

Supporting Information (11 pages)

A Highly Chemoselective Oxidation of Alcohols to Carbonyl Products with Iodosobenzene Diacetate Mediated by Chromium(III)(salen) Complexes: Synthetic and Mechanistic Aspects

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Experimental Section

General Aspects. ¹H- and ¹³C-NMR spectra were recorded on a Bruker AC 200 (¹H: 200 MHz, ¹³C: 50 MHz) or a Bruker AC 250 (¹H: 250 MHz, ¹³C: 63 MHz) spectrometer with CHCl₃ (δ 7.26) for the ¹H and CDCl₃ (δ 77.0) for the ¹³C resonances as internal reference standards. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. GC-MS analysis was conducted on a MD 800 mass spectrometer, coupled with a Fisons Instruments GC 8000. A DB-Wax column was employed as stationary phase and He gas was used as carrier: 50 °C (3 min isotherm) to 240 °C (4 °C/min).

ESI-MS analysis was performed by utilizing a TSQ 7000 tandem-mass spectrometer system, equipped with an ESI interface (Finnigan MAT). Data acquisition and evaluation were conducted with a ICIS 8.1 software (Finnigan MAT). For sample injection, a Rheodyne 8125 with 5- μ l sample loop was used. Acetonitrile at a flow rate of 50 μ l/min was employed as solvent. For pneumatically assisted electrospray ionization, the spray-capillary voltage was set to 4.0 kV and the temperature of the heated inlet capillary was 200 °C. Nitrogen was used as sheath gas (80 psi). Positive ions were detected with a total scan duration of 3.0 s for a single full spectrum (mass range m/z 150 to 2000). The MS-MS experiments for the product-ion scans (mass range m/z 150 to 2000) were performed at a collision gas pressure of 260 mPa with Ar gas and the collision energy was set to 25 or 35 eV with a total scan duration of 3.0 s for a single spectrum.

Materials. Iodosobenzene was prepared by hydrolysis of the corresponding diacetate according to the literature method.¹³ Iodosobenzene diacetate was obtained from Merck. The alcohols **1a**, **1c**, **1g** and **1k** were commercially available (Merck, Aldrich). The alcohols **1b**¹⁴, **E-1d**¹⁵, **Z-1d**¹⁶, **1e**¹⁷, **1f**¹⁸, **E-1h**¹⁴, **Z-1h**¹⁵, **1i**¹⁹, **1j**^{12a}, **1l**²⁰, **1m**²¹, **1n**²² were synthesized in analogy to known methods. The ¹⁸O-labeled alcohol **¹⁸O-1c** was prepared by equilibrating the alcohol **1c** with highly enriched ¹⁸O-labeled water (94.5 atom%) according to the literature procedure.²³

The chromium complex [Cr^{III}(salen)]Cl [**A(Cl)**] was obtained according to the literature procedure⁶ and the complexes [Cr^{III}(salen)]TfO [**A(TfO)**] and [Cr^{III}(salen)]PF₆ [**A(PF₆)**] were made from **A(Cl)** by anion exchange according to the known procedure.²⁴ The authentic oxo complexes [Cr^V(salen)(O)]TfO [**D(TfO)**] and [Cr^V(salen)(O)]PF₆ [**D(PF₆)**] were prepared by oxidation of the respective [Cr^{III}(salen)]X complex with iodosobenzene or its diacetate

derivative by following the literature method.^{9a,b} Since the oxidation of the complex $[\text{Cr}^{\text{III}}(\text{salen})]\text{TfO}$ [**A(TfO)**] by $\text{PhI}(\text{OAc})_2$ is not reported in the literature, the experimental procedure of this reaction is described below.

Oxidation of $[\text{Cr}^{\text{III}}(\text{salen})]\text{TfO}$ [A(TfO)**] by $\text{PhI}(\text{OAc})_2$.** To a solution of the complex **A(TfO)** (51.0 mg, 0.100 mmol) in 5 mL CH_3CN was added $\text{PhI}(\text{OAc})_2$ (35.4 mg, 0.110 mmol) at ca. 20 °C under an Ar gas atmosphere. After ca. 5 min, the yellow solution turned to dark-green. The reaction mixture was concentrated after 1 h to 2 mL and dry Et_2O was added slowly. The black-green precipitate (37 mg, 79%) was collected by filtration. The IR spectrum of this solid material matched well with that of the authentic oxo complex $[\text{Cr}^{\text{III}}(\text{salen})(\text{O})]\text{TfO}$ [**D(TfO)**], which showed a characteristic stretching band at 995 cm^{-1} for the $\text{Cr}=\text{O}$ group.^{9a,b}

