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Enantioselective reduction of α,β-unsaturated ketones by *Geotrichum candidum*, *Mortierella isabellina* and *Rhodotorula rubra* yeast

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Abstract—The reduction of 3-methyl-4-phenyl-3-buten-2-one and its phenyl-substituted derivatives by microorganisms was investigated. Growing cells of *Mortierella isabellina* DSM1414 and *Geotrichum candidum* LOCK 105 strains reduced α,β-unsaturated ketones to the corresponding secondary alcohols in high enantiomeric excess (94–99%), whereas the *Rhodotorula rubra* M18D3 strain converted the same compounds into optically active ketones as the major products with only trace amounts of the corresponding saturated and unsaturated alcohols.

1. Introduction

Optically active secondary alcohols and ketones are well known as important chiral building blocks in the pharmaceutical, agrochemical, and fragrance industries. Moreover, when prepared by biotechnological methods, they can find a wide application as natural aromas for the food industry.[1]

Quite a large number of papers and reviews[1–5] have been published to date on the microbiological reduction of unsaturated carbonyl compounds. Most of them deal with baker's yeast (*Saccharomyces cerevisiae*)-mediated reactions, although recently some other microorganisms, such as *Beauveria sulfurescens* ATCC 7159,[2] *Pichia stipitis* CCT 2617,[5] and *Pyrococcus furiosus* DSM 3638,[6] have also been used in the reduction of some ketones and aldehydes. The available literature data indicate that the microbiological reduction of α-substituted enones may lead to several types of products in various proportions, the preferred structure of which depends on the substrate and microorganism and is therefore difficult to predict. Fuganti et al., using *S. cerevisiae* in the reduction of α,β-unsaturated ketones obtained the corresponding allylic alcohol as the main product with small amounts of the saturated alcohol,[7a] whereas Sakai et al. reported the formation of the corresponding saturated chiral ketone[7b] in the same reaction. Moreover, the reduction of the carbon–carbon double bond is in most cases accompanied by the formation of various amounts of saturated alcohol.[7c] For example, the reduction of 4-(furan-2-yl)-but-3-en-2-one with resting cells of *Geotrichum candidum* G38 gave a mixture of the saturated ketone and saturated alcohol with an excellent enantiomeric excess. From the results published to date it seems to be obvious that the course of the reduction depends on the relative activities of the two groups of enzymes produced by the microorganism. The data also suggest that the enoate reductase-catalyzed reduction of the carbon–carbon double bond is a faster process and probably the primary step of the reaction if both reductases are produced. Since reduction of a non-activated C=C bond is rather difficult,[2,5,8,9] reduction of the carbonyl group by the dehydrogenase occurs in all probability as the second stage of the process.

Herein we present the results of our investigation on the reduction of α,β-unsaturated alkyl-aryl ketones carried out with microorganisms of the *Fungi imperfecti* and *Zygomyces* groups.

2. Results and discussion

2.1. Microbial reduction of 4-aryl-3-methyl-3-buten-2-ones 1a–e by the *Rhodotorula rubra* M18D3

The bioreductions of 3-methyl-4-phenyl-3-buten-2-one **1a** and its phenyl substituted derivatives **1b–e** were performed with whole cells of the *R. rubra* M18D3 yeast in a 2%

