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Synthesis of Racemic and Enantiomerically Enriched α-Oxyfunctionalized Benzocyclanones and Chromanones by Dimethyldioxirane and Dimethyldioxirane/Mn(III) salen System[#]

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Summary. Enolacetates of benzocyclanones and chromanones were synthesized and treated with dimethyldioxirane and the asymmetric oxidizing system dimethyldioxirane/chiral, non-racemic Mn(III) salen complex/axial ligand. The latter reagent resulted in the corresponding enantiomerically enriched cyclic α-hydroxy ketones and their acetates in moderate-to-good yields and modest enantioselectivity under mild and neutral conditions from tetralone and chromanone. On the contrary, flavanone provided poor yields due to the competitive C–H insertion at position 2. The use of *R*,*R*-Mn(III)salen catalyst induced an *S* absolute configuration at the position α in the whole series.

Keywords. Dioxirane; Enantioselective epoxidation; Enolacetates; *Jacobsen-Katsuki*'s catalyst.

Introduction

α-Hydroxy ketones, particularly in their enantiopure form, are important synthetic building blocks and, therefore, their synthesis has received great attention in the last decades. Among the various approaches the oxidation of enol derivatives **2** including enolates **3** by an electrophilic oxidant is one of the most prominent methods of high synthetic value (Scheme 1).

The oxidation of enol derivatives **2** results in the formation of epoxide intermediates **4** giving the alcohols **5** by hydrolysis and/or the rearranged α-oxyfunctionalized ketones **6** depending on the structure of the starting material.

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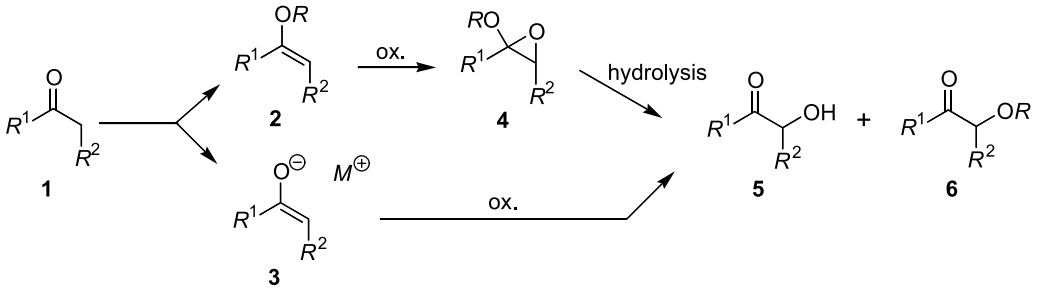
[#] Dedicated to Prof. *Waldemar Adam* on the occasion of his retirement



Scheme 1

Alkyl enol ethers **2** ($R =$ alkyl) have been oxidized by HOF • *Me*CN complex to yield α-ketols **5** [1]. When methyl trifluoromethyl dioxirane (*MTMD*) or dimethyldioxirane (*DMD*) was applied as oxidant, the intermediate (spiro)acetals **4** ($R =$ alkyl) have been isolated [2]. An enantioselective version utilizing *Ph*IO and non-racemic Mn(III) salen complexes (*Jacobsen-Katsuki*'s catalysts) has also been developed [3], in this latter case α-hydroxyacetals have been obtained due to the solvolysis of the intermediate. *Adam et al.* [4] used peracids, H_2O_2, *Ph*IO, and bleach in combination with a chiral, non-racemic Mn(III) salen complex for this purpose. Silyl enol ethers **2** ($R = TMS$, *TBDMS*) have been oxidized by a wide variety of oxidants such as peracids [5], lead tetrabenzoate [6], lead tetraacetate [7], osmium tetroxide [8], *DMD* [9], oxaziridine [10], and *tert*-butyl hydroperoxide (*THBP*) in the presence of titanium silicalite-1 [11]. The products were epoxides **4** ($R = TMS$), α-silyloxy ketones **6** ($R = TMS$), or ketols **5** depending on the conditions used. Several asymmetric oxidations of silyl enol ethers by using *Ph*IO [12, 13] or bleach [13] in combination with a chiral, non-racemic Mn(III) salen complex or by an optically active dioxirane generated *in situ* from Oxone® and a fructose-derived ketone (*Shi*'s ketone) have been performed [14]. Enol esters **2** ($R =$ acyl, phosphinyl) were also frequent substrates affording mainly the epoxides **4** ($R =$ acyl, phosphinyl) on oxidation by peracids [15, 16] or *DMD* [9b, 17]. Enantioselective epoxidations of enolacetates by Oxone® and *Shi*'s ketone have also been reported [14a].

It is noteworthy that ketones with high enol content could directly be oxidized to α-hydroxyketones **5** by *DMD* [18]. However, the one-pot oxidation of metal enolates by various electrophilic oxidants is a far more frequently used procedure. Such transformation was performed by using direct oxygenation followed by the reduction of the intermediate hydroperoxide [19] or by treating the enolate with *Vedejs*' reagent (MoO_5 • *HMPA* (Mo*OPH*)) [20], oxaziridines [10, 21], *bis*(trimethylsilyl) peroxide (*BTSP*) [22], and *DMD* [18, 23, 24]. Enantioselective, reagent-controlled α-hydroxylations upon treatment by chiral, non-racemic oxaziridines such as (+)-(camphorsulfonyl)oxaziridine have also been reported [10, 21]. Alternatively, a substrate-controlled approach utilizing titanium enolates with chiral ligands and *DMD* and 3-phenyl-2-phenylsulfonyloxaziridine (*PPO*) as oxygen source has also been developed [25].

