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Highly enantioselective undirected catalytic hydroxylation of benzylic CH_2 groups with H_2O_2

Roman V. Ottenbacher, Evgenii P. Talsi, Konstantin P. Bryliakov

Novosibirsk State University, Pirogova 1, Novosibirsk 630090, Russia
Boreskov Institute of Catalysis, Pr. Lavrentieva 5, Novosibirsk 630090, Russia

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ABSTRACT

Chiral *bis*-amine-*bis*-pyridine Mn complexes of the type [$LMn^{II}(OTf)_2$] (L is 2,2′-bipyrrolidine derived chiral ligand, bearing trifluoroethoxy and methyl substituents), efficiently catalyze the enantioselective hydroxylation of organic substrates at benzylic CH_2 positions with H_2O_2. The use of β-polyfluorinated alcohols instead of CH_3CN as the reaction solvents enhances the yield of chiral secondary alcohol from 5–6% up to 50–70%. The enantiomeric purity of the alcohol can be further increased (up to 97% *ee*) by diluting the mixture with CH_3CN at late stage, which facilitates stereoconvergent oxidative kinetic resolution of the alcohol formed. Using this one-pot sequential asymmetric hydroxylation/oxidative kinetic resolution approach, the oxidation of a series of 3,4-dihydrocoumarin derivatives and 3,4-dihydroquinolinone has been realized, affording the target 4-hydroxo compounds in 40–60% isolated yield and in up to 93% *ee*. Besides the 4-hydroxo derivatives, formation of 3,4-epoxidation and 3,4-desaturation byproducts has been observed in some cases, thus providing evidence for unprecedented substrate-dependent hydroxylase/desaturase/epoxidase reactivity of *bis*-amine-*bis*-pyridine Mn complexes.

1. Introduction

Designing transition-metal based catalyst systems for the stereoselective C-H oxidation of complex organic molecules has attracted significant interest [1–21] and turned into a hot topic of homogeneous catalysis in the last decade. In 2012–2014, Simonneaux with co-workers reported on the possibility of asymmetric benzylic C-H oxidation of ethylbenzene derivatives with "green" oxidant hydrogen peroxide. The reaction took place in the presence of soluble chiral Mn porphyrin complex **1** (Fig. 1A) and its Fe counterpart, affording the corresponding 1-arylalcohols with 32–57% *ee* [22,23].

A complementary approach, based on catalyzed oxidative desymmetrization, was proposed by Milan, Bietti and Costas, who applied chiral manganese complexes **2** and **3** (Fig. 1B) for the oxidation of mono-substituted cyclohexanes with H_2O_2 in the presence of carboxylic acid additives, documenting good to very high selectivity for the ketonization at the γ position [24]. With cyclopropanecarboxylic acid, the best catalytic additive in the series, γ-ketones having up to 96% *ee* were obtained. Another oxidative desymmetrization method was developed by Sun and Nam with co-workers who used C_1-symmetrical benzimidazole-derived complex **4** for the oxidation of complex spirocyclic β-ketones to the corresponding β,β'-diketones in up to 98% *ee* (Fig. 1C) [25]. Subsequently, the authors reported similarly high enantioselectivities for the oxidation of Boc-protected spirocyclic oxindoles and dihydroquinolines in the presence of 2 mol.% of the same catalyst **4** [26]. Noticeably, the reaction afforded a mixture of the chiral oxygenated products (Fig. 1C), and, depending on the reaction conditions, preferential formation of either the oxo or the hydroxo derivatives was documented.

In recent years, we sought novel catalytic approaches to chemo- and enantioselective C-H hydroxylation of organic molecules bearing CH_2 or CH groups, mostly relying on chiral manganese complexes as catalysts and hydrogen peroxide as the oxidant [27–30]. For the sake of synthetic generality, we intentionally focused on *undirected* [19] oxidations, that would effectively work without aid of catalyst-substrate chelation or substrate-specific supramolecular binding, thus welcoming broad scope of potential substrates. Achieving high regio- and stereoselectivity in undirected oxidations entirely relies on engineering a proper chiral environment around the catalytic site at the stereodetermining step of the reaction. This is a challenging task; very recently, an elegant attempt to fundamentally address it has been reported, based on inserting the catalytically active synthetic metal complex inside

E-mail address: bryliako@catalysis.ru (K.P. Bryliakov)

