Organic Chemistry

Potentially hexadentate bisazine dioximate ligands: "correct" synthetic procedure and encapsulation reactions of the iron(II) ion

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Condensation of diacetyl monoxime hydrazone with diacetyl, hexane-3,4-dione, and glyoxal in MeOH afforded potentially hexadentate bisazine dioximes. The crystal and molecular structure of the condensation product with diacetyl was established by X-ray diffraction analysis. The reactions of the resulting azine oximes with Fe^{2+} ions in the presence of Lewis acids were studied.

Key words: azomethines, Schiff bases, X-ray diffraction analysis, clathrochelates.

Clathrochelate polynuclear complexes,* polyclathrochelate complexes,** and the corresponding macropolycyclic ligands are being extensively studied as models of biological systems (biomimetics), synthetic precursors of molecular electronic devices, and receptors of cations, anions, and neutral molecules.[1—4] General approaches to the synthesis of polyene clathrochelates of these types have been developed previously.[3—5] The polyazomethine ligands are necessary building blocks for the construction of polyene polyclathrochelates and polynuclear clathrochelates. Tetradentate ligands (in particular, diacetyl azine dioxime ($DAOH_2$) and its analogs $IAOH_2$ and $TMAOH_2$; Scheme 1) were readily synthesized according to a known procedure.[5,6] To the contrary, attempts to apply this procedure to the preparation of potentially hexadentate azomethine ligands were unsuccessful.[7] Previously, we have failed to synthesize hexadentate azine oxime $TAOH_2$ (see Scheme 1) in an aqueous medium, and this ligand was prepared by condensation of dry monoxime hydrazone (DHO) with diacetyl in anhydrous methanol.[3] In the present study, the reactions of oxime hydrazones with α-dicarbonyl compounds in aqueous and alcoholic media were examined in detail by physicochemical methods and procedures for the synthesis of the $TAOH_2$ ligand and its analogs were developed. We also examined the reactions of the resulting ligands with iron(II) ions in the presence of cross-linking agents, *viz.*, Lewis acids.

* Complexes containing two or more metal ions encapsulated in a three-dimensional cavity of the macrobicyclic ligand.

** Complexes containing two or more isolated fragments with an encapsulated metal ion.

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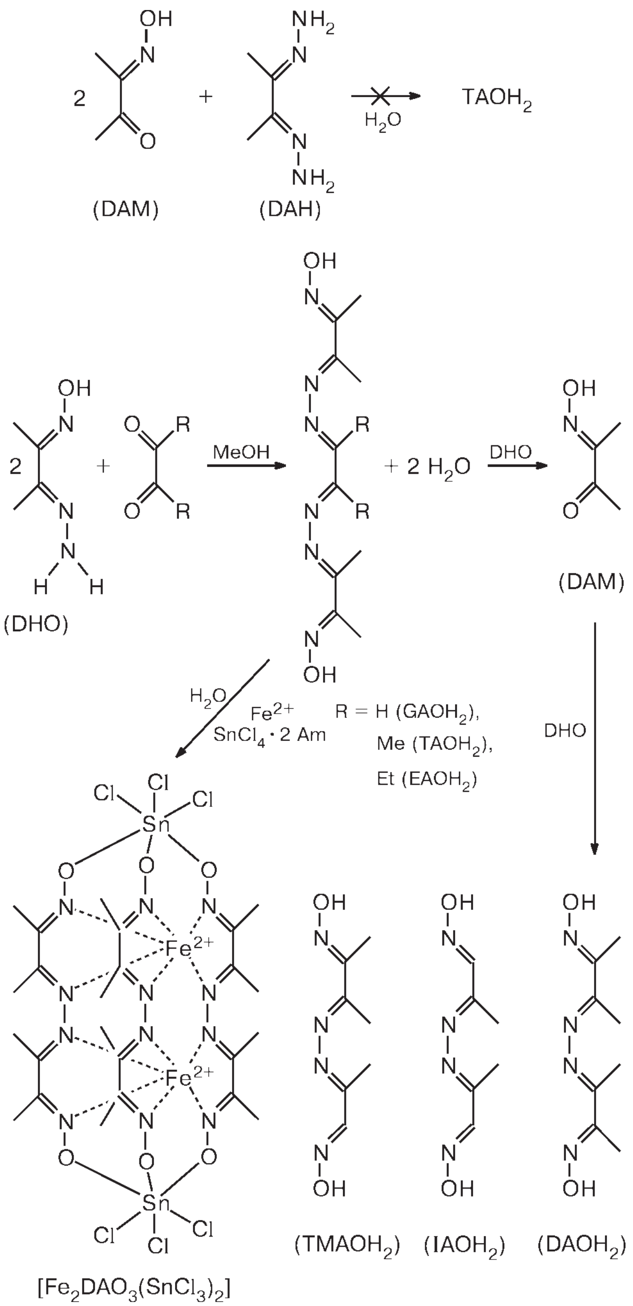
Scheme 1



