

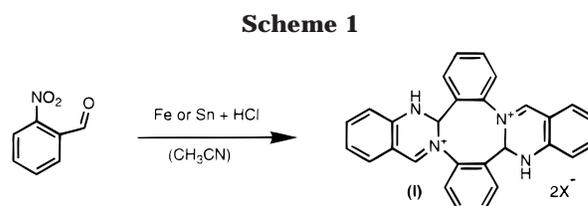
Direct Reduction of *o*-Nitrobenzaldehyde to 4b,5,15b,16-Tetrahydrodibenzo[3,4:7,8]-[1,5]diazocino[2,1-*b*:6,5-*b*]diquinazoline-11,22-dium cation (H₂TAAB²⁺) Salts with Simultaneous Formation of Alternative Geometric Isomers of [H₂TAAB]²⁺

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The tetrameric cation 4b,5,15b,16-tetrahydrodibenzo[3,4:7,8][1,5]diazocino[2,1-*b*:6,5-*b*]diquinazoline-11,22-dium (I) derived from *o*-aminobenzaldehyde (often abbreviated as H₂TAAB²⁺, constitutes an extremely convenient starting material for the preparation of a variety of macroheterocyclic compounds.¹ These include the ligands H₄TAAB (II) and H₈TAAB (III), which have been found to be highly selective extractants for copper² as well as forming various transition-metal complexes of the ligand TAAB (IV), which resemble porphyrins. The latter materials have been successfully used for myoglobin modeling³ and for quantitative oxygen determination.⁴ Several of these complexes show remarkable anticancer activity,⁵ while at least one is a pronounced superoxide dismutase mimic⁶ and an active nuclease.⁷ All previously known routes to these materials require *o*-aminobenzaldehyde as the starting material. H₂TAAB salts (I), for example, can easily be obtained by the acidification of *o*-aminobenzaldehyde.^{1,8} The preparation of *o*-aminobenzaldehyde itself, however, involves a tedious workup with steam distillation from a tarry reaction mixture, offering very limited opportunities for derivatization.⁹ Here, we report an alternative convenient route to H₂TAAB salts based on the direct reduction of *o*-nitrobenzaldehyde.



The reduction of *o*-nitrobenzaldehyde with a variety of reducing agents has been studied in great detail. Depending on the reducing agent and the experimental conditions, one can obtain *o*-aminobenzaldehyde,⁹ anthranil,¹⁰ and several other products.¹¹ We expected that direct reduction of *o*-nitrobenzaldehyde to H₂TAAB salts might be achievable by a method that combined two necessary features: (1) a reducing agent that normally converts nitro- into amino-group functionality but leaves aldehyde groups untouched and (2) a highly acidic medium (pH < 1) in which transformation of *o*-aminobenzaldehyde to H₂TAAB salts takes place readily.

Among several methods tested, the best results have been obtained from the historic Béchamp reduction.¹² Iron or tin react rapidly with *o*-nitrobenzaldehyde in a mixture of hydrochloric acid and certain neutral organic solvents (Scheme 1). The color of the reaction mixture turns bright red, which is very characteristic for H₂TAAB salts. Trichlorostannate(II) or tetrachloroferrate(II) H₂TAAB salts crystallize spontaneously after some minutes with 63 and 84% yields, respectively. This is better than the overall yield of I (about 50%) from the previously known route.^{1,8} The process does not occur without the addition of organic solvent, which seems to be the only reason the reaction was not discovered early in the development of organic chemistry. Such an addition of organic solvents to the reaction mixture has occasionally been applied in the Béchamp reduction,¹³ but to the best of our knowledge, not to the reduction of *o*-nitrobenzaldehyde. In our case, acetonitrile acts as the best additive; the second best is propylene carbonate, despite its partial hydrolysis by hydrochloric acid.

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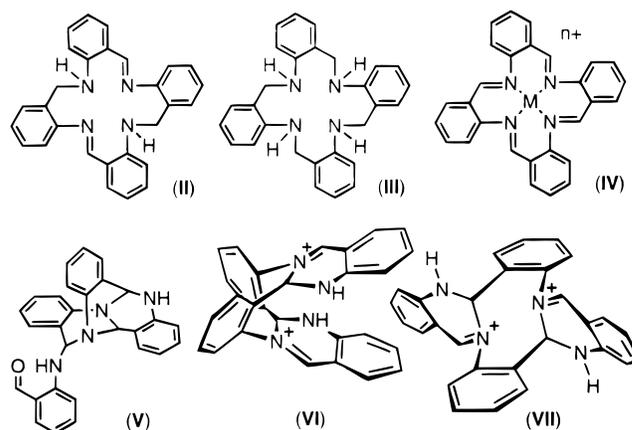
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The standard reactions of H₂TAAB salts, including BH₄⁻ reduction to II, are unaffected by the presence of