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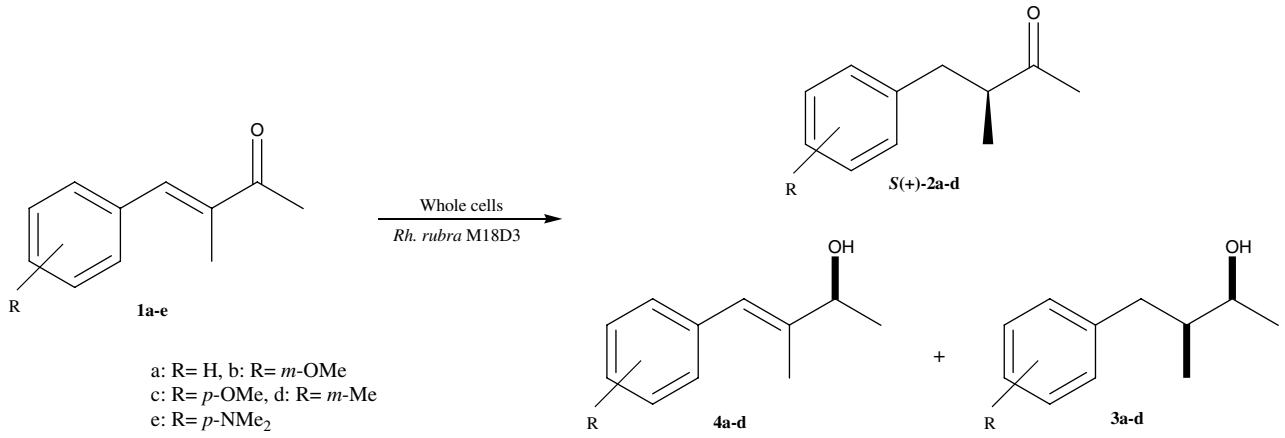


Scheme 1.

glucose solution at 30 °C. Incubation of **1a**–**e** with a suspended culture of the yeast gave the corresponding (*S*)-saturated chiral ketones **2a**–**d** as the major products in 32–49% isolated yields; the corresponding saturated **3a**–**d** and unsaturated alcohols **4a**–**d** were obtained in small amounts (Scheme 1). Attempted separation of the saturated and unsaturated alcohol mixtures was unsuccessful. It is interesting that the *R. rubra* yeast failed to reduce **1e**; even with prolonged incubation time (120 h) no trace of the reduction products was detected.

The results of the reactions starting with substrates **1a**–**e** are presented in Table 1. As it may be seen, the enantiomeric excesses (ee %) of the 4-aryl-3-methylbutan-2-ones (**2a**–**d**) prepared by reduction of the corresponding α,β-unsaturated ketones with *R. rubra* M18D3 were rather moderate; the 4-dimethylamino derivative did not react at all. The results also indicate that the reductive biotransformation of **1a**–**d** is a two-step process, the carbon–carbon double bonds being reduced faster then the carbonyl group. This observation is consistent with the results reported by Sakai et al.[7b] for reductions carried out with baker's yeast (*S. cerevisiae*). The data in Table 1 also indicate that the enantiomeric excesses of the corresponding saturated ketones were highest with the *meta*-substituted derivatives **2b** and **2d**. The absolute (*S*) configurations of the prepared **2a**–**d** were established by comparing the signs of specific rotations with those reported in the literature.[7b,10]

2.2. Reductions of 1a–e by *Mortierella isabellina* DSM 1414 and *G. candidum* LOCK 105

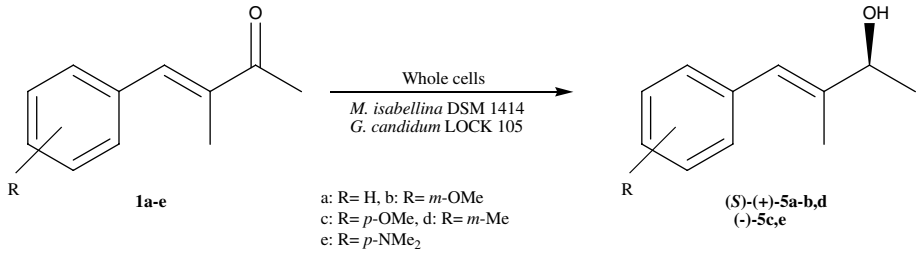
For the purpose of improving the enantiomeric purities and yields of the saturated ketones **2**, we investigated the reduction of α,β-unsaturated ketones of type **1** with other microorganisms. Growing cells of *M. isabellina* DSM 1414 (Mi) and *G. candidum* LOCK 105 (Gc) fungi were selected as the most promising ones. Under conditions similar to those described above for the reaction with *R. rubra* M18D3, the reduction by *M. isabellina* gave only the corresponding optically active unsaturated alcohols **5a**–**e** obtained in 12–65% isolated yields and rather high enantiomeric purities. The reduction of **1a** by *G. candidum* cells gave also satisfactory results, but conversions of **1b** and **1d** by this microorganism were low, in the range of 20%, and most of the substrates were left unchanged. The 4-methoxy- and 4-dimethylamino-derivatives **1c** and **1e** did not react at all (Scheme 2 and Table 2).