Experimental

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer in DMSO-d_6. The chemical shifts were measured relative to the signals of the residual protons (δ_H 2.50) and the signals of the ^{13}C nuclei (δ_C 39.5) of the solvent (are given with respect to Me_4Si in the δ scale). The assignment of the signals in the ^{13}C NMR spectra was made by recording the spectra both with ^{1}H—^{13}C spin-spin coupling and decoupling. The mass spectra (EI) were recorded on a quadrupole Finnigan MAT INCOS 50 mass spectrometer (the ionizing voltage was 70 eV; the temperature of the ionization chamber was 150 °C). The IR spectra (KBr pellets) were measured on a Specord M-80 instrument in the range 400—4000 cm^{-1}. The UV-vis spectra (solutions in THF) were recorded on a Perkin—Elmer Lambda 9 spectrophotometer in the range 220—600 nm.

Diacetyl hydrazone oxime (DHO) was synthesized according to a procedure reported previously;[8] Et_2O was dried with a Na wire, MeOH was dried with magnesium methoxide. All synthetic procedures were carried out in air. Diacetyl, hexane-3,4-dione, and glyoxal were purchased from Fluka.

3,6,7,10-Tetramethyl-4,5,8,9-tetraazadodeca-3,5,7,9-tetraene-2,11-dione dioxime ($TAOH_2$). A solution of diacetyl (4.4 mL, 0.05 mol) in anhydrous MeOH (50 mL) was added to a solution of DHO (11.5 g, 0.1 mol) in anhydrous MeOH (150 mL). The reaction mixture was kept at ~20 °C for 12 h. Then a finely crystalline yellow-orange precipitate that formed was filtered off and washed successively with a small amount of MeOH, a large amount of dry Et_2O until an impurity of $DAOH_2$ disappeared (the purity of the product was monitored by ^{1}H and ^{13}C NMR spectroscopy as described below), and a small amount of hexane. The solid residue was dried *in vacuo*. The yield was 11 g (79%). Found (%): C, 51.49; H, 7.16; N, 30.07. $C_{12}H_{20}N_6O_2$. Calculated (%): C, 51.43; H, 7.14; N, 30.00. IR, ν/cm^{-1}: 983, 1053, 1126 (NO), 1602 multiplet (CN). ^{1}H NMR, δ: 1.94, 2.01, and 2.03 (all s, 6 H each, Me); 11.73 (s, 2 H, NOH). ^{13}C{^{1}H} NMR, δ: 9.3, 12.5, and 12.8 (all Me); 154.4, 154.6, and 155.7 (all C=N). MS, *m/z* (I_{rel} (%)): 280 [M$^+$] (24); 263 [M$^+$ – OH] (40); 181 [M$^+$ – HON=C(Me)—C(Me)=N] (100). UV, λ_{max}/nm ($\varepsilon \cdot 10^{-3}$/L mol^{-1} cm^{-1}): 257 (20), 292 (22).

