Relative reactivity of substituted acetophenones in enantioselective biocatalytic reduction catalyzed by plant cells of *Daucus carota* and *Petroselinum crispum*

A.R. Chanysheva, T.E. Vorobyova, V.V. Zorin

PII: S0040-4020(19)30821-X

DOI: https://doi.org/10.1016/j.tet.2019.130494

Reference: TET 130494

To appear in: *Tetrahedron*

Received Date: 23 April 2019

Revised Date: 9 July 2019

Accepted Date: 31 July 2019

Please cite this article as: Chanysheva AR, Vorobyova TE, Zorin VV, Relative reactivity of substituted acetophenones in enantioselective biocatalytic reduction catalyzed by plant cells of *Daucus carota* and *Petroselinum crispum*, *Tetrahedron* (2019), doi: https://doi.org/10.1016/j.tet.2019.130494.

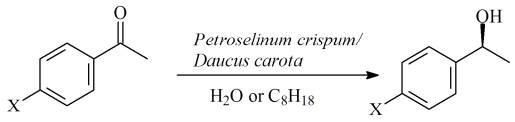
Graphical Abstract

Relative reactivity of substituted acetophenones in enantioselective biocatalytic reduction catalyzed by plant cells of *Daucus carota* and *Petroselinum crispum*

Leave this area blank for abstract info.

A.R. Chanysheva[a,] ∗, T.E. Vorobyova[a] and V.V. Zorin[a]

[a] *Department of Biochemistry and Technology of Microbiological Industries, Ufa State Petroleum Technological University, ul. Kosmonavtov, 1, Ufa, Russia*



S-alcohol

X= H; *p*-OCH_3; *p*-Cl; *p*-Br; *p*-NO_2.

Tetrahedron
journal homepage: www.elsevier.com

Relative reactivity of substituted acetophenones in enantioselective biocatalytic reduction catalyzed by plant cells of *Daucus carota* and *Petroselinum crispum*

A.R. Chanysheva[a,] ∗, T.E. Vorobyova[a] and V.V. Zorin[a]

[a] *Department of Biochemistry and Technology of Microbiological Industries, Ufa State Petroleum Technological University, Ufa, Russia*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Enantioselective bioreduction
Plant cells
Acetophenones
Hammett's correlation
Relative reactivity
S-alcohols

ABSTRACT

We have examined enantioselective bioreduction of acetophenone and its substituted derivatives into corresponding *S*-alcohols catalyzed by *Daucus carota* and *Petroselinum crispum* plant cells in water and isooctane. We found that the nature of the substituent has a profound effect on the relative reactivity of substituted acetophenones and enantioselectivity of biocatalytic reduction. Electron-withdrawing substituents –Br and $–NO_2$ enhance the initial rate of reaction and yields of products, while electron-donating substituent $–OCH_3$ decreases them. The reduction rates and yields of products in water were noticeably higher in comparison with similar reductions conducted in isooctane. Correlations between the initial reaction rate and the substituent constant (σ^+) in the aromatic ring characterizing its nature were established. Comparison of ρ constants of bioreduction catalyzed by *D. carota* and *P. crispum* shows that the sensitivity of the reduction to the nature of the substituents is more significant in the case of *D. carota* biocatalyst. Comparison of ρ constants for *D. carota* and *P. crispum* in water and isooctane indicates that the sensitivity of bioreduction to the nature of the substituent tends to increase from water to isooctane.

∗ Corresponding author. Tel.: +7-927-085-0852; e-mail: aliyach@mail.ru

1. Introduction

Enantioselective bioreduction of prochiral ketones is an important transformation in organic synthesis. Biocatalytic reduction can be performed using whole cell plant and microbial systems, as well as isolated enzymes. Enantioselective bioreduction catalyzed by various plant cells is an efficient and simple method due to its high enantioselectivity and mild reaction conditions. *Daucus carota* cells are widely used in enantioselective biocatalysis due to their ability to produce secondary alcohols with excellent yields and optical purity. In addition, *Petroselinum crispum, Nicotiana tabacum, Apium graveolens, Cucumis sativus, Solanum tuberosum, Pisum sativa* were previously reported to have a high synthetic potential in asymmetric reduction of functionally substituted carbonyl compounds.[1–19]

Enantioselective bioreduction of prochiral ketones, in particular substituted acetophenones, implies the participation of oxidoreductases in the process of hydride ion transfer from NADH to the carbonyl group. The rate and efficiency of this process may depend on the electron density of the carbonyl group, which can be changed in the presence of electron-donating or electron-withdrawing substituents in the aromatic ring. The effect of these substituents' nature on the enantioselectivity of bioreduction is not very well understood.