The (*S*) configuration of (+)-**5a**,**b** and **d** was established by comparing the signs of the specific rotations with those described[11] in the literature. However, the isolated unsaturated alcohols **5c** and **e** exhibit opposite rotation of polarized light (they are levorotatory compounds) and their configurations are not described in the literature. We attempted to determine the absolute configuration of **5c** by Mosher's method[12a,b] (comparison of ^{1}H NMR spectra of esters obtained in the reaction of **5c** with both

Table 1. Yields of optically active ketones **2a**–**d** prepared by bioreduction of **1a**–**e** by *Rhodotorula rubra* M18D3[a]

Entry	Product	Ar	Time (h)	Conv. (%)[b]	Yield[c] (%)	ee[d] (%)	$[\alpha]_D$	*c* ($CHCl_3$)
1	**2a**	C_6H_5–	22	64	44	46	+19.0[e]	2.11
2	**2b**	*m*-MeO–C_6H_4–	23	66	49	71	+36.6	2.33
3	**2c**	*p*-MeO–C_6H_4–	24	55	32	38	+14.3	2.09
4	**2d**	*m*-Me–C_6H_4–	24	61	41	65	+28.4	2.40
5	**2e**	*p*-Me_2N–C_6H_4–	120	—	—	—	—	

[a] Conditions: 0.08 mmol of ketone/3.0 g wet biomass, 3.0 mL of 2% glucose solution/1.5 g wet biomass at 30 °C.
[b] Conversion of unsaturated ketone was determined by GC analysis.
[c] Isolated yield of **2a**–**d** after column chromatography.
[d] Enantiomeric excesses were determined by HPLC using Chiralcel OD-H column in comparison with racemic compounds.
[e] Lit.[7b] $[\alpha]_D = +33.6$ (*c* 2.74, EtOH).



Scheme 2.

Table 2. Yields of unsaturated ketones **5a–e** obtained by bioreduction of **1a–e** by *Mortierella isabellina* (Mi)[a] and *Geotrichum candidum* (Gc)[a]

Entry	Substrate	Microorganism	Time (h)	Conv. (%)[b]	Yield[c] (%)	ee[d] (%)	$[\alpha]_D$	*c* ($CHCl_3$)
1	**1a**	Mi	6	81	65	97	+6.5[e]	2.81
2	**1b**	Mi	24	59	35	94	+7.4	2.66
3	**1c**	Mi	24	51	23	77	−16.7	1.36
4	**1d**	Mi	24	56	31	94	+7.2	2.18
5	**1e**	Mi	48	65	12	43	−0.4	1.50
6	**1a**	Gc	2	47	24	98	+6.8[e]	2.74
7	**1b**	Gc	3	18	16	99	+4.3	1.27
8	**1c**	Gc	48	—	—	—	—	—
9	**1d**	Gc	3	25	19	98	+7.7	2.50
10	**1e**	Gc	48	—	—	—	—	—

[a] Conditions: 0.08 mmol of ketone/4.0 g wet biomass, 3.0 mL of 2% glucose solution/1.5 g wet biomass at 30 °C.
[b] Conversion was determined by GC analysis.
[c] Isolated yield after column chromatography.
[d] Enantiomeric excesses were determined by chiral HPLC analysis using Chiralcel OD-H column in comparison with racemic compounds.
[e] Lit.[11] $[\alpha]_D = +3.2$ (*c* 0.5, $CHCl_3$).

enantiomers of methoxyphenylacetic acid (MPA)) but these attempts were unsuccessful. The spectra of the resulting diastereomeric esters taken in a $CDCl_3$ solution showed opposite signs of $\Delta\delta$ of two neighboring groups of protons on the same side of the asymmetry center and therefore cannot be used for configurational assignment. Assuming that this could be caused by the presence of the unsaturated carbon–carbon double bond in close proximity to the stereogenic center, hydrogenation of the optically active unsaturated derivative **5c** was used to obtain the appropriate saturated alcohol, which was next esterified with MPA enantiomers. Unfortunately, investigations of ^1H NMR spectra of the obtained diastereomeric esters also failed to give unequivocal results.

