2.982(8) Å). This clearly represents an entirely different bonding system from the one discussed here.

Evidently, the bonding of the thiolate sulfur to four equivalent copper atoms is electron-deficient, since RS⁻ has only three lone pairs in addition to the C-S bond pair. The copper atoms are sufficiently separated that the cluster may be described in terms of noninteracting square-pyramidal CSCu₄ units. This geometry favors the bonding, since two of the copper atoms can interact with the sulfur p_x orbital (the S-C axis is the z direction), and the other two with p_y . All four copper atoms can interact with an inward-pointing sp_z hybrid. It is thus possible to accommodate the four available electron pairs in bonding molecular orbitals (Figure 3), the next highest orbital being



Figure 3. Schematic molecular orbital diagram for the $CSCu_4$ unit. Symmetry labels correspond to idealized C_{4v} symmetry.

nonbonding (or slightly antibonding, to the extent that the copper orbitals overlap). Inclusion of the sulfur $d_{x^2-y^2}$ orbital might stabilize the b₁ orbital slightly, but would provide no additional bonding electrons. The bond lengths indicate that this sixcenter, eight-electron system is tightly bound.

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A New Asymmetric Formylation of Aldehydes**

Andreas Kirschning,* Gerald Dräger, and Alexander Jung

Formylation of aldehydes is of major importance in synthesis.^[11] The formyl anion is typically employed in a masked form; thus masked α -hydroxy aldehydes, carboxylic acids, or esters are formed, which subsequently have to be unmasked. The most commonly applied formylating agents are heteroatom-stabilized (often sulfur-stabilized) carbanions. Control of the configuration of the newly formed stereogenic center at C-2 has been achieved either by an α -positioned chiral center in the substrate^[2, 3] or by chiral auxiliaries in the carbanion.^[4] In the latter case achiral aldehydes may be used but liberation of the carbonyl group is often accompanied with irreversible loss of the chiral auxiliary.^[5]

In contrast, our strategy uses a formyl anion equivalent that homologates aldehydes in the primary step in such a way that prochirality at the former aldehyde carbon atom is retained. Then the hydroxy group at C-2 is enantioselectively introduced and the masked formyl group at C-1 liberated simultaneously. Ketene O,O-acetals **1** are ideal for this new formylation strategy, because they can be prepared from aldehydes in the Horner-Wittig reaction,^[6] and they give intermediate diols **2** in the Sharpless asymmetric dihydroxylation (AD)^[7] that spontaneously collapse to α -hydroxy carboxylates (Scheme 1).



Scheme 1. Asymmetric formylation of aldehydes via ketene O,O-acetals.

In order to carry out this formylation sequence most efficiently, the Horner–Wittig step had to be optimized. Quantitative formation of the metalated diethoxymethyl diphenyl phosphine oxide^[8] was best achieved by use of lithium diisopropylamide (LDA) or potassium diisopropylamide (KDA) in THF. In contrast to earlier reports by van der Gen et al.,^[9] a minimum deprotonation time of two hours and a temperature of -110 °C is important. Under these conditions the dark red anion is quantitatively generated. Use of complexating agents like HMPA or crown ethers did not result in improved yields.^[10] Addition of aldehydes **3a**–**h** afforded stable phosphine oxides **4a**–**h** after

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COMMUNICATIONS

| Aldehyde | R | Cation [a] | Phosphine oxide (Yield [%])[b] | Hydroxyester (Yield [%])[c, d] | AD-mix x [(D ee [%] | HQ)2PHAL] Config. | AD-mix β [(D ee [%] | HQD) ₂ PHAL] Config. |
|----------|-------------------|------------|-----------------------------------|-----------------------------------|------------------------|----------------------|------------------------|------------------------------------|
| 3a | | K | 4a (89) | 5a (76, 68) | 98.4 | 2 <i>S</i> | 99.9 | 2 R |
| 3b | | К | 4b (84) | 5 b(68, 57) | 93 [e] | 2 <i>S</i> | 95[e] | 2 R |
| 3c | <u>}-</u> | К | 4c (72) | 5c (88, 63) | 69.7 | 2 <i>S</i> | 80.3 | 2 <i>R</i> |
| 3d | MeO | K | 4d (92) | 5d (71, 65) | 86.1 | 2 <i>S</i> | 88.0 | 2 R |
| 3e | Me ₂ N | Li | 4e (71) | 5e (23, 16) | — [f] | _ | — [f] | _ |
| 3f | \sim | Li | 4f (71) | 5f (73, 52) | 95.7 | 2 <i>S</i> | 93.5 | 2 <i>R</i> |
| 3g | Me Me | Li | 4g (55) | 5g (49, 27) [g] | 92.6 | 2 <i>S</i> | 92.4 | 2 R |
| 3h | | Li | 4h (34) | 5h (94, 32) | >95(de)[h] | 2 S, 4 R | >95(de)[h] | 2 R, 4 R |