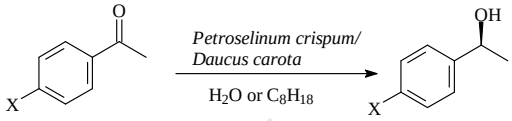
Correlations between bioreduction rate of acetophenone derivatives and the nature of substituents catalyzed by isolated rat liver dehydrogenase and recombinant ketoreductases were previously described by Uwai K. et al.[20] and Zhu D. et al.[21]

In this report, we examined how the nature of substituents in a series of acetophenones affects the rate and direction of bioreduction catalyzed by plant cells of *D. carota* and *P. crispum*.

2. Results and Discussion

We investigated the kinetics and enantioselectivity of bioreduction of functionally substituted acetophenones catalyzed by plant cells of *D. carota* and *P. crispum*, which are known to exhibit a rather high reductase activity [2-19].

Acetophenone **1a** and its derivatives: 4-chloroacetophenone **2a**, 4-bromoacetophenone **3a**, 4-nitroacetophenone **4a**, 4-methoxyacetophenone **5a** were reduced enantioselectively by using *D. carota* or *P. crispum* in water (substrate concentration 20 mmol/l, biocatalyst concentration 100 g/l) at 23 -27 °C for 96 hours to produce *S*-1-phenylethanol **1b**, *S*-1-(4-chlorophenyl)ethanol **2b**, *S*-1-(4-bromophenyl)ethanol **3b**, *S*-1-(4-nitrophenyl)ethanol **4b** and *S*-1-(4-methoxyphenyl)ethanol **5b**, respectively. The conversion and enantiomeric excess (ee) of products were determined by enantioselective GC and polarimetry analysis (Scheme 1).



S-alcohol X= H; *p*-OCH_3; *p*-Cl; *p*-Br; *p*-NO_2.

Scheme 1 - Biocatalytic reduction of acetophenone and its substituted derivatives 1a-5a catalyzed by D. carota or P. crispum plant cells.

The obtained results indicate that the nature of the substituent in the aromatic ring significantly impacts the reaction rate and the yields of products. Electron-withdrawing substituents –Br and –NO_2 enhance the initial rate of reaction, while electron-donating substituent –OCH_3 slows down the initial reaction rate (Figure 1). Such effect of substituents in the aromatic ring on the initial rate of reactions involving nucleophilic agents was previously observed in various reaction series.[22]

The sensitivity of reactions to the nature of the substituent is determined by the type of reaction and by position of the substituent in the aromatic ring. There is often a correlation between the initial reaction rate and the substituent constant characterizing its nature.

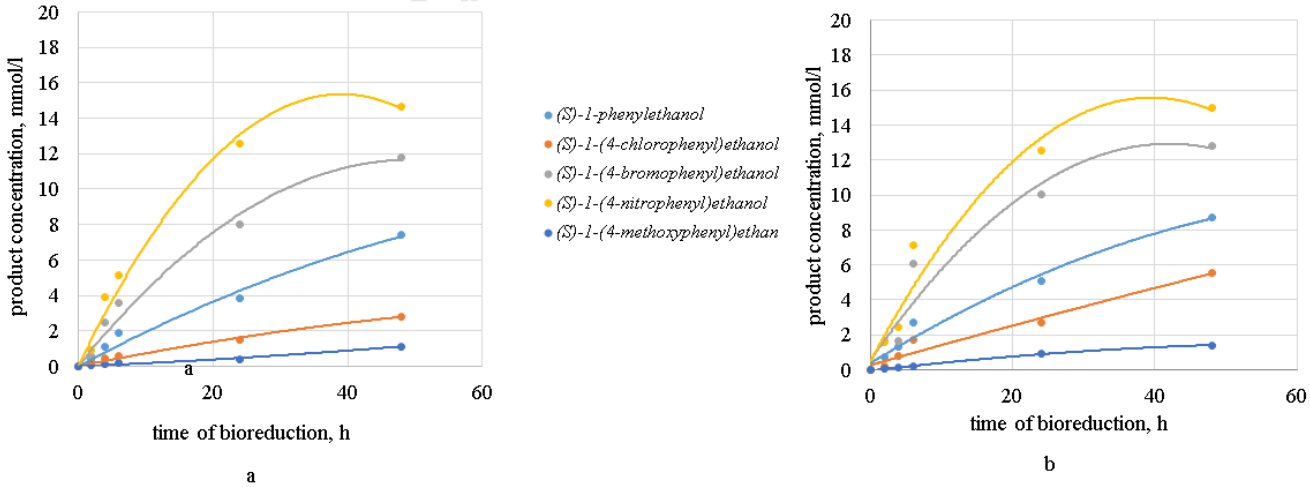


Figure 1 - Kinetics of formation of substituted *S*-1-phenylethanols **1b-5b** in biocatalytic reduction of acetophenone and its derivatives **1a-5a** in the presence of a). *D. carota*; b). *P. crispum* (T = 23-27 ° C, solvent - water, substrate concentration 20 mmol/l, biocatalyst concentration 100 g/l).