6,7-Diethyl-3,10-dimethyl-4,5,8,9-tetraazadodeca-3,5,7,9-tetraene-2,11-dione dioxime ($EAOH_2$) was prepared according to a procedure analogous to that described above for $TAOH_2$ with the use of hexane-3,4-dione (6 mL, 0.05 mol) instead of diacetyl, the total volume of the solvent being increased to 500 mL. The finely crystalline pale-yellow product was obtained in a yield of 6.5 g (42%). Found (%): C, 54.47; H, 7.83; N, 27.31. $C_{14}H_{24}N_6O_2$. Calculated (%): C, 54.55; H, 7.79; N, 27.27. IR, ν/cm^{-1}: 995, 1037, 1058, 1136 (NO), 1600 multiplet (CN). ^{1}H NMR, δ: 0.93 (t, 6 H, $CH_2C\underline{H}_3$, J = 7.4 Hz); 1.96 and 2.03 (both s, 6 H each, Me); 2.55 (q, 4 H, $C\underline{H}_2CH_3$, J = 7.4 Hz); 11.73 (s, 2 H, NOH). ^{13}C{^{1}H} NMR, δ: 9.2 (Me); 11.1 ($\underline{C}H_3CH_2$); 12.9 (Me); 19.6 ($\underline{C}H_2CH_3$); 154.3, 154.8, and 159.0 (all C=N). MS, *m/z* (I_{rel} (%)): 308 [M$^+$] (27), 291 [M$^+$ – OH] (30), 209 [M$^+$ – HON=C(Me)—C(Me)=N] (100). UV, λ_{max}/nm ($\varepsilon \cdot 10^{-3}$/L mol^{-1} cm^{-1}): 247 (14), 261 (19), 296 (19).

3,10-Dimethyl-4,5,8,9-tetraazadodeca-3,5,7,9-tetraene-2,11-dione dioxime ($GAOH_2$) was prepared analogously to $TAOH_2$ with the use of a 40% aqueous solution of glyoxal (7.25 g, 0.05 mol) instead of diacetyl. The precipitate that formed during the first 20 min was filtered off and discarded. The finely crystalline pale-yellow product was obtained in a yield of 3.2 g (25%). Found (%): C, 47.56; H, 6.44; N, 33.30. $C_{10}H_{16}N_6O_2$. Calculated (%): C, 47.62; H, 6.35; N, 33.33. IR, ν/cm^{-1}: 998, 1056, 1142 (NO), 1596 multiplet (CN). ^{1}H NMR, δ: 1.99 and 2.07 (both s, 6 H each, Me); 7.91 (s, 2 H, HC=N); 11.92 (s, 2 H, NOH). ^{13}C{^{1}H} NMR, δ: 9.4 and 13.0 (both Me); 153.3 (Me$\underline{C}$=N—N); 154.5 (HC=N); 161.1 (Me$\underline{C}$=NOH). MS, *m/z* (I_{rel} (%)): 252 [M$^+$] (29), 235 [M$^+$ – OH] (74), 218 [M$^+$ – 2 OH] (53), 153 [M$^+$ – HON=C(Me)—C(Me)=N] (100). UV, λ_{max}/nm ($\varepsilon \cdot 10^{-3}$/L mol^{-1} cm^{-1}): 258 (18), 307 (26).

X-ray diffraction study. Pale-yellow crystals of azine oxime $TAOH_2$ suitable for X-ray diffraction analysis were prepared by slow cooling of a saturated (at 60 °C) solution of $TAOH_2$ in DMSO. The X-ray data were collected from a platelet-like single crystal of dimensions 0.42×0.30×0.06 mm. At 110(1) K, the crystals of composition $TAOH_2 \cdot 2DMSO$ (M = 436.6) are triclinic, a = 5.2872(9) Å, b = 5.2979(10) Å, c = 19.911(3) Å, α = 88.086(5)°, β = 86.905(5)°, γ = 86.049(5)°, V = 555.3(2) $Å^3$, space group $P\bar{1}$, Z = 1, d_{calc} = 1.305 g cm^{-3}. The intensities of 3856 independent reflections were measured on a Bruker SMART 1K CCD diffractometer (R_{int} = 0.0247, ω scanning technique, $2\theta_{max}$ = 64°).[9] The semiempirical absorption correction (μ = 0.273 mm^{-1}) was applied using the SADABS program;[10] the maximum and minimum transmission coefficients are 0.928 and 0.377, respectively.