Table 1. Asymmetric formylation of aldehydes 3a-h: yields, configurations and enantioselectivities

[a] Optimal cation. [b] Yield of isolated product after column chromatography. [c] The first value in the parentheses refers to the yield of isolated product based on phosphine oxides 4a-h. [d] The second value in the parentheses is the overall yield based on aldehydes 3a-h. [e] Determined from the ¹H NMR spectra of both diastereomeric Mosher esters. [f] Racemic mixture. [g] Reduced yield due to volatile ketene acetal. [h] Determined from ¹H NMR spectra.

aqueous workup. These phosphine oxides could be chromatographed on silica gel and fully characterized or used directly for the next step (Table 1). In some cases the potassium salt of diethoxymethyl diphenyl phosphine oxide reacted more efficiently. The yields of the isolated products were considerably reduced for enolizable aldehydes like 3g and 3h. In the following the corresponding ketene acetals 1 were liberated by KOtBupromoted elimination.^[11] After concentration of the reaction mixture at 0 °C the crude product was enantioselectively oxidized to afford the α -hydroxy carboxylates 5a - h in moderate to good overall yield (Table 1).^[12] In most cases ketene acetal formation and the following asymmetric dihydroxylation process proceeds almost quantitatively. Under the phase-transfer conditions employed, proton-induced hydrolysis of the ketene acetals to the corresponding carboxylates did not occur. However, oxidation is best performed in an inverse manner by adding the precooled AD-mixture to 1.

Except for 4-dimethylaminobenzaldehyde (**3e**), all aldehydes were formylated with a high degree of enantioselectivity. The lower *ee* values for dihydrochinin (DHQ) ligands than for dihydrochinidin (DHQD) ligands is a phenomenon often observed for the AD-process.^[13] The formation of racemate **5e** may be caused by competition between the amino group in **6** and the chiral ligand for the binding site of the osmium complex. To test this hypothesis, a mixture of ketene acetals **6** and **7** were oxidized under AD-conditions, and in a second experiment **6** was oxidized first and ketene acetal **7** added after complete transformation (Scheme 2). Again the *ee* values of the oxidation products for both experiments scarcely differed from those obtained under standard conditions (racemate for 5e and >99 and 95.1% ee, respectively for 5a). Therefore the amino group of neither the ketene acetal 6 nor the product 5e deactivates the chiral catalyst. Probably either the polarity of the dimethylamino group in 6 prevents binding of the chiral ligand to the osmate complex or (more likely) 5e undergoes rapid racemization. In fact, when the ee of 5b was redetermined after three months of storage at -10 °C the value had dropped from 93% down to 83%.

In summary, we present a new asymmetric formylation method for aldehydes that affords α -hydroxy carboxylates with high enantiomeric purity. Unlike common one-carbon homologations of aldehydes, we utilize prochiral ketene O,O-acetals as intermediates. In view of new chiral ligands for the AD-process that have recently been disclosed by Sharpless and co-workers,^[13, 14] this process may be improved further.

Experimental Section

4: To a solution of LDA or KDA [15] (1.1 mmol) in dried THF (15 mL) under nitrogen at $-110 \,^{\circ}\text{C}$ was added diethoxymethyl diphenyl phosphine oxide (0.35 g, 1.2 mmol) in dried THF (2 mL) over a period of 30 min. After 1.5 h at ambient temperature freshly purified aldehyde 3 (1.0 mmol) in dried THF (2 mL) was added to the dark red solution. The reaction mixture decolorized immediately, was hydrolyzed after 15 min with water (4 mL) and allowed to warm to room temperature. After addition of brine (10 mL) and dichloromethane (10 mL) the layers were separated. The aqueous phase was washed with dichloromethane (5 ×), and the combined organic extracts were dried (MgSO₄) and concentrated in vacuo. The crude product can either be purified by column chromatography on silica gel or can be

used directly for the next reaction. In this case, traces of water were removed by codistillation with toluene prior to use.

5: The adduct 4 (1 mmol) was dissolved in dried THF (15 mL) under nitrogen and treated with freshly sublimed potassium *tert*-butoxide (12.3 mg, 1.1 mmol) in THF (2 mL) at 0 °C. After 15 min the solution was concentrated under reduced pressure (with cooling in an ice bath) to a volume of appoximately 1 mL. A suspension of "AD-mix" (1.4 g; that



Scheme 2. AD competition experiment with ketene acetals 6 and 7: a) 6, 3h, 0° C, then addition of 7, 12h, 0° C; b) 6, 7, 12h, 0° C.

is, 1 mol% (DHQ)2-PHAL for AD-mix-α or (DHQD)2-PHAL for AD-mix-β) in water (5 mL) and tert-butanol (5 mL) was prepared at room temperature, cooled to 0 °C, and added to the precooled ketene acetal. After addition of methanesulfonamide (95 mg, 1.02 mmol) the suspension was vigorously stirred overnight at 0 °C and reduced with sodium sulfite (1.5 g). Stirring was continued for 30 min at 0 $^\circ \text{C}$ and after an additional 15 min at room temperature water (5 mL) and dichloromethane (20 mL) were added. The aqueous layer was extracted with dichloromethane $(5 \times)$, and the combined organic extracts were dried (MgSO₄), concentrated under reduced pressure, and purified by column chromatography on silica gel.