The classic description of such correlations is performed by the Hammett equation[22]:

$$\lg(V_X/V_H) = \rho\sigma \qquad (1)$$

where V_X - the initial rate of substituted *S*-1-phenylethanols **2b-5b** formation, mmol·s^{-1}/l;

V_H - the initial rate of *S*-1-phenylethanol **1b** formation, mmol·s^{-1}/l;

σ – the Hammett constant;

ρ – the reaction series constant.

Calculation of experimentally obtained initial rates of bioreduction of substituted acetophenones and comparison of the $lg(V_X/V_H)$ values and the substituent constants σ[22] showed poor correlation in accordance with the Hammett equation.

In contrast, application of the modified Hammett equation using the σ^+ constants, suggesting that the substituent participates in direct polar conjugation with the electron-withdrawing transition state, showed a good correlation between $lg(V_X/V_H)$ values and σ^+ constants.[22] (Table 1, Figure 2).

Table 1. Kinetic parameters in the bioreduction of acetophenone and its substituted derivatives **1a-5a** catalyzed by *D. carota* or *P. crispum* cells

Daucus carota					*Petroselinum crispum*				
Alcohol (X)	V_X	(V_X/V_H)	$lg(V_X/V_H)$	σ^+	Alcohol (X)	V_X	(V_X/V_H)	$lg(V_X/V_H)$	σ^+
1b (H)	$7{,}77\cdot10^{-5}$	1	0	0	1b (H)	$9{,}02\cdot10^{-5}$	1	0	0
2b (Cl)	$3{,}05\cdot10^{-5}$	0,39	-0,41	0,035	2b (Cl)	$5{,}41\cdot10^{-5}$	0,60	-0,22	0,035
3b (Br)	$17{,}2\cdot10^{-5}$	2,21	0,34	0,025	3b (Br)	$11{,}5\cdot10^{-5}$	1,28	0,11	0,025
4b (NO_2)	$26{,}9\cdot10^{-5}$	3,46	0,54	0,74	4b (NO_2)	$17{,}2\cdot10^{-5}$	1,91	0,28	0,74
5b (OCH_3)	$1{,}25\cdot10^{-5}$	0,16	-0,8	-0,648	5b (OCH_3)	$0{,}97\cdot10^{-5}$	0,11	-0,96	-0,648

substrate concentration 20 mmol/l, biocatalyst concentration 100 g/l, T=23-27 °C, solvent – water

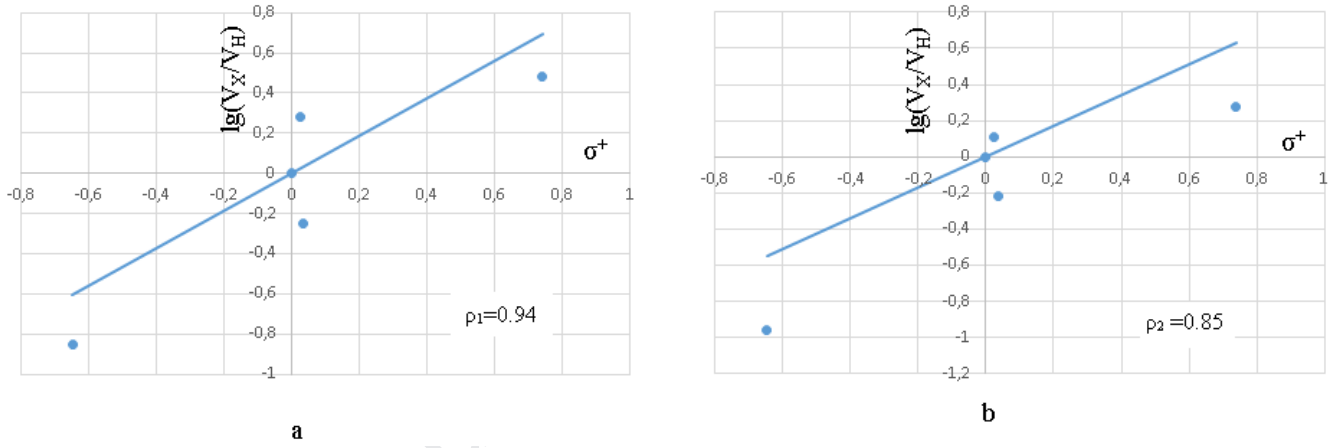


Figure 2 – Correlations between experimentally obtained $lg(V_X/V_H)$ and σ^+ values in the bioreduction of substituted acetophenones **1a-5a** catalyzed by a). *D. carota* or b). *P. crispum* at 23-27 ° C in water

The hydride ion transfer to the carbonyl group by NADH occurs in the process of enatioselective bioreduction of acetophenones **1a-5a** to the corresponding alcohols **1b-5b**. The favorable combination of polar factors that occurs in transition state in case of electron-withdrawing substituents is positively reflected in the values of the initial reaction rates.

