aliph.), 1 675 (C=O), 1 615, 1 590 (C=C, arom.), 1 485, 1 470 (C=C, C—H). ^{1}H NMR spectrum ($CDCl_3$): 1·50 m, 12 H; 4·30 t, 4 H; 6·70–7·00 m, 4 H; 7·25–7·55 m, 2 H; 7·85 dd, 2 H; 10·62 s, 2 H. Mass spectrum (*m/z*, rel %.): 386 (M^+, 11), 139 (39), 121 (100), 120 (47), 110 (17), 92 (12), 69 (22), 55 (17). For $C_{22}H_{26}O_6$ (386·4) calculated: 68·39% C, 6·74% H; found: 68·29% C, 6·84% H.

N,N′-Disalicyloyl-1,4-butanediamine (*X*)

1,4-Butanediamine (8·88 g, 0·11 mol) was carefully added to 30·40 g (0·20 mol) methyl salicylate placed in a distillation flask in an ice bath. The reaction mixture was left to stand in an ice bath at 0–5°C for half an hour and then heated gradually in an oil bath at atmospheric pressure to 150°C, whereupon methanol was gradually distilled off. The total reaction time was 2 h. After

the reaction was completed, 32·30 g (98%) of crude product was obtained. An aliquot part of the product (2 g) was purified by means of column chromatography (200 g silica gel; benzene–ethyl acetate 4 : 1) to give 0·96 g (47%) of pure product *X*. Recrystallization from ethyl acetate gave 0·56 g (28%) of pure compound *X*, m.p. 180°C. IR spectrum (KBr, ν_{max}): 3 550–3 410 (O—H, N—H), 3 060 (C—H, arom.), 2 940 (C—H, aliph.), 1 640 (C=O), 1 585, 1 535 (C=C, arom.), 1 535, 1 500 (C—N—H), 1 445, 1 365 (C—H), 1 325, 1 260 (C—N). ^{1}H NMR spectrum ($(CD_3)_2$.CO): 1·60 m, 4 H; 3·45 m, 4 H; 6·85 m, 4 H; 7·35 m, 2 H; 7·88 dd, 2 H; 8·81 t, 2 H; 12·75 s, 2 H. Mass spectrum (*m/z*, rel. %): 328 (M^+, 22), 191 (21), 190 (22), 179 (23), 164 (12), 121 (100), 120 (18), 93 (22), 70 (78), 65 (29). For $C_{18}H_{20}O_4N_2$ (328·4) calculated: 65·85% C, 6·10% H, 8·54% N; found: 65·85% C, 6·25% H, 8·37% N.

5-Nitro-1,2-bis(salicyloyloxy)ethane (*XI*), 5′,5″-Dinitro-1,2-bis(salicyloyloxy)ethane (*XII*) and 3′,5″-Dinitro-1,2-bis(salicyloyloxy)ethane (*XIII*)

Concentrated precooled nitric acid (10 cm^3) was carefully added to the precooled solution of 1,2-bis(salicyloyloxy)ethane (A, X = O, see Scheme 2; 1·51 g, 5 . 10^{-3} mol) in 20 cm^3 glacial acetic acid. Reaction mixture was left in an ice bath at 0–5°C for half an hour and after that at room temperature for 24 h. Reaction mixture was then poured into cold water (300 cm^3), the precipitated solid was filtered off giving 1·65 g (82%) air-dried crude mixture of products. An aliquot part (1 g) was purified by means of column chromatography (100 g silica gel; benzene–ether–glacial acetic acid 200 : 1 : 0·25) to give 0·060 g (5%) of compound *XI*, 0·13 g (11%) of compound *XII* and 0·27 g (22%) of compound *XIII*. Recrystallizations from methylene chloride–hexane (1 : 1) gave 0·051 g (4%) of pure compound *XI*, m.p. 132–133°C; 0·12 g (10%) of pure compound *XII*, m.p. 168–169°C and 0·195 g (16%) of pure compound *XIII*, m.p. 144–145°C.

Synthesis of XII *from 5-nitromethyl salicylate.* 1,2-Ethanediol (0·017 g, 2·8 . 10^{-4} mol) and *p*-toluenesulphonic acid (0·02 g, 10^{-4} mol) were added to the solution of methyl 5-nitrosalicylate (0·11 g, 5·7 . 10^{-4} mol) in N,N-dimethylformamide (1 cm^3). The obtained mixture was refluxed for 16 h at 165–170°C. Reaction mixture was poured then into water (100 cm^3). The solid was filtered off giving 0·020 g (18%) of air-dried crude product. Recrystallization from 95% ethanol gave 0·010 g (9%) of pure compound *XII*.