ESI-MS Characterization of Cr(salen) Complexes. An aliquot of 5 μL from a 1.2 mM stock solution of the complex $[\text{Cr}^{\text{III}}(\text{salen})]\text{TfO}$ [**A(TfO)**] in CH_3CN was analyzed by ESI-MS. It showed the ion peaks of m/z 318.2 $[\text{Cr}^{\text{III}}(\text{salen})]^+$, m/z 359.4 $[\text{Cr}^{\text{III}}(\text{salen})\{\text{CH}_3\text{CN}\}]^+$ and m/z 400.2 $[\text{Cr}^{\text{III}}(\text{salen})\{\text{CH}_3\text{CN}\}_2]^+$. The ESI-MS analysis of the authentic oxo complex $[\text{Cr}^{\text{V}}(\text{salen})(\text{O})]\text{TfO}$ [**D(TfO)**], which was prepared by oxidation of **A(TfO)** with PhIO according to the literature procedure^{9a,b}, showed the ion peak m/z 333.8 $[\text{Cr}^{\text{V}}(\text{salen})(\text{O})]^+$. The complex obtained from the oxidation of **A(TfO)** with $\text{PhI}(\text{OAc})_2$ also showed the ion peak m/z 333.8 (Figure 1).

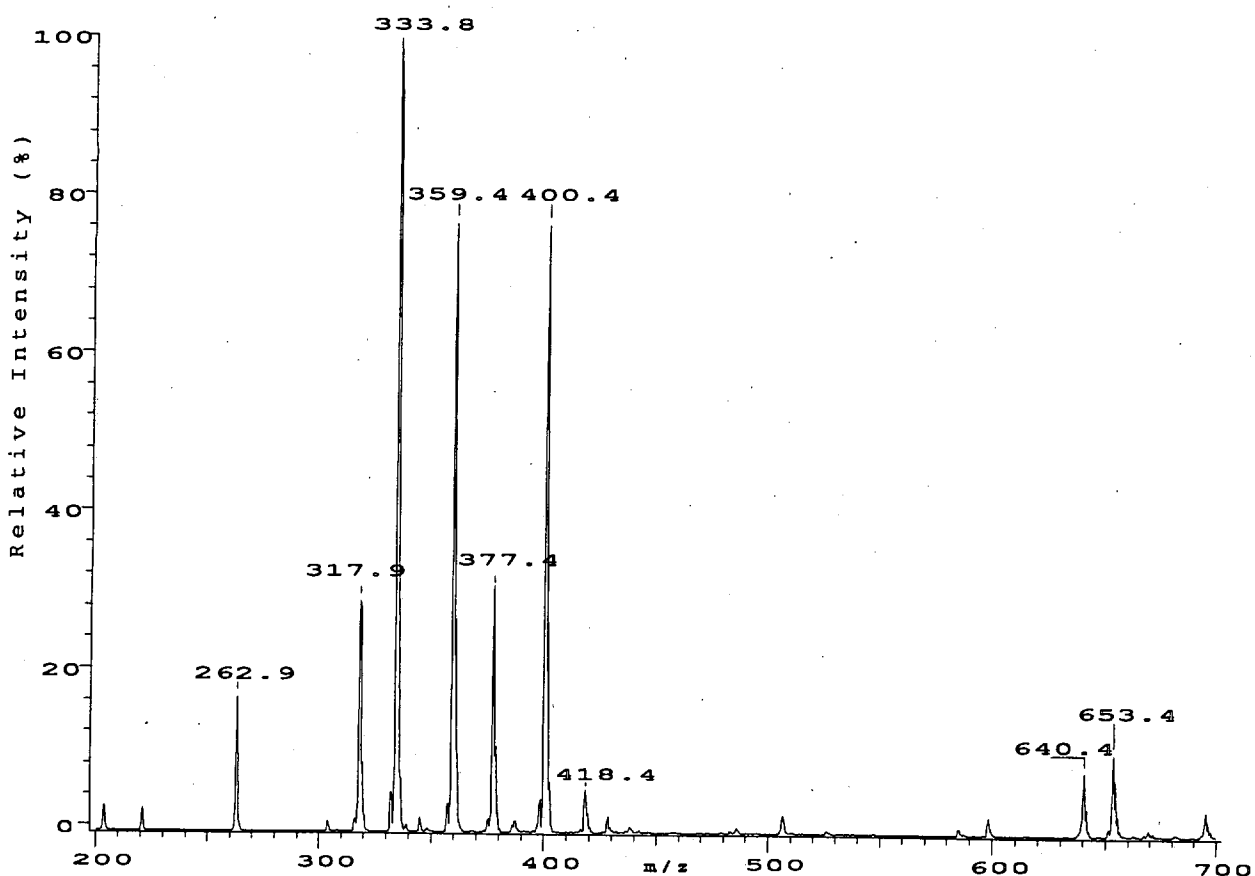


Figure 1 Electrospray mass spectrum of the reaction mixture of the $[\text{Cr}^{\text{III}}(\text{salen})]\text{TfO}$ complex with $\text{PhI}(\text{OAc})_2$ in CH_3CN .

To characterize additional chromium species formed in the reaction of $\text{A}(\text{TfO})$ with $\text{PhI}(\text{OAc})_2$, a 1.2 mM solution of the complex $\text{A}(\text{TfO})$ and $\text{PhI}(\text{OAc})_2$ (1.5 equiv) in CH_3CN was stirred at 20 °C for 12 min. A 5- μL sample from this solution was analyzed by ESI-MS (Figure 1). The following ion peaks were observed: m/z 640.4 (8%) $[\text{Cr}^{\text{III}}(\text{salen})\{\text{PhI}(\text{OAc})_2\}]^+$ (B^+), m/z 377.4 (31%) $[\text{Cr}^{\text{IV}}(\text{salen})(\text{OAc})]^+$ (C^+), and m/z 333.8 (100%) $[\text{Cr}^{\text{V}}(\text{salen})(\text{O})]^+$ (D^+), together with the three ion peaks detected in the CH_3CN solution of the complex $\text{A}(\text{TfO})$ without oxygen source.