The exception is *p*-chloroacetophenone **2a**. The initial reduction rate of **2a** is significantly lower than the expected value (Fig. 2), estimated by interpolating the resulting dependence. It apparently can be explained by a specific effect of this substrate on the catalyst.

In order to study the possible inhibitory effect of *p*-chloroacetophenone **2a** on the biocatalyst, we carried out transformation of acetophenone **1a** by *D. carota* cells under the same reaction conditions for 24 hours in the presence of a small additive of *p*-chloroacetophenone (2.5%). Bioreduction resulted in formation of corresponding *S*-1-phenylethanol **1b** with 7% yield. Reduction of ketone **1a** under similar conditions (24 hours) in the absence of 2.5% *p*-chloroacetophenone **2a** results in production of alcohol **1b** with a yield of 20%. In the case of biotransformation in the presence of *p*-chloroacetophenone (2.5%) for 96 hours the yield of *S*-1-phenylethanol **1b** is 22%. The inhibitory effect increases with the increase in the concentration of *p*-chloroacetophenone **2a** (7.5%) during bioreduction of acetophenone **1a**. In this case, the yield of *S*-1-phenylethanol **1b** decreased to 5% (24h), and - 16% (96h). These results most likely reflect the assumption of the inhibitory effect of ketone **2a** on the biocatalyst.

We compared the ρ constants of bioreduction catalyzed by *D. carota* (1) and *P. crispum* (2) and found that ρ_2 =0.85 is lower than ρ_1=0.94. Thus, the sensitivity of the reduction to the nature of the substituents is more significant in the case of *D. carota* biocatalyst.

The nature of the substituent also affects the product yields and the enantioselectivity of the process (Table 2).

Table 2. Yield and enantiomeric excess (ee) of alcohols **1b-5b** in bioreduction of ketones **1a-5a** catalyzed by *D. carota* and *P. crispum* in water

	Daucus carota		Petroselinum crispum		
Alcohol (X)	Yield, %	Enantiomeric excess (ee), %	Alcohol (X)	Yield, %	Enantiomeric excess (ee), %
1b (H)	50	98	1b (H)	76	82
2b (Cl)	27	68	2b (Cl)	59	90
3b (Br)	70	98	3b (Br)	69	94
4b (NO_2)	83	97	4b (NO_2)	74	95
5b (OCH_3)	5	71	5b (OCH_3)	14	72

T=23-27 °C, t=96 hours, substrate concentration 20 mmol/l, biocatalyst concentration 100 g/l

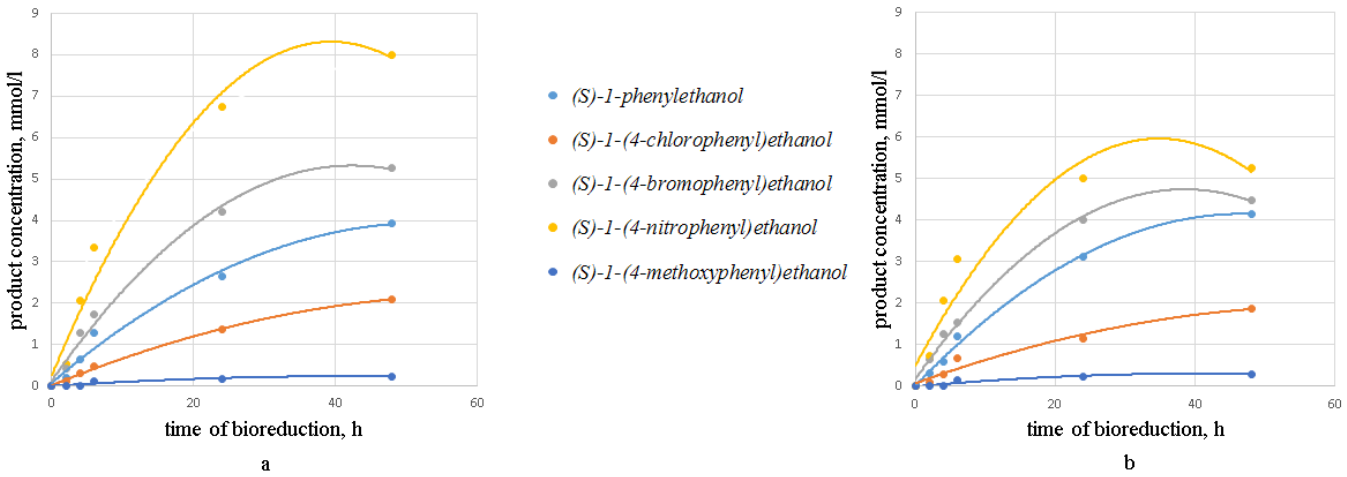
Organic compounds, including alkylaromatic ketones, have limited solubility in aqueous media. Thus, it is important to study the possibility of enantioselective bioreduction catalyzed by *D. carota* and *P. crispum* plant cells in organic solvents.