The structure was solved by direct methods and refined by the full-matrix least-squares method based on F^2 with anisotropic thermal parameters for nonhydrogen atoms. The positions of the H atoms were revealed from the difference Fourier synthesis and refined isotropically. A total of 191 parameters were refined. All calculations were carried out using the SHELXTL PLUS 5.0 program package.[11] The final reliability factors were as follows: $R_1(F)$ = 0.048, based on 3086 observed reflections with $I > 2\sigma(I)$; $wR_2(F^2)$ = 0.124, $GOOF$ = 1.029 based on all 3853 reflections used at the final stage of the refinement. The atomic coordinates were deposited with the Cambridge Structural Database.

Results and Discussion

Attempts to use the procedure involving condensation of diacetyl monoxime (DAM) with diacetyl dihydrazone (DAH) in water (see Scheme 1), which has been proposed previously,[7] for the synthesis of azine oxime $TAOH_2$ were unsuccessful and the desired product was not obtained. According to the ^1H and ^{13}C NMR spectroscopic data, oxime hydrazone, which was generated by the 1 : 1 condensation, dominated the mixture of the reaction products. Thus, the ^1H NMR spectrum of the product has signals of four nonequivalent Me groups with equal intensities. The $^{13}C\{^1H\}$ NMR spectrum shows signals of four nonequivalent azomethine fragments along with signals of four nonequivalent Me groups. The authors of the cited study[7] failed to correctly identify the reaction product based only on the data from elemental analysis and UV spectroscopy. Efforts to synthesize potentially hexadentate azine oximes $TAOH_2$, $EAOH_2$, and $GAOH_2$ by condensation of oxime hydrazone DHO with the corresponding active α-dicarbonyl compound (see Scheme 1) in MeOH were much more successful (attempts to carry out the synthesis in 1,4-dioxane, MeCN, Et_2O, or THF either at room temperature or upon heating failed). However, this pathway is also complicated by side reactions and requires that the conditions of the synthesis be carefully followed. It should be noted that an attempt to use acid catalysis for acceleration of condensation failed. In the latter case, an amount of by-products, which crystallized together with the target azine oximes, was substantially increased. Since water, which was generated in the course of the reaction and present in the solvent, is responsible for the major side reaction giving rise to diacetyl azine dioxime ($DAOH_2$) (see Scheme 1), care must be taken to avoid the presence of water in the solvent, a large excess of the solvent should be used (to reduce the water concentration), and the reaction time must be closely controlled (on the one hand, it is necessary to ensure the maximum possible degree of condensation and provide crystallization of the product and, on the other hand, the amount of $DAOH_2$ increases with time). According to our data, the optimum reaction time is ~12 h. The succeeding fractions contained substantially larger amounts of $DAOH_2$. Azine oximes thus obtained are difficult to purify because of their low solubility and tendency to undergo disproportionation. The procedure of choice for the purification of potentially hexadentate azine oximes $TAOH_2$, $EAOH_2$, and $GAOH_2$ is based on the fact that their solubilities in Et_2O are approximately equal to that of $DAOH_2$. Thus, the reaction products (although with substantial losses) were obtained with a purity of >95% (according to the ^1H and ^{13}C NMR spectroscopic data) when a finely crystalline precipitate that formed in the course of the reaction was washed with this solvent. On the whole, the ^1H and ^{13}C NMR spectra (along with the data from elemental analysis and mass spectrometry) made it possible to unambiguously identify the products obtained (Figs. 1—3) and to control their synthesis and purification. As can be seen from Fig. 1, the degree of purification of azine oxime $TAOH_2$ upon washing with dry Et_2O can be followed by ^1H NMR spectroscopy from the relative intensities of the signals of the methyl and oxime groups of an $DAOH_2$ impurity (these signals are shifted upfield by 0.05 and 0.03 ppm, respectivey, compared to those of $TAOH_2$).

