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# 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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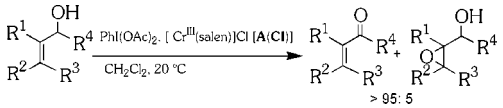
## ABSTRACT




**The catalytic oxidation of the allylic alcohols 1d−n with iodosobenzene diacetate, mediated by the [$Cr^{III}$(salen)]X complex, affords the respective enones in excellent chemoselectivity for $Cl^-$ as counterion [complex A(Cl)], while for the counterions $TfO^-$ [complex A(TfO)] and $PF_6^-$ [complex A($PF_6$)] nearly equal amounts of enone and epoxide are observed. This counterion-dependent oxidation of allylic alcohols by $Cr^{III}$(salen) complexes is rationalized in terms of Lewis acid catalysis by the complex A(Cl) and redox catalysis for A(TfO) and A($PF_6$).**

The oxidation of alcohols to carbonyl products is a pivotal transformation in organic chemistry, which has received much attention over the years, especially the search for versatile and selective reagents in catalytic applications.[1] Particularly in the past decade, the oxidizing properties of hypervalent iodine compounds[2] have been of increasing interest, of which the highly utilized pentavalent iodine reagents stand out, namely, the Dess−Martin periodinane[3] and its direct precursor *o*-iodoxybenzoic acid.[4] Despite their utility and popularity, a serious disadvantage of such iodine(V) oxidants is their explosive nature, which obliges their *impromptu* generation, since these potentially dangerous reagents should not be stocked.[5]

In contrast, the facile, safe to use, readily available, and persistent iodine(III) oxidants, e.g., iodosobenzene[6,7] and most notably its diacetate,[5,8] have, in comparison, not been used very much. Consequently, only few selective catalytic oxidations with iodine(III) reagents are known, especially

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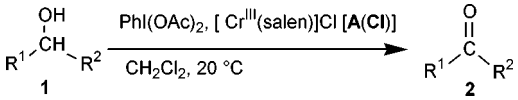
of alcohols to carbonyl products. Transition-metal catalysis[9] has been quite effective in the use of the heterogeneous iodosobenzene: Kochi[9a,b] employed $Cr^{III}$(salen) complexes to epoxidize catalytically olefins by PhIO, which Gilheany[9c] recently applied to asymmetric epoxidations. The feasibilty of oxidizing catalytically allylic alcohols to enones was demonstrated by Hill[9d] for cyclohexen-3-ol, who employed heterotungstate complexes of chromium(III) with PhIO. We have recently reported[6] that quite generally allylic alcohols may be chemoselectively transformed to the corresponding enones by the $Cr^{III}$(salen)/PhIO oxidant under catalytic conditions.

The use of iodosobenzene diacetate [$PhI(OAc)_2$] for selective catalytic oxidations, which is readily soluble in organic media, is still more limited. In one early report,[8a] it was shown that ruthenium catalyzes the oxidation of alcohols by $PhI(OAc)_2$, as demonstrated for saturated aliphatic and benzylic alcohols. Very recently,[5] an effective and convenient polymer-supported $PhI(OAc)_2$ reagent was developed for the oxidation of alcohols catalyzed by KBr in aqueous media, but primary alcohols were further oxidized to carboxylic acids. The latter report prompts us to communicate our preliminary results on the usefulness of $PhI(OAc)_2$ for the efficient and highly chemoselective oxidation of a variety of alcohols **1** to their carbonyl products **2** (Scheme 1),

**Scheme 1.** Chemoselective Oxidation of Alcohols **1** by Iodosobenzene Diacetate, Catalyzed with $Cr^{III}$ Complex **A(Cl)**




catalyzed by $Cr^{III}$(salen) complexes under homogeneous conditions.