Moreover, it is not obvious that the influence of the nature of substituents on the bioreduction of acetophenones **1a-5a** in organic solvents will be similar to reductions conducted in water.

Therefore, we studied bioreduction of substituted acetophenones **1a-5a** catalyzed by *D. carota* or *P. crispum* cells under the same conditions in isooctane (which is less toxic among other organic solvents) (Scheme 1).

We found that the presence of a substituent in the aromatic ring has the same significant effect on the reaction rate and the yields and ees of products as in the case of bioreductions carried out in water solutions. The electron-withdrawing substituents –Br and $–NO_2$ enhance the initial rates of reaction, while the electron-donating substituent $–OCH_3$ slows it down (Figure 3, Table 3).

Figure 3 - Kinetics of *S*-1-phenylethanol **1b** and its substituted derivatives **2b-5b** formation in the reaction of biocatalytic reduction of acetophenone derivatives **1a-5a** in the presence of a). *D. carota*; b). *P. crispum* (T = 23-27 ° C, solvent - isooctane, substrate concentration 20 mmol/l, biocatalyst concentration 100 g/l).



The reduction rates of ketones **1a-5a** in the presence of *D. carota* and *P. crispum* in isooctane are noticeably lower in comparison with a similar reductions conducted in water. This is probably due to a change of lipophilic-hydrophilic balance in the globular structure of the enzyme responsible for the reduction process, which leads to a decrease in its catalytic activity. In this case, the enantioselectivity also depends on the nature of the substituent.

Graphic dependence (Figure 4) of $\lg(V_X/V_H)$ parameter on σ^+ indicates satisfactory correlation of these values (Table 4). Ketone **2a** is the exception as in the case of bioreduction carried out in water.

Table 3. Yield and enantiomeric excess (ee) of alcohols **1b-5b** in bioreduction of ketones **1a-5a** catalyzed by *D. carota* and *P. crispum* in isooctane

	Daucus carota		*Petroselinum crispum*		
Alcohol (X)	Yield, %	Enantiomeric excess (*ee*), %	Alcohol (X)	Yield, %	Enantiomeric excess (*ee*), %
1b (H)	24	94	1b (H)	22	90
2b (Cl)	17	94	2b (Cl)	14	91
3b (Br)	28	94	3b (Br)	29	93
4b (NO_2)	33	94	4b (NO_2)	26	94
5b (OCH_3)	2,5	74	5b (OCH_3)	2	73

T=23-27 °C, t=96 hours, substrate concentration 20 mmol/l, biocatalyst concentration 100 g/l

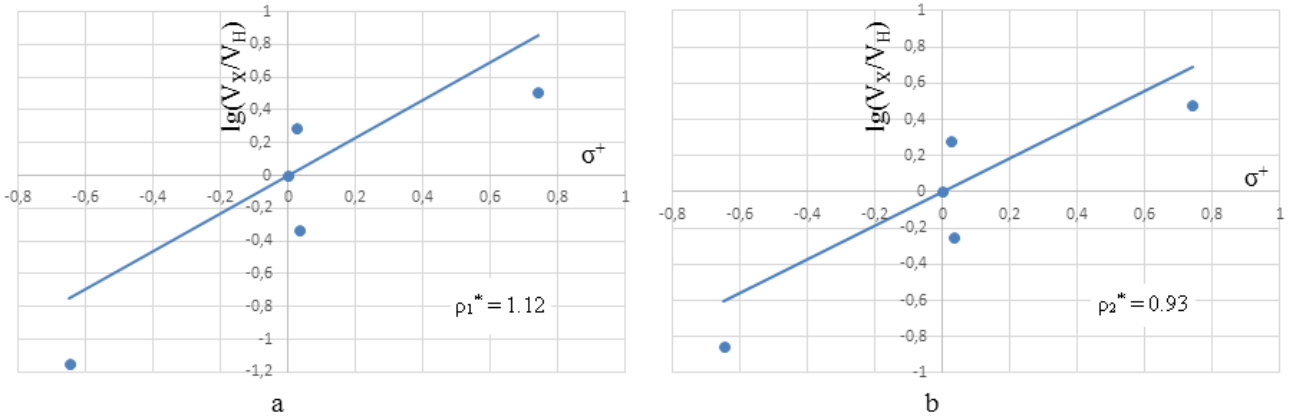


Figure 4 – Correlations between experimentally obtained lg (V_X/V_H) and σ+ values in the bioreduction of substituted acetophenones (1a-5a) by a). D. carota or b). P. crispum at 23-27 ° C in isooctane