Contrary to some earlier reports[13a] describing the reduction of α,β-unsaturated carbonyl compounds with *S. cerevisiae* and to the results obtained by us with *R. rubra* M18D3, the selective reduction of carbonyl group by Mi and Gc suggests that enoate reductases responsible for double bond reduction are either not produced by these microorganisms or their activity is very low. Moreover, the results indicate the possibility of a selective carbonyl group reduction in the presence of an activated double bond by the suitably selected microorganism. Attempts at the reduction of 4-(4-methoxyphenyl)- and 4-(4-dimethylaminophenyl)-3-methyl-3-buten-2-ones **1c** and **1e**, respectively, with *G. candidum* LOCK 105 were unsuccessful; no trace of the reaction products could be detected. However, the reductions of **1a**,**b** and **d** by both investigated strains were unidirectional and gave optically active unsaturated secondary alcohols in excellent enantiomeric excesses. The results suggest that the presence and position of substituents in the phenyl ring of the enones **1a–e** have no crucial influence on the stereoselectivity of their reduction by *M. isabellina* DSM 1414 and *G. candidum* LOCK 105, though in the absence of any substituent the conversions and yields were highest. It is also interesting to note that the reaction time for the reduction by *G. candidum* LOCK 105 was considerably shorter than that required by *M. isabellina* DSM 1414.

3. Conclusions

It has been shown that the *M. isabellina* DSM 1414 and *G. candidum* LOCK 105 strains are active and very selective biocatalysts in the reduction of 3-methyl-4-phenyl-3-buten-2-one and its various phenyl substituted analogs; the corresponding unsaturated alcohols of high enantiomeric excess were the only products. On the other hand, *R. rubra* M18D3 preferably reduced the carbon–carbon double bond with lower selectivity. It is also evident that a careful selection of the microorganism would make it possible to direct the reaction toward one or the other reducible center of 4-aryl-3-methyl-3-buten-2-ones.

4. Experimental

4.1. General

^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded with Varian Mercury 400 MHz spectrometer in

$CDCl_3$ solution, and chemical shifts (δ) are reported in parts per million. Optical rotations were measured in $CHCl_3$ using a PolAAr 32 and a Jasco P-1020 polarimeter. Enantiomeric excesses (ee %) were determined by HPLC analysis on a Thermo-Separation Products P-100 instrument with Chiralcel OD-H column in *n*-hexane/*iso*-propanol as the eluent in comparison with racemates. The biotransformation reactions were monitored by GC with Hewlett–Packard Model 5890 II MSD 5972A chromatograph with Helium as the carrier gas. Preparative chromatographic separations were carried on Merck silica gel 60 (230–400 mesh).

4.2. Synthesis of enones 1a–e

The starting 4-aryl-3-methyl-3-buten-2-ones were prepared as previously described.[13a,b]

4.2.1. 3-Methyl-4-phenyl-3-buten-2-one 1a. Yield 75%; yellow oil; bp 133–135 °C/13 mmHg; lit.[14] yield 85%; bp 127–130 °C/12 mmHg.

4.2.2. 4-(3-Methoxyphenyl)-3-methyl-3-buten-2-one 1b. Yield 33%; yellow oil; lit.[13a] yield 38%.

4.2.3. 4-(4-Methoxyphenyl)-3-methyl-3-buten-2-one 1c. Yield 46%; yellow oil; lit.[13a] yield 32%.