Compound XI. IR spectrum (KBr, ν_{max}): 3 500–3 240 (O—H), 3 100 (C—H, arom.), 2 960, 2 915 (C—H, aliph.), 1 680 (C=O), 1 630, 1 620, 1 530, 1 485 (–NO_2), 1 590 (C=O), 1 385 (–NO_2). ^{1}H NMR spectrum ($CDCl_3$): 4·75 s, 4 H; 6·90 m, 2 H; 7·05 d, 1 H; 7·45 m, 1 H; 7·85 dd, 1 H; 8·33 dd, 1 H; 8·80 d, 1 H. For $C_{16}H_{13}O_8N$ (347·3) calculated: 55·33% C, 3·75% H, 4·03% N; found: 55·99% C, 3·84% H, 4·11% N.

Compound XII. IR spectrum (KBr, ν_{max}): 3 430 (O—H), 3 095 (C—H, arom.), 2 980, 2 920 (C—H, aliph.), 1 685 (C=O), 1 625, 1 525, 1 485 (–NO_2), 1 585, 1 525 (C=C, arom.), 1 445, 1 390 (C—H), 1 340 (–NO_2). ^{1}H NMR spectrum ($CDCl_3$): 4·80 s, 4 H; 7·05 d, 2 H; 8·25 dd, 2 H; 8·73 d, 2 H; 10·40 s, 2 H. Mass spectrum (*m/z*, rel. %): 210 (100), 165 (88), 164 (20), 120 (50), 92 (22). For $C_{16}H_{12}O_{10}N_2$ (392·3) calculated: 48·98% C, 3·06% H, 7·14% N; found: 49·09% C, 3·23% H, 7·03% N.

Compound XIII. IR spectrum (KBr, ν_{max}): 3 500–3 400 (O—H), 3 095 (C—H, arom.), 2 980, 2 920 (C—H, aliph.), 1 675 (C=O), 1 615, 1 525 (–NO_2), 1 580 (C=C, arom.), 1 480 (C—H), 1 340 (–NO_2). ^{1}H NMR spectrum ($CDCl_3$): 4·75 s, 4 H; 7·05 2 dd, 2 H; 8·15 dd, 2 H; 8·30 dd, 1 H; 8·75 d, 1 H. For $C_{16}H_{12}O_{10}N_2$ (392·3) calculated: 48·98% C, 3·06% H, 7·14% N; found: 49·13% C, 3·30% H, 7·26% N.

5′,5″-Dinitro-N,N′-disalicyloyl-1,2-ethanediamine (*XIV*)

Procedure A. Concentrated precooled nitric acid (2·4 cm^3, 3 . 10^{-2} mol) was carefully added to a solution of N,N′-disalicyloyl-1,2-ethanediamine (A, X = NH, see Scheme 2; 1·38 g, 5 . . 10^{-3} mol) in glacial acetic acid (60 cm^3) placed in an ice bath. The reaction mixture was left to stand half an hour at 0–5°C, after that at room temperature for 24 h. Reaction mixture was then poured into cold water (300 cm^3), the solid was filtered off, washed with water and air-dried giving 1·19 g (66%) of crude mixture of products. By means of column chromatography on silica gel (100 g, benzene–ether–glacial acetic acid 100 : 6 : 1) 0·19 g (10%) of pure compound *XIV* was obtained. Recrystallization from acetone–hexane (1 : 1) gave 0·16 g (9%) of pure compound *XIV*, m.p. >260°C.

Procedure B. Triethylamine (1·83 cm^3, 1·3 . 10^{-2} mol) and 1,2-ethanediamine (0·44 cm^3, 6·7 . 10^{-3} mol) were added to a solution of methyl 5-nitrosalicylate (2·60 g, 1·3 . 10^{-2} mol) in N,N-dimethylformamide (6 cm^3). The obtained solution was heated for 12 h at 85–90°C. Reaction mixture was then poured into water (400 cm^3) and hydrochloric acid (1 : 1) was added (to pH 4). The solid was filtered off and air-dried giving 1·80 g (70%) of crude product. Column chromatography (150 g silica gel, chloroform–acetone–glacial acetic acid 100 : 10 : 0·1) gave 0·63 g (24%) of pure compound *XIV*. Recrystallization from dioxane gave 0·38 g (15%) of pure compound *XIV*.