Table 4. Kinetic parameters in the bioreduction of acetophenone and its substituted derivatives **1a-5a** catalyzed by *D. carota* or *P. crispum* cells

Daucus carota					*Petroselinum crispum*				
Alcohol (X)	V_X	(V_X/V_H)	$lg(V_X/V_H)$	σ^+	Alcohol (X)	V_X	(V_X/V_H)	$lg(V_X/V_H)$	σ^+
1b (H)	$4{,}44\cdot10^{-5}$	1	0	0	1b (H)	$4{,}79\cdot10^{-5}$	1	0	0
2b (Cl)	$2{,}08\cdot10^{-5}$	0,47	-0,33	0,035	2b (Cl)	$2{,}70\cdot10^{-5}$	0,56	-0,25	0,035
3b (Br)	$8{,}68\cdot10^{-5}$	1,95	0,29	0,025	3b (Br)	$9{,}31\cdot10^{-5}$	1,94	0,28	0,025
4b (NO_2)	$14{,}3\cdot10^{-5}$	3,22	0,51	0,74	4b (NO_2)	$14{,}9\cdot10^{-5}$	3,11	0,48	0,74
5b (OCH_3)	$0{,}35\cdot10^{-5}$	0,07	-1,15	-0,648	5b (OCH_3)	$0{,}65\cdot10^{-5}$	0,14	-0,85	-0,648

substrate concentration 20 mmol/l, biocatalyst concentration 100 g/l, T=23-27 °C, solvent – isooctane

In general, a similar dependence of the influence of substituents on the reaction rate is observed for both isooctane and aqueous medium.

However, a comparison of $\rho_1 = 0.94$ with $\rho_1^* = 1.12$ and also $\rho_2 = 0.85$ with $\rho_2^* = 0.93$ for *D. carota* and *P. crispum* in water and isooctane, respectively, shows that the sensitivity of bioreduction to the nature of the substituent tends to increase from water to isooctane.

3. Conclusions

In this study, we examined enantioselective bioreductions of a series of substituted arylketones into corresponding *S*-alcohols catalyzed by *Daucus carota* and *Petroselinum crispum* plant cells in water and isooctane.

We investigated how the nature of substituents in a series of acetophenones affects the rate and direction of bioreduction using *D. carota* and *P. crispum* plant cells. Our resuts suggest that the nature of the substituent in the aromatic ring and solvent significantly impact the reaction rate and the yields of products. Electron-withdrawing substituents –Br and $–NO_2$ enhance the initial rate of reaction and yields of products, while electron-donating substituent $–OCH_3$ decreases them. In addition, we observed that the reduction rates and yields of products in isooctane are noticeably lower in comparison with similar reductions conducted in water.

Correlations between the initial reaction rate and the substituent constant (σ^+) in the aromatic ring characterizing its nature were established. We compared the ρ constants of bioreduction catalyzed by *D. carota* and *P. crispum* and found that the sensitivity of the reduction to the nature of the substituents is more significant in the case of *D. carota* biocatalyst.

Comparison of ρ constants for *D. carota* and *P. crispum* in water and isooctane shows that the sensitivity of bioreduction to the nature of the substituent tends to increase from water to isooctane.

4. Experimental

4.1. General information

Acetophenone, *para*-nitro-, methoxy-, chloro- and bromoacetophenones were purchased from commercial sources.

Racemic alcohols were prepared from the corresponding ketones by reduction with $NaBH_4$.

Fresh carrots (*D. carota*) and parsley (*P. crispum*) were purchased from a local market.

Gas chromatographic analyses were performed on Khromatek-crystall-5000.2 with flame-ionization detector. Enantioselective column Astec CHIRALDEXB-PM (30m×0.25mm×0.12μm); column temperature 100°C (**1b**), 120°C (**2b**, **5b**), 130°C (**3b**),150°C (**4b**); oven temperature 250 °C, detector temperature 250 °C; helium as a carrier gas, flow rate 14.2 mL/min. For more efficient chromatographic separation of enantiomeric alcohols, its acetyl derivatives were obtained.

