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Asymmetric reduction of nitroalkenes with baker's yeast

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Abstract—Various α,β-disubstituted and trisubstituted nitroalkenes were chemoselectively reduced with baker's yeast to the corresponding nitroalkanes. Stereoselectivities of the reduction of α,β-disubstituted nitroalkenes were modest to low, and e.e.s up to 52% were obtained. Trisubstituted nitroalkenes could be reduced to the corresponding nitroalkanes with excellent enantioselectivities, moderate diastereoselectivities and in good yield.

1. Introduction

Because the nitro group can be easily transformed into other functionalities including amine and carbonyl groups,[1] aliphatic nitro compounds are versatile synthetic building blocks. They are considered to be valuable intermediates for the preparation of various biologically active compounds[2] such as alkaloids,[3,4] steroids,[5,6] amino acid derivatives,[7–10] enzyme inhibitors,[11] and of interest to us, cobyric acid.[12] Considerable efforts have been made to develop synthetic methods for chiral nitro compounds. For example, the diastereoselective nitroaldol reaction with chiral aldehydes,[13] the stereoselective Michael addition reaction of nitroalkanes or nitroalkenes,[14–20] the [4+2] or [3+2] cycloaddition reaction of nitroalkenes,[21,22] and nitroolefination reactions using chiral nitroenamines[23,24] have been reported. However, the use of chiral auxiliaries is necessary in these reactions, and a catalytic method of chiral induction would be preferable.

The microbial reduction of carbonyl compounds is known to be a powerful tool for the synthesis of chiral alcohols.[25] In particular, baker's yeast (*Saccharomyces cerevisiae*) is one of the most widely investigated biocatalysts because it is inexpensive, versatile and readily available.[26,27] In contrast to the carbonyl reduction, only a few investigations on the asymmetric reduction of carbon–carbon double bonds have been reported. Most reports involve the reduction of olefins conjugated with a carbonyl group.[28–33] There have been few papers on the reduction of the carbon–carbon double bond of nitroalkenes.[34–39] Herein, we report the novel stereoselective reduction of trisubstituted nitroalkenes with baker's yeast. The baker's yeast reduction of β,β-disubstituted nitroalkenes affords (*R*)-nitroalkanes enantioselectively,[35,36] while α,β-disubstituted nitroalkenes are transformed into almost racemic saturated nitroalkanes in both aqueous[37] and organic solvent systems.[38,39]

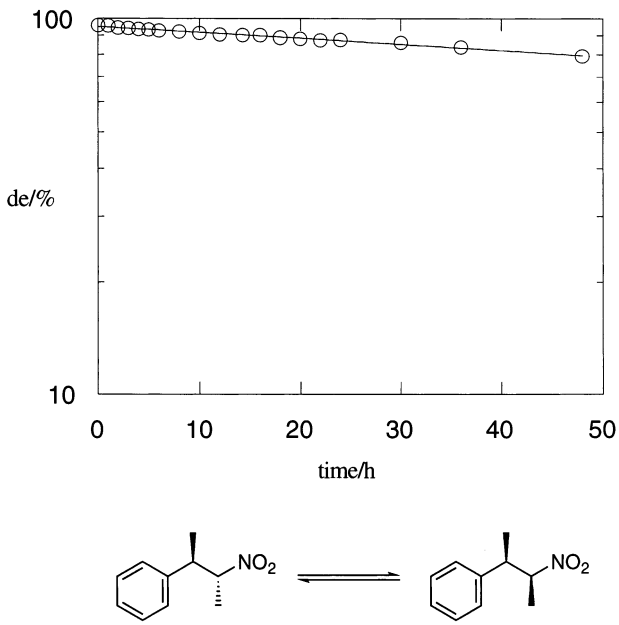

Figure 1. Epimerization of (±)-*erythro*-3-phenyl-2-nitrobutane under microbial reduction conditions.

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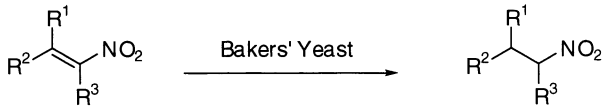


1a - t 2a - t

a R^1=H R^2=Ph R^3=Me
b R^1=Ph R^2=H R^3=Me
c R^1=H R^2=*o*-Cl-Ph R^3=Me
d R^1=H R^2=*m*-Cl-Ph R^3=Me
e R^1=H R^2=*p*-Cl-Ph R^3=Me
f R^1=H R^2=*o*-Me-Ph R^3=Me
g R^1=H R^2=*o*-Me-Ph R^3=Me
h R^1=H R^2=*p*-Me-Ph R^3=Me
i R^1=H R^2=*o*-MeO-Ph R^3=Me
j R^1=H R^2=*m*-MeO-Ph R^3=Me
k R^1=H R^2=*p*-MeO-Ph R^3=Me
l R^1=H R^2=*c*-C_6H_{12} R^3=Me
m R^1=H R^2=*i*-Pr R^3=Me
n R^1=H R^2=*t*-Bu R^3=Me
o R^1=H R^2=Ph R^3=Et
p R^1=Ph R^2=H R^3=Et
q R^1=H R^2=*o*-Me-Ph R^3=Et
r R^1=H R^2=*m*-Me-Ph R^3=Et
s R^1=H R^2=*p*-Me-Ph R^3=Et
t R^1=H R^2=Ph R^3=Pr

Scheme 1.

2. Results and discussion

In the earlier report, the non-stereoselective reduction of α,β-disubstituted nitroalkenes with microbes was attributed to racemization of the product because of acidity of the α-proton.[34] At first, the rate of racemization of the product under the same conditions as the microbial reduction was evaluated by measuring the epimerization rate at the α-carbon of *erythro*-3-phenyl-2-nitrobutane. The results are shown in Fig. 1. The half life of the epimerization reaction was estimated to be 188 hours under the reaction conditions, which suggests that the low stereoselectivities observed were not a result of non-enzymatic racemization of the product, because the reduction with yeast was completed within several hours.

Since there remained a possibility that the microbial reduction of nitroalkenes would proceed with high stereoselectivity, we studied the details of the stereoselectivity of baker's yeast reduction of various α,β-disubstituted nitroolefins (Scheme 1). Twenty aromatic and aliphatic nitroalkenes were synthesized and subjected to baker's yeast reduction. We chose the reduction of (*E*)-2-nitro-1-phenylpropene **1a** and (*E*)-2-nitro-1-phenyl-1-butene **1o** as typical models. The reduction of **1a** proceeded rapidly giving the corresponding nitroalkane (*S*)-**2a** chemoselectively, but the stereoselectivity was low with an e.e. of 12%. Elongation of the substituent at the α-position to an ethyl group increased the stereoselectivity, giving an e.e. of 39%.