Recently, we have disclosed that the combination of *DMD* and *Jacobsen*'s catalyst is a useful and efficient reagent for the enantioselective epoxidation of chromenes [26] and isoflavones [27] with ee values up to 93% under mild and

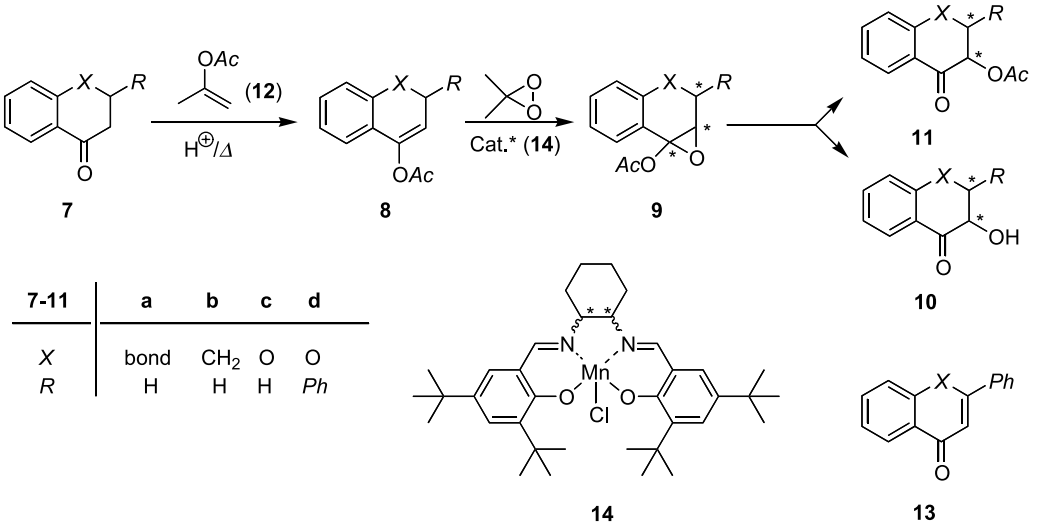
neutral conditions. In continuation of this work we wished to test our system in α-oxyfunctionalization, as well. Cyclic ketones were used as substrates for our studies since

(i) these derivatives were much more rarely used model compounds and fewer procedures have been developed for their asymmetric oxidation, moreover,
(ii) usually poorer enantioselective discrimination was observed in their reaction probably due to the fixed cyclic system. *E.g.*, *Reddy* and *Thornton* [12] reported only 14–62% ee in the oxidation of cyclic silyl enol ethers by *Ph*IO and Mn(III) salen complexes. Similarly, a poor (20–30%) enantioselectivity was found [28] in the oxidation of 1-(trimethylsilyloxy)-3,4-dihydronaphtalene by *Ph*IO or bleach and *Jacobsen*'s catalyst, a reagent which was very efficient for acyclic substrates [13]. We have chosen enol acetates **2** ($R = Ac$) as starting materials owing to the higher persistency of the intermediates **4** and in the hope that the lower reactivity of enol acetates toward the oxidant may result in a higher enantioselectivity.

Results and Discussion

Starting material enolacetates **8a**–**8d** have been synthesized by the classical acid-catalyzed transesterification of the corresponding ketones **7a**–**7d** and isopropenyl acetate (**12**) using modified *Saito*'s conditions [29].

When enolacetates **8a**–**8c** were allowed to react with *DMD* (as acetone solution) [30] without any chiral catalyst mixtures of α-hydroxy ketones **10a**–**10c** and α-acetoxy ketones **11a**–**11c** were obtained in moderate yields (15–57% and 34–48%, respectively) and no intermediate **9** could be detected (Scheme 2). Oxidation of chromanone derivative **8c** gave lower yields due to the instability of products **10c** and **11c**, particularly α-ketol **10c** was sensitive for the exposure to air.



Scheme 2

The immediate formation of secondary products **10** and **11** by ring-opening of the oxirane functionality can be explained by the presence of a small amount of water in the *DMD* solution. When the oxidation was performed in the presence of anh. K_2CO_3 as additive, the intermediate 1-acetoxy-1,2-epoxytetralin (**9b**) was obtained in excellent yield but other enolacetates **8a** and **8c** gave only the secondary products, again. The treatment of 4-acetoxy-2-phenyl-2*H*-1-chromene (**8d**) with *DMD* in the presence of anh. K_2CO_3 resulted in the formation of *trans*-3-hydroxyflavanone (*trans*-**10d**) (40%), *trans*-3-acetoxyflavanone (*trans*-**11d**) (25%), and flavone (**13**) (10%). The complete diastereoselectivity of the reaction is noteworthy, no *cis* diastereomers could be detected in the reaction mixture by ^{1}H NMR.

To our best knowledge, this was the first isolation of epoxide **9b**, although Spanish authors [31] postulated its intermediacy in the photolysis of enolacetate **8b**. The observed high lability of α-acetoxy epoxides **9** can be attributed to various reasons. These epoxides are known to be sensitive to traces of acid [16, 32]. *Shi* and coworkers [14a] purified α-benzoyloxy epoxides on silica pretreated with N*Et*$_3$. In the non-selective bleach/Mn(III) salen-mediated oxidation of 2-acetoxy-1,3-cycloalkadienes *Jacobsen et al.* [33] obtained only the corresponding α-hydroxy and α-acetoxy ketone derivatives. Any ring-strain seems to increase the lability of the epoxides **9**. Tetralines still show modest stability since 1-benzoyloxy-1,2-epoxytetraline has been also prepared [14a] but incorporation of the larger oxygen heteroatom in the cyclanone ring or the change for a five-membered indane ring makes the epoxide unstable.