^{1}H and ^{13}C NMR spectra were measured on Bruker AM-300 and AMX-300 spectrometeres. As internal δ (0.00) for standards served TMS ^{1}H NMR and $CDCl_3$ δ (77.0) for ^{13}C NMR spectroscopy.

GC-MS analyses were performed using GCMS-QP2010S Shimadzu. A mass spectrometer with an ion trap detector in full scan mode under electron impact ionization (70 eV) in the 35-500 amu range was used. The chromatographic column used for the analysis was an HP-1MS capillary column (30 m×0.25 mm×0.25 μm). The vaporizer temperature was 280°C, the ionization chamber temperature was 200°C. Helium was used as carrier gas, at a flow rate of 1.1 mL/min. The injections were performed in mode at 100 -230 °C at a heating rate of 20°C/min.

The absolute configurations of the compounds were determined with «Optical Activity Limited» model AA-55.

4.2. Reduction of ketones by D. carota or P. crispum

Ketones **1a-5a** (20mmol) were added to a suspension of freshly cut *D. carota* or *P. crispum* (15 g) in distilled water or isooctane (70 ml) under constant stirring in a conical Erlenmayer flask. The reaction mixture was then placed in an orbital shaker (150 rpm) at room temperature. After achieving the necessary conversions, the suspension was filtered, and *D. carota* or *P.crispum* were washed three times with water. The filtrates were extracted with diethyl ether (3 × 125 mL). The organic phase was dried over $MgSO_4$, evaporated and monitored by GLC.

*4.2.1. S-1-phenylethanol (**1b**)*

^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=1.40 d (3H, CH_3), 4.74 q (1H, CH), 7.20-7.28 m (5H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ=25.18 (1C, CH_3), 70.05 (1C, CH), 125.34 (2C, CH_{Ar}), 127.18 (1C, CH_{Ar}), 128.28 (2C, CH_{Ar}), 145.92 (1C, CH_{Ar}). GC/MS (m/z (%)): 122 ([M]$^+$, 30), 107 (85), 79 (100), 78 (23), 77 (57), 51 (23), 50 (11), 44 (17),43 (39), 39 (10).

*4.2.2. S-1-(4-chlorophenyl)ethanol (2**b**)*

^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=1.29 d (3H, CH_3), 5.35 q (1H, CH-O), 7.34 m (4H, $4CH_{Ar}$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ=26.14 (CH_3), 67.86 (CH-OH), 127.59 ($2CH_{Ar}$), 128.33 ($2CH_{Ar}$), 131.35 (C_{Ar}-Cl), 146.63 (C_{Ar}). GC/MS (m/z (%)): 155 ([M]$^+$, 20), 143 (25), 141 (93), 139 (38), 113 (40), 77 (100), 75 (22), 51 (23), 44 (58), 43 (59).

*4.2.3. S-1-(4-bromophenyl)ethanol (**3b**)*

^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=1.29 d (3H, CH_3), 4.69 q (1H, C<u>H</u>-OH), 7.28 d (2H, $2CH_{Ar}$), 7.46 d (2H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ=26.04 (CH_3), 67.96 (CH-OH), 119.85 ($2CH_{Ar}$), 127.98 ($2CH_{Ar}$), 131.25 (C_{Ar}-Br), 146.98 (C_{Ar}). GC/MS (m/z (%)): 202 ([M]$^+$, 12), 186 (39), 184 (43), 156 (21), 121 (26), 78 (45), 77 (100), 51 (26), 50 (19), 43 (69).

*4.2.4. S-1-(4-nitrophenyl)ethanol (**4b**)*

^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=1.45 d (3H, CH_3), 4.85 q (1H, C<u>H</u>-OH), 7.6 d (2H, $2CH_{Ar}$), 8.16 d (2H, $2CH_{Ar}$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ=25.96 (1C, CH_3), 67.88 (1C, CH-OH), 123.67 ($2CH_{Ar}$), 126.81 ($2CH_{Ar}$), 146.6 (1C, C_{Ar}), 155.62 (C_{Ar}-NO_2). GC/MS (m/z (%)): 244 ([M$^+$], 7), 150 (100), 134 (5), 120 (10), 104 (29), 92 (15), 89(9), 76 (18), 50 (16), 42 (8).

*4.2.5. S-1-(4-methoxyphenyl)ethanol (**5b**)*

^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ=1.28 d (3H, CH_3), 3.7 s (3H, CH_3-O), 4.65 q (1H, C<u>H</u>-OH), 6.85 d (2H, $2CH_{Ar}$), 7.23 d (2H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ=26.27 (CH_3), 55.37 (CH_3-O), 68.11 (CH-OH), 113.73 ($2CH_{Ar}$), 126.86 ($2CH_{Ar}$), 139.69 (C_{Ar}), 158.36 (C_{Ar}-O). GC/MS (m/z (%)): 152 ([M]$^+$, 25), 137 (100), 134 (18), 109 (53), 94 (30), 91 (15), 77 (30), 65 (14), 44 (16), 43 (29).