4.2.4. 4-(3-Methylphenyl)-3-methyl-3-buten-2-one 1d. Yield 43%; yellow oil; bp 80–81 °C/0.13 mmHg; lit.[15] bp 126–127 °C/2 mmHg; ^{1}H NMR ($CDCl_3$) δ ppm: 2.05 (d; 3H; CH_3–CH=; $J = 1.2$ Hz); 2.39 (s; 3H; CH_3–Ar); 2.46 (s; 3H; CH_3–CO); 7.15–7.31 (m; 4H (aromatic H)); 7.50 (s; 1H; CH=); ^{13}C NMR ($CDCl_3$) δ ppm: 12.9; 21.4; 25.8; 126.7; 128.3; 129.3; 130.4; 135.8; 137.5; 138.0; 139.9; 200.3.

4.2.5. 4-(4-Dimethylaminophenyl)-3-methyl-3-buten-2-one 1e. Yield 89%; yellow solid; mp 121–122 °C (from petroleum ether); lit.[13b] (Yield 100%); mp 122–123 °C (from petroleum ether); ^{1}H NMR ($CDCl_3$) δ ppm: 2.10 (s; 3H; CH_3–CH=); 2.44 (s; 3H; CH_3–CO); 3.03 (s; 6H; $2 \times CH_3$–N); 6.71–7.43 (m; 4H (aromatic H)); 7.46 (s; 1H; CH=); ^{13}C NMR ($CDCl_3$) δ ppm: 12.9; 25.7; 40.1; 111.6; 123.5; 131.8; 133.3; 140.7; 150.4; 200.1.

The ^{1}H NMR spectra of compounds **1a**–**c** were consistent with those reported in the literature.

4.3. Microorganisms

The DSM 1414 strain of *M. isabellina* was purchased from German Collection of Microorganisms and Cell Cultures (DSMZ). The LOCK 105 strain of *G. candidum* was generously gifted by the Centre of Industrial Microorganisms Collection, Institute of Fermentation Technology and Microbiology in Lodz, Poland. The M18D3 strain of *R. rubra* (Demme) was generously donated by the Institute of Environmental Engineering Systems, Warsaw University of Technology.

4.4. Cultivation of microorganisms

A suitable liquid medium was sterilized at 120 °C for 15 min. Every microorganism was grown on a plate with agar medium for 3 days at 27 °C until well sporulated. Spores from the surface culture were used to inoculate flasks containing sterile liquid medium, next incubated at 30 °C for 3 days on a rotary shaker at 140 rpm.

The fungal mycelium was collected by filtration in the case of the fungi *G. candidum* LOCK 105 and *M. isabellina* DSM 1414 or by centrifugation in the case of the yeast *R. rubra* M18D3.

4.4.1. Growth medium for *M. isabellina* DSM 1414. Malt extract (30 g), soya peptone (3 g), were dissolved in 1.0 L of distilled water, adjust pH to 5.6.

4.4.2. Growth medium for *G. candidum* LOCK 105. Yeast extract (10 g), peptone from soybeans (5 g), glycerol (30 g), K_2HPO_4 (3.12 g), KH_2PO_4 (11.18 g) were dissolved in 1.0 L of distilled water.

4.4.3. Growth medium (YM) for *R. rubra* (Demme) M18D3. Yeast extract (3 g), malt extract (3 g), peptone from soybeans (5 g), and glucose (10 g) were dissolved in 1.0 L of distilled water.

4.5. General bioreduction procedure for of α,β-unsaturated ketones 1a–e by *R. rubra* M18D3

Wet mycelium (46 g) was suspended in a flask containing 92 mL of 2% glucose solution and 1.23 mmol of substrate in a minimum amount of ethanol. The mixture was shaken at 30 °C and 140 rpm and the conversion was monitored by gas chromatography. After an appropriate time, a few grams of Celite® and ethyl acetate (50 mL) were added to the reaction mixture and stirring was continued for 15 min. The mixture was then filtered and the supernatant was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and the solvent was evaporated under reduced pressure. The crude mixture was separated by column chromatography on silica gel with hexane/ethyl acetate (5:1 v/v) as an eluent yielding (*S*)-4-aryl-3-methyl-2-butanone **2a**–**d** as the main product and small amounts of the saturated and unsaturated alcohol. The enantiomeric excess was determined by HPLC analysis using Chiracel OD-H column. However, in the case of the chiral saturated ketones (**2a**,**b**,**d**) it was necessary to reduce them to the corresponding alcohols. ^{1}H, ^{13}C NMR spectra of the isolated products are presented below.