Under the mild homogeneous conditions of ca. 20 °C in $CH_2Cl_2$ and a 1:0.1:1.5 ratio of substrate **1**:catalyst **A(Cl)**:$PhI(OAc)_2$, the corresponding $\alpha,\beta$-unsaturated carbonyl products **2** were obtained from the allylic alcohols **1d**−**n** essentially exclusively in good to excellent yields (Table 1; entries 4−16). This procedure is a major improvement over our previously reported[6] heterogeneous procedure using PhIO. No further oxidation of the aldehydes, derived from the primary alcohols **1k, 1m**, and **1n** (entries 13, 15, and 16), to the respective carboxylic acid was observed. Oxidation of the saturated (**1a**,**b**) and benzylic (**1c**) substrates to the corresponding ketones was also achieved (entries 1−3), but the saturated substrates showed moderate reactivity and were converted in only 50−60% even after long (21−24 h) reaction times. Conspicuous is the fact that no ring-opened product was observed for the cyclopropyl derivative **1b** (entry 2), which implys that cyclopropylcarbinyl radicals do not intervene.[10]

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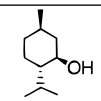
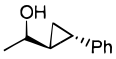
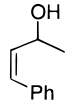
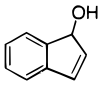
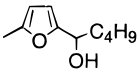
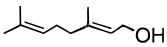
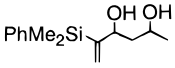
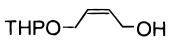
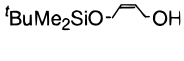
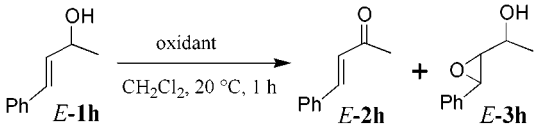
**Table 1.** Oxidation of Alcohols **1** with Iodosobenzene Diacetate, Catalyzed by the [$Cr^{III}$(salen)]Cl Complex[a]

| | alcohols | time (h) | convn[b] (%) | mb[b] (%) | yield[b,c] ketone **2** (%) |
|---|---|---|---|---|---|
| 1 |  (**1a**) | 24 | 48 | 97 | 96 |
| 2 |  (**1b**) | 21 | 60 | 95 | 92 |
| 3 |  (**1c**) | 5 | 67 | 99 | 99 |
| 4 |  (*E*-**1d**) | 6 | 92 | 71 | 77 |
| 5 |  (*Z*-**1d**) | 4 | 56 | 73 | 69 (92:8) |
| 6 |  (**1e**) | 6 | 92 | 70 | 67 |
| 7 |  (**1f**) | 6 | 85 | 72 | 66 |
| 8 |  (**1g**) | 5 | 95 | 91 | 96 |
| 9 |  (*E*-**1h**) | 4 | 86 | 97 | 90 |
| 10 |  (*Z*-**1h**) | 4 | 48 | 92 | 82 (91:9) |
| 11 |  (**1i**) | 5 | 95 | 96 | 93 |
| 12 |  (**1j**) | 6 | 94 | 91 | 69[d] |
| 13 |  (**1k**) | 4 | 92 | 84 | 82 |
| 14 |  (**1l**) | 5 | 83 | 95 | 93[e] |
| 15 |  (**1m**) | 4 | 78 | 85 | 81 (93: 7) |
| 16 |  (**1n**) | 4 | 66 | 98 | 92 (94: 6) |

[a] Reaction conditions: $PhI(OAc)_2$ (1.5 equiv), catalyst **A(Cl)** (0.1 equiv), $CH_2Cl_2$, 20 °C. [b] Determined by $^1H$ NMR analysis of the crude reaction mixture with dimethyl isophthalate as internal standard; error ± 5% of the stated values. mb stands for mass balance. [c] Yields of the respective carbonyl products **2** based on 100% conversion of the alcohol **1**; <5% epoxy alcohol was found. In parentheses are given *cis*:*trans* ratios of the respective enone **2** (cf. Supporting Information). [d] Minor amounts of (ca. 10%) ring-expansion product (ref 12a) were found. [e] Observed in 95:5 allylic versus aliphatic regioselectivity.