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[SnCl₃] and [FeCl₄] anions. However, the [FeCl₄] salt hydrolyses unusually easily, with the reaction to tris-anhydrotetramer V going to completion by addition of water to the crystalline material.¹⁴ The iron(II) and tin(II) in the anions also provide additional synthetic possibilities. H₂TAAB(FeCl₄) transforms into Fe-(TAAB)Cl₂¹⁵ on addition of triethylamine under anaerobic conditions. Reaction of either red or yellow H₂TAAB-(SnCl₃)₂ with copper(II) acetate gives the Cu(I) TAAB complex directly,¹⁶ previously prepared by a two-step synthetic route.¹⁷ Finally, H₂TAAB(SnCl₃)₂ and H₂-TAAB(FeCl₄) can readily be transformed into other H₂-TAAB salts by anion metathesis upon addition of the corresponding acid in acetonitrile.

H₂TAAB(SnCl₃)₂ Alternative Geometric Isomers

Whereas iron reduction of *o*-nitrobenzaldehyde results in only one crystalline product, which is red, the tin reduction normally gives a mixture of yellow and red crystals. Under certain conditions, these products can be obtained separately: lower temperatures and greater acidity facilitate formation of the red product, while higher temperatures (boiling water bath) and lower acidity favor the yellow product. Analytical data (C, N, H, Sn, Cl) indicate that the two products are isomeric, their compositions corresponding to H₂TAAB(SnCl₃)₂ (C₂₈H₂₂N₄Sn₂Cl₆). The two compounds show no sign of interconversion in the solid state even at elevated temperature. Trichlorostannate is the only anion known so far that can stabilize two different isomers of H₂TAAB salts. The geometry and packing peculiarities of this anion in combination with the geometry of the organic cation may be such that almost equal energies of the crystal lattices are observed for the red and the yellow isomer; consequently, both isomers are forming simultaneously.

The structures of the red tetrachloroferrate(II) and trichlorostannate(II) H₂TAAB salts appear to be identical to those of previously characterized H₂TAAB salts, since their NMR, IR, MS, and electronic spectra are extremely similar.¹ The nature of the yellow isomer is less obvious, with a contrast between the NMR and IR spectra, similar in both forms, and distinct electronic spectra.

It has now been possible to resolve the nature of the isomerization by X-ray characterization of the red and yellow tin salts (Figures 1 and 2). As expected, analogously to all previously structurally characterized H₂-TAAB salts,^{8,18} the red isomer of H₂TAAB(SnCl₃)₂ has the saddle conformation (VI) (Figure 1). The yellow isomer has the same structural formula, but with a unique twisted geometry (VII) (Figure 2). Thus, the yellow and red H₂TAAB(SnCl₃)₂ salts represent a relatively rare case

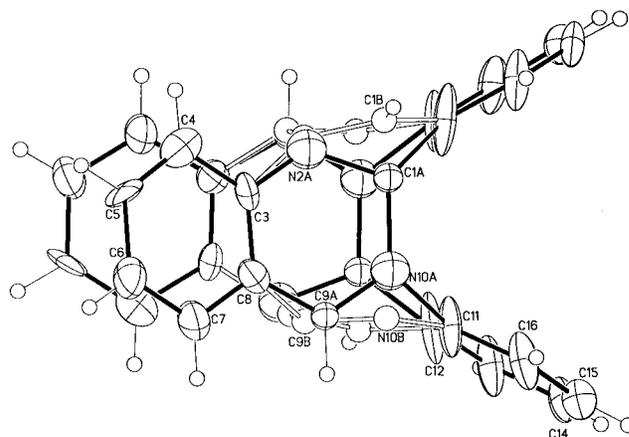


Figure 1. View of the 2-fold symmetric cation of the red isomer of [H₂TAAB]²⁺ 2[SnCl₃]⁻, showing the alternative connectivity of the disordered central section with solid and open bonds. Ellipsoids drawn at 50% probability. The form of the ellipsoids in the C11–C16 ring show clearly that the disorder also affects these atoms, although the separation between the two positions is less than in the central section.

of isomerism, based on two different geometries possible for eight-membered rings.

Experimental Section

General Methods. Reagents were obtained from commercial sources and used as received. Combustion analyses were performed by the Analytical Laboratory of the Institute of Physical Chemistry and tin analyses by the Analytical Laboratory of the Institute of General and Inorganic Chemistry (Kiev, Ukraine).