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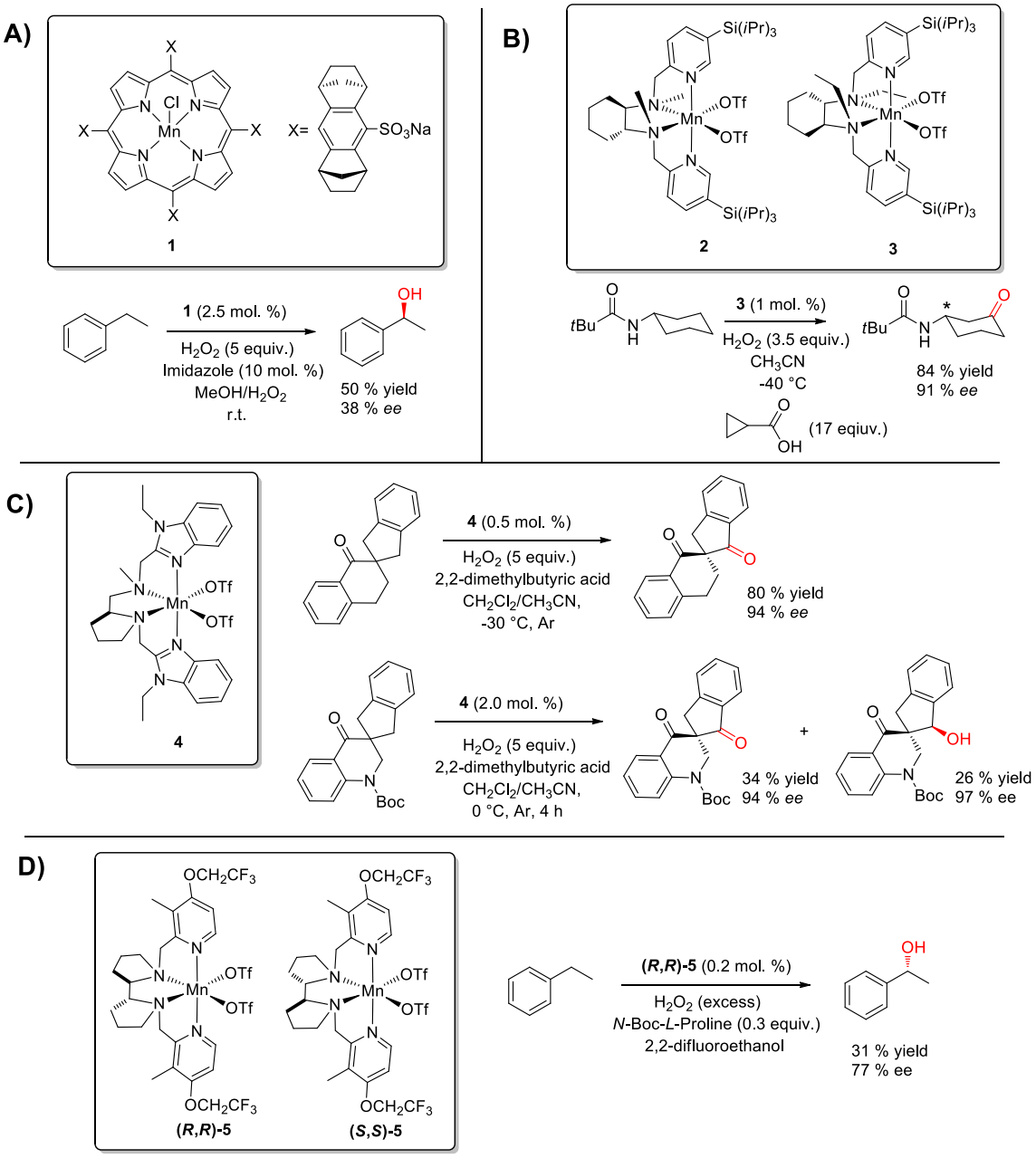


Fig. 1. Examples of manganese catalyzed stereoselective C-H oxidations with H_2O_2.

an enzyme [31]. Such sophisticated approach, yet in some cases providing high enantioselectivities in benzylic hydroxylation of arylalkanes to secondary alcohols (12–80% *ee*; 98% *ee* in one case), ensured relatively low alcohol yields (2.3–44%).

In case of hydroxylations of CH_2 groups, there has been additional complication, caused by the fact that the target product, *sec*-alcohol, has weaker and more electron rich C-H bond than the substrate itself, which entails its higher reactivity towards C-H bond breaking by electrophilic oxidants, eventually leading to ketone formation. In effect, in acetonitrile as solvent, benzylic CH_2 oxidations typically result in low alcohol yields, not exceeding 5–6% [27,28]. However, the alcohol reactivity could be effectively attenuated by using the "polarity reversal" approach, suggested by Bietti and Costas with co-workers. The key feature of the latter approach is the use of β-polyfluorinated alcohols that act as strong hydrogen-bond donors, thus reducing the nucleophilicity of the target alcohol and hence suppressing its overoxidation to the ketone [32]. In effect, we found that in 2,2-difluoroethanol, complexes **(*R*,*R*)-5** and **(*S*,*S*)-5** (Fig. 1D) catalyzed the benzylic hydroxylation of a series of simple arylalkanes in up to 30–35% yield and 77% *ee* [29].

Such improvement in the alcohol yield, yet encouraging, is still insufficient for preparative syntheses. Conducting the reaction in even more polar medium (by e.g. replacing 2,2-difluoroethanol with 2,2,2-trifluoroethanol) would not help, since, while enhancing the alcohol yield, deteriorates the enantioselectivity of its formation [29]. Herewith, we present an alternative, one-pot sequential asymmetric C-H oxidation/kinetic resolution approach, ensuring higher 1-phenylethanol yield (40%) and higher enantioselectivity at the same time (up to 97% *ee*). Using such approach, 3,4-dihydrocoumarin derivatives and 3,4-dihydroquinolinone can also be hydroxylated at position 4, affording potentially biologically

relevant derivatives featuring *sec*-alcohol moieties in 40–60% isolated yields and good to high enantioselectivities (82–93% *ee*). Mechanistic details of the oxidation are discussed briefly.