The crystal and molecular structure of azine oxime $TAOH_2$ was established by X-ray diffraction method. The $TAOH_2$ molecule occupies a special position in an inversion center. This molecule is nearly planar with the transoid arrangement of the Me substituents (Fig. 4, Table 1). The largest deviation from the plane of the molecule (0.066(2) Å) is observed for the O(1) atom. The geometric parameters of the $TAOH_2$ and DMSO molecules have standard values.

Each $TAOH_2$ molecule crystallizes with two DMSO molecules of solvation. The crystal packing consists of the alternating layers of the major and solvate molecules. This layered structure is, apparently, responsible for instability of the crystals in air at room temperature. The major and solvate molecules are linked *via* the O(1)—H(1O)...O(1S) hydrogen bonds (O(1)—H(1O), 0.81(3) Å; H(1O)...O(1S), 1.87(3) Å; O(1)...O(1S), 2.685(1) Å; the O(1)—H(1O)...O(1S) angle is 176(2)°; see Fig. 4).

The reactions of the resulting azine oximes with the Fe^{2+} ions in the presence of Lewis acids (in particular,

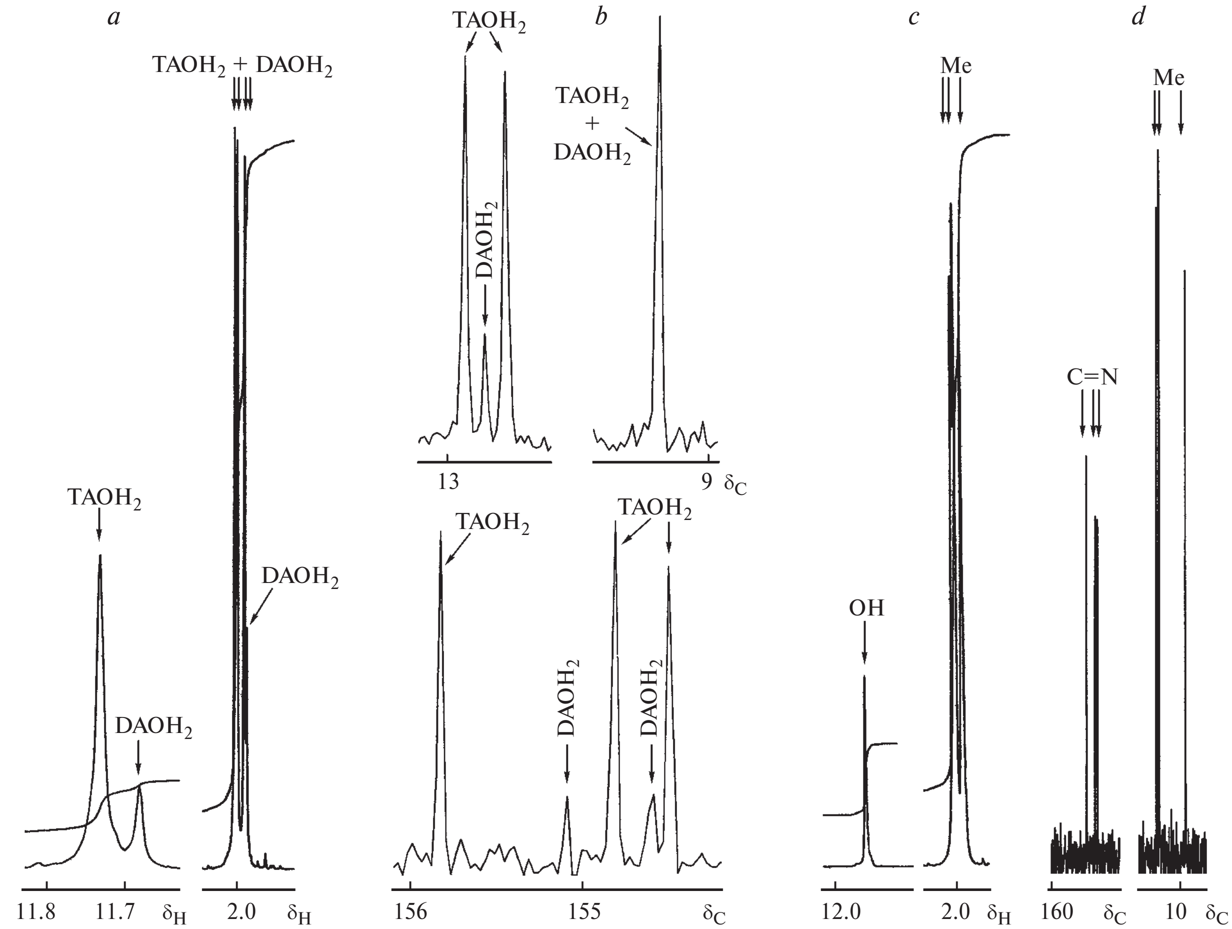


Fig. 1. Fragments of the ^{1}H and ^{13}C{^{1}H} NMR spectra (in DMSO-d_6) of a crude sample of $TAOH_2$ containing an impurity of $DAOH_2$ (*a* and *b*, respectively) and a sample of $TAOH_2$ after washing with Et_2O (*c* and *d*, respectively).

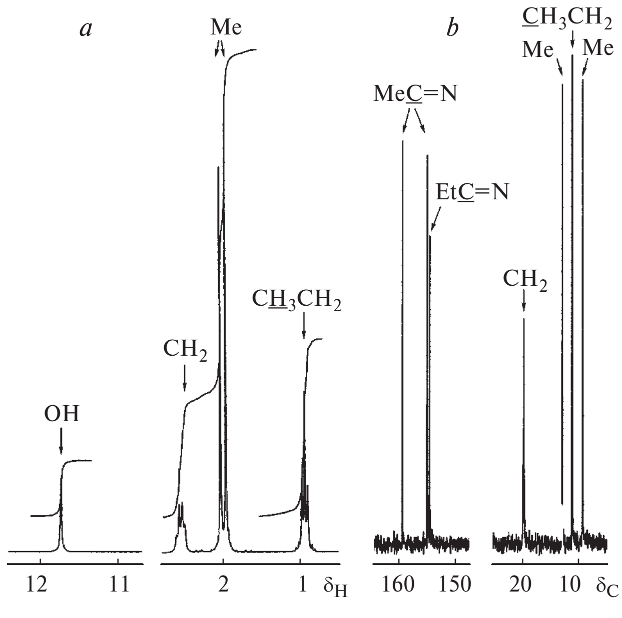


Fig. 2. Fragments of the ^{1}H (*a*) and ^{13}C{^{1}H} (*b*) NMR spectra of a solution of $EAOH_2$ in DMSO-d_6.

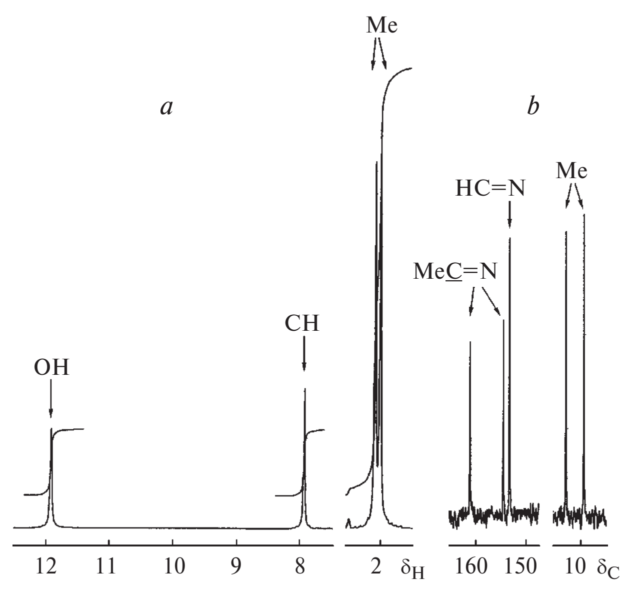


Fig. 3. Fragments of the ^{1}H (*a*) and ^{13}C{^{1}H} (*b*) NMR spectra of a solution of $GAOH_2$ in DMSO-d_6.