Mapping the reactivity of the stable epoxide **9b** we found that it reacted smoothly in the presence of acids even with silica gel to afford 2-hydroxytetralone (**10b**) and 2-acetoxytetralone (**11b**). The formation of acetate **11b** in a thermal process (*vide infra*) could be excluded since a prolonged (50 h) heating of epoxide **9b** gave the mixture of **10b** and **11b** only in a very low (13%) conversion.

The asymmetric epoxidation of enolacetate **8b** by *DMD* and *Jacobsen*'s catalyst **14** was tested next (Table 1). Enantioselectivity was determined by measuring the optical rotation of the isolated pure epoxide **9b** after a fast short-column chromatography to remove the catalyst. Attempts to determine ee values by chiral HPLC failed due to the slow hydrolysis of the product **9b** during the sample preparation and the elution. On the basis of our experiments with different catalyst loading we chose amounts of 10 mol% for the further oxidations. By switching from *R*,*R*-**14** to *S*,*S*-**14**, nearly the same optical purity was measured for the other enantiomer. This observation clearly proves an asymmetric oxidation process.

In the 1980s *Kochi* and coworkers [34] observed that efficiency of metal salen catalysts can be improved by adding donor ligands and this finding was also successfully used in the *Jacobsen-Katsuki* epoxidation [35, 36]. In our previous work we have also perceived the beneficial effect of nitrogen-containing axial ligands both on the yields and ee values [26a, 27b]. Therefore, we have performed oxidation of enolacetate **8b** by using imidazole, *N*-methylimidazole, 4-picoline *N*-oxide, and 4-phenylpyridine *N*-oxide (*PPNO*) (*ca.* 40 mol%) as axial ligand and, as expected, an improved enantiopurity of both the intermediate epoxide **9b** and the cleaved products **10b** and **11b** was observed. The data summarized in Table 1 clearly show the advantageous effect of the ligands, the best enantioselectivities were obtained by using imidazole or *PPNO* (ee values up to 66% for **10b** and 58%

Table 1. Results of the synthesis of chiral, non-racemic epoxide **9b** by oxidation with *DMD* and Mn(III) salen catalyst **14** and their silica gel-induced ring-opening to alcohol **10b** and acetate **11b**

Catalyst (**14**)		Axial ligand		Epoxide **9b**		Alcohol **10b**[a]			Acetate **11b**[b]		
Config.	Amount/ mol%	Type	Amount/ mol%	Yield/ %	$[\alpha]_D$	Yield/ %	Config.	ee[c]/ %	Yield/ %	Config.	ee[c]/ %
R,*R*-(−)	10.2	none	–	52	+26.2	38	*S*-(−)	26	31	*S*-(−)	20
S,*S*-(+)	6.3	none	–	60	−16.5	37	*R*-(+)	33	49	*R*-(+)	30
S,*S*-(+)	10.2	none	–	39	−23.3	39	*R*-(+)	20	47	*R*-(+)	26
S,*S*-(+)	14.9	none	–	19[d]	−5.9	23	*R*-(+)	33	31	*R*-(+)	30
S,*S*-(+)	10.2	imidazole	42.9	26	−40.1	17	*R*-(+)	66	21	*R*-(+)	49
S,*S*-(+)	10.2	*N*-Me-imidazole	42.8	34	−39.1	17	*R*-(+)	52	28	*R*-(+)	52
S,*S*-(+)	10.2	4-picoline *N*-oxide	40.2	45	−36.2	32	*R*-(+)	47	30	*R*-(+)	36
S,*S*-(+)	10.2	*PPNO*[e]	40.0	[f]	–	59	*R*-(+)	62	17	*R*-(+)	58

[a] Absolute configuration was determined on the basis of the sign of specific rotation [21, 53]
[b] Absolute configuration was determined on the basis of the sign of specific rotation [21]
[c] Determined by HPLC
[d] Contaminated with alcohol **10b** and acetate **11b**
[e] *PPNO* = 4-phenylpyridine *N*-oxide
[f] Decomposed to alcohol **10b** and acetate **11b** during chromatography

for **11b**). The major enantiomer of both the alcohol and the acetate had the same absolute configuration; the formation of *R*-(+)-**10b** and *R*-(+)-**11b** was preferred in the presence of *S*,*S*-(+)-**14**.

In continuation we checked our optimized system (*DMD*/10 mol% **14**/ 40 mol% imidazole or *PPNO*) in the oxidation of heterocyclic enolacetates **8c** and **8d** and the results are shown in Tables 2 and 3.

Oxidation of both substrates resulted in poor ee values without axial ligands but considerably higher enantioselectivity was obtained in the presence of imidazole or *PPNO*. As before, these two additives gave comparable ee values (up to 50% for alcohols and 45% for acetates) but the values were somewhat lower than those found for the tetralone derivatives. It seems that the incorporation of oxygen into the ring decreases the stereodifferentiation in the attack of the chiral Mn(V) salen

Table 2. Results of the enantioselective oxidation of enolacetate **8c** with *DMD* and Mn(III) salen catalyst (*R*,*R*)-**14** (10 mol%)

DMD/equiv.	Axial ligand[a]	Alcohol **10c**			Acetate **11c**		
		Yield/%	Config.[b]	ee/%	Yield/%	Config.[c]	ee/%
4.0	none	19	*S*-(−)	8	24	*S*-(−)	8
2.9	imidazole	26	*S*-(−)	37	23	*S*-(−)	33
2.5	*PPNO*	16	*S*-(−)	33	16	*S*-(−)	31