In the whole cell reaction, it is frequently observed that unsatisfactory stereoselectivity is the result of the simultaneous action of several enzymes that have opposite stereochemistry toward the same substrate.[40,41] In such a case, modification of reaction conditions often changes the stereoselectivity of the reaction. Stereoselectivities under various reaction conditions such as pH of the reaction medium, addition of an additive, substrate concentration, and reaction temperature were investigated, and the results are summarized in Table 1. As shown in Table 1, lowering the pH of the reaction medium shifted the stereochemistry towards the opposite configuration but the stereoselectivity was low (entries 2 and 3). The presence of methyl vinyl

Table 1. Baker's yeast reduction of nitroolefins **1a** and **1o** under various reaction conditions

Entry	Substrate	Conditions[a]	Reaction time (h)	Yield[b] (%)	% E.e.	Config.[c]
1	**1a**	–	2	91	12	*S*
2	**1a**	pH 5.0	5	89	5	*S*
3	**1a**	pH 4.0	6	7	5	*R*
4	**1a**	[MVK][d] 15 mM	6	7	20	*S*
5	**1a**	[glucose] 0.84 M	7	72	17	*S*
6	**1a**	[S] 7.5 mM	1	89	19	*S*
7	**1o**	–	5	58	39	
8	**1o**	[S] 7.5 mM	3	65	41	
9	**1o**	[S] 3.8 mM	1	78	44	
10	**1o**	25°C	8	62	44	
11	**1o**	15°C	23	55	52	

[a] Water 30 mL, dry baker's yeast 5 g, [S] 15 mM, ethanol 1 mL.
[b] Isolated yield.
[c] Ref. 30.
[d] Methyl vinyl ketone.

Table 2. Baker's yeast reduction of disubstituted nitroolefins **1a–t**

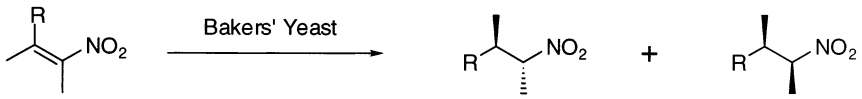
Substrate	Reaction time (h)	Yield (%)	% E.e.
1a	2	81	12
1b	1.5	79	13
1c	1.5	52	4
1d	3	47	2
1e	3	51	7
1f	5	65	3
1g	3	61	2
1h	7	58	0
1i	5	72	3
1j	3	68	9
1k	5	66	45
1l	5	63	4
1m	2	48	10
1n	5	57	4
1o	5	58	39
1p	4	55	34
1q	32	16	9
1r	12	23	7
1s	9	52	40
1t	24	48	19

ketone[40,42] (MVK) or glucose as additives slightly increased the selectivity (entries 4 and 5). The stereoselectivity of microbial reduction is often dependent upon the substrate concentration,[43] and reducing the substrate concentration led again to a slight increase in selectivity (entries 6, 8 and 9). The stereoselectivity increased further on lowering the reaction temperature (entries 10 and 11). Although these results suggest that many enzymes participate in the reduction of nitroalkenes, no considerable changes in stereoselectivity were observed in all the reactions investigated.

Since modifying the reaction conditions had no marked effect on the outcome of the reactions, we investigated the effect of structural variations of the substrate on the stereoselectivity of the microbial reduction. Various α,β-disubstituted nitroalkenes **1a–t** were prepared and subjected to reduction with baker's yeast, and the results are listed in Table 2. The stereoselectivity was not influenced by the structural difference between geometrical isomers, i.e. (*E*)- and (*Z*)-isomers. The reduction of (*E*)- and (*Z*)-1-phenyl-2-nitropropenes, **1a** and **b**, gave the nitroalkanes **2** in e.e.s of 12 and 13%, respectively. Similarly, (*E*)- and (*Z*)-1-phenyl-2-nitro-1-butenes, **1o** and **1p**, were transformed into nitroalkane **2** in e.e.s of 39 and 34%, respectively. Aliphatic nitroalkenes **1l–n** were also reduced to the corresponding nitroalkanes with low stereoselectivity. In the reduction of the series of aromatic nitroalkenes **1a–k**, the stereoselectivity of the reduction was influenced by the phenyl ring substituent. Only the reduction of the *para*-methoxyphenyl derivative **1k** afforded the nitroalkane **2k** in a moderate e.e. of 45% and the other substrates were reduced with little selectivity. This reaction has been reported previously and afforded the racemic product in both aqueous[37] and organic solvent systems.[38,39] Placing an ethyl group α to the nitro group led to increased stereoselectivity, while increasing the length of the substituent further to a propyl group retarded the reaction and led to a decrease in the stereoselectivity.

We next applied the microbial reduction to trisubstituted nitroalkenes (Scheme 2). The results are summarized in Table 3. Substitution at the β-position retards the reaction. Although diastereoselectivities in the reduction of the trisubstituted olefins **3** were moderate, enantioselectivities were satisfactory, 82–98% e.e., giving 3-aryl-2-nitrobutanes **4** and **5**. In contrast to the reduction of disubstituted nitroalkenes, the stereoselectivity was influenced by the structural difference between geometrical isomers. The reduction of (*Z*)-isomer **3a** was found to be more enantioselective than that of the (*E*)-isomer **3b** and a substituent on the phenyl ring also affected the reactivity and stereoselectivity. The *o*-chloro derivative **3c** could not be reduced with this microbe. The reduction of *p*-chloro derivative **3e** was the most diastereoselective, giving **4** in high e.e. of 94%. The diastereoisomers thus obtained were readily separable from each other by column chromatography on silica gel, allowing enantiomerically pure isomers of **4** and **5** to be obtained without difficulty.

The enantiomeric excesses of the products were determined as follows. The nitro compounds were reduced to amines with ammonium formate catalyzed by palladium on carbon,[44,45] followed by conversion to their amides by reaction with (+)-α-methoxy-α-(trifluoro-



3a - e **4a - e** **5a - e**

a R=Ph
b R=Ph (*E*-isomer)
c R=*o*-Cl-Ph
d R=*m*-Cl-Ph
e R=*p*-Cl-Ph

Scheme 2.

Table 3. Baker's yeast reduction of trisubstituted nitroolefins **3a–e**

Substrate	Yield[a] (%)	% D.e. of **4**	% E.e. of **4**	% E.e. of **5**
3a	72	20	98	97
3b	54	19	87	83
3c	Nr[b]	–	–	–
3d	52	36	82	81
3e	67	43	94	92

[a] Isolated yield.
[b] Not reduced.

methyl)-α-phenylacetyl chloride. Enantio- and diastereomeric excesses in the products were determined by GLC.

