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[23] (*R*)-**3a** = dichloro[4*R*, 5R-2,2-dimethyl-$\alpha,\alpha,\alpha',\alpha'$-tetraphenyl-1,3-dioxolane-4,5-dimethanolato(2-)-*O*,*O'*]titanium. (*R*)-**3b** = dichloro[4*R*,5*R*-2,2-dimethyl-$\alpha,\alpha,\alpha',\alpha'$-tetra(1-naphthyl)-1,3-dioxolane-4,5-dimethanolato(2-)-*O*,*O'*]titanium. The two corresponding TADDOL ligands are commercially available.
[24] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-145414 ([(*R*)-**3a**(DME)]) and CCDC-145415 ([(*R*)-**3b**-(NCMe)$_2$]). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
[25] A representative experimental procedure is as follows: Complex **3b** (10.3 mg, 0.0125 mmol) was added to a solution of β-ketoester **1d** in acetonitrile (0.25 mmol in 1 mL), and the mixture was stirred until a clear yellow solution was obtained (5 min). To this was added a saturated F-TEDA solution (2.0 mL; 0.145 mol L^{-1}; 0.29 mmol) in MeCN. After 7 min, TLC (TBME/hexane 1/5, R_f(starting material) = 0.36, R_f(product) = 0.50; detection by UV and/or phosphomolybdic acid; TBME = *tert*-butyl methyl ether) indicated complete conversion. The reaction mixture was extracted with water (50 mL) and TBME (30 mL), the organic phase was filtered through Al_2O_3 (1 g; washed with additional TBME) and evaporated. Liquid chromatography (TBME/hexane 1/20*)* gave **2d** (49 mg; 82 %) of as colorless oil (70.8 % *ee* by HPLC).
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Octahedral SeO_6^{6-} and Square-Pyramidal SeO_5^{4-}, Two New Oxoselenate Anions[**]

Helmut Haas and Martin Jansen[*]

For kinetic as well as thermodynamic reasons cations in tetrahedral and octahedral complexes usually show a lower Lewis acidity than in three- or fivefold coordination. We have therefore considered the main driving force for the surprisingly smooth acid–base reaction of the addition of O^{2-} to SeO_4^{2-} in the synthesis of Li_4SeO_5[1] to be the formation of a collective solid-state structure $A_4A'B_5$, thus the order variant of an AB structure type,[2] and the associated gain in lattice energy. Also the unexpected coordination polyhedron (CN = 5, trigonal-bipyramidal) was attributed to this overriding structure-chemical argument. That such explanations are not applicable, is confirmed by the preparation of two other oxoselenates, for which at first glance there are no structural features apparent that stabilize a hexaoxo- or pentaoxo anion.

For the Na_2O/Na_2SeO_4 system the solid-state reaction at a molar ratio of the starting materials of 1:2[3] under standard pressure gave $Na_6Se_2O_9$, which contains hexaoxoselenate(VI) and tetraoxoselenate(VI) anions, whereas at a ratio of 1:1 under hydrostatic pressure Na_4SeO_5 was formed. The single-crystal structure analysis[4] confirmed in the first case that according to the formulation $Na_{12}(SeO_6)(SeO_4)_3$ an octahedral orthoselenate anion had been obtained for the first time (Figure 1). This displays the point symmetry O_h within the margins of error of the structure determination. The dimensions of the tetrahedral SeO_4^{2-} ions ($\bar{d}_{\text{Se-O}} = 163.6$ pm, O-Se-O = 109.53°) are comparable with those of already known oxoselenates(VI) with tetrahedral anions (cf. Na_2SeO_4[6] with $\bar{d}_{\text{Se-O}} = 164.8$ pm). The increase of the average Se–O bond

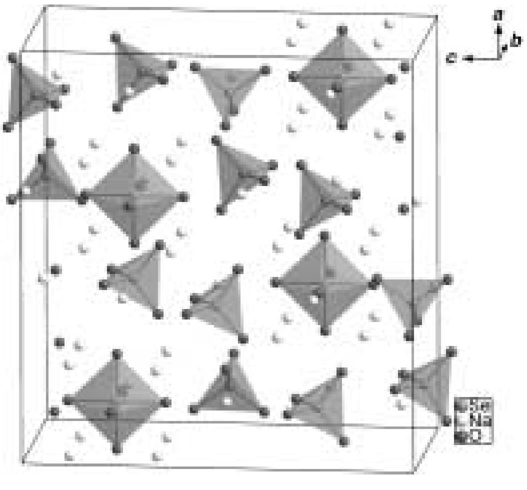

Figure 1. Crystal structure of $Na_6Se_2O_9$ (perspective representation).