General Procedure for the Oxidation of Alcohols **1** with Iodobenzene Diacetate Catalyzed by Chromium(III)(salen) Complexes

To a solution of the substrate **1** (0.3-0.5 mmol) and 0.1 equiv of the catalyst [Cr^{III}(salen)]X in 3-5 mL of CH₂Cl₂ was added 1.5 equiv of PhI(OAc)₂. After stirring for the time specified in the Table 1, the reaction mixture was adsorbed on silica gel (2-3 g) by careful evaporation of the solvent (20 °C, 300-400 mbar). The adsorbed material was transferred to a small Buchner funnel, on which had been placed a silica-gel (4-5 g) pad, and washed under suction (300-400 mbar) first once with petroleum ether (30-50 mL) to remove iodobenzene and then once with Et₂O (40-60 mL) to obtain the carbonyl products **2** and unreacted alcohols as mixture. This treatment was necessary to remove the paramagnetic chromium species, which cause severe line broadening in the NMR spectrum and prevent quantitative product analysis. After evaporation (20 °C, 100-400 mbar) of the solvent, the crude product mixture was analyzed by ¹H-NMR spectroscopy for conversions, mass balance, yields and chemoselectivities.

The carbonyl products **2a**, **c**, **e**, **f**, **g** and **k** were identified by comparison with the authentic samples (commercially available). The carbonyl compounds **2b**²⁵, *E*-**2d**²⁶, *Z*-**2d**²⁷, *E*-**2h**²⁸, *Z*-**2h**²⁸, **2i**²⁹, **2j**^{8b}, **2l**²⁰, **2m**²¹, **2n**³⁰ and the epoxy alcohol *E*-**3h**³¹ were characterized by comparison of their NMR data with those reported in the literature.

Preparative Oxidation of the Alcohols *E*-**1h**, **1k**, **1m** and **1n**

The preparative oxidations were performed in the presence of a catalytic amount of NaOAc (0.2 equiv), because this external base enhanced the conversion at decreased reaction time.