In order to determine the absolute configuration of **4a** by single-crystal X-ray analysis using the anomalous dispersion effect of a heavy atom, **4a** was reduced to an amine as above, which was recrystallized from ethanol as hydrochloride salt **6**. Full-matrix refinements using anomalous dispersion factors for all non-hydrogen atoms of **6** resulted in an *R* factor of 0.0844 for (2*R*,3*R*) and 0.0945 for the other enantiomorph. Consequently, the hydrochloride **6** has the (2*R*,3*R*)-configuration (Fig. 2). Use of the Flack parameter (–0.01(2)) also confirmed this assignment.[46] Thus, it is concluded that **4a** and **5a** resulting from yeast reduction have (2*R*,3*R*)- and (2*S*,3*R*)-configurations, respectively. Since the reduction of chloro derivatives **4d** and **4e** catalyzed by palladium on carbon also gave amine **6**, the absolute configurations of **4d**,**e** and **5d**,**e** were determined to be (2*R*,3*R*) and (2*S*,3*R*), respectively, by comparing their retention times of GLC with those obtained as above.

3. Conclusion

The baker's yeast reduction of nitroalkenes affords the corresponding nitroalkanes chemoselectively. The stereoselectivity of the reduction is strongly influenced by the substitution pattern of the substrate. The reduction of α,β-disubstituted nitroalkenes occurs with low stereoselectivity. The baker's yeast reduction of trisubstituted nitroalkenes proceeds with satisfactory enantioselectivity, while the diastereoselectivity is modest. The absolute configuration of the products was determined by single-crystal X-ray analysis using the anomalous dispersion effect.

4. Experimental

4.1. Instruments

^{1}H NMR spectra were recorded on a Varian VXR-200 spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as an internal reference. Gas chromatograms were recorded on a Shimadzu GC-14B (OV-1701, 25 m and OV-1, 25 m) gas chromatograph. IR spectra were recorded on a Japan Spectroscopic FT/IR-5300 spectrometer. X-Ray crystallographic studies were made on a Rigaku AFC7R diffractometer with filtered Cu-Kα radiation and a rotating anode generator.

4.2. Materials

Organic reagents and solvents were purchased from Nacalai Tesque Co., Wako Pure Chemical Ind., Ltd., Tokyo Kasei Kogyo Co., Ltd., Kanto Chemical Co., Inc. and Aldrich Chemical Co. Dry baker's yeast was purchased from Oriental Yeast Co. and stored in a refrigerator.

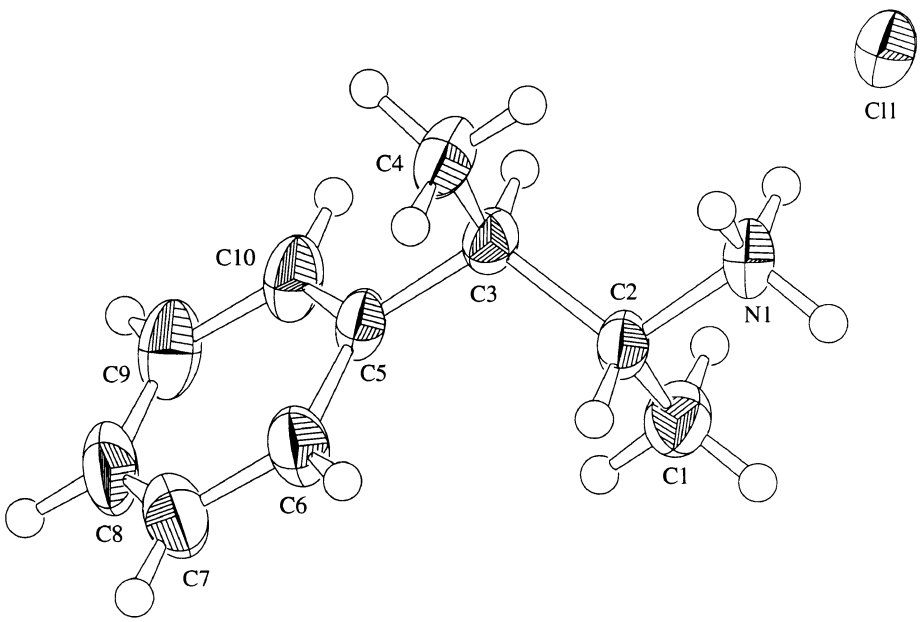


Figure 2. The ORTEP drawing of **6**. One molecule is omitted for clarity.

4.3. General procedure for the preparation of (*E*)-α,β-disubstituted nitroalkenes 1

The aldehyde (20 mmol) and ammonium acetate (20 mmol) were heated to reflux in nitroethane or 1-nitropropane (40 mL) overnight. The solvent was removed and the organic materials were extracted with ethyl acetate from water. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a crude product. The purification methods, the isolated yields, and their spectral data are shown below.

4.3.1. (*E*)-1-Phenyl-2-nitropropene 1a. Purified by recrystallization from ethanol; 67% yield; mp 63–64°C; ^{1}H NMR ($CDCl_3$, TMS): δ 2.46 (3H, s), 7.45 (5H, s) and 8.10 (1H, s); IR (KBr): 1518 and 1323 cm^{-1}; anal. calcd for $C_9H_9NO_2$: C, 66.25; H, 5.56; N, 8.58%. Found: C, 66.42; H, 5.52; N, 8.60%.

4.3.2. (*E*)-1-(2′-Chlorophenyl)-2-nitropropene 1c. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 92% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 2.35 (3H, s), 7.32–7.52 (4H, m) and 8.19 (1H, s); IR (neat): 1524 and 1327 cm^{-1}; anal. calcd for $C_9H_8NO_2Cl$: C, 54.70; H, 4.08; N, 7.09%. Found: C, 54.54; H, 4.11; N, 7.07%.

4.3.3. (*E*)-1-(3′-Chlorophenyl)-2-nitropropene 1d. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 75% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 2.44 (3H, s), 7.28–7.42 (4H, m) and 8.01 (1H, s); IR (neat): 1522 and 1327 cm^{-1}; anal. calcd for $C_9H_8NO_2Cl$: C, 54.70; H, 4.08; N, 7.09%. Found: C, 54.73; H, 4.07; N, 7.13%.

4.3.4. (*E*)-1-(4′-Chlorophenyl)-2-nitropropene 1e. Purified by recrystallization from ethanol; 95% yield; mp 84–85°C; ^{1}H NMR ($CDCl_3$, TMS): δ 2.44 (3H, s), 7.35–7.47 (4H, m) and 8.04 (1H, s); IR (KBr): 1512 and 1312 cm^{-1}; anal. calcd for $C_9H_8NO_2Cl$: C, 54.70; H, 4.08; N, 7.09%. Found: C, 54.76; H, 4.09; N, 7.11%.