2. Results and discussion

Among the fluorinated alcohols tested in this and our previous studies [27–30], hexafluoroisopropanol (HFIP) is the strongest hydrogen-bond donor (HBD) solvent [32]. Therefore, in agreement with our expectations, it has been found to ensure the highest 1-phenylethanol yield (ca. 65%) upon ethylbenzene oxidation in the presence of **(*R*,*R*)-5** (0.2 mol.%) and 2-ethylhexanoic acid (Fig. 2). On the other hand, in HFIP, the enantiomeric purity of 1-phenylethanol product does not exceed 48%, which is substantially lower than the figure of 61% *ee* documented in 2,2-difluoroethanol (DFE). At first sight, this makes the use of HFIP solvent not so beneficial from the practical perspective.

However, it was shown that the asymmetric induction in arylalkanes oxidation may arise at both the C-H oxidation step itself, and the concomitant oxidative kinetic resolution, thus leading to progressive *ee* increase over the reaction course [28,29]. Apparently, the higher overall oxidation enantioselectivity in DFE is partly accounted for by higher contribution of kinetic resolution, as compared to the reaction in HFIP, since in the latter case, the alcohol is substantially deactivated toward further oxidation to ketone. Keeping in mind that the kinetic resolution should be facilitated when passing from stronger to weaker hydrogen bond donor solvents, we have attempted finding a reasonable compromise between the alcohol yield and its enantiomeric purity by conducting the reaction in mixed solvents (containing variable shares of HFIP and weaker HBDs). The results are presented in Table 1. *N*-Boc-*L*-proline (Fig. 3), which previously demonstrated its efficiency in C-H oxidations (in combination with **(*R*,*R*)-5**) [28,29], was used as the chiral catalytic additive. One can see that with reducing the share of HFIP in the mixture, the alcohol enantiopurity increases, but its maximum yield decreases (Table 1, entries 1–6). In effect,

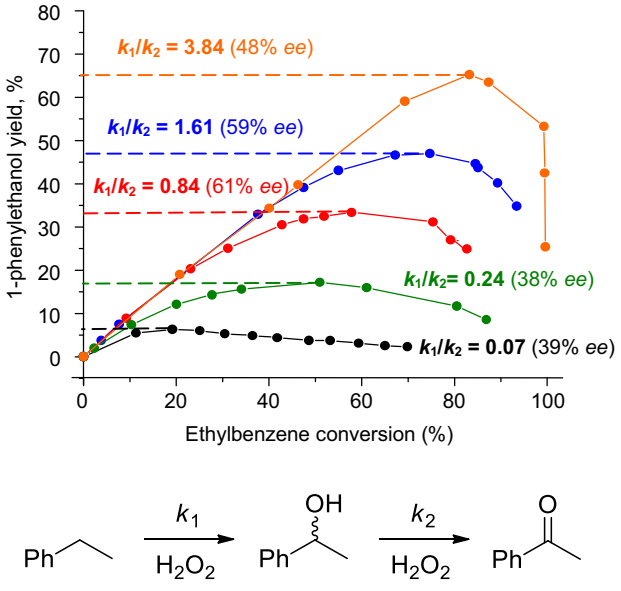


Fig. 2. 1-Phenylethanol yield vs. conversion for the oxidation of ethylbenzene (0.1 mmol) in the presence of **(*R*,*R*)-5** (0.2 mol.%) and 2-ethylhexanoic acid (0.1 mmol) at −30 °C in acetonitrile (black), 2-fluoroethanol (olive), 2,2-difluoroethanol (red), 2,2,2-trifluoroethanol (blue), and 1,1,1,3,3,3-hexafluoro-2-propanol (orange). k_1/k_2 values (according to the formal two-step kinetic scheme, cf. Ref. [29]) and alcohol enantiomeric excess at maximum yield are given for each curve.

in HFIP/CH_3CN, the enantioselectivity as high as 88% *ee* was achieved, but the alcohol yield was as low as 27% (entry 6).

In order to combine as far as possible the benefits of the solvent components, HFIP (advantage: high alcohol yield) and CH_3CN (advantage: high *ee*), we have modified the experimental procedure as follows. The oxidation of ethylbenzene was started in pure HFIP; upon achieving the expected maximum alcohol yield, the mixture was diluted with equal volume of CH_3CN, and the reaction was continued in order to improve the alcohol enantiomeric purity by oxidative kinetic resolution. In such a manner, 1-phenylethanol having 93–97% *ee* can be obtained in 38–41% yield (entries 7–10 of Table 1), which values are considerably high if compared with the direct catalytic C-H hydroxylation methods existing to date. The plot of ethanol and acetophenone amounts, as well as alcohol *ee* vs. oxidation equiv. for the experiment in entry 8 of Table 1 is displayed in Fig. 4. One can see that the alcohol *ee* is virtually constant (ca. 50% *ee*) before the addition of CH_3CN, indicating the absence of kinetic resolution in HFIP. Adding CH_3CN results in sharp enantioenrichment, accompanied by decrease of the alcohol amount due to its further oxidation to acetophenone (Fig. 4).