Conditions for the determination of the enantiomeric excesses of the α -hydroxycarboxylates 5 by GC analysis on a chiral heptakis(2,6-di-O-methyl-3-O-pentyl)-βcyclodextrin column (all isothermal with a flow rate of 1.5 mLmin^{-1}): 5a: 100 °C, 52.7 min (2S), 48.6 min (2R); 5c: 115°C, 104.1 min (2S), 98.6 min (2R); 5d: 131°C, 52.1 min (2S), 47.9 min (2R); 5e: 145 °C, 64.7 min (2S), 62.3 min (2R); 5f: 107 °C, 42.8 min (2S), 41.0 min (2R); 5g: 65 °C, 38.7 min (2S), 36.7 min (2R).

The absolute configuration was deduced from comparison of CD-spectra with those of authentic (2R)-5a (positive Cotton-effect for (2S)-5a-h; negative Cotton-effect for (2R)-**5a**-**h**) with authentic (2R)-**5a**).

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Constitution of the Iodyl Cation**

Martin Jansen* and Ralph Müller

The syntheses and crystal chemistry of ternary oxides can be categorized into three classes depending on the oxide basicity or the acidity of the appropriate binary components.^[1] The largest group of ternary oxides consists of binary components with strongly different oxide basicities. As a rule these contain complex anions (e.g. in $K_6[Co_2O_7]$) that are formed through O^{2-1} transfer.^[2] Combinations of binary oxides with similar basicities (e.g. $MgAl_2O_4$) often are referred to as double oxides. The investigation of ternary oxides of nonmetals, of which both components preferably act as acids with other oxides as in systems containing iodine oxides, has more or less been neglected until recently. Although a large number of such phases have been identified through their "fingerprints", mainly with vibrational spectra, their composition and constitution have, as a rule, not been reliably clarified. This fact applies especially to cases where iodine oxide appears as oxide base and crystallochemically takes over the cationic function. Of these ternary oxides, mainly known as iodosyl and iodyl compounds, only the crystal structure of $(IO)_2SO_4$ or $I_2O_3 \cdot SO_3$ could be substantiated until recently.^[3] The polymeric and mixed valency $I_3O_6^+$ cation in $(I_3O_6)HSO_4$ has now also been elucidated.^[4] The details given on the iodyl cation IO_2^+ are contradictory and generally lack a reliable experimental basis.^[5] The iodyl cation is reported to exist as a monomer in solutions.^[6] A polymeric constitution similar to the structure of solid selenium(IV) oxide has been suggested for the solid state.^[7] This unsatisfactory state of iodine-oxygen chemistry is mainly caused by the unusually large variety of compounds within these systems, which makes it a laborious task to prepare single-phase products.^[8] Furthermore, the preparation of crystals is impeded by the polymeric nature and thermal lability of the iodine-oxygen compounds.

If the reaction parameters of the system $I_2O_5/SO_3/H_2O$ (beside concentration and temperature, the time required for the establishment of equilibrium is a critical factor) are adjusted in such a way that $(IO_2)_2S_2O_7$ is the first phase to exceed its solubility product, it precipitates as a

coarse crystalline product. The analysis of the crystal structure contradicts all earlier suggestions for the structure of the iodyl cation,^[9] and reveals it to be a dimer $I_2O_4^{2+}$ (Figure 1). The variation of I-O bond lengths within this unit is remarkable. The two shortest I-O distances and the asymmetrical I-O-I bridges suggest a monomeric, angular IO_2^+ (bond angle at iodine: 98°, isoelectronic with SO_2). If not examined in detail the dimensions of the $S_2O_7^{2-}$ anion do not present any peculiarities.

This rigorous description as an ionic crystal of $I_2O_4^{2+}$ cations and



Figure 1. Crystal structure of $I_2O_4^{2+}$. Selected bond lengths [pm] and angles ["]: I1-O8 201.2(7), 11-O10 190.9(8), 11-O11 174.0(12), I2-O8 190.7(7), 12-09 175.2(6), 12-010 199.4(8); O8-I1-O10 77.0(3), O8-11-O11 98.2(20), O10-11-O11 98.8(20), O8-I2-O10 77.5(3), 08-12-09 97.4(20), O9-I2-O10 98.0(20).

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