4.3.5. (*E*)-1-(2′-Methylphenyl)-2-nitropropene 1f. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 86% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 2.32 (3H, s), 2.34 (3H, s), 7.19–7.36 (4H, m) and 8.17 (1H, s); IR (neat): 1520 and 1327 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90%. Found: C, 67.75; H, 6.29; N, 7.91%.

4.3.6. (*E*)-1-(3′-Methylphenyl)-2-nitropropene 1g. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 89% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 2.40 (3H, s), 2.45 (3H, s), 7.21–7.39 (4H, m) and 8.06 (1H, s); IR (neat): 1518 and 1323 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90%. Found: C, 67.65; H, 6.28; N, 7.89%.

4.3.7. (*E*)-1-(4′-Methylphenyl)-2-nitropropene 1h. Purified by recrystallization from ethanol; 79% yield; mp 53–54°C; ^{1}H NMR ($CDCl_3$, TMS): δ 2.40 (3H, s), 2.46 (3H, s), 7.26 (2H, d, J=8.3 Hz), 7.35 (2H, d, J=8.3 Hz) and 8.07 (1H, s); IR (KBr): 1522 and 1321 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90%. Found: C, 67.74; H, 6.24; N, 7.87%.

4.3.8. (*E*)-1-(2′-Methoxyphenyl)-2-nitropropene 1i. Purified by recrystallization from ethanol; 78% yield; mp 51–52°C; ^{1}H NMR ($CDCl_3$, TMS): δ 2.39 (3H, s), 3.89 (3H, s), 6.93–7.05 (2H, m), 7.28–7.46 (2H, m) and 8.29 (1H, s); IR (KBr): 1512, 1321 and 1248 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74; N, 7.25%. Found: C, 62.35; H, 5.79; N, 7.21%.

4.3.9. (*E*)-1-(3′-Methoxyphenyl)-2-nitropropene 1j. Purified by recrystallization from ethanol; 49% yield; mp 42–43°C; ^{1}H NMR ($CDCl_3$, TMS): δ 2.45 (3H, s), 3.84 (3H, s), 6.94–7.04 (3H, m), 7.33–7.42 (1H, m) and 8.05 (1H, s); IR (KBr): 1510, 1319 and 1254 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74; N, 7.25%. Found: C, 62.18; H, 5.73; N, 7.29%.

4.3.10. (*E*)-1-(4′-Methoxyphenyl)-2-nitropropene 1k. Purified by recrystallization from ethanol; 48% yield; mp 46–47°C; ^{1}H NMR ($CDCl_3$, TMS): δ 2.47 (3H, s), 3.87 (3H, s), 6.98 (2H, d, J=8.8 Hz), 7.43 (2H, d, J=8.8 Hz) and 8.08 (1H, s); IR (KBr): 1494, 1302 and 1258 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74; N, 7.25%. Found: C, 62.20; H, 5.84; N, 7.22%.

4.3.11. (*E*)-1-Cyclohexyl-2-nitropropene 1l. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 87% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.10–1.41 (5H, m), 1.54–1.83 (5H, m), 2.02–2.35 (4H, m) and 6.94 (1H, d, J=10.1); IR (neat): 2930, 2855, 1520 and 1331 cm^{-1}; anal. calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.93; N, 8.28%. Found: C, 63.73; H, 8.93; N, 8.34%.

4.3.12. (*E*)-4-Methyl-2-nitro-2-pentene 1m. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 58% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.11 (6H, d, J=6.6 Hz), 2.17 (3H, s), 2.47–2.72 (1H, m) and 6.95 (1H, d, J=10.3 Hz); IR (neat): 1524 and 1333 cm^{-1}; HRMS found: m/z 129.0794; calcd for $C_6H_{11}NO_2$ [M]$^+$: 129.0790.

4.3.13. (*E*)-4,4-Dimethyl-2-nitro-2-pentene 1n. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 32% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.23 (9H, s), 2.29 (3H, s) and 7.20 (1H, s); IR (neat): 1524 and 1327 cm^{-1}; anal. calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78%. Found: C, 58.35; H, 9.21; N, 9.95%.

4.3.14. (*E*)-1-Phenyl-2-nitro-1-butene 1o. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 63% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.28 (3H, t, J=7.4 Hz), 2.86 (2H, q, J=7.4 Hz), 7.44 (5H, s) and 8.02 (1H, s); IR (neat): 1520 and 1331 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90%. Found: C, 67.50; H, 6.23; N, 7.93%.

4.3.15. (*E*)-1-(2′-Methylphenyl)-2-nitro-1-butene 1q. Purified by recrystallization from ethanol; 76% yield;

mp 41–42°C; ^{1}H NMR ($CDCl_3$, TMS): δ 1.21 (3H, t, $J=7.3$ Hz), 2.33 (3H, s), 2.73 (2H, q, $J=7.3$ Hz), 7.19–7.37 (4H, m) and 8.09 (1H, s); IR (KBr): 1518 and 1327 cm^{-1}; anal. calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33%. Found: C, 69.03; H, 6.87; N, 7.34%.

4.3.16. (*E*)-1-(3′-Methylphenyl)-2-nitro-1-butene 1r. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 72% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.28 (3H, t, $J=7.4$ Hz), 2.40 (3H, s), 2.86 (2H, q, $J=7.4$ Hz), 7.21–7.39 (4H, m) and 7.99 (1H, s); IR (neat): 1518 and 1331 cm^{-1}; anal. calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33%. Found: C, 69.07; H, 6.94; N, 7.36%.

4.3.17. (*E*)-1-(4′-Methylphenyl)-2-nitro-1-butene 1s. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 89% yield; mp 32–33°C; ^{1}H NMR ($CDCl_3$, TMS): δ 1.27 (3H, t, $J=7.4$ Hz), 2.40 (3H, s), 2.87 (2H, q, $J=7.4$ Hz), 7.33 (2H, d, $J=8.3$ Hz), 7.33 (2H, d, $J=8.3$ Hz) and 8.00 (1H, s); IR (KBr): 1503 and 1316 cm^{-1}; anal. calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33%. Found: C, 69.19; H, 6.78; N, 7.29%.