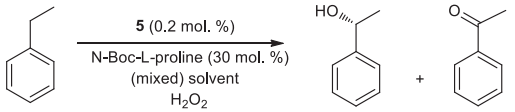
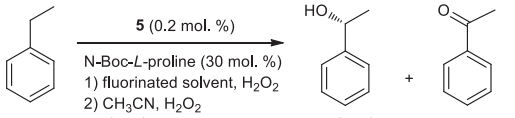
Next, the oxidation of several complex substrates, mostly Boc-protected 3,4-dihydroquinolinones, representing common motifs of bioactive molecules [13,33–35], and related compounds, was examined (Table 2). *N*-Carbobenzyloxyproline (*N*-Cbz-*D*-proline) and *N*-Boc-prolines (Fig. 3) have emerged as the best catalytic additives, ensuring the highest yield and enantioselectivity of the 4-hydroxo product at the same time (entries 2 vs. 3 and 4 vs. 5 of Table 2), while *N*-carbobenzyloxy-2-piperidinecarboxylic acid (*N*-Cbz-*L*-ppca) showed inferior result (entry 1 of Table 2). Encouragingly, the 4-hydroxo product isolated yields in several cases reached 50–60%, which may hold practical promise. We notice that the product enantiomeric purities up to 92% *ee* can be achieved in HFIP even *without* assistance of kinetic resolution: in Table 2, entries 1–14, CH_3CN was not added to the reaction mixtures.

The structure of the substrate affects the oxidation outcome. Replacing the Boc protecting group with benzoyl one resulted in an improved 4-hydroxo product yield, albeit having slightly lower *ee* (cf. entries 9 and 3). Moreover, 3,4-dihydrocoumarin, close analog of 3,4-dihydroquinolinones, converted to the chiral product in good yield and enantioselectivity (entry 10). On the other hand, α-tetralone converted predominantly to 2,3-dihydronaphthalene-1,4-dione, while no ketoalcohol was found among the reaction products (entry 11). 6-Methoxy substituted Boc protected 3,4-dihydroquinolinone did not react at all under the conditions (entry 13). The substrate bearing 6-*o*-tolyl substituent readily reacted under the conditions, affording a rich mixture of unidentified products rather than any 4-hydroxo derivative (entry 14).

In the experiments of Table 2, the reactions were conducted until quantitative substrate conversion was achieved or the substrate conversion stopped growing, despite further H_2O_2 and Mn complex additions. In some cases, recovered starting material (r.s.m.) was isolated after column workup in significant amounts. The corresponding values, where available, are reported in Table 2 together with the major product yields.

We have attempted recruiting the kinetic resolution in order to enhance the product *ee*, using the same approach as for the oxidation of ethylbenzene, i.e. by diluting the reaction mixture with CH_3CN after having achieved maximum 4-hydroxo product yield, and adding extra H_2O_2. This modification indeed improved the product *ee* by 5–6 percent points (Table 2, entries 15 and 16 vs. 2), without meaningful deterioration of isolated yield. In contrast to ethylbenzene oxidations, the reaction dramatically decelerates when the starting substrate is depleted, since the resulting hydroxylated derivative is very poorly reactive under the conditions. In effect, kinetic resolution can make rather limited contribution to the isolated yield and *ee*. Reducing the solvent polarity, exempli-

Table 1
Oxidation of ethylbenzene with H_2O_2 in the presence of chiral manganese complexes.[a]

No	catalyst	solvent (v/v)	substrate conversion % [b]	alcohol yield, % [b]	A/K [c]	alcohol *ee* (%) [b]	config.
							
1	***(R,R)*-5**	HFIP	95	71	6.9	49	(*R*)
2	***(R,R)*-5**	HFIP:TFE (6:1)	98	68	5.5	57	(*R*)
3	***(R,R)*-5**	HFIP:DFE (3:1)	81	55	8.2	58	(*R*)
4	***(R,R)*-5**	HFIP:MeOH (3:1)	95	43	1.5	77	(*R*)
5	***(R,R)*-5**	HFIP:CH_3CN (3:1)	92	41	1.25	79	(*R*)
6	***(R,R)*-5**	HFIP:CH_3CN (1:1)	70	27	0.82	88	(*R*)
							
7	***(R,R)*-5**	HFIP:TFE (6:1)	98	41	0.88	89	(*R*)
8	***(R,R)*-5**	HFIP [d]	99	39	0.85	94	(*R*)
9	***(S,S)*-5** [e]	HFIP [d]	98	40	0.96	93	(*S*)
10	***(S,S)*-5** [e,f]	HFIP [d]	98	38	0.90	97	(*S*)

[a] At −40 °C; [substrate]:[Mn] = 100 μmol:0.2 μmol, solvent (0.2 mL). DFE and TFE are di- and trifluoroethanol, respectively.
[b] Determined by chiral HPLC. Maximum alcohol yield values achieved are reported.
[c] Alcohol/ketone ratio.
[d] Pure HFIP is solid at the reaction temperature, so 30% H_2O_2 (20 μL) was added to the mixture, then the latter was thermostated at −40 °C, and finally the catalyst was added as solid. See SI for further details.
[e] *N*-Boc-*D*-proline was used as additive.
[f] Experiment in entry 9 to which extra portion of H_2O_2 was added.