Alcohol E-1h. To a solution of the alcohol *E-1h* (0.148 g, 1.00 mmol) in CH₂Cl₂ (10 mL), the complex **A(Cl)** (0.039 g, 0.10 mmol), NaOAc (0.017 g, 0.200 mmol) and PhI(OAc)₂ (0.483 g, 1.50 mmol) were added successively. The reaction mixture was stirred at 20 °C for 4 h to achieve full conversion of the alcohol. The work-up of the reaction mixture according to the general procedure and subsequent flash silica-gel chromatography (80 : 20 mixture of petroleum ether/Et₂O as eluent) afforded the ketone *E-2h* (0.13 g, 89%) and the epoxide *E-3h* (0.06 g, 3.6%) as colorless oil.

Alcohol 1k. The above procedure was applied for the oxidation of the alcohol **1k** (0.116 g, 0.750 mmol) with PhI(OAc)₂ (0.362 g, 1.12 mmol) in the presence of the complex **A(Cl)** (0.029 g, 0.075 mmol) and NaOAc (0.011 g, 0.160 mmol). The reaction was completed after 3 h, and the respective aldehyde **2k** was formed as the only product. Since **2k** is a low boiling product, the yield (91%) was determined by ¹H-NMR analysis with dimethyl isophthalate as internal standard. For this purpose, the crude product was purified by flash silica-gel chromatography (85 : 15 mixture of petroleum ether/Et₂O as eluent), the solution was concentrated under vacuum (20°C, 350 mbar) and a sample of the concentrated solution was analyzed by ¹H-NMR spectroscopy.

Alcohol 1m. A sample of 0.103 g (0.600 mmol) **1m** was oxidized with PhI(OAc)₂ (0.290 g, 0.900 mmol) in the presence of the complex **A(Cl)** (0.023 g, 0.060 mmol) and NaOAc (0.010 g, 0.120 mmol) in CH₂Cl₂ (10 mL). After work-up according to the general procedure, the ¹H-NMR analysis of the crude reaction mixture showed the enones *Z/E-2m* in a ratio of

86:14. Silica-gel chromatography afforded 0.015 g (14.6 %) of **Z-2m** and 0.067 g (65%) of **E-2m** (*Z*:*E* ratio 19 : 81), and 6.00 mg (5.8%) of the starting alcohol **1m** was recovered.

Alcohol 1n. A sample of **1n** (0.121 g, 0.600 mmol) was oxidized with $\text{PhI}(\text{OAc})_2$ (0.290 g, 0.900 mmol) in the presence of the complex **A (Cl)** (0.023 g, 0.060 mmol) and NaOAc (0.010 g, 0.120 mmol) in CH_2Cl_2 (10 mL). After standard work-up, the $^1\text{H-NMR}$ analysis of the crude reaction mixture showed the enones *Z/E* **-2n** in a ratio of 95:5. Silica-gel chromatography afforded 0.015 g (12.4%) of **Z-2n** and 0.076 g (62.8%) of **E-2n** (*Z/E* ratio 17: 83), and 10.0 mg (8.2%) of the starting alcohol **1n** was recovered.

Product Studies in Oxidation of the Allylic Alcohol *E*-2h

Stoichiometric Oxidation. To a solution of the alcohol ***E*-1h** (7.40 mg, 0.050 mmol) in CH_2Cl_2 (2 mL) was added 0.060 mmol of the authentic oxo complex **D(TfO)** or **D(PF₆)** in the absence or presence of PPNO (0.120 mmol) and the reaction mixture was stirred at ca. 20 °C for 0.5 h or 1 h. After work-up according to the general procedure, the crude reaction mixture was analyzed by $^1\text{H-NMR}$ spectroscopy with dimethyl isophthalate as an internal standard for conversion, mass balance and product distribution (chemoselectivity). The data are given in Table 2.

Catalytic Oxidation. To a solution of the alcohol ***E*-1h** (14.8 mg, 0.100 mmol) and 0.10 mmol of the Cr^{III} (salen) complex (specified in Table 2) was added either $\text{PhI}(\text{OAc})_2$ or PhIO (0.15 mmol) in the presence or absence of PPNO (0.02 mmol). The reaction mixture was stirred at ca. 20 °C for 0.5 h or 1 h. After work-up according to the general procedure,

the crude reaction mixture was analyzed by $^1\text{H-NMR}$ spectroscopy with dimethyl isophthalate as an internal standard (data in Table 2).

^{18}O -Labeling Experiments

Stoichiometric Oxidation. To a solution of 12.4 mg (0.100 mmol) $^{18}\text{O-1c}$ (^{18}O content $90 \pm 5\%$) in CH_2Cl_2 (3 mL) was added the oxo complex **D(TfO)** (62.5 mg, 0.120 mmol). The reaction mixture was stirred at ca. 20 °C and monitored by TLC. After 50 h, the reaction was worked up according to the general procedure, except no petroleum-ether wash was employed.