4.4. General procedure for the preparation of (*Z*)-α,β-disubstituted nitroalkenes 1

Nitroethane or 1-nitropropane (20 mmol) was added to benzaldehyde (20 mmol) at 0°C and stirred for 5 min. Chromatographic alumina (Merck, activity I) was added to the mixture and stirred for 1 h at room temperature. After standing for 23 h, the alumina was washed with dichloromethane. The filtered extract was evaporated at reduced pressure to give crude 2-nitroalkanol, which was used without further purification.

Copper(I) chloride (0.20 g) and 1,3-dicyclohexylcarbodiimide (20 mmol) were added to a solution of 2-nitroalkanol in diethyl ether (10 mL) at room temperature under an atmosphere of argon for 48 h. The mixture was filtered and the filtrate was evaporated at reduced pressure to give a crude mixture of (*E*)- and (*Z*)-isomers of nitroalkene. The purification methods, the isolated yields and their spectral data are shown below.

4.4.1. (*Z*)-1-Phenyl-2-nitropropene 1b. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 15% yield; mp 45–46°C; ^{1}H NMR ($CDCl_3$, TMS): δ 2.36 (3H, s), 6.48 (1H, s) and 7.21–7.37 (5H, m); IR (KBr): 1528 and 1350 cm^{-1}; anal. calcd for $C_9H_9NO_2$: C, 66.25; H, 5.56; N, 8.58%. Found: C, 66.12; H, 5.58; N, 8.53%.

4.4.2. (*Z*)-1-Phenyl-2-nitro-1-butene 1p. Purified by column chromatography on silica gel with hexane/ethyl acetate (20/1); 19% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.21 (3H, t, $J=7.4$ Hz), 2.69 (2H, q, $J=7.4$ Hz), 6.37 (1H, s) and 7.22–7.37 (5H, m); IR (neat): 1524 and 1373 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90%. Found: C, 67.62; H, 6.28; N, 7.91%.

4.5. General procedure for the preparation of 2-aryl-2-butenes

To a stirred suspension of ethyltriphenylphosphonium bromide (50 mmol) in dry diethyl ether (200 mL) was added a solution of butyl lithium in hexane (34 mL, 1.59 mM) at room temperature under an argon atmosphere. After 4 h, the acetophenone or its derivative (52 mmol) was added, and the mixture was stirred under reflux overnight. The mixture was filtered, and the filtrate was washed with water and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a crude product, which was purified by column chromatography on silica gel with hexane. The isolated yields and their spectral data are shown below.

4.5.1. 2-Phenyl-2-butene. 62% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.59 (3H, dq, $J=6.9$, 1.5 Hz), 1.79 (3H, dq, $J=6.8$, 1.0 Hz), 2.01–2.04 (3H, 3H, m), 5.56 (1H, qq, $J=6.9$, 1.4 Hz), 5.86 (1H, qq, $J=6.8$, 1.3 Hz) and 7.16–7.39 (5H, 5H, m); IR (neat): 3023, 1495, 1441, 754 and 698 cm^{-1}; anal. calcd for $C_{10}H_{12}$: C, 90.85; H, 9.15%. Found: C, 90.66; H, 9.24%.

4.5.2. 2-(2′-Chlorophenyl)-2-butene. 56% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.40 (3H, dq, $J=6.8$, 1.6 Hz), 1.77 (3H, dq, $J=6.8$, 1.1 Hz), 1.96–1.99 (3H, 3H, m), 5.48 (1H, qq, $J=6.8$, 1.5 Hz), 5.62 (1H, qq, $J=6.8$, 1.5 Hz) and 7.08–7.41 (5H, 5H, m); IR (neat): 3056, 3030, 1472, 1431, 1047, 1034 and 754 cm^{-1}; anal. calcd for $C_{10}H_{11}Cl$: C, 72.07; H, 6.65%. Found: C, 71.91; H, 6.65%.

4.5.3. 2-(3′-Chlorophenyl)-2-butene. 56% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.58 (3H, dq, $J=7.0$, 1.6 Hz), 1.79 (3H, dq, $J=6.9$, 1.1 Hz), 1.98–2.01 (3H, 3H, m), 5.58 (1H, qq, $J=6.9$, 1.5 Hz), 5.88 (1H, qq, $J=6.9$, 1.4 Hz) and 7.04–7.35 (5H, 5H, m); IR (neat): 3056, 3030, 1593, 1562, 1080, 997 and 781 cm^{-1}; anal. calcd for $C_{10}H_{11}Cl$: C, 72.07; H, 6.65%. Found: C, 71.94; H, 6.57%.

4.5.4. 2-(4′-Chlorophenyl)-2-butene. 52% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.58 (3H, dq, $J=7.0$, 1.5 Hz), 1.79 (3H, dq, $J=6.9$, 1.1 Hz), 1.98–2.01 (3H, 3H, m), 5.57 (1H, qq, $J=7.0$, 1.5 Hz), 5.85 (1H, qq, $J=6.9$, 1.4 Hz) and 7.10–7.33 (5H, 5H, m); IR (neat): 3030, 1491, 1092, 837 and 812 cm^{-1}; anal. calcd for $C_{10}H_{11}Cl$: C, 72.07; H, 6.65%. Found: C, 72.28; H, 6.76%.

4.6. General procedure for the preparation of 3-aryl-2-nitro-2-butenes 3

Nitric acid (4.5 g) and sulfuric acid (two drops) were added dropwise to stirred acetic anhydride (30 mL) at 0°C. A solution of 2-aryl-2-butene (25 mmol) in acetic anhydride (10 mL) was added dropwise to the mixture. After 20 min, water (150 mL) was added and the mixture was stirred for 30 min at room temperature. The organic materials were extracted with diethyl ether. The organic layer was neutralized with saturated sodium hydrogen carbonate, washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave crude 3-acetoxy-3-aryl-2-nitrobutane, which was used without further purification.

To a solution of 3-acetoxy-3-aryl-2-nitrobutane in chloroform (50 mL) was added triethylamine (4 mL) and the mixture was refluxed overnight. The mixture was neutralized with diluted hydrochloric acid, washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a crude product, which was purified by column chromatography on silica gel with hexane/ethyl acetate (20/1). The isolated yields and their spectral data are shown below.

4.6.1. (*Z*)-3-Phenyl-2-nitro-2-butene 3a. 49% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 2.09 (3H, q, J=1.5 Hz), 2.23 (3H, q, J=1.5 Hz) and 7.18–7.43 (5H, m); IR (neat): 1520 and 1343 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90%. Found: C, 67.86; H, 6.31; N, 7.86%.

4.6.2. (*E*)-3-Phenyl-2-nitro-2-butene 3b. 14% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 2.12 (3H, q, J=1.1 Hz), 2.32 (3H, q, J=1.1 Hz) and 7.13–7.35 (5H, m); IR (neat): 1522 and 1352 cm^{-1}; anal. calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90%. Found: C, 67.64; H, 6.42; N, 7.89%.