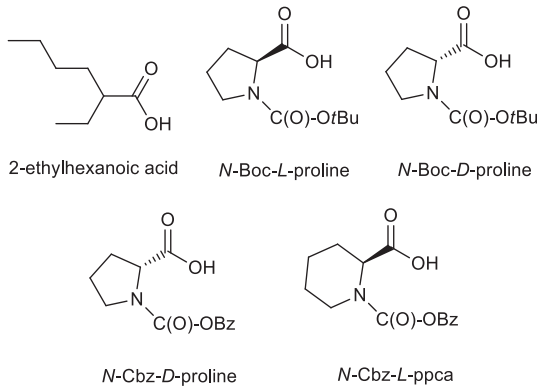


Fig. 3. Structures of catalytic additives used in this work.

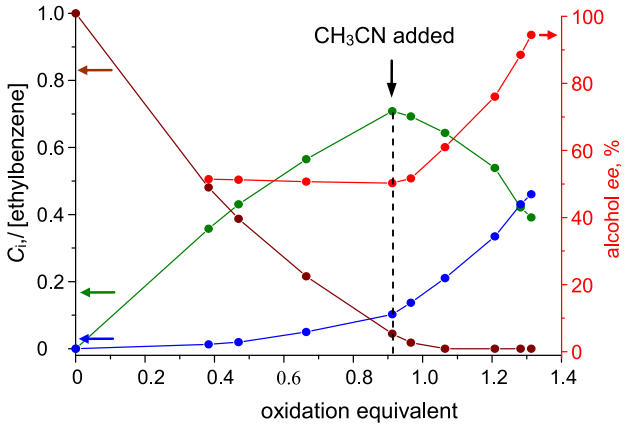


Fig. 4. Amounts of ethylbenzene (brown), alcohol (olive), ketone (blue), and of alcohol *ee* (red) in the course of ethylbenzene oxidation by the systems ***(R,R)*-5**/Boc-(*L*)-Pro/H_2O_2 vs. oxidation equivalent ({[1-phenylethanol] + 2 × [acetophenone]}/[ethylbenzene]$_0$).

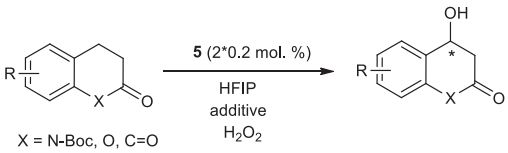
fied by using CH_3CN/DFE mixture as solvent (Table 2, entry 17) is not beneficial, deteriorating both the yield and *ee*.

The oxidation procedure is scalable, as has been witnessed by performing the oxidation of 1-benzoyl-3,4-dihydroquinolin-2(1H)-one at 1 mmol scale (Scheme 1). Moreover, using the one-pot asymmetric oxidation / oxidative kinetic resolution procedure, the enantiomeric excess of the resulting chiral 4-hydroxo product was improved by 5% points, at the expense of the slightly reduced isolated yield (cf. Scheme 1 vs. entry 9 of Table 2).

Curiously, it turned out that in the course of oxidation of benzoyl-protected (Scheme 1) and Boc-protected 3,4-dihydroquinolinone **6** (Scheme 2A), the major isolated by-products appeared to be the corresponding Boc-chromene 3,4-epoxides (8–15% isolated yield). The mechanism of its formation is particularly interesting. First of all, the generation of epoxide via oxidation of the 4-hydroxo product was ruled out: no epoxide was found upon oxidation of **7** (Scheme 2B, see SI for details). One could hypothesize that substrate **6** under the reaction conditions, in addition to Mn catalyzed hydroxylation [36], can undergo manganese catalyzed desaturation (Scheme 2C) [37,38], with subsequent, also manganese catalyzed epoxidation of the intermediate **9** (Scheme 2C) [39]. However, the formation of desaturation product **9** has not been detected by HPLC in the course of the oxidation of **6** (Scheme 2C). Moreover, the independently synthesized **9** itself was very poorly reactive toward oxidation in the presence of Mn catalyst **5** under the conditions (see SI for details), affording trace amounts of unidentified products rather than any epoxide (Scheme 2C).

Contrastingly, the oxidation of 3,4-dihydrocoumarin **10** (Scheme 3A), in addition to the 4-hydroxo major product **11**, allowed the isolation of both the 3,4-desaturation and 3,4-epoxidation byproducts in a ca. 10:1 ratio (Scheme 3A; see SI for HPLC details and NMR characterization). Notably, the Mn-catalyzed oxidation of coumarin **12** smoothly afforded the corresponding epoxide as the major product (Scheme 3B). Furthermore, the oxidation of *unprotected* 3,4-dihydroquinolinone **14** yielded the corresponding 4-hydroxo derivative **15** as a *minor* product (12%), with the desaturation product **16** prevailing with its 32%

Table 2
Asymmetric oxidations with H_2O_2 in the presence of chiral manganese complexes **5**.[a]