To assess whether the counterion of the $Cr^{III}$(salen) complex affects the chemoselectivity of the allylic alcohol

**Table 2.** Product Studies for the Catalytic and Stoichiometric Oxidation of the Allylic Alcohol *E*-**1h** by Iodosobenzene and Its Diacetate, Catalyzed by the [$Cr^{III}$(salen)]X Complexes




| | oxidant (equiv) | additive | convn[a] (%) | mb[a] (%) | chemoselectivity **2h**:**3h**[a,b] |
|---|---|---|---|---|---|
| 1 | **A(Cl)** (0.1), | none | 29 | 99 | >95:05 |
| 2 | $PhI(OAc)_2$ (1.5) | PPNO | 22 | 96 | >95:05 |
| 3 | **A(Cl)** (0.1), | none | 17 | 97 | 95:05 |
| 4 | PhIO (1.5) | PPNO | 28 | 94 | 94:06 |
| 5 | **A(TfO)** (0.1), | none | 48 (21) | 65 (87) | 96:04 (73:27) |
| 6 | $PhI(OAc)_2$ (1.5) | PPNO | 36 | 91 | 58:42 |
| 7 | **A(TfO)** (0.1), | none | 91 (70) | 50 (66) | 89:11 (74:26) |
| 8 | PhIO (1.5) | PPNO | 51 | 93 | 54:46 |
| 9 | **A($PF_6$)** (0.1), | none | 77 | 59 | 68:32 |
| 10 | PhIO (1.5) | PPNO | 49 | 93 | 48:52 |
| 11 | **D(TfO)** (1.1) | none | 40 (28) | 83 (94) | 67:33 (55:45) |
| 12 | | PPNO | 55 | 86 | 51:49 |
| 13 | **D($PF_6$)** (1.1) | none | 33 | 75 | 61:39 |
| 14 | | PPNO | 93 | 98 | 42:58 |

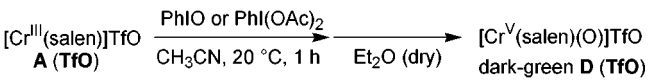
[a] Determined as in Table 1. In parentheses are given the values for 0.5 h reaction time. [b] The diastereomer *E*-**3h** was found in a *erytro*:*threo* ratio of ca. 85:15 (±5% of the stated value) as determined by $^1H$ NMR analysis of the crude reaction mixture.

oxidation, product studies have been carried by employing the allylic alcohol *E*-**1h** as the model substrate. $Cr^{III}$(salen) complexes with different counterions under a variety of reaction conditions were used, and the results (Table 2) show a very high chemoselectivity (≥95:5) in favor of the enone **2h** for the complex **A(Cl)** and $PhI(OAc)_2$ (entries 1 and 2). The chemoselectivity for $PhI(OAc)_2$ is higher than that for PhIO (entries 3 and 4), irrespective of whether the additive 4-phenylpyridine *N*-oxide (PPNO) was employed. For the triflate complex **A(OTf)**, a high (96: 4) chemoselectivity was obtained for $PhI(OAc)_2$ without the PPNO additive (entry 5), but a poor (58:42) chemoselectivity was obtained with PPNO (entry 6); similar results were found for PhIO (entries 7 and 8). The diminution in the chemoslectivity is still more pronounced in the case of $PF_6^-$ complex and PhIO, for which a low enone/epoxide ratio was obtained with and without PPNO (entries 9 and 10).

In the absence of PPNO, the high chemoselectivity after 1 h is accompanied by a low mass balance, while after 0.5 h the mass balance is higher but the chemoselectivity is not as good (entries 5 and 7). The lower mass balance indicates that the epoxide is decomposed due to the Lewis acidity of the Cr(salen) complex, which falsifies the chemoselectivity results. Presumably, the ligated PPNO reduces the Lewis acidity of the Cr(salen) complex and the epoxide decomposition is avoided. Indeed, a good mass balance was obtained for the 0.5-h run in the presence of PPNO (data not shown).