4.5.1. (*S*)-(+)-3-Methyl-4-phenyl-2-butanone 2a. ^{1}H NMR ($CDCl_3$) δ ppm: 1.09 (d; 3H; CH_3–CH; $J = 6.8$ Hz); 2.09 (s; 3H; CH_3–CO); 2.56 (dd; 1H; Ar–CHH–CH; $J = 13.6$ Hz; $J = 8.0$ Hz); 2.83 (m; 1H; CH_3–CH(CO)CH_2); 3.00 (dd; 1H; Ar–CHH–CH; $J = 13.6$ Hz; $J = 6.8$ Hz); 7.14–7.30 (m; 5H (aromatic H)).

4.5.2. (*S*)-(+)-4-(3-Methoxyphenyl)-3-methyl-2-butanone 2b. ^{1}H NMR ($CDCl_3$) δ ppm: 1.09 (d; 3H; CH_3–CH; $J = 6.8$ Hz); 2.10 (s; 3H; CH_3–CO); 2.53 (dd; 1H;

Ar–CH_2–CH; $J = 13.6$ Hz; $J = 8$ Hz); 2.82 (m; 1H; CH_3–CH(CO)CH_2); 2.98 (dd; 1H; Ar–CHH–CH; $J = 13.6$ Hz; $J = 6.8$ Hz); 3.79 (s; 3H; CH_3O–Ar); 6.69–7.22 (m; 4H (aromatic H)).

4.5.3. (*S*)-(+)-4-(4-Methoxyphenyl)-3-methyl-2-butanone 2c. ^{1}H NMR ($CDCl_3$) δ ppm: 1.07 (d; 3H; CH_3–CH; $J = 6.8$ Hz); 2.08 (s; 3H; CH_3–CO); 2.51 (dd; 1H; Ar–CHH–CH; $J = 13.6$ Hz; $J = 7.6$ Hz); 2.79 (m; 1H; CH_3–CH(CO)CH_2); 2.93 (dd; 1H; Ar–CHH–CH; $J = 13.6$ Hz; $J = 6.8$ Hz); 3.78 (s; 3H; CH_3O–Ar); 6.81–7.08 (m; 4H (aromatic H)).

4.5.4. (*S*)-(+)-4-(3-Methylphenyl)-3-methyl-2-butanone 2d. ^{1}H NMR ($CDCl_3$) δ ppm: 1.09 (d; 3H; CH_3–CH; $J = 7.2$ Hz); 2.10 (s; 3H; CH_3–CO); 2.32 (s; 3H; CH_3–Ar); 2.52 (dd; 1H; Ar–CHH–CH; $J = 13.6$ Hz; $J = 7.6$ Hz); 2.82 (m; 1H; CH_3–CH(CO)CH_2); 2.96 (dd; 1H; Ar–CHH–CH; $J = 13.6$ Hz; $J = 6.4$ Hz); 6.94–7.19 (m; 4H (aromatic H)); ^{13}C NMR ($CDCl_3$) δ ppm: 16.18; 21.34; 28.81; 38.78; 48.77; 125.87; 126.93; 128.23; 129.67; 137.92; 139.54; 212.23.