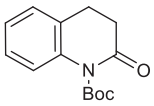
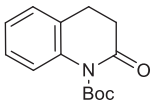
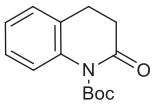
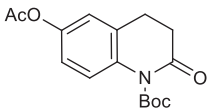
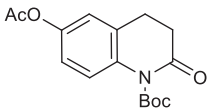
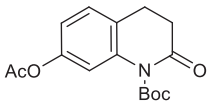
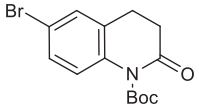
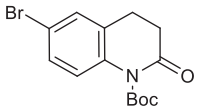
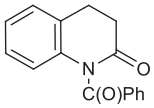
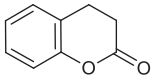
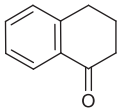
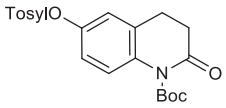
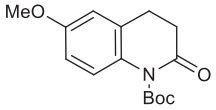
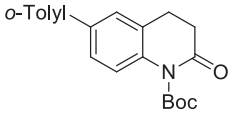
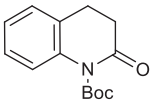
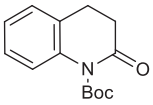
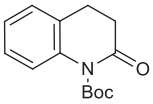
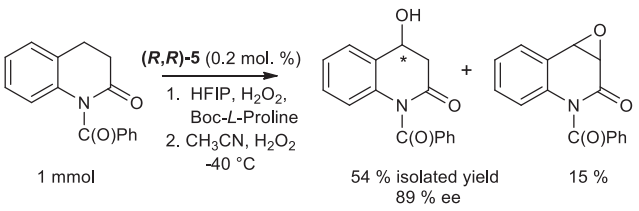
No	substrate	catalyst	additive	4-hydroxo product yield (%) [b]	4-hydroxo product *ee* (%) [c]
1		***(R,R)*-5**	*N*-Cbz-*L*-ppca	35 (16% r.s.m.)	76
2		***(R,R)*-5**	*N*-Boc-*L*-proline	42	87[d]
3		***(S,S)*-5**	*N*-Cbz-*D*-proline	55	89[d]
4		***(S,S)*-5**	*N*-Cbz-*D*-proline	35 (45% r.s.m.)	78
5		***(S,S)*-5**	*N*-Boc-*D*-proline	51 (16% r.s.m.)	82
6		***(S,S)*-5**	*N*-Boc-*D*-proline	52 (15% r.s.m.)	72
7		***(S,S)*-5**	*N*-Cbz-*D*-proline	42 (49% r.s.m.)	92
8		***(S,S)*-5**	*N*-Boc-*D*-proline	34 (50% r.s.m.)	92
9		***(S,S)*-5**	*N*-Cbz-*D*-proline	60	84
10		***(S,S)*-5**	*N*-Boc-*D*-proline	52 (29% r.s.m.)	85
11		***(S,S)*-5**	*N*-Boc-*D*-proline	–[e]	–
12		***(S,S)*-5**	*N*-Boc-*D*-proline	38 (43% r.s.m.)	81
13		***(S,S)*-5**	*N*-Cbz-*D*-proline	no reaction	–

Table 2 (*continued*)

No	substrate	catalyst	additive	4-hydroxo product yield (%) [b]	4-hydroxo product *ee* (%) [c]
14		***(S,S)*-5**	*N*-Boc-*D*-proline	–[f]	–
15[g]		***(S,S)*-5**	*N*-Boc-*D*-proline	47[h]	93
16[g]		***(R,R)*-5**	*N*-Boc-*L*-proline	41[i]	92
17[j]		***(S,S)*-5**	*N*-Boc-*D*-proline	29[k]	89

[a] At −40 °C; [substrate]: [additive]: [Mn] = 200 μmol: 60 μmol: 0.4 μmol; solvent (HFIP): 0.4 mL, 30% H_2O_2 (60 μL) was added to the mixture, then the latter was thermostated at −40 °C, and finally the catalyst was added as solid; the mixture was stirred overnight, and 2 μmol aliquots were analyzed by chiral HPLC to monitor the reaction progress. Extra portions of H_2O_2 were added until achieving nearly quantitative substrate conversion or dramatic reaction deceleration. The 4-hydroxylated products were isolated by column chromatography (SI).
[b] Isolated yields; the isolated amounts of recovered starting material (r.s.m.) are reported where available.
[c] Determined by chiral HPLC (SI).
[d] Products in entries 2 and 3 had opposite optical configuration (see HPLC traces in the SI).
[e] 2,3-dihydronaphthalene-1,4-dione (67%) was the major oxidation product.
[f] A number of (minor) products was formed, 4-hydroxy product was not found.
[g] After nearly quantitative substrate conversion, the mixture was diluted with equal volume of CH_3CN, and extra portion of oxidant was added.
[h] By-product: epoxide **8** (Scheme 1), 11% isolated yield (76% *ee*).
[i] By-product: epoxide **8**, 8% isolated yield (73% *ee*).
[j] The reaction was conducted in CH_3CN/DFE (10:3 v/v).
[k] By-product: epoxide **8**, 13% isolated yield (90% *ee*).



Scheme 1. Oxidation of 1-benzoyl-3,4-dihydroquinolin-2(1H)-one at 1 mmol scale.

(Scheme 3C). In this case, the epoxide was not found at all (cf. recent results of Bach with co-workers [20]).