4.6.3. (*Z*)-3-(2′-Chlorophenyl)-2-nitro-2-butene 3c. 43% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 1.97 (3H, q, J=1.6 Hz), 2.21 (3H, q, J=1.6 Hz), 7.13–7.18 (1H, m), 7.26–7.34 (2H, m) and 7.43–7.48 (1H, m); IR (neat): 1524 and 1345 cm^{-1}; anal. calcd for $C_{10}H_{10}NO_2Cl$: C, 56.75; H, 4.76; N, 6.62%. Found: C, 56.79; H, 4.85; N, 6.54%.

4.6.4. (*Z*)-3-(3′-Chlorophenyl)-2-nitro-2-butene 3d. 34% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 2.09 (3H, q, J=1.5 Hz), 2.19 (3H, q, J=1.5 Hz), 7.07–7.12 (1H, m), 7.20–7.26 (1H, m) and 7.34–7.36 (2H, m); IR (neat): 1522 and 1345 cm^{-1}; anal. calcd for $C_{10}H_{10}NO_2Cl$: C, 56.75; H, 4.76; N, 6.62%. Found: C, 56.73; H, 4.81; N, 6.59%.

4.6.5. (*Z*)-3-(4′-Chlorophenyl)-2-nitro-2-butene 3e. 37% yield; ^{1}H NMR ($CDCl_3$, TMS): δ 2.09 (3H, q, J=1.5 Hz), 2.20 (3H, q, J=1.5 Hz), 7.12–7.19 (2H, m) and 7.37–7.43 (2H, m); IR (neat): 1522 and 1343 cm^{-1}; anal. calcd for $C_{10}H_{10}NO_2Cl$: C, 56.75; H, 4.76; N, 6.62%. Found: C, 56.62; H, 4.78; N, 6.54%.

4.7. General procedure for the reduction of α,β-disubstituted nitroalkenes by baker's yeast

Nitroalkene (2.5 mmol) dissolved in ethanol (5.0 mL) was added to a stirred suspension of dry baker's yeast (25 g) in water (150 mL) at 35°C. The reaction was followed by gas chromatography. When the substrate was consumed completely or after 24 h, the reaction was worked up as follows. Acetone (150 mL) was added to the reaction mixture and the mixture was filtered through hyflo super-cel®. The residue was washed three times with acetone and the washing solution was combined with the filtrate. The mixture was evaporated under reduced pressure to 100 mL and the organic materials were extracted with diethyl ether. The ether solution was dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a crude product, which was purified by column chromatography on silica gel with hexane/ethyl acetate (20/1). The yields and the enantiomeric excesses are summarized in Table 2. The spectral data are shown below.

4.7.1. 1-Phenyl-2-nitropropane 2a. ^{1}H NMR ($CDCl_3$, TMS): δ 1.54 (3H, d, J=6.7 Hz), 3.00 (1H, dd, J=6.8, 14.0 Hz), 3.32 (1H, dd, J=7.5, 14.0 Hz), 4.69–4.86 (1H, m) and 7.14–7.32 (5H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48%. Found: C, 65.35; H, 6.75; N, 8.45%.

4.7.2. 1-(2′-Chlorophenyl)-2-nitropropane 2c. ^{1}H NMR ($CDCl_3$, TMS): δ 1.59 (3H, d, J=6.7 Hz), 3.19 (1H, dd, J=6.1, 14.1 Hz), 3.40 (1H, dd, J=8.1, 14.1 Hz), 4.84–5.02 (1H, m), 7.16–7.26 (3H, m) and 7.36–7.41 (1H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_9H_{10}NO_2Cl$: C, 54.15; H, 5.05; N, 7.02%. Found: C, 54.17; H, 5.21; N, 6.84%.

4.7.3. 1-(3′-Chlorophenyl)-2-nitropropane 2d. ^{1}H NMR ($CDCl_3$, TMS): δ 1.56 (3H, d, J=6.7 Hz), 2.99 (1H, dd, J=6.5, 14.1 Hz), 3.30 (1H, dd, J=7.7, 14.1 Hz), 4.69–4.86 (1H, m), 7.02–7.07 (1H, m), 7.17 (1H, s) and 7.24–7.27 (2H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_9H_{10}NO_2Cl$: C, 54.15; H, 5.05; N, 7.02%. Found: C, 53.93; H, 5.10; N, 6.86%.

4.7.4. 1-(4′-Chlorophenyl)-2-nitropropane 2e. ^{1}H NMR ($CDCl_3$, TMS): δ 1.55 (3H, d, J=6.7 Hz), 2.99 (1H, dd, J=6.4, 14.1 Hz), 3.29 (1H, dd, J=7.8, 14.1 Hz), 4.67–4.84 (1H, m), 7.07–7.13 (2H, m) and 7.26–7.32 (2H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_9H_{10}NO_2Cl$: C, 54.15; H, 5.05; N, 7.02%. Found: C, 54.34; H, 5.17; N, 6.93%.

4.7.5. 1-(2′-Methylphenyl)-2-nitropropane 2f. ^{1}H NMR ($CDCl_3$, TMS): δ 1.55 (3H, d, J=6.6 Hz), 2.33 (3H, s), 2.98 (1H, dd, J=6.9, 13.9 Hz), 3.38 (1H, dd, J=7.5, 13.9 Hz), 4.68–4.88 (1H, m) and 7.04–7.19 (4H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%. Found: C, 66.92; H, 7.38; N, 7.82%.

4.7.6. 1-(3′-Methylphenyl)-2-nitropropane 2g. ^{1}H NMR ($CDCl_3$, TMS): δ 1.54 (3H, d, J=6.6 Hz), 2.33 (3H, s), 2.96 (1H, dd, J=6.9, 13.9 Hz), 3.29 (1H, dd, J=7.5, 13.9 Hz), 4.69–4.86 (1H, m) and 6.94–7.26 (4H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%. Found: C, 66.81; H, 7.35; N, 7.77%.

4.7.7. 1-(4′-Methylphenyl)-2-nitropropane 2h. ^{1}H NMR ($CDCl_3$, TMS): δ 1.52 (3H, d, J=6.6 Hz), 2.31 (3H, s), 2.96 (1H, dd, J=6.9, 14.3 Hz), 3.27 (1H, dd, J=7.4, 14.3 Hz), 4.66–4.83 (1H, m), 7.04 (2H, d, J=8.1 Hz) and 7.12 (2H, d, J=8.1 Hz); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%. Found: C, 66.93; H, 7.23; N, 7.67%.