GC-MS analysis of the crude mixture revealed a 1:1 mixture (51: 49) of the ketone and starting alcohol, and the ^{18}O contents were 84% for $^{18}\text{O-2c}$ and 91% for the unreacted alcohol $^{18}\text{O-1c}$ (error $\pm 5\%$). The ^{18}O content was determined by the GC-MS analysis from the relative intensities of the molecular ions m/z 122 and 124 for the carbonyl compounds **2c** and $^{18}\text{O-2c}$ and m/z 126 and 124 for the alcohols **1c** and $^{18}\text{O-1c}$.

Catalytic Oxidation. To a solution of $^{18}\text{O-1c}$ (12.4 mg, 0.100 mmol) and the complex **A(Cl)** (5.00 mg, 0.100 mmol) in CH_2Cl_2 (3 mL) was added either $\text{PhI}(\text{OAc})_2$ or PhIO (0.15 mmol). The reaction mixture was stirred at 20 °C and the conversion monitored by TLC. Work-up after 6 h, and analysis of the crude reaction mixture as above gave ^{18}O contents of 90% and 87% (error $\pm 5\%$) for the $^{18}\text{O-2c}$ with $\text{PhI}(\text{OAc})_2$ and with PhIO .

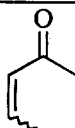
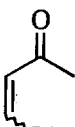
Control Experiments

To assess whether $\text{PhI}(\text{OAc})_2$ may oxidize the alcohol **1** directly, a solution of the alcohol *E*-**1h** (29.6 mg, 0.200 mmol) and $\text{PhI}(\text{OAc})_2$ (97.0 mg, 0.300 mmol) in CH_2Cl_2 (4 mL) was stirred without any $\text{Cr}^{\text{III}}(\text{salen})$ complex at 20 °C for 6 h. The reaction mixture was worked up according to the general procedure and directly submitted to $^1\text{H-NMR}$ spectroscopy. The analysis showed < 5% conversion of the alcohol *E*-**1h** and a high mass balance (> 95%).

To scrutinize the effect of the base NaOAc on the catalytic oxidation of the alcohol, the oxidation of the alcohol *E*-**1h** (44.5 mg, 0.300 mmol) with $\text{PhI}(\text{OAc})_2$ (145 mg, 0.450 mmol) and the complex **A(Cl)** (11.0 mg, 0.030 mmol) was carried out in the presence of catalytic amounts of NaOAc (11.0 mg, 0.060 mmol) in 4 mL CH_2Cl_2 at 20 °C. TLC analysis revealed complete conversion of *E*-**1h** within 3 h. After work-up according to the general procedure, the quantitative $^1\text{H-NMR}$ analysis of the crude reaction mixture showed a high yield (98%) of enone *E*-**2h** and high mass balance (98%).

Acid-Catalyzed *Z/E* Isomerization of the Enones **2d and **2h**.** A 90:10 or >95:5 mixture of *Z/E* isomers of the enone **2d** or **2h** was dissolved in normal CDCl_3 (contains traces of HCl) or in acid-free CDCl_3 (filtered through basic Al_2O_3), and the *Z/E* ratio was determined at different time intervals by $^1\text{H-NMR}$ spectroscopy (Table 4). The enone *Z*-**2h** was also isomerized on silica gel during chromatographic purification. The crude enone product, obtained by catalytic oxidation of *Z*-**1h**, showed a *Z/E* ratio of 91:9 (Table 1, entry 10). After silica-gel chromatography of the crude product, the *Z/E* ratio changed to 15:85.

Table 4 Acid-Catalyzed *Z/E* Isomerization of the Enones **2d** and **2h**.

substrate	solvent	time (min)	<i>Z</i> : <i>E</i> ratio
 2d	CDCl ₃	0	90:10
	CDCl ₃	50	32:68
	CDCl ₃ ^a	40	90:10
 2h	CDCl ₃	0	>95:05
	CDCl ₃	30	75:25
	CDCl ₃	300	10:90
	CDCl ₃ ^a	20	>95:05
	CDCl ₃ ^a	300	>95:05

^aCDCl₃ was filtered through basic Al₂O₃.

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