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lengths with the increase of the coordination number from 4 (SeO_4^{2-}) to 6 (SeO_6^{6-}) by 11.8% corresponds to that for the transition from WO_4^{2-} to WO_6^{6-} (12.2%). The highly charged SeO_6^{6-} ion is stabilized by eight sodium ions, one located above each face, and by an additional six sodium ions, one located at each corner of the octahedron. The resulting unit $SeO_6Na_8Na_6'$ (Figure 2) resembles a $M_6X_8X_6'$ building block from transition metal cluster chemistry.[7] In analogy to $MoCl_2$ these are linked through four common sodium atoms (Na′) to give layers (Figure 3). In contrast to the Cl bridges in $Mo_6Cl_8Cl_6'$, the Na bridges here are almost linear. The SeO_4^{2-} ions are located in the holes between four $(SeO_6)O_8$ cubes and above and below the bridging sodium ions.

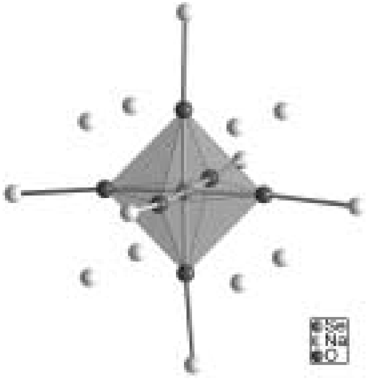

Figure 2. $(SeO_6)Na_8Na_6'$ building block in $Na_6Se_2O_9$. Bond lengths [pm] and angles [°]: Se1-O3 180.8(2) 2 ×, Se1-O4 181.4(2), Se1-O6 182.4(2), Se1-O9 183.8(2), Se1-O7 184.3(2); O3-Se1-O3 179.16(11), O3-Se1-O4 90.27(6) 2 ×, O3-Se1-O6 89.73(6) 2 ×, O4-Se1-O6 179.69(11), O3-Se1-O9 90.32(5) 2 ×, O4-Se1-O9 89.49(11), O6-Se1-O9 90.20(11), O3-Se1-O7 89.68(5) 2 ×, O4-Se1-O7 90.29(12), O6-Se1-O7 90.02(12), O9-Se1-O7 179.77(11).

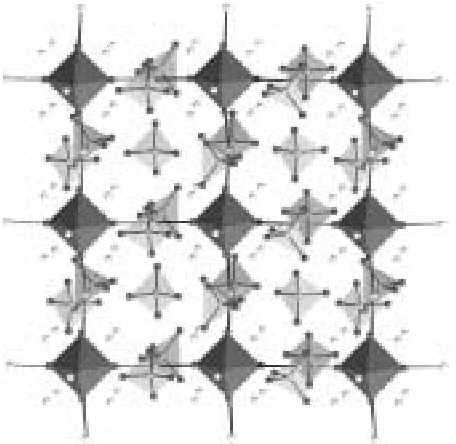

Figure 3. Layer of $Na_6Se_2O_9$.

Na_4SeO_5 only forms if a hydrostatic pressure of at least 2.5 GPa is used in the solid-state reaction. It precipitates in the form of a microcrystalline powder, thus the structure was determined by X-ray powder diffraction methods[8, 9] (Figure 4). According to the structure analysis a new type of structure is present in which square-pyramidal SeO_5^{4-} ions are observed for the first time (Figure 5). These are, however, so distorted that they can hardly be described with the ideal point symmetry C_{4v}. The increase of the average Se–O bond lengths with the increase of the coordination number from 4 (SeO_4^{2-}) to 5 (SeO_5^{4-}) by 8.0% lies significantly below the value for the octahedral SeO_6^{6-} ion and in the same range as for the trigonal-bipyramidal SeO_5^{4-} ion (6.7%). The SeO_5^{4-} ions are arranged in the structure such that four selenium atoms span a near ideal square with an edge length of 510.1 pm, and the polyhedra are directed so that an oxygen atom from the basal plane of one square pyramid is directed toward the selenium atom of a neighboring polyhedron (Figure 5). This appears to indicate a 5+1 coordination at selenium, however, the shortest Se–O distance between two polyhedra (330.2 pm) lies above that of the van der Waals distance. That, nevertheless, a bonding interaction is present, is evident from the fact that this oxygen atom displays the longest Se–O distance in the SeO_5 polyhedron. The polyhedral arrangement can be derived from $(NbF_5)_4$,[10] in which the four corner-shared NbF_6 octahedra likewise span a square. If this square is stretched isotropically and it is assumed that each polyhedron retains one of the two bridging atoms in its coordination sphere, a polyhedral arrangement is achieved such as that found in Na_4SeO_5. The positions of the selenium,