4b,5,15b,16-Tetrahydrodibenzo[3,4:7,8][1,5]diazocino-[2,1-*b*:6,5-*b*]diquinazoline-11,22-diium Trichlorostannate-(II), H₂TAAB(SnCl₃)₂, Red Isomer (VI). Concentrated hydrochloric acid (37%) (4 mL) was added dropwise at 5 °C to a mixture of *o*-nitrobenzaldehyde (1 g), acetonitrile (4 mL), and excess tin powder (3 g); the reaction mixture was kept overnight at room temperature. Product precipitated as large red crystals, yield 0.91 g (63%). Spectroscopic data for red isomer H₂TAAB-(SnCl₃)₂: FAB-MS (positive) *m/z* 413 and 431 corresponding to HTAAB⁺ and TAAB(H₃O)⁺; FAB-MS (negative) *m/z* 225 and 429 corresponding to SnCl₃⁻ and TAAB(OH)⁻; IR (KBr) 3442, 3286, 1628, 1559, 1476, 754 cm⁻¹; UV/vis (acetonitrile) 454 (5590); ¹H NMR data are identical to those previously described for H₂-TAAB cation (ref 1). Anal. Calcd for C₂₈H₂₂N₄Sn₂Cl₆: C, 38.90; H, 2.56; N, 6.48; Sn, 27.46; Cl, 24.60. Found: C, 38.70; H, 2.32; N, 6.59; Sn, 27.62; Cl, 24.69.

4b,5,15b,16-Tetrahydrodibenzo[3,4:7,8][1,5]diazocino-[2,1-*b*:6,5-*b*]diquinazoline-11,22-diium Trichlorostannate-(II), H₂TAAB(SnCl₃)₂, Yellow Isomer (VII). Hydrochloric acid (33%) (4 mL) was added in several portions (exothermic!) to the mixture of *o*-nitrobenzaldehyde (1 g), acetonitrile (4 mL), and excess tin powder (3 g); reflux 20 min. The hot solution was drained from the excess tin before crystallization started, yield 1.02 g (71.3%). Spectroscopic data for yellow isomer H₂TAAB(SnCl₃)₂: FAB-MS (positive) *m/z* 411, 413, and 429 corresponding to (TAAB – H)⁺, HTAAB⁺ and TAAB(OH)⁺; FAB-MS (negative) *m/z* 225 and 429 corresponding to SnCl₃⁻ and TAAB(OH)⁻; IR (KBr) 3442, 3229, 1624, 1558, 1490, 763 cm⁻¹; UV/vis (acetonitrile) 300 nm (10⁴), 364 (5590); ¹H NMR data are identical to those previously described for H₂TAAB cation (ref 1). Anal. Calcd for C₂₈H₂₂N₄Sn₂Cl₆: C, 38.90; H, 2.56; N, 6.48; Sn, 27.46; Cl, 24.60. Found: C, 39.07; H, 2.42; N, 6.47; Sn, 27.49; Cl, 24.72.

4b,5,15b,16-Tetrahydrodibenzo[3,4:7,8][1,5]diazocino-[2,1-*b*:6,5-*b*]diquinazoline-11,22-diium Tetrachloroferrate-(II), H₂TAAB(FeCl₄). Concentrated hydrochloric acid (37%) (18 mL) was added in small portions (exothermic!) to the stirred mixture of *o*-nitrobenzaldehyde (5 g), acetonitrile (20 mL), and

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(15) Spectroscopic data for Fe(TAAB)Cl₂: FAB-MS (positive) *m/z* 468 corresponding to FeTAAB⁺; UV/vis are identical to those previously described for FeTAAB²⁺.

(16) Spectroscopic data for Cu(TAAB)Cl: FAB-MS (positive) *m/z* 475 corresponding to CuTAAB⁺; UV/vis are identical to those previously described for CuTAAB⁺.

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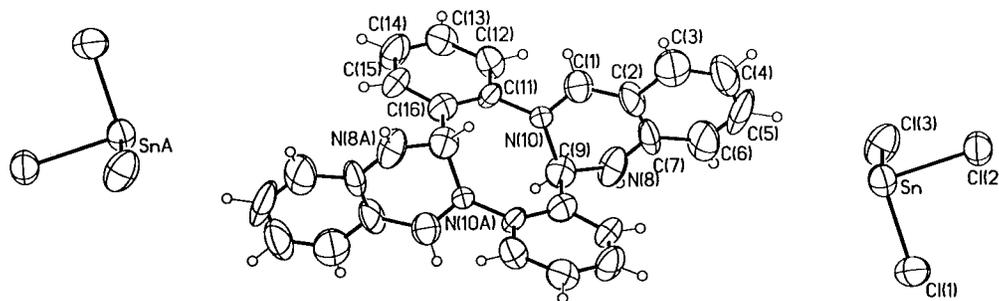


Figure 2. View of the centrosymmetric cation and symmetry related anions of the yellow isomer of $[\text{H}_2\text{TAAB}]^{2+} 2[\text{SnCl}_3]^-$.