4.7.8. 1-(2′-Methoxyphenyl)-2-nitropropane 2i. ^{1}H NMR ($CDCl_3$, TMS): δ 1.53 (3H, d, J=6.7 Hz), 3.05 (1H, dd, J=6.5, 13.5 Hz), 3.27 (1H, dd, J=7.7, 13.5 Hz), 3.84 (3H, s), 4.83–5.00 (1H, m) and 6.84–7.30 (4H, m); IR (neat): 1549 and 1248 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17%. Found: C, 61.27; H, 6.80; N, 7.11%.

4.7.9. 1-(3′-Methoxyphenyl)-2-nitropropane 2j. ^{1}H NMR ($CDCl_3$, TMS): δ 1.55 (3H, d, J=6.7 Hz), 2.98 (1H, dd, J=7.0, 13.8 Hz), 3.31 (1H, dd, J=7.4, 13.8 Hz), 3.79 (3H, s), 4.70–4.87 (1H, m), 6.69–6.83 (3H, m) and 7.20–7.28 (1H, m); IR (neat): 1551 and 1263 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17%. Found: C, 61.81; H, 6.81; N, 7.12%.

4.7.10. 1-(4′-Methoxyphenyl)-2-nitropropane 2k. ^{1}H NMR ($CDCl_3$, TMS): δ 1.53 (3H, d, J=6.7 Hz), 2.95 (1H, dd, J=6.7, 14.1 Hz), 3.25 (1H, dd, J=7.5, 14.1 Hz), 3.78 (3H, s), 4.65–4.82 (1H, m) and 7.14–7.32 (4H, m); IR (neat): 1549 and 1245 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17%. Found: C, 61.55; H, 6.88; N, 7.09%.

4.7.11. 1-Cyclohexyl-2-nitropropane 2l. ^{1}H NMR ($CDCl_3$, TMS): δ 0.80–2.04 (16H, m) and 4.61–4.79 (1H, m); IR (neat): 2926, 2853 and 1551 cm^{-1}; anal. calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.00; N, 8.18%. Found: C, 62.94; H, 10.08; N, 8.12%.

4.7.12. 4-Methyl-2-nitropentane 2m. ^{1}H NMR ($CDCl_3$, TMS): δ 0.92 (3H, d, J=6.5 Hz), 0.96 (3H, d, J=6.3 Hz), 1.40–1.62 (5H, m), 1.92–2.03 (1H, m) and 4.62–4.72 (1H, m); IR (neat): 1553 cm^{-1}; anal. calcd for $C_6H_{13}NO_2$: C, 54.94; H, 9.99; N, 10.68%. Found: C, 55.18; H, 10.18; N, 10.46%.

4.7.13. 4,4-Dimethyl-2-nitropentane 2n. ^{1}H NMR ($CDCl_3$, TMS): δ 0.93 (9H, s), 1.04 (1H, dd, J=3.7, 8.8 Hz), 1.53 (3H, d, J=6.7 Hz), 2.21 (1H, dd, J=8.8, 15.1 Hz) and 4.63–4.79 (1H, m); anal. calcd for $C_7H_{15}NO_2$: C, 57.90; H, 10.41; N, 9.65%. Found: C, 58.81; H, 10.57; N, 10.19%.

4.7.14. 1-Phenyl-2-nitrobutane 2o. ^{1}H NMR ($CDCl_3$, TMS): δ 0.98 (3H, t, J=7.4 Hz), 1.73–2.14 (2H, m), 3.03 (1H, dd, J=5.9, 14.1 Hz), 3.26 (1H, dd, J=8.5, 14.1 Hz), 4.56–4.70 (1H, m) and 7.13–7.36 (5H, m); IR (neat): 1549 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%. Found: C, 66.78; H, 7.34; N, 7.79%.

4.7.15. 1-(2′-Methylphenyl)-2-nitrobutane 2q. ^{1}H NMR ($CDCl_3$, TMS): δ 0.98 (3H, t, J=7.3 Hz), 1.73–2.17 (2H, m), 2.33 (3H, s), 3.05 (1H, dd, J=6.1, 14.4 Hz), 3.28 (1H, dd, J=8.3, 14.4 Hz), 4.54–4.69 (1H, m) and 7.06–7.18 (4H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25%. Found: C, 68.21; H, 7.91; N, 7.16%.

4.7.16. 1-(3′-Methylphenyl)-2-nitrobutane 2r. ^{1}H NMR ($CDCl_3$, TMS): δ 0.97 (3H, t, J=7.4 Hz), 1.72–2.13 (2H, m), 2.32 (3H, s), 2.98 (1H, dd, J=6.0, 14.1 Hz), 3.22 (1H, dd, J=8.5, 14.1 Hz), 4.55–4.69 (1H, m) and 6.93–7.24 (4H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25%. Found: C, 68.46; H, 7.95; N, 7.10%.

4.7.17. 1-(4′-Methylphenyl)-2-nitrobutane 2s. ^{1}H NMR ($CDCl_3$, TMS): δ 0.97 (3H, t, J=7.4 Hz), 1.72–2.12 (2H, m), 2.31 (3H, s), 2.98 (1H, dd, J=5.9, 14.0 Hz), 3.21 (1H, dd, J=8.5, 14.0 Hz), 4.53–4.67 (1H, m), 7.03 (2H, d, J=8.3 Hz) and 7.11 (2H, d, J=8.3 Hz); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25%. Found: C, 68.18; H, 7.88; N, 7.29%.

4.8. General procedure for the reduction of trisubstituted nitroalkenes by baker's yeast

The procedure described for α,β-disubstituted nitroalkenes was followed using baker's yeast (50 g) and water (250 mL). The yields, diastereomeric excesses, and enantiomeric excesses are summarized in Table 3. The spectral data are shown below.

4.8.1. (2*R*,3*R*)-3-Phenyl-2-nitrobutane 4a. $[\alpha]_D^{20}$=+8.5 (*c* 1.0, EtOH), e.e.=98%; ^{1}H NMR ($CDCl_3$, TMS): δ 1.31 (3H, d, J=6.6 Hz), 1.32 (3H, d, J=6.9 Hz), 3.22 (1H, dq, J=10.0, 6.9 Hz), 4.67 (1H, dq, J=10.0, 6.6 Hz) and 7.15–7.40 (5H, m); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%. Found: C, 66.89; H, 7.38; N, 7.81%.