In addition to these catalytic oxidations (Table 2, entries 1−10), stoichiometric reactions with authentic $Cr^V$(salen)(O) complexes **D(TfO)** and **D($PF_6$)** were examined (entries 11−14). The triflate [**D**(**TfO**)] and hexafluorophosphate [**D**(**$PF_6$**)] derivatives were prepared by oxidation of the respective $Cr^{III}$(salen) complexes with PhIO or $PhI(OAc)_2$ (Scheme 2). When the stoichiometric conditions were applied

**Scheme 2.** Reaction of [$Cr^{III}$(salen)]TfO with Iodosobenzene and Its Diacetate




to the model substrate *E*-**1h**, nearly equal amounts of enone *E*-**2h** and epoxide *E*-**3h** were obtained in the absence (entries 11 and 13) and the presence of PPNO (entries 12 and 14). These poor chemoselectivities for the stoichiometric oxidations match those for the catalytic ones in the presence of the PPNO additive (entries 6, 8, and 10). It may, therefore, be concluded that in the catalytic oxidations mediated by the [$Cr^{III}$(salen)]TfO [**A(TfO)**] and [$Cr^{III}$(salen)]$PF_6$ [**A($PF_6$)**] complexes, presumably the [$Cr^V$(salen)(O)] species **D** serves as the actual oxidant.

Since the complexes [$Cr^V$(salen)(O)]X are paramagnetic and possesses radical character, the present allylic oxidation may follow C−H insertion by way of the established oxygen-rebound mechanism.[11] To scrutinize this mechanistic possibilty, oxidation experiments were performed with the $^{18}O$-labeled alcohol $^{18}O$-**1c** (Table 3). In the stoichiometric (first

**Table 3.** Oxidation of Alcohol $^{18}O$-**1c** by the $Cr^V$(salen)(O) Complexes under Stoichiometric and Catalytic Conditions

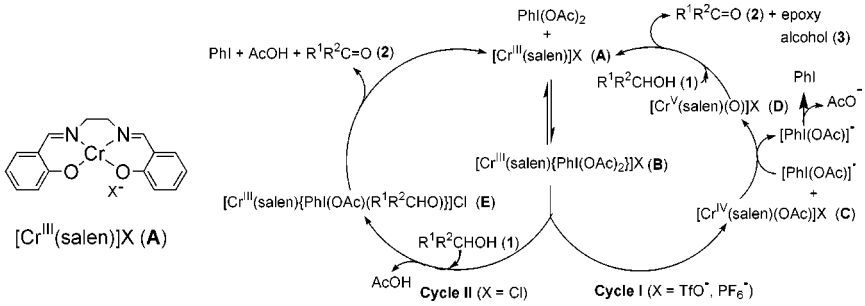
| oxidant (equiv) | time (h) | convn (%) | $^{18}O$ content $^{18}O$-**2c**[b] (%) |
|---|---|---|---|
| [$Cr^V$(salen)(O)]TfO (1.1) | 51 | 51 | 84 |
| [$Cr^{III}$(salen)]Cl (0.1), PhIO (1.5) | 8 | 95 | 89 |
| [$Cr^{III}$(salen)]Cl (0.1), $PhI(OAc)_2$ (1.5) | 6 | 95 | 90 |

[a] The $^{18}O$ content of the initial alcohol $^{18}O$-**1c** was 90 ± 5%. [b] The $^{18}O$ content was determined by mass-spectral analysis in terms of the relative intensities for the respective molecular ions (*m*/*z* 122 and 124), error ± 5% of the stated value.

entry) as well as catalytic (second and third entries) oxidations, the initial $^{18}O$ content (90 ± 5%) of $^{18}O$-**1c** was essentially retained (≥85%) in the carbonyl product $^{18}O$-**2c**. These $^{18}O$-labeling experiments indicate that this oxidation is not a C−H insertion; otherwise isotopic dilution would have had to occur. Moreover, the stoichiometric oxidation of $^{18}O$-**1c** was very slow (first entry) compared to the catalytic

(11) Hamada, T.; Irie, R.; Mihara, J.; Hamachi, K.; Katsuki, T. *Tetrahedron* **1998**, *54*, 10017−10028.