[a] 40 mol% of axial ligand were added
[b] Absolute configuration was determined on the basis of the sign of specific rotation [54]
[c] Absolute configuration was deduced from the $Sc(OTf)_3$-mediated hydrolysis of (−)-**11c** giving (−)-**10c** [55]

Table 3. Results of the enantioselective oxidation of enolacetate **8d** with DMD and Mn(III) salen catalyst (*R*,*R*)-**12** (10 mol%)

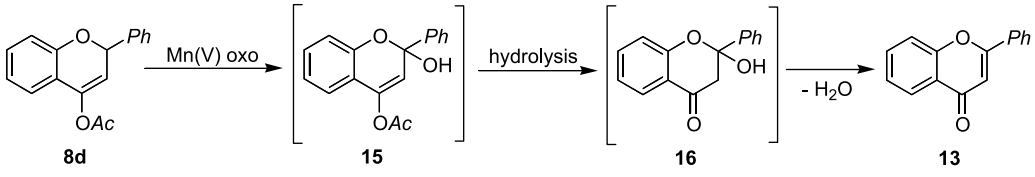
DMD/equiv.	Axial ligand[a]	Alcohol **10d**			Acetate **11d**			Flavone (**13**) Yield/%
		Yield/%	Config.[b]	ee/%	Yield/%	Config.[b]	ee/%	
7.0	none	29	*2R*,*3R*-(−)	2	2.5	n.d.	n.d.	37
6.5[b]	none	29	*2R*,*3R*-(−)	4	3	*2S*,*3S*-(−)	3	42
5.4	imidazole	12	*2S*,*3S*-(+)	44	13	*2S*,*3S*-(−)	45	52
6.0	*PPNO*	11	*2S*,*3S*-(+)	50	8	*2S*,*3S*-(−)	35	73

[a] 40 mol% of axial ligand were added

[b] Absolute configuration was determined on the basis of the sign of rotation [51]

oxo complex on the double bond of enolacetate. Absolute configuration of products **10c**, **11c**, *trans*-**10d**, and *trans*-**11d** has been assigned on the basis of the sign of the specific rotation or by chemical correlation. When the oxidation was performed by using catalyst *R*,*R*-(−)-**14**, all these products had the same *S* absolute configuration at stereogenic center C-3. This observation is in accordance with the preferred configuration of tetralones (*vide supra*).

Data given in Table 3 have also revealed another interesting point. Namely, when enolacetate **8d** was oxidized by *DMD* without catalyst **14** the major products were *trans*-**10d** and *trans*-**11d** (in 65% total isolated yields, see Experimental) but the amount of the previous by-product flavone (**13**) was highly increased when *Jacobsen*'s catalyst was applied. The use of catalyst **14** combined with axial ligands led to the formation of **13** as major product (in isolated yields up to 73%). Due to this unfortunate side reaction the asymmetric α-oxyfunctionalization of flavanone has no significant synthetic value. The preferred formation of flavone (**13**) can be explained by the increased reactivity of the oxidizing species, *i.e.* the Mn(V) salen oxo complex, compared to *DMD*. The more reactive oxidizing agent can attack not only the C=C double bond but competitively the doubly activated (*benzylic* and *allylic* at the same time) position 2 of the enolacetate **8d**, too, forming the 2-hydroxylated intermediate **15** by a C–H insertion reaction. This intermediate **15** affords flavone (**13**) after hydrolysis and water elimination (Scheme 3). The ease of this latter elimination step has been documented [37a]. It is noteworthy that the oxidation of flavanones by *DMD* was also reported but it takes place very slowly on the parent compound **7d** and requires the activation of C-2 by electron-donating substituents in ring B [37].