4.6. General procedure for bioreduction of α,β-unsaturated ketones 1a–e by *G. candidum* LOCK 105 and *M. isabellina* DSM1414

Wet mycelium (63 g) was suspended in 126 mL of 2% glucose solution and 1.26 mmol of substrate **1a–e** in least amount of ethanol was added. The mixture was shaken at 30 °C and 140 rpm and the conversion was monitored by gas chromatography. After an appropriate reaction time, ethyl acetate (70 mL) was added to the reaction mixture and stirring was continued for 15 min. The biomass was filtered off and the supernatant was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The crude mixture was separated by column chromatography on silica gel with hexane/ethyl acetate as the eluent affording 4-aryl-3-methyl-3-buten-2-ol **5a–e**. The enantiomeric excesses were determined by HPLC analysis using a Chiracel OD-H column (in *n*-hexane/*i*-propanol, 95:5; 0.6 mL/min). ^{1}H, ^{13}C NMR spectra of the isolated products are reported below.

4.6.1. (*S*)-(+)-3-Methyl-4-phenyl-3-buten-2-ol 3a. ^{1}H NMR ($CDCl_3$) δ ppm: 1.37 (d; 3H; CH_3–CH; $J = 6.4$ Hz); 1.89 (s; 3H; CH_3–C=); 4.39 (q; 1H; CH–OH; $J = 6.4$ Hz); 6.52 (s; 5H; CH=); 7.20–7.36 (m; 5H (aromatic H)).

4.6.2. (*S*)-(+)-4-(3-Methoxyphenyl)-3-methyl-3-buten-2-ol 3b. ^{1}H NMR ($CDCl_3$) δ ppm: 1.36 (d; 3H; CH_3–CH; $J = 6.4$ Hz); 1.89 (s; 3H; CH_3–C=); 3.81 (s; 3H; CH_3–O–Ar); 4.37 (q; 1H; CH–OH; $J = 6.4$ Hz); 6.49 (s; 1H; CH=); 6.76–7.27 (m; 4H (aromatic H)); ^{13}C NMR ($CDCl_3$) δ ppm: 13.47; 21.71; 55.11; 73.52; 111.85; 114.49; 121.47; 124.16; 129.00; 139.00; 141.88; 159.27.

4.6.3. (−)-4-(4-Methoxyphenyl)-3-methyl-3-buten-2-ol 3c. ^{1}H NMR ($CDCl_3$) δ ppm: 1.35 (d; 3H; CH_3–CH; $J = 6.4$ Hz); 1.88 (s; 3H; CH_3–C=); 3.81 (s; 3H; CH_3–O–Ar); 4.36 (q; 1H; CH–OH; $J = 6.4$ Hz); 6.44 (s; 1H; CH=); 6.86–7.23 (m; 4H (aromatic H)); ^{13}C NMR ($CDCl_3$) δ ppm: 13.26; 21.70; 55.19; 73.78; 113.50; 123.92; 130.08; 130.14; 139.88; 158.02.

4.6.4. (*S*)-(+)-4-(3-Methylphenyl)-3-methyl-3-buten-2-ol 3d. ^{1}H NMR ($CDCl_3$) δ ppm: 1.37 (d; 3H; CH_3–CH; $J = 6.4$ Hz); 1.89 (s; 3H; CH_3–C=); 2.36 (s; 3H; CH_3–Ar); 4.38 (q; 1H; CH–OH; $J = 6.4$ Hz); 6.49 (s; 1H; CH=); 7.04–7.25 (m; 4H (aromatic H)); ^{13}C NMR ($CDCl_3$) δ ppm: 13.35; 21.41; 21.71; 73.66; 124.43; 125.95; 127.13; 127.96; 129.67; 137.52; 137.58; 141.37.

4.6.5. (−)-4-(4-Dimethylaminophenyl)-3-methyl-3-buten-2-ol 3e. ^{1}H NMR ($CDCl_3$) δ ppm: 1.35 (d; 3H; CH_3–CH; $J = 6.4$ Hz); 1.90 (s; 3H; CH_3–C=); 2.96 (s; 6H; $2 \times CH_3$–N); 4.37 (q; 1H; CH–OH; $J = 6.4$ Hz); 6.41 (s; 1H; CH=); 6.69–7.24 (m; 4H (aromatic H)); ^{13}C NMR ($CDCl_3$) δ ppm: 13.25; 21.65; 40.54; 40.62; 74.13; 112.16; 124.49; 129.87; 130.28; 138.09; 149.00.

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