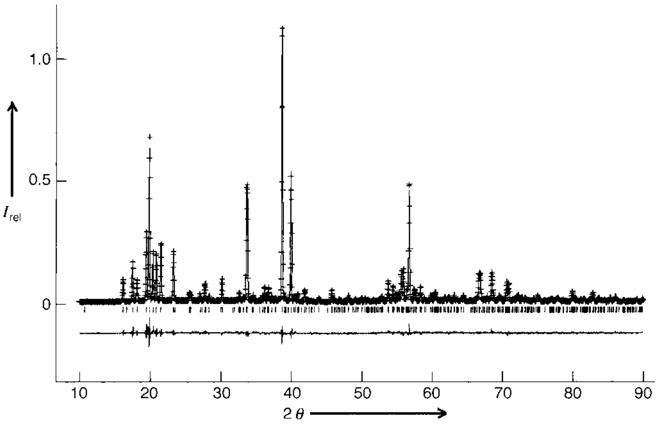

Figure 4. Powder diffraction diagram of Na_4SeO_5. Top: Measured (data points) and calculated intensities (solid line), bottom: difference plot.

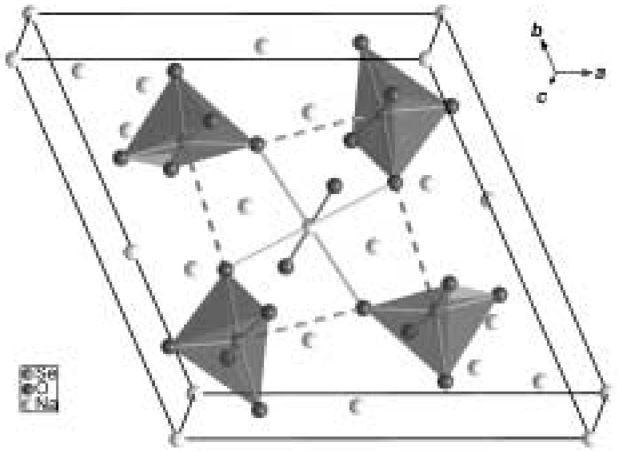

Figure 5. Crystal structure of Na_4SeO_5. Bond lengths [pm]: Se1-O1 172.8(8), Se1-O2 173.2(8), Se1-O6 181.3(7), Se1-O8 176.5(7), Se1-O10 176.6(7), Se2-O3 181.5(7), Se2-O4 177.2(8), Se2-O5 172.9(8), Se2-O7 172.9(8), Se2-O9 178.0(8).

sodium, and four of the oxygen atoms can be described in a monoclinic space group, and the unit cell can be transformed accordingly into a monoclinic one. Only one oxygen position is not consistent with this cystallographic description. The knowledge of the structure of the isotypic compound Na_4MoO_5,[11] however, substatiates the structure analysis and clarifies the observed pseudosymmetry in favor of the low symmetry space group in the triclinic system.

Experimental Section

$Na_6Se_2O_9$ was prepared by the solid-state reaction of Na_2O with Na_2SeO_4 in a molar ratio of 1:2 in a closed silver crucible sealed in a glass ampule. Na_4SeO_5 was prepared by the solid-state reaction of Na_2O with Na_2SeO_4 in a molar ratio 1:1 in a sealed silver tube under a pressure of 2.5 GPa (piston-cylinder-press[12]). In both cases, the reaction time was two days and the reaction temperature was 500 °C. Na_2O was prepared according to reference [13], and Na_2SeO_4 (purum p.a. $> 99\%$, Fluka) was dried under vacuum prior to reaction (10^{-3} mbar, 400 °C, 24 h).