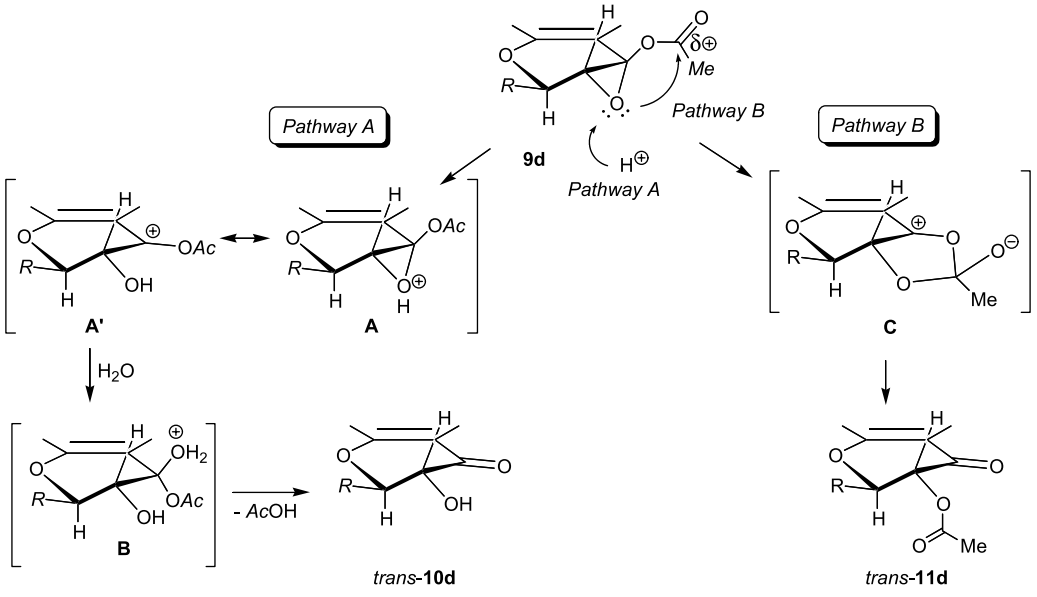
Scheme 3

The transformation of α-acetoxy epoxides into α-acetoxy ketones has been known for a long time and the suggested mechanisms are reviewed [38]. This rearrangement can take place both upon treatment of acids (or silica gel, as in our case) and heating. The configuration at the position adjacent to the ketone group is usually retained in the presence of acids but the thermal procedure may give either the product with inverted [14a, 38] or, in some particular case [38, 39], with retained configuration. This duality indicates the existence of at least two independent mechanisms. Considering the facts that in our reactions

(i) the obtained α-hydroxy- and α-acetoxybenzo(hetera)cyclanones had the same absolute configuration and the formation of α-hydroxy ketones does not entail the breaking of the C_α–O bond,
(ii) the oxyfunctionalization of flavanone (**7d**) took place with complete diastereoselectivity, and
(iii) the possibility of thermolysis was excluded (*vide supra*) we suggest the mechanism shown in Scheme 4 to account all the listed observations the ring opening of intermediate **9d** is depicted.

The formation of alcohol *trans*-**10d** can be interpreted in terms of a protonation of the epoxide giving the oxonium ion **A** and its resonance stabilized form **A′**. The hydration of the latter species followed by elimination of acetic acid from the intermediate **B** results in the product *trans*-**10d**. The pathway leading to *trans*-**11d** involves an intramolecular migration of the acetyl group *via* a zwitterion with a dioxolan ring (**C**) which leaves the C_α–O bond intact.

As mentioned before, catalyst *R*,*R*-(−)-**14** induced a preferred *S* whereas catalyst *S*,*S*-(+)-**14** induced *R* absolute configuration of the α-hydroxy and α-acetoxy ketones. These selectivities are consistent with the configurations expected on the basis of a recently published model of the transition state [36b and the references



Scheme 4

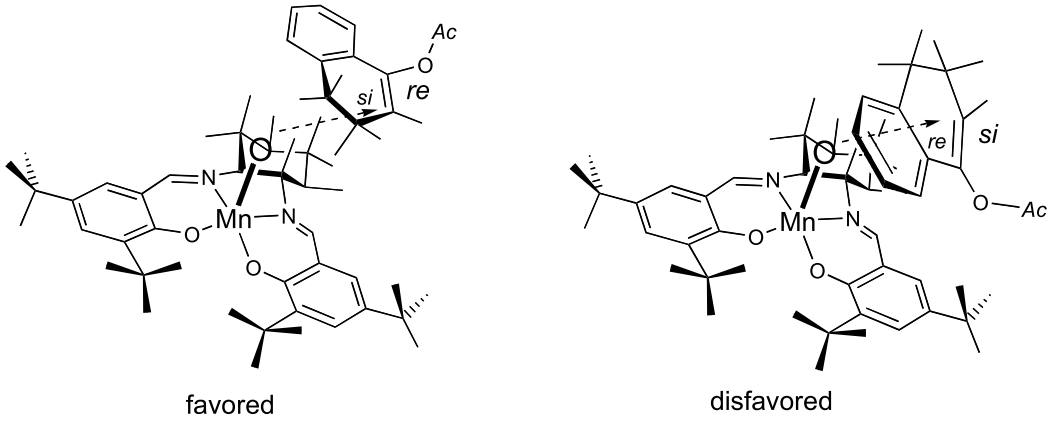


Fig. 1. Suggested way of attack of substrate **8b** on *Jacobsen*'s catalyst

cited therein]. The two possible approaches of an enolacetate to the oxidizing species are shown for catalyst *S*,*S*-(+)-**14** and substrate **8b** in Fig. 1.

The enolacetate comes to the Mn(V) oxo complex of folded structure from the open side above the phenyl ring of the catalyst (*Katsuki* trajectory, $\phi \cong -90°$) with a parallel or slightly skewed side-on approach. Approach from the opposite side ($\phi \cong 90°$) is hindered due to the substituted phenyl group of the catalyst lying above the plane of the cyclohexyl ring. From the two possible orientations of the enolacetate, the attack to its *si* face is favored because of less steric repulsion. This attack leads to *R* configuration at position 2 which is retained in the products **10b** and **11b**. In the case of attack to the *re* face the benzene ring and the acetoxy group of the substrate **8** come too close to the phenyl ring of the salen unit bearing two bulky *tert*-butyl groups which make this approach highly disfavored (Fig. 1).

In conclusion, the asymmetric oxidation of enolacetates of benzocyclanones and chromanone **8a**–**8c** by *DMD*/chiral, non-racemic Mn(III) salen complex/axial ligand system offers a new method for the synthesis of enantiomerically enriched cyclic α-hydroxy ketones **10a**–**10c** and their acetates **11a**–**11c** with moderate-to-good yields and modest enantioselectivities under mild and neutral conditions. 4-Acetoxy-2-phenyl-2*H*-1-chromene (**8d**) reacts smoothly with *DMD* itself to afford the corresponding α-oxyfunctionalized products **10d** and **11d** with complete *trans* diastereoselectivity but the chiral reagent provides only flavone (**13**) as the major product. The stereochemical control of the epoxidation is in accordance with the side-on approach to the Mn(V) oxo complex along the *Katsuki* trajectory.