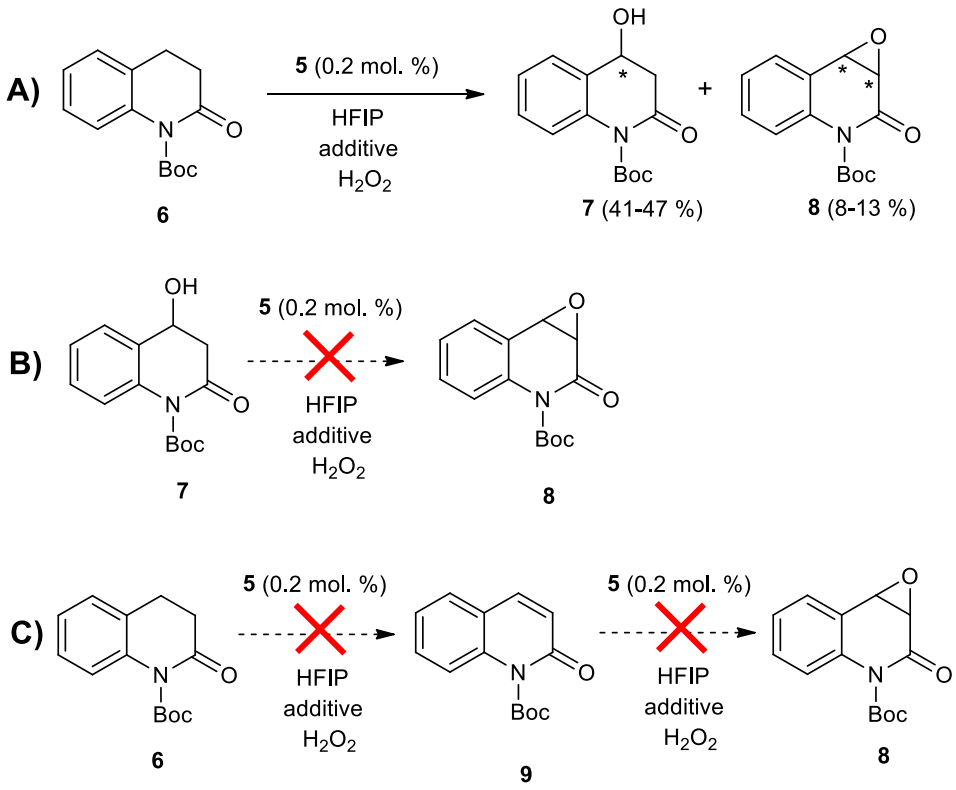
Overall, these results clearly demonstrate the substrate-dependent mixed hydroxylase/desaturase/epoxidase reactivity of manganese catalysts **5**. To the best of our knowledge, such switchable triple reactivity has been unprecedented for synthetic biomimetic catalyst systems.

The data collected so far do not provide unequivocal evidence in favor of the common pathway of epoxide formation via epoxidation of the initially formed olefinic substrate. At least, Boc-protected 3,4-dihydroquinolinone **6** is not desaturated, and Boc-protected quinolinone **9** is not epoxidized under the reaction conditions. At the same time, formation of coumarin 3,4-epoxide **13** via consecutive 3,4-dihydrocoumarin **10** desaturation and further 3,4-epoxidation of coumarin **12** seems to be plausible under the conditions. The desaturation pathway (Scheme 4, bottom) is apparently an alternative to the oxygen rebound hydroxylation mechanism (Scheme 4, top), possibly occurring via common intermediate in a solvent cage (shown in square brackets in Scheme 4) [37,38]. Apparently, in the case of the *unprotected* 3,4-dihydroquinolinone **14**, the desaturation pathway is favored by quinolinone/oxyquinoline tautomerism, resulting in aromatization, while in the case of Boc-protected **6** there is no such driving force, which leads to prevalence of the 4-hydroxylation product.