4.8.2. (2*S*,3*R*)-3-Phenyl-2-nitrobutane 5a. $[\alpha]_D^{20}$=+91.5 (*c* 1.0, EtOH), e.e.=97%; ^{1}H NMR ($CDCl_3$, TMS): δ 1.33 (3H, d, J=7.2 Hz), 1.56 (3H, d, J=6.7 Hz), 3.38 (1H, dq, J=8.4, 7.2 Hz), 4.72 (1H, dq, J=8.4, 6.7 Hz) and 7.17–7.37 (5H, m); IR (neat): 1549 cm^{-1}; anal. calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82%. Found: C, 66.91; H, 7.42; N, 7.81%.

4.8.3. (2*R*,3*R*)-3-(3′-Chlorophenyl)-2-nitrobutane 4d. $[\alpha]_D^{20}$=+7.5 (*c* 1.0, EtOH), e.e.=82%; ^{1}H NMR ($CDCl_3$, TMS): δ 1.31 (3H, d, J=6.9 Hz), 1.33 (3H, d, J=6.6 Hz), 3.22 (1H, dq, J=9.9, 6.9 Hz), 4.64 (1H, dq, J=9.9, 6.6 Hz), 7.04–7.10 (1H, m), 7.17–7.19 (1H, m) and 7.26–7.30 (2H, m); IR (neat): 1553 cm^{-1}; anal. calcd for $C_{10}H_{12}NO_2Cl$: C, 56.21; H, 5.66; N, 6.56%. Found: C, 56.38; H, 5.69; N, 6.44%.

4.8.4. (2*S*,3*R*)-3-(3′-Chlorophenyl)-2-nitrobutane 5d. $[\alpha]_D^{20}$=+54.8 (*c* 0.90, EtOH), e.e.=81%; ^{1}H NMR ($CDCl_3$, TMS): δ 1.32 (3H, d, J=7.2 Hz), 1.57 (3H, d, J=6.7 Hz), 3.36 (1H, dq, J=8.6, 7.2 Hz), 4.70 (1H, dq, J=8.6, 6.7 Hz), 7.06–7.11 (1H, m) and 7.18–7.26 (3H, m); IR (neat): 1549 cm^{-1}; anal. calcd for $C_{10}H_{12}NO_2Cl$: C, 56.21; H, 5.66; N, 6.56%. Found: C, 56.39; H, 5.75; N, 6.35%.

4.8.5. (2*R*,3*R*)-3-(4′-Chlorophenyl)-2-nitrobutane 4e. $[\alpha]_D^{20}$=+8.2 (*c* 1.0, EtOH), e.e.=94%; ^{1}H NMR ($CDCl_3$, TMS): δ 1.31 (3H, d, J=6.9 Hz), 1.32 (3H, d, J=6.6 Hz), 3.23 (1H, dq, J=9.8, 6.9 Hz), 4.62 (1H, dq, J=9.8, 6.6 Hz), 7.12 (2H, dt, J=8.9, 2.3 Hz) and 7.33 (2H, dt, J=8.9, 2.3 Hz); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{10}H_{12}NO_2Cl$: C, 56.21; H, 5.66; N, 6.56%. Found: C, 56.29; H, 5.69; N, 6.56%.

4.8.6. (2*S*,3*R*)-3-(4′-Chlorophenyl)-2-nitrobutane 5e. $[\alpha]_D^{20}$=+82.6 (*c* 1.0, EtOH), e.e.=92%; ^{1}H NMR ($CDCl_3$, TMS): δ 1.33 (3H, d, J=7.2 Hz), 1.57 (3H, d, J=6.7 Hz), 3.34 (1H, dq, J=8.7, 7.2 Hz), 4.68 (1H, dq, J=8.7, 6.7 Hz), 7.13 (2H, dt, J=8.7, 2.2 Hz) and 7.29 (2H, dt, J=8.7, 2.2 Hz); IR (neat): 1551 cm^{-1}; anal. calcd for $C_{10}H_{12}NO_2Cl$: C, 56.21; H, 5.66; N, 6.56%. Found: C, 56.29; H, 5.70; N, 6.52%.

4.9. Determination of enantiomeric excess of nitroalkane

Anhydrous ammonium formate (7 mmol) was added to a stirred suspension of nitroalkane (1 mmol) and palladium on carbon (10%, 0.05 g) in dry methanol (2 mL) and the mixture was stirred for 6 h at room temperature under an atmosphere of argon. The mixture was filtered and the filtrate was evaporated at reduced pressure. The residue was dissolved in a mixture of ethyl acetate and water. The organic layer was separated and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a corresponding amine, which was used without further purification.

To a solution of amine (6 mg) and dry pyridine (three drops) in dry benzene (1 mL) was added (+)-α-methoxy-α-(trifluoromethyl)-α-phenylacetyl (MTPA) chloride (30 μL) and stirred at room temperature under an atmosphere of argon overnight. To the solution was added *N*,*N*-dimethyl-1,3-propanediamine (three drops) and stirred for 5 min. The solution was washed three times with diluted hydrochloric acid and five times with saturated sodium hydrogen carbonate and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave an amide. The diastereomeric excess of the amide was determined by gas chromatography (capillary column, OV-1701 or OV-1).

4.10. Determination of the absolute configuration of 4a

3-Phenyl-2-nitropropane **4a** obtained from baker's yeast reduction was converted to the corresponding amine as described above. Hydrogen chloride was bubbled through the solution of the amine in diethyl ether. The resulting precipitate **6** was recrystallized from ethanol. A colorless prismatic crystal, crystal size 0.2×0.3×0.5 mm, monoclinic, space group $P2_1$ (no. 4), $a=12.542(1)$, $b=5.583(2)$, $c=15.920(1)$ Å, $\beta=107.323(7)°$, $V=1064.2(3)$ Å^3, $Z=4$, $D_c=1.16$ g/cm^3, μ(Cu-Kα)=27.52 cm^{-1} was used for data collection. The structure was solved by direct methods (SIR-92)[47] and expanded using Fourier techniques (DIRDIF-94).[48] All the calculations were performed using the teXsan crystallographic software package of Molecular Structure Corporation. The final cycle of full-matrix least-squares refinement was based on 3764 observed reflections ($I>1.50\sigma(I)$) and 217 variable parameters and gave $R=0.084$ and $R_w=0.101$. The value of the goodness of fit indicator was 1.17.

4.11. Preparation of (±)-*erythro*-3-phenyl-2-nitrobutane 4a

Palladium on carbon (10%, 0.1 g) was added to a solution of (*Z*)-3-phenyl-2-nitro-2-butene (5 mmol) in diethyl ether (50 mL) and the suspension was stirred under an atmosphere of hydrogen for 6 h. The suspension was filtered and the filtrate was evaporated at reduced pressure to give a crude product, which was purified by column chromatography on silica gel with hexane/ethyl acetate (20/1), giving the product in 72% yield.

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