**Scheme 3.** Mechanism for the $Cr^{III}$(salen)-Catalyzed Oxidation of Allylic Alcohols by Iodosobenzene Diacetate; **Cycle I** for the Redox Chemistry and **Cycle II** for the Lewis Acid Activation




reactions (second and third entries). This finding suggests that some species other than the $[Cr^{V}(salen)(O)]^{+}$ complex may be involved in the catalytic oxidation.

To provide a clue as to the nature of the active species, the reaction mixture from the oxidation of the $[Cr^{III}(salen)]X$ complex by $PhI(OAc)_2$ without any alcohol was analyzed by ESI-MS (cf. Supporting Information). Also, the mass peaks *m*/*z* 640.4 (8%) and 377.4 (31%) were found, which correspond to the ions with the compositions $[Cr^{III}(salen)\{PhI(OAc)_2\}]^{+}$ (**B**$^{+}$) and $[Cr^{IV}(salen)(OAc)]^{+}$ (**C**$^{+}$), in addition to the mass peak *m*/*z* 333.8 (100%) for $[Cr^{V}(salen)(O)]^{+}$ (**D**$^{+}$). Their formation (Scheme 3) may be rationalized in terms of ligation of $PhI(OAc)_2$ with the $Cr^{III}$(salen) complex **A** to afford the adduct **B** and subsequent electronic reorganization (**Cycle I**) with elimination of the PhI(OAc)$^{\bullet}$ radical to generate the $Cr^{IV}$(salen)(OAc) complex (**C**). Electron transfer between the latter and the PhI(OAc)$^{\bullet}$ radical[12] leads to $Cr^{V}$(salen)(O) complex (**D**), an established oxidant.

Unquestionably, a rather complex mechanism (Scheme 3) operates in this counterion-dependent catalytic oxidation of alcohols by the $[Cr^{III}(salen)]X$ complex **A** with PhIO or $PhI(OAc)_2$. Nevertheless, the previously presented chromium complexes **B**−**D**, proposed as potential oxidants in the catalytic redox chemistry of **Cycle I** (Scheme 3) for the nonnucleophilic counterions $TfO^{-}$ and $PF_6^{-}$, are not enough to rationalize the results for the nucleophilic $Cl^{-}$ counterion; consequently, additional species appear to be involved. It must be stressed that for the synthesis the $Cr^{III}$(salen)Cl complex is the more valuable one, because the enone **2** is produced exclusively in high yields under mild conditions (Table 1). In contrast, for the $TfO^{-}$ and $PF_6^{-}$ counterions, the chemoselectivity is poor since under most conditions nearly equal amounts of enone and epoxide are formed (Table 2).

To account for this counterion-dependent mechanistic dichotomy, we propose the Lewis acid activation in **Cycle II** (Scheme 3). The pertinent product-branching point is the $Cr^{III}$(salen) complex **B**, for which, in the case where X = Cl, the chromium metal assists the exchange of an acetate group in the ligated $PhI(OAc)_2$ for a substrate molecule, alcohol **1**, to generate the complex **E**. Base-catalyzed deprotonation of the alcoholate affords carbonyl product **2**, with concurrent elimination of iodobenzene and acetate ion (shown as AcOH in the **Cycle II**). In fact, when NaOAc is added in catalytic amounts (20 mol %) as external base, the reactivity is significantly enhanced (cf. Supporting Information).

**Acknowledgment.** We thank the DFG (SFB 347) and the Fonds der Chemischen Industrie for financial support. S.H. thanks the Alexander-von-Humboldt-Foundation for a postdoctoral fellowship (1999−2000).

**Supporting Information Available:** Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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