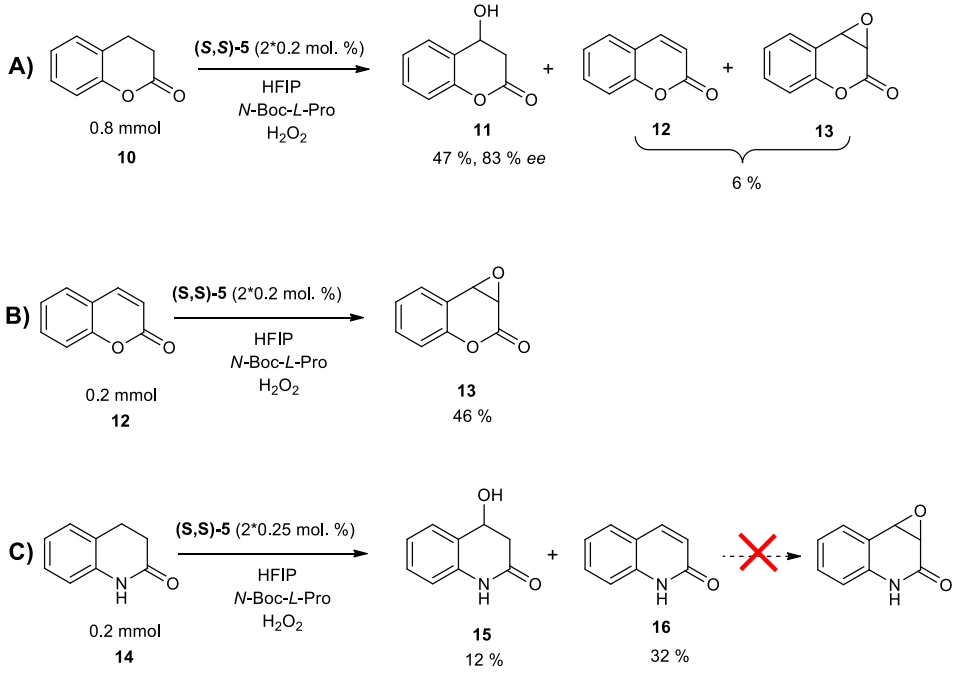
3. Conclusions

One-pot sequential asymmetric benzylic C-H hydroxylation/oxidative kinetic resolution procedure has been developed using ethylbenzene as model substrate, ensuring improved yield (40%) and enantiomeric excess (up to 97% *ee*) of 1-phenylethanol. This catalytic approach relies on the easily prepared chiral *bis*-amine-*bis*-pyridine manganese complexes as catalysts (used at 0.2–0.4 mol.% loadings), and "green" H_2O_2 as oxidant. The synthetic potential of this approach has been exemplified by the enantioselective hydroxylation of 3,4-dihydroquinolinone derivatives and their structural analogs, affording potentially biologically relevant derivatives with *sec*-alcohol moieties in 40–60% isolated yields and good to high enantioselectivities (up to 93% *ee*), which holds practical promise. The proposed approach offers the best yield / enantioselectivity combination in the synthesis of chiral secondary alcohols via metal-catalyzed direct CH_2 hydroxylations with H_2O_2. We believe that this simple but highly efficient and stereoselective catalytic approach can find use in late stage functionalization of complex organic molecules of pharmaceutical relevance. Further studies will be aimed at broadening the substrate scope and improving the yield of the chiral hydroxylated products.

Analysis of the reaction products, besides the target 4-hydroxy compounds, in some cases witnesses the formation of the corresponding 3,4-epoxidation and (for the oxidation of 3,4-dihydrocoumarin and unprotected 3,4-dihydroquinolinone) 3,4-desaturation byproducts, thus providing the first example of substrate-dependent triple hydroxylase/desaturase/epoxidase reactivity of bioinspired *bis*-amine-*bis*-pyridine manganese complexes.



Scheme 2. Formation of major oxidation products in the oxidation of *tert*-butyl 2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate **6** (A). Examined reaction pathways for epoxide formation: (B), (C).



Scheme 3. Oxidation of 3,4-dihydrocoumarin (A), coumarin (B), and 3,4-dihydroquinolinone (C).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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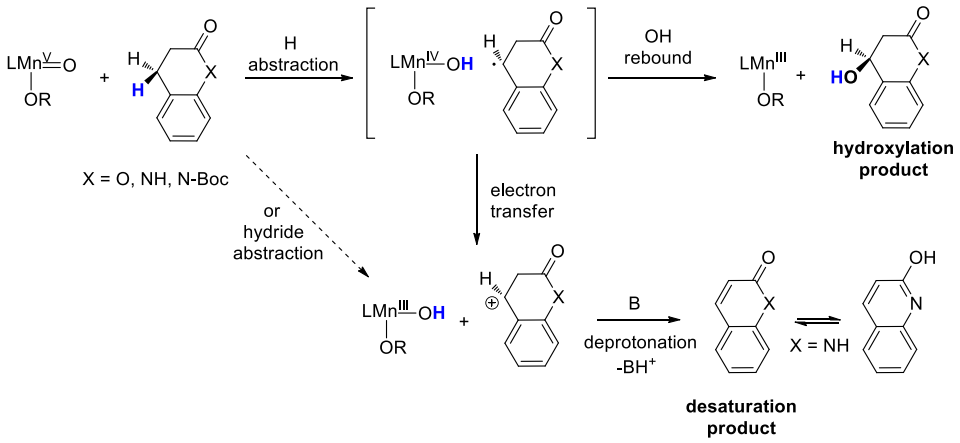

Scheme 4. Proposed competivive hydroxylation/desaturation reaction pathways in Mn catalyzed oxidations.

viding access to the spectral and analytical facilities, and Mr. V.N. Konev for HPLC measurements for entry 9 of Table 2 and Scheme 1.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcat.2020.08.005.

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[39] We notice that the epoxides samples isolated from the reaction mixtures in entries 15 and 16 of Table 2, had opposite stereoconfigurations (see SI for HPLC traces), which corroborates the key role of the chiral Mn based catalysts ((S,S)-5 and (R,R)-5, respectively) in their formation. Asymmetric epoxidations, catalyzed by chiral aminopyridine and structurally related Mn complexes, have been extensively studied; for selected examples, see: (a) M. Wu, B. Wang, S. Wang, C. Xia, W. Sun, Org. Lett. 11 (2009) 3622-3625; (b) O. Cussó, I. Garcia-Bosch, D. Font, X. Ribas, J. Lloret-Fillol, M. Costas, Org. Lett. 15 (2013) 6158-6161. (c) R.V. Ottenbacher, D.G. Samsonenko, E.P. Talsi, K.P. Bryliakov, ACS Catal. 4 (2014) 1599-1606.