Experimental

All solvents and reagents were purchased from commercial suppliers and used as received. Caroate® (potassium monoperoxysulfate), the triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, was used as received from Peroxid-Chemie GmbH (Höllriegelskreuth, Germany). *DMD* solution was prepared as indicated in Ref. [30], its peroxide content was determined by iodometry. Melting points were determined on a *Boetius* hot-stage apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer 16 PC FT-IR instrument in KBr pellets unless otherwise specified. ^{1}H and ^{13}C NMR data were recorded on Bruker WP 200SY and Bruker AM400 spectrometers. Chromatographic separations were performed

using 70–230 or 230–400 mesh (Merck) silica gel. Thin-layer chromatography (TLC) was carried out on Macherey-Nagel silica plates (0.25 mm layer thickness). HPLC analyses were performed with a Hewlett-Packard chromatograph with Chiralcel OB (**10a**, **11a**) or OD (**10c**, **10d**, **11c**, **11d**) (250 mm × 0.46 cm) chiral columns, (eluent: *n*-hexane:2-propanol = 9:1, *v*/*v*). Optical rotations were measured at 20°C with a Perkin-Elmer 341 instrument at 589 nm (cell width = 100 mm). Elemental analyses (C, H) were conducted using the Carlo Erba 1106 EA instrument; their results were found to be in good agreement (±0.2%) with the calculated values.

*General Method for the Preparation of Enolacetates **8a**, **8c**, and **8d***

To a solution of the corresponding ketone **7a**–**7c** (27.00 mmol) in 2-acetoxypropene (**12**) (16 cm^3, 0.145 mmol), 0.4 g (4.162 mmol) of methanesulfonic acid were added and the mixture was stirred at reflux temperature for 24 h under N_2 atmosphere. After cooling to room temperature it was diluted with toluene (100 cm^3) and washed with a saturated solution of $NaHCO_3$ (20 cm^3). The organic phase was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: toluene:*Et*O*Ac* = 4:1, *v*/*v*).

1-Acetoxyindene (**8a**)

White crystals, 3.283 g (62%); mp 40–41°C (Ref. [40] 45–46°C); ^{1}H NMR spectrum was found to be identical with the one described in Ref. [40].

4-Acetoxy-2H-1-chromene (**8c**)

Yellowish crystals, 4.311 g (74%); mp 49.5–50.5°C (Ref. [29] bp 150–152°C/1.733 kPa); ^{1}H NMR spectrum was found to be identical with the one described in Ref. [29].

4-Acetoxy-2-phenyl-2H-1-chromene (**8d**)

Yellowish crystals, 3.523 g (49%); mp 52–54°C (Ref. [40] oil); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.50$ (d, $J = 7.8$ Hz, 2′,6′-H), 7.36 (m, 3′,4′,5′-H), 7.14 (m, 7-H), 7.10 (dd, $J = 7.2$, 1.2 Hz, 5-H), 6.88 (m, 6-H), 6.80 (d, $J = 8.4$ Hz, 8-H), 6.08 (d, $J = 3.7$ Hz, 2-H), 5.62 (d, $J = 3.7$ Hz, 3-H), 2.30 (s, 3H, Ac); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 168.5$ (s, Ac), 153.9 (s, C-8a), 142.6 (s, C-4), 140.0 (s, C-1′), 130.4 (d, 5-C), 128.7 (d, 3′,5′-C), 127.3 (m, 2′,4′,6′-H), 121.4, 121.0 (2d, 6,7-C), 118.2 (s, C-4a), 116.3 (d, C-8), 111.6 (d, C-3), 79.6 (d, C-2), 20.9 (q, Ac).

1-Acetoxy-3,4-dihydronaphtalene (**8b**)

In a three-necked flask fitted with a *Vigreux* column and equipped with a gas inlet, a mixture of 1-tetralone (**7b**) (13.885 g, 94.99 mmol), 2-acetoxypropene (**12**) (22 cm^3, 0.199 mmol), and methanesulfonic acid (0.550 g, 5.722 mmol) was stirred under N_2 atmosphere for 23 h while the head temperature was kept below 60°C. The mixture was diluted with *n*-hexane (100 cm^3), saturated $NaHCO_3$ solution (150 cm^3) was added, and it was stirred for 15 min at room temperature. The brown crystals formed were filtered off, dissolved in CH_2Cl_2 (10 cm^3), and the solution was filtered through a mixture of silica gel and $MgSO_4$ (1:1). The filtrate was concentrated under reduced pressure and the oily residue was allowed to stand with *n*-hexane to give 13.624 g (76%) of **8b** as light brown crystals. Mp 54–56°C (Ref. [40] 54–56°C); ^{1}H NMR spectrum was found to be identical with the one described in Ref. [40].