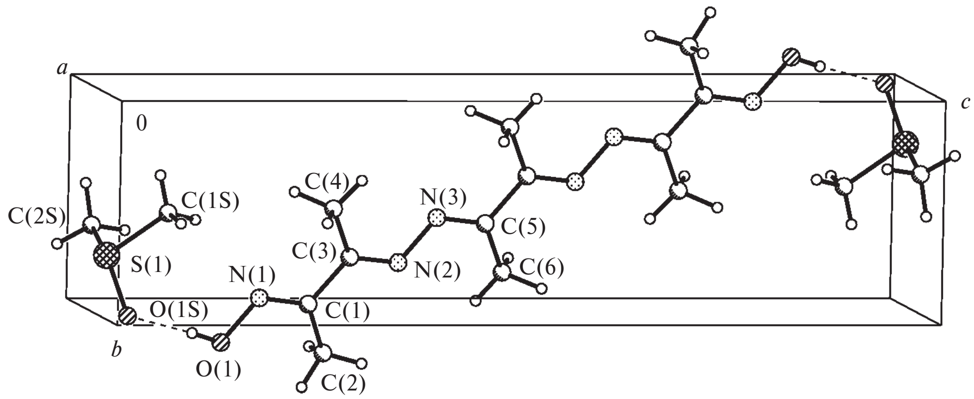


Fig. 4. Overall view of the crystal structure of $TAOH_2 \cdot 2DMSO$.

$SnCl_4$) as cross-linking agents followed an unusual pathway. Even in aprotic media (for example, in dry MeCN), the reactions always gave only one clathrochelate complex $[Fe_2DAO_3(SnCl_3)_2]$ (see Scheme 1) in essential yield (~20%) instead of the expected trinuclear clathrochelates $[Fe_3L_3(SnCl_3)_2]^{2+}$ (L = TAO^{2-}, EAO^{2-}, or GAO^{2-}). This product has been studied in detail previously.[5] In the course of the reaction, the starting azine oximes, apparently, underwent disproportionation with elimination of the central fragment to form a very stable and poorly soluble binuclear clathrochelate, which was removed from the reaction medium due to its low solubility. Evidently, in the case of the resulting potentially hexadentate azine oximes, it is necessary to use softer cross-linking agents for the synthesis of trinuclear clathrochelates.

On the whole, condensation of oxime hydrazones with active carbonyl compounds in dry lower alcohols seems to be the most efficient procedure for the synthesis of azine oximes. In particular, this is associated with high solubility of the reaction components and low solubility of the resulting azine oxime in these alcohols, which causes the shift of the equilibrium toward the latter compound due to precipitation of the solid product. In addition, the solvent is able to bind water liberated upon condensation.

Table 1. Selected bond lengths (d) and bond angles (ω) in the $TAOH_2$ molecule

Bond	d/Å	Angle	ω/deg
O(1)—N(1)	1.3970(13)	C(1)—N(1)—O(1)	112.63(10)
N(1)—C(1)	1.291(2)	N(1)—C(1)—C(3)	114.39(10)
C(1)—C(3)	1.477(2)	N(1)—C(1)—C(2)	124.91(11)
C(1)—C(2)	1.496(2)	N(2)—C(3)—C(1)	114.28(10)
C(3)—N(2)	1.298(2)	C(1)—C(3)—C(4)	119.44(10)
C(3)—C(4)	1.499(2)	C(3)—N(2)—N(3)	113.88(10)
N(2)—N(3)	1.3970(14)	C(5)—N(3)—N(2)	113.77(10)
N(3)—C(5)	1.296(2)	N(3)—C(5)—C(5)*	114.32(13)
C(5)—C(5)*	1.484(2)	N(3)—C(5)—C(6)	126.68(11)
C(5)—C(6)	1.499(2)		

* The atom generated from the basis atom by the symmetry operation $-x + 1, -y + 1, -z + 1$.

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