Compound XIV. IR spectrum (KBr, ν_{max}): 3 550–3 380 (O—H, N—H), 3 100 (C—H, arom.), 2 920 (C—H, aliph.), 1 640 (C=O), 1 605 (C=C, arom.), 1 550, 1 510, 1 475 ($-NO_2$), 1 475, 1 425 (C—H), 1 335, 1 300 ($-NO_2$). ^{1}H NMR spectrum (DCON$(CD_3)_2$): 3·74 s, 4 H; 7·15 d, 2 H; 8·31 dd, 2 H; 8·92 d, 2 H; 9·16 s, 2 H. For $C_{16}H_{14}O_8N_4$ (390·3) calculated: 49·23% C, 3·59% H, 14·36% N; found: 48·98% C, 3·32% H, 13·96% N.

RESULTS AND DISCUSSION

For calculation of particular acidity constant by method of iteration[7], 15–18 values of absorbance measured at different pH corresponding to 30–70% dissociation of the compound being diprotic acid were used. Iteration was continued until there was no significant difference between succesive values of K_1 and K_2. The average results for pK_1 and pK_2 given in Table I fall within the range ±0·06 and ±0·10, respectively.

Compounds *XII* and *XIV* are the strongest acids, due to two nitro groups present in their molecules showing strong negative inductive and resonance effect.

In the case of compound *XIV* an additional intramolecular hydrogen bonding (between hydrogen from NH and oxygen from phenolic OH) is possible, influencing dissociation of phenolic OH.

Differences in acidity constants especially in the case of the amides *VIII*–*X* in respect to the esters *I*–*VII* can be explained in the same way as in our previous paper[2].

On the basis of the stability constants of the UO_2^{2+}-complexes with ligands *I*–*X*, *XII* and *XIV* (Table II) it can be concluded that the prepared compounds may serve as suitable ligands for complexation of UO_2^{2+}-ion. Ligands *I*–*VII* and *VIII*–*X*

differ mutually with respect to both the functional group involved and the length of methylene chain linking the two salicylic rings. However, on the basis of the stability constants (log β) of the UO_2^{2+}-complexes with novel compounds it can be concluded that the length of methylene chain influences ligand affinity towards UO_2^{2+}-ion.

The complexes of UO_2^{2+}-ions with the ligands of diester type (*I*–*VII*) are more stable than the complexes of the ligands of amide type (*VIII*–*X*).

The UO_2^{2+}-complexes with compounds of the amide type exhibit relatively lower stability, which can be partly explained in terms of formation of the intramolecular hydrogen bond between the NH group and undissociated or dissociated phenolic function.

TABLE I

The acidity constants of compounds *I*–*X*, *XII* and *XIV* in 61·10% aqueous ethanol at (25 ± 1)°C (μ = 0·5 (LiCl))

Compound[a]	pK_1[b]	pK_2[b]	Compound[a]	pK_1[b]	pK_2[b]
I[c]	9·45	9·89	*VII*	9·99	10·38
II[c]	9·64	10·03	*VIII*[c]	8·48	9·28
III	9·79	10·65	*IX*[c]	8·53	9·17
IV[c]	9·66	10·10	*X*	8·71	10·39
V	9·83	10·77	*XII*	5·34	6·14
VI	9·93	10·60	*XIV*	5·02	6·12

[a] See Schemes 1 and 2; [b] estimated errors in pK_1 are ±0·06, in pK_2 ±0·10; [c] ref.[2].

TABLE II

The stability constants (log β) of UO_2^{2+}-complexes with ligands *I*–*X*, *XII* and *XIV* in 61·10% aqueous ethanol (μ = 0·5 (LiCl))

Ligand	log β[a]	Ligand	log β[a]
I	18·27	*VII*	19·35
II[b]	18·51	*VIII*	16·83
III	19·17	*IX*	16·66
IV[b]	18·95	*X*	18·01
V[b]	19·34	*XII*	10·45
VI	19·22	*XIV*	10·40

[a] Estimated error in log β is ±0·05; [b] ref.[8].

Presence of nitro groups in the disubstituted ligands (*XII* and *XIV*) diminishes (due to a negative resonance effect) their complexing affinity towards UO_2^{2+}-ion. However, due to an enhanced acidity (caused by the presence of *p*-NO_2 groups) of the phenolic function, these ligands are efficient agents for binding UO_2^{2+}-ion in acidic media.

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