1-Acetoxy-1,2-epoxytetralin (**9b**, $C_{12}H_{12}O_3$)

1-Acetoxy-3,4-dihydronaphthalene (**8b**, 380 mg, 2.019 mmol) and anh. K_2CO_3 (1.00 g) were added to a solution of *DMD* in acetone (83 cm^3, 0.049 *M*, *ca.* 2.01 equiv) and the mixture was allowed to react at

−20°C for 2 h. The insoluble part was filtered off and the solvent was removed under reduced pressure at room temperature. The crude product was recrystallised from *n*-hexane to afford 346 mg (84%) of epoxide **9b** as white crystals. Mp 96–98°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.43$ (dd, $J = 7.3$, 2.5 Hz, 8-H), 7.26 (m, 6,7-H), 7.15 (dd, $J = 8.0$, 2.5 Hz, 5-H), 3.88 (d, $J = 2.7$ Hz, 2-H), 2.56–2.86 (m, 2H, 4-H), 2.40 (m, 3-H_{eq}), 2.26 (s, 3H, Ac), 2.02 (m, 1H, 3-H_{ax}); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 169.0$ (s, C=O), 136.0 (s, C-8a), 130.9 (s, C-4a), 128.9, 128.5, 126.3, 125.1 (m, C-5,6,7,8), 79.8 (s, C-1), 62.0 (d, C-2), 24.9 (t, C-4), 21.5 (t, C-3), 20.8 (q, Ac); IR (KBr): $\bar{\nu} = 2908$, 1746 (C=O), 1426, 1376, 1216 (C–O–C), 1180, 1064 (C–O–C), 974, 760 cm^{-1}.

Typical Procedure for the Enantioselective Oxidation of Enolacetate ***8b***

A *DMD* solution in acetone (164 cm^3, 0.051 *M*, *ca.* 2.02 equiv) was added to the solution of enolacetate **8b** (779 mg, 4.139 mmol) and *R*,*R*-(−)-*Jacobsen*'s catalyst (*R*,*R*-**14**) (271 mg, 0.427 mmol) and the mixture was stirred at room temperature for 10 min. The solvent was removed under reduced pressure at room temperature. The crude oily residue was passed through a silica gel pad wetted with *n*-hexane:*Et*O*Ac* (1:1, *v*/*v*) to remove the catalyst. The eluted fraction was concentrated under reduced pressure and the residue was treated with *n*-hexane to yield crystalline epoxide **9b**. Further experimental details are given in Table 1.

Typical Procedure for the Silica Gel-induced Ring-opening of 1-Acetoxy-1,2-epoxytetralin (***9b***) *to 2-Hydroxytetralone* (***10b***) *and 3-Acetoxytetralone* (***11b***)

A mixture of racemic epoxide **9b** (275 mg, 1.346 mmol), silica gel (1.5 g), and CH_2Cl_2 (25 cm^3) was stirred at room temperature for 17 h, the completion of the reaction was checked by TLC (*n*-hexane:*Et*O*Ac* = 1:1, *v*/*v*). After filtration the solvent was removed *in vacuo* and the residue (mixture of 48% alcohol **10b** and 52% acetate **11b** according to ^{1}H NMR) was submitted to column chromatography (eluent: toluene:*Et*O*Ac* = 4:1, *v*/*v*) to give 77 mg (35%) of 2-hydroxytetralone (**10b**) and 109 mg (40%) of 2-acetoxytetralone (**11b**).

2-Hydroxytetralone (**10b**)

Yellow oil (Ref. [41] mp 36–37°C, Ref. [23] "slightly yellow coloured oil which darkens on exposure on air"); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 8.15$ (dd, $J = 7.7$, 1.3 Hz, 5-H), 7.54 (m, 7-H), 7.26–7.39 (m, 6,8-H), 4.40 (dd, $J = 13.5$, 5.4 Hz, 2-H), 3. 81 (br s, 2-OH), 3.10 (m, 2H, 4-H), 2.52 (m, 3-H_{eq}), 2.02 (m, 3-H_{ax}).

2-Acetoxytetralone (**11b**)

White crystals; mp 66.5–68°C (Ref. [21] 58–59°C, Ref. [42] 72–73°C); ^{1}H NMR spectrum was found to be identical with the one described in Ref. [21].

The same reaction conditions were also applied to the chiral, non-racemic epoxide **9b** obtained in the presence of catalyst **14** (*vide supra*), the results are shown in Table 1.

When 2-acetoxytetralone (**11b**) was treated under the same conditions for 50 h no reaction was observed.

Acid-induced Ring-opening of 1-Acetoxy-1,2-epoxytetralin (***9b***)

Trifluoroacetic acid (209 mg, 1.833 mmol) was added to the solution of racemic epoxide **9b** (211 mg, 1.033 mmol) in methanol (15 cm^3) and stirred at room temperature for 10 min, the completion of the reaction was checked by TLC (toluene:*Et*O*Ac* = 4:1, *v*/*v*). The mixture was evaporated under reduced

pressure. The residue (mixture of 91% alcohol **10b** and 9% acetate **11b** according to ^{1}H NMR) was submitted to column chromatography (eluent: toluene:*Et*OAc = 4:1, *v*/*v*) to give 143 mg (85%) of 2-hydroxytetralone (**10b**) and 19 mg (9%) of 2-acetoxytetralone (**11b**).

Base-induced Ring-opening of 1-Acetoxy-1,2-epoxytetralin (***9b***)

Anh. K_2CO_3 (1.000 g, 7.236 mmol) was added to the solution of epoxide **9b** (240 mg, 1.175 mmol) in methanol (15 cm^3) and stirred at room temperature under N_2 atmosphere for 10 min, the completion of the reaction was checked by TLC (toluene:*Et*OAc = 4:1, *v*/*v*). After filtration the solvent was removed under reduced pressure. The residue was submitted to column chromatography (eluent: toluene:*Et*OAc = 4:1, *v*/*v*) to give 164 mg (86%) of 2-hydroxytetralone (**10b**).