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[4] a) X-ray crystal structure analysis of $Na_6Se_2O_9$: orthorhombic, space group *Pnma* (no. 62), $a = 1577.2(7)$, $b = 781.7(3)$, $c = 1475.5(7)$ pm, $V = 1819.1(18)$ Å^3, $\rho_{calcd} = 3.205\ g\,cm^{-3}$, $Z = 4$, $\mu(Mo_{K\alpha}) = 8.428\ mm^{-1}$, $F(000) = 1648$, $\lambda = 0.71073$ Å, Bruker-Smart-CCD diffractometer, graphite monochromator, crystal dimensions $0.2 \times 0.2 \times 0.2$ mm, $T = 293$ K, 36800 measured, 5226 symmetry-independent reflections, 182 refined parameters; structure solution by direct methods.[5] The sodium and oxygen positions were determined by a subsequent difference-Fourier synthesis. All atom positions were refined anisotropically to give $R1 = 0.030$ and $wR2 = 0.058$. b) Further details on the crystal structure investigations may be obtained from the Fachinformationszentrum Karlsruhe, 76344 Eggenstein-Leopoldshafen, Germany (fax: (+49) 7247-808-666; e-mail: crysdata@fiz-karlsruhe.de), on quoting the depository numbers CSD-411402 ($Na_6Se_2O_9$) and CSD-411401 (Na_4SeO_5).

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[9] X-ray crystal structure analysis of Na_4SeO_5: space group $P\bar{1}$; $a = 988.3(1)$, $b = 988.4(1)$, $c = 558.6(1)$ pm, $\alpha = 96.25(1)^\circ$, $\beta = 96.24(1)^\circ$, $\gamma = 113.41(1)^\circ$, $V = 490.8(1) \times 10^6\ pm^3$; $Z = 4$, $\rho_{calcd} = 3.551\ g\,cm^{-3}$; Stoe-Stadi-P transmission powder diffractometer, $Cu_{K\alpha 1}$ radiation, germanium monochromator, linear position-sensitive detector (Stoe-Mini-PSD), capillary measurement, 8000 data points, measurement range: $10 < 2\theta < 90$, total measurement time: 24 h, 778 observed reflections, 57 refined positional parameters, 21 temperature parameters, Rietveld refinement: $R_p = 0.0783$, $R_{wp} = 0.1037$, $R_F = 0.0773$.[4b]

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Total Synthesis of (+)-Ratjadone**

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Ratjadone (**1**) was isolated in 1994 by Höfle et al. from *Sorangium cellulosum* (So ce360) collected as a soil sample at Cala Ratjada (Mallorca, Spain).[1] It is similar in both structure and its biological profile to polyketides like leptomycin,[2] callystatin A,[3] and other related compounds.[4] Ratjadone shows high cytotoxicity in cultured mouse cell lines (L929) with an IC_{50} value of 50 pg mL^{-1} and it inhibits the growth of the HeLa cell line (KB3.1) at remarkably low concentrations (40 pg mL^{-1}). In addition, it shows other interesting biological effects (e.g. changes in the cell morphology and growth of yeast) and a narrow spectrum of antifungal activity with MIC values (MIC = mimimal inhibiting concentration) ranging from 0.04 to 0.6 µg mL^{-1} for *Mucor hiemalis*, *Phythophthora drechsleri*, *Ceratocystis ulmi*, and *Monila brunnea*.[5] Despite these promising biological properties, neither the exact mode of action nor the molecular targets are known.

Here we report the first total synthesis of ratjadone.[6] Our highly convergent approach allows the rapid assembly of various ratjadone derivatives for the identification of biologically active substructures. Since only the relative stereochemistry of the tetrahydropyran moiety (C17–C21) was known at the outset of this synthesis, it was necessary to design a flexible strategy that would allow the formation of all possible stereoisomers.[7] The structure of ratjadone reveals the diene systems as attractive sites for the retrosynthetic disassembly (Scheme 1). We dissected ratjadone into three fragments, the tetrahydropyran subunit **A**, the phosphonium salt **B**, and the aldehyde **C**. In the synthesis, fragments **B** and **C** were joined by a Wittig reaction followed directly by a Heck coupling for the connection with the **A** fragment.

The synthesis of **A** began with the transformation of the known aldol product **2**[8] into the Weinreb amide[9] followed by protection of the hydroxy group (TBS) and subsequent reduction with Dibal-H to generate aldehyde **3** (Scheme 2). The all-*syn* stereo triad (C19, C20, C21) of the **A** fragment was generated by a vinylogous Mukaiyama aldol reaction.[10] The reaction of **3** with the ketene acetal **4** and $BF_3 \cdot OEt_2$ as the Lewis acid gave the α,β-unsaturated ester **5** with a selectivity of 3:1 in favor of the desired Felkin–Ahn product. After silylation of the hydroxy group and reduction of the ester functionality, the allylic alcohol **6** was diastereoselectively epoxidized ($de > 95\%$ in favor of the *anti* isomer) with *m*CPBA.[11] Removal of the TBS protecting groups with TBAF was followed by treatment with amberlyst-15 to induce the intramolecular 6-*exo* ring closure.[12] This key step generates

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