iron (5.6 g). After the vigorous reaction was complete, the reaction mixture was spontaneously separated in two layers. Product crystallized in the upper layer under cooling, yield 4.25 g (84%). Spectroscopic data for $\text{H}_2\text{TAAB}(\text{FeCl}_4)$: FAB-MS (positive) m/z 413 corresponding to HTAAB^+ ; FAB-MS (negative) m/z 161 corresponding to FeCl_3^- ; UV/vis(acetonitrile) 450 (3830); ^1H NMR data are identical to those previously described for $\text{H}_2\text{-TAAB}$ cation (ref 1). Anal. Calcd for $\text{C}_{28}\text{H}_{22}\text{N}_4\text{FeCl}_4$: C, 54.92; H, 3.60; N, 9.15; Fe, 9.13; Cl, 23.21. Found: C, 54.73; H, 3.81; N, 9.22; Fe, 8.98; Cl, 23.42.

Crystal Data. **VI:** $[\text{C}_{28}\text{H}_{22}\text{N}_4]^{2+} 2[\text{SnCl}_3]^-$, $M = 864.58$, monoclinic, space group $P2/c$ $a = 9.4638(11)$ Å, $b = 9.8450(12)$ Å, $c = 16.886(2)$ Å, $\beta = 90.573(2)^\circ$, $U = 1573.2(3)$ Å³, $T = 153(2)$ K, $Z = 2$, $D(\text{calcd}) = 1.817$ Mg/m³, $F(000) = 832$; $\mu(\text{Mo K}\alpha) = 2.123$ mm⁻¹. Crystal character: red plates. Crystal dimensions $0.25 \times 0.20 \times 0.04$ mm. 6282 reflections measured, 2213 unique [$R(\text{int}) = 0.0822$]. Absorption correction by ψ -scan; minimum and maximum transmission factors: 0.56, 0.93. Goodness-of-fit on F^2 was 1.098, $R1$ [for 1252 reflections with $I > 2\sigma(I)$] = 0.0901, $wR2 = 0.1807$. Data/restraints/parameters 2213/12/179. Largest difference Fourier peak and hole 0.726 and -0.822 e Å⁻³.

VII: $[\text{C}_{28}\text{H}_{22}\text{N}_4]^{2+} 2[\text{SnCl}_3]^-$, $M = 864.58$, monoclinic, space group $P2(1)/n$, $a = 10.4018(5)$ Å, $b = 9.1126(3)$ Å, $c = 16.4358(7)$ Å, $\beta = 90.082(3)^\circ$, $U = 1557.91(11)$ Å³, $T = 293(2)$ K, $Z = 2$, $D(\text{calcd}) = 1.843$ Mg m⁻³, $F(000) = 840$; $\mu(\text{Mo K}\alpha) = 2.144$ mm⁻¹. Crystal character: small yellow blocks. Crystal dimensions $0.44 \times 0.24 \times 0.16$ mm. $R1$ [for 3151 reflections with $I > 2\sigma(I)$] = 0.0958, $wR2 = 0.1697$. Goodness-of-fit on F^2 was 1.535. Data/restraints/parameters 4583/24/183. Extinction coefficient 0.0004(6). Largest difference Fourier peak and hole 0.758 and -0.671 e Å⁻³.

Data Collection and Processing. Siemens SMART¹⁹ three-circle system with CCD area detector, graphite-monochroma-

tized Mo K α radiation ($\lambda = 0.71073$ Å). Unit cell constants by least-squares refinement on numerous reflection positions. Temperature maintained with the Siemens LT-2 system. Both types of crystals were small and weakly diffracting.

Structure Analysis and Refinement. Structures solved by direct methods using SHELXS²⁰ (TREF) with additional light atoms found by Fourier methods. The crystal of VII was found to be twinned, and the data were deconvoluted and refined using the method of Sparks.²¹ For VI, the central portion of the cation is disordered with bonds either between C1 and N10 or C2 and N9. It was refined with 50% occupancies for these central atoms and with equivalent distances restrained to be equal.

Hydrogen atoms were added at calculated positions and refined using a riding model. Anisotropic displacement parameters were used for all non-H atoms, apart from the disordered atoms in VI; H atoms were given isotropic displacement parameters equal to 1.2 times the equivalent isotropic displacement parameter of the atom to which the H atom is attached. The weighting scheme was calculated by $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$, where $P = (F_o^2 + 2F_c^2)/3$. VII: $a = 0.04$, $b = 0.3$. VI: $a = 0.041$, $b = 14$. Refinement used SHELXL96.²² The weak diffraction coupled with the twinning and disorder account for the relatively poor final R values achieved.

Additional material available from the Cambridge Crystallographic Data Centre comprises coordinates, thermal parameters, and bond lengths and angles.

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Supporting Information Available: X-ray crystallographic data for compounds VI and VII (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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