Typical Procedure for the One-step Synthesis of Racemic α-Hydroxy Ketones **10a–10c** *and α-Acetoxy Ketones* **11a–11c**

A *DMD* solution in acetone (45 cm^3, 0.069 *M*, *ca.* 2.03 equiv) was added to enolacetate **9b** (287 mg, 1.523 mmol) and the mixture was stirred at room temperature until completion of the reaction (monitored by TLC, toluene:*Et*OAc = 4:1, *v*/*v*). Then it was concentrated *in vacuo* and submitted to column chromatography (eluent: toluene:*Et*OAc = 4:1, *v*/*v*) to give 141 mg (57%) of 2-hydroxytetralone (**10b**) and 123 mg (40%) of 2-acetoxytetralone (**11b**).

Analogous treatment of enolacetate **8a** afforded 2-hydroxyindanone (**10a**, 31%) and 2-acetoxytetralone (**11a**, 48%).

2-Hydroxyindanone (**10a**)

Yellowish oil (Ref. [43] mp 34–36°C, Ref. [44] colourless, viscous liquid, bp 152°C/0.267 kPa); ^{1}H NMR spectrum was found to be identical with the one described in Ref. [45].

2-Acetoxyindanone (**11a**)

White crystals; mp 68–70°C (Ref. [43] bp 124–128°C/13 Pa, Ref. [44] bp 140°C/0.267 kPa); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.85$ (d, $J = 7.5$ Hz, 4-H), 7.65 (m, 6-H), 7.45 (m, 5,7-H), 5.45 (dd, $J = 8.0$, 5.0 Hz, 2-H), 3.67 (dd, $J = 17.1$, 8.0 Hz, 3-H_{cis}), 3.05 (dd, $J = 17.1$, 5.0 Hz, 3-H_{trans}), 2.20 (s, 3H, Ac); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 201.2$ (s, C-1), 170.4 (s, Ac), 150.3 (s, C-4a), 135.8 (d, C-5), 134.4 (s, C-7a), 128.1 (d, C-7), 126.6 (d, C-4), 124.4 (d, C-6), 74.0 (d, C-2), 33.4 (t, C-3), 20.7 (q, Ac).

Analogous treatment of enolacetate **8c** afforded 3-hydroxy-4-chromanone (**10c**, 15%) and 3-acetoxy-4-chromanone (**11c**, 34%).

When the reaction was repeated in the presence of 1.000 g (7.236 mmol) of anh. K_2CO_3 using 2.8 equiv of *DMD* 22% alcohol **10c** and 36% acetate **11c** were obtained.

3-Hydroxy-4-chromanone (**10c**)

Pale yellow crystals; mp 51–55°C (Ref. [45] 58–59°C); ^{1}H NMR spectrum was found to be identical with the one described in Ref. [46].

3-Acetoxy-4-chromanone (**11c**)

Pale yellow crystals; mp 66–68°C (Ref. [47] 74°C); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.91$ (dd, $J = 7.8$, 1.7 Hz, 5-H), 7.55 (m, 7-H), 7.05 (m, 6, 8-H), 5.66 (dd, $J = 11.4$, 5.6 Hz, 3-H), 4.45 (dd, $J = 11.3$, 5.6 Hz, 2-H_{eq}), 4.40 (dd, $J = 11.4$, 11.3 Hz, 2-H_{ax}), 2.25 (s, 3H, Ac); ^{13}C NMR (100 MHz,

$CDCl_3$): $\delta = 188.0$ (s, C-4), 169.5 (s, Ac), 161.3 (s, C-8a), 136.4 (d, C-7), 127.6 (d, C-5), 122.1 (d, C-6), 119.8 (s, C-4a), 177.8 (d, C-8), 69.4 (d, C-3), 68.3 (t, C-2), 20.5 (q, Ac).

One-step Synthesis of Racemic trans-3-Hydroxyflavanone (***10d***) *and trans-3-Acetoxyflavanone* (***10d***)

A *DMD* solution in acetone (180 cm^3, 0.069 *M*, *ca.* 4.00 equiv) was added to a mixture of 4-acetoxy-2-phenyl-2*H*-1-chromene (**8d**, 827 mg, 4.106 mmol) and anh. K_2CO_3 (1.013 g, 7.329 mmol) and allowed to react at $-20°C$. After filtration the solvent was removed *in vacuo* at room temperature and the residue was submitted to column chromatography (eluent: toluene:*Et*O*Ac* = 4:1, *v*/*v*) to yield 251 mg (40%) of alcohol **10d**, 140 mg (25%) of acetate **11d**, and 66 mg (10%) of flavone (**13**).

trans-3-Hydroxyflavanone (**10d**)

White crystals; mp 182–185°C (Ref. [48] 183–184°C, Ref. [49] 188°C); ^{1}H NMR spectrum was found to be identical with the one described in Ref. [50].

trans-3-Acetoxyflavanone (**11d**)

White crystals; mp 92–95°C (Ref. [50] 96–97°C); ^{1}H NMR spectrum was found to be identical with the one described in Ref. [51].

Flavone (**13**)

White crystals; mp 93–96°C (Ref. [52] 97°C).

Typical Procedure for the Enantioselective Oxidation of Enolacetates **8c** *and* **8d**

A *DMD* solution in acetone (180 cm^3, 0.058 *M*, *ca.* 2.90 equiv) was added to the mixture of enolacetate **8c** (697 mg, 3.665 mmol), imidazole (100 mg, 1.469 mmol), and *R*,*R*-(−)-Jacobsen's catalyst (*R*,*R*-**12**) (240 mg, 0.378 mmol) and stirred at room temperature for 6 h. The solvent was removed under reduced pressure at room temperature and the residue was submitted to column chromatography (eluent: *n*-hexane:*Et*O*Ac* (4:1, *v*/*v*)). Further experimental details are shown in Tables 2 and 3.

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