Acknowledgement

This study was funded by the Ministry of Education and Science of Russian Federation (grant no. 4.6451.2017/8.9).

References

1. Matsuda, T.; Yamanaka, R.; Nakamura K. *Tetrahedron: Asymmetry* **2009**, *20*, 513–557.
2. Scarpi, D.; Occhiato, E.; Guarna, A. *Tetrahedron: Asymmetry* **2005**, *16*, 1479–1483.
3. Omori, A. T.; Lobo, F.G.; Goncalves do Amaral, A. C.; de Oliveira, C. de Souza. J. Mol. Catal. B: Enzym. **2016**, *127*, 93–97.
4. Ishihara, K.; Hamada, H.; Hirata, T.; Nakajima, N. *J. Mol. Catal. B: Enzym.* **2003**, *23*, 145–170.
5. Gašo-Sokač, D; Nujić, M.; Bušić, V.; Habuda-Stanić, M. *Croat. J. Food Sci. Technol.* **2014**, *6 (1)*, 51-60.
6. Bruni, R.; Fantin, G.; Maietti, S.; Medici, A.; Pedrini, P.; Sacchetti, G. *Tetrahedron: Asymmetry* **2006**, *17*, 2287–2291.
7. Maczka, W. K.; Mironowicz, A. *Tetrahedron: Asymmetry* **2004**, *15*, 1965–1967.
8. Chang Xu; Yang Zhonghua; Zeng Rong; Yang Gai; Yan Jiabao *Chinese Journal of Chemical Engineering* **2010**, *18*, 1029-1033.
9. Majewska, E.; Mironowicz, A. *Tetrahedron Letters* **2013**, *54(47)*, 6331–6332.
10. Baskar, B.; Ganesh, S.; Lokeswari, T.S.; Chadha, A. *J. Mol. Catal. B: Enzym.* **2004**, *27*, 13–17.
11. Xiang Liu; Zheng Guang Pan; Jian He Xu; He Xing Li. *Chinese Chemical Letters* **2010**, *21*, 305-308.
12. Chanysheva, A. R.; Yunusova, G. V.; Vorobyova, T. E.; Zorin, V. V. *Russian Journal of General Chemistry* **2016**, *86*, 3021–3024.
13. Chanysheva, A.R.; Vorobyova, E.N.; Zorin, V.V. *Russian Journal of General Chemistry* **2017**, *87*, 3259–3262 .

14. Lacheretz, R.; Pardo, D. G.; Cossy, J. *Organic Letters* **2009**, *11*, 1245-1248.
15. Villa, R.; Molinari, F. *J. Nat. Prod.* **2008**, *71*, 693–696.
16. Yang, Zhong-Hua; Zeng, Rong; Yang, Gai; Wang, Yu; Li; Li-Zhen; Lv, Zao-Sheng; Yao, Man; Lai, Bin. *J. Ind. Microbiol. Biotechnol.* **2008**, *35*, 1047–1051.
17. Shimoda, K.; Kubota, N.; Hamada, Hatsuyuki.; Hamada, Hiroki. *Tetrahedron Letters.* **2006**, *47*, 1541–1544.
18. Chanysheva, A.R.; Sheiko, E.A.; Zorin, V.V. *Russian Journal of General Chemistry* **2018**, *88*, 2934–2936.
19. Blanchard, N.; P. V. de Weghe *Org. Biomol. Chem.* **2006**, *4*, 2348- 2353.
20. Uwai, K.; Konno, N.;Yasuta, Y.; Takeshita M. *Bioorg. Med. Chem*. **2008**, *16*, 1084-1089.
21. Zhu, M.; Rios, B.R.; Rozzell, J. D.; Hua, L. *Tetrahedron: Asymmetry* **2005**, *16*, 1541–1546.
22. Gordon, A. J.; Ford, R. A. *The Chemist's Companion: A Handbook of Practical Data, Techniques, and References* John Wiley & Sons, Inc., **1973**, p. 560.

Highlights

- Enantioselective biocatalysis
- Enantioselective bioreduction of substituted acetophenones catalyzed by plant cells
- The effect of substituent on the relative reactivity of substituted acetophenones
- Correlation between the initial reaction rate and the substituent constant (σ^+) in bioreduction
- Sensitivity of the reduction to the substituent type for *D. carota* and *P. crispum* biocatalyst
- Sensitivity of the bioreduction to the substituent type in water and isooctane