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# Ketoreductase catalyzed stereoselective bioreduction of α-nitro ketones†

Zexu Wang,[a,b] Xiaofan Wu,[c] Zhining Li,[a,b] Zedu Huang *[a,b] and Fener Chen*[a,b]

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We report here the stereoselective bioreduction of α-nitro ketones catalyzed by ketoreductases (KREDs) with publicly known sequences. YGL039w and RasADH/SyADH were able to reduce 23 class I substrates (1-aryl-2-nitro-1-ethanone (**1**)) and ten class II substrates (1-aryloxy-3-nitro-2-propanone (**4**)) to furnish both enantiomers of the corresponding β-nitro alcohols, with good-to-excellent conversions (up to >99%) and enantioselectivities (up to >99% ee) being achieved in most cases. To the best of our knowledge, KRED-mediated reduction of class II α-nitro ketones (1-aryloxy-3-nitro-2-propanone (**4**)) is unprecedented. Select β-nitro alcohols, including the synthetic intermediates of bioactive molecules (*R*)-tembamide, (*S*)-tembamide, (*S*)-moprolol, (*S*)-toliprolol and (*S*)-propanolol, were stereoselectively synthesized in preparative scale with 42% to 90% isolated yields, showcasing the practical potential of our developed system in organic synthesis. Finally, the advantage of using KREDs with known sequence was demonstrated by whole-cell catalysis, in which β-nitro alcohol (*R*)-**2k**, the key synthetic intermediate of hypoglycemic natural product (*R*)-tembamide, was produced in a space–time yield of 178 g $L^{-1}$ $d^{-1}$ as well as 95% ee by employing the whole cells of a recombinant *E. coli* strain coexpressing RasADH and glucose dehydrogenase as the biocatalyst.

## Introduction

Ketoreductases (KREDs) are NAD(P)H-dependent enzymes displaying a broad substrate spectrum for the reduction of prochiral ketones to the corresponding chiral alcohols.[1] Undoubtedly KREDs are some of the most common and sophisticated biocatalysts utilized in the industrial syntheses of pharmaceuticals, mainly due to their excellent stereoselectivity, good stability and environmental compatibility.[1a,2] Ketones with a substituent α to the carbonyl group (α-substituted ketones) represent an important class of substrates for KREDs, because the resulting alcohols are bifunctional.[3] In this regard, KREDs catalyzing the asymmetric reduction of α-azido ketones, α-nitrile ketones, α-hydroxy ketones and α-halo ketones are well-documented.[4] In contrast, the bioreduction of α-nitro ketones has been scarcely studied, which is surprising given that the resulting β-nitro alcohols are well-recognized synthetic intermediates that can undergo a variety of useful transformations,[3,5] such as conversion to β-amino alcohols, which are privileged structural elements present in many pharmaceuticals and bioactive natural products (Fig. 1).[6] β-Amino alcohols are also widely used as chiral ligands and auxiliaries in organic syntheses.[7]

When we initiated our project, the bioreduction of α-nitro ketones was exclusively performed using whole cells of baker's yeast, *Comamonas testosterone*, and *Candida parapsilosis* (Scheme 1).[8] However, most of those studies, only demonstrated limited substrate scope (mainly aliphatic α-nitro ketones) and only accessed one enantiomer of the β-nitro alcohol products. These low stereoselectivities can be attributed to the presence of multiple KREDs in the whole cell system, some with opposite stereochemical preferences.[8d] Therefore, we decided to systematically investigate the biore-

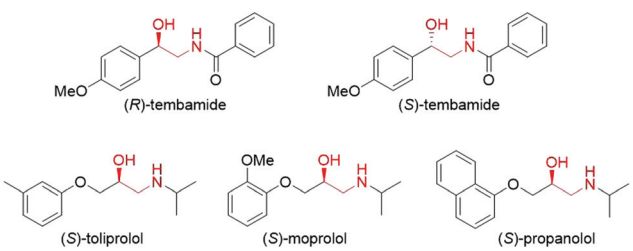


**Fig. 1** Select examples of bioactive natural products and pharmaceutical molecules containing vicinal amino alcohol moiety.

[a]*Engineering Center of Catalysis and Synthesis for Chiral Molecules, Department of Chemistry, Fudan University, 220 Handan Road, Shanghai, 200433, P. R. China. E-mail: huangzedu@fudan.edu.cn, rfchen@fudan.edu.cn*
[b]*Shanghai Engineering Research Center of Industrial Asymmetric Catalysis of Chiral Drugs, 220 Handan Road, Shanghai, 200433, P. R. China*
[c]*College of Chemical Engineering, Fuzhou University, 2 Xueyuan Road, Fuzhou, 350100, P. R. China*

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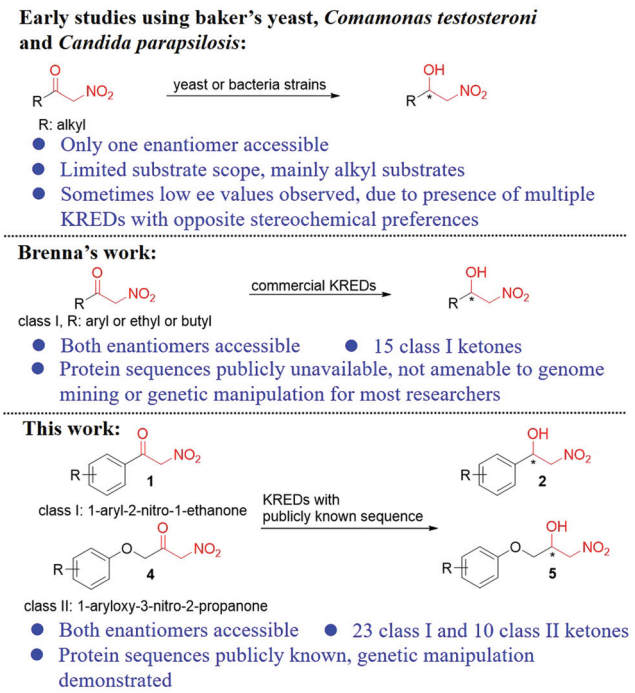



**Scheme 1** Different approaches to the stereoselective bioreduction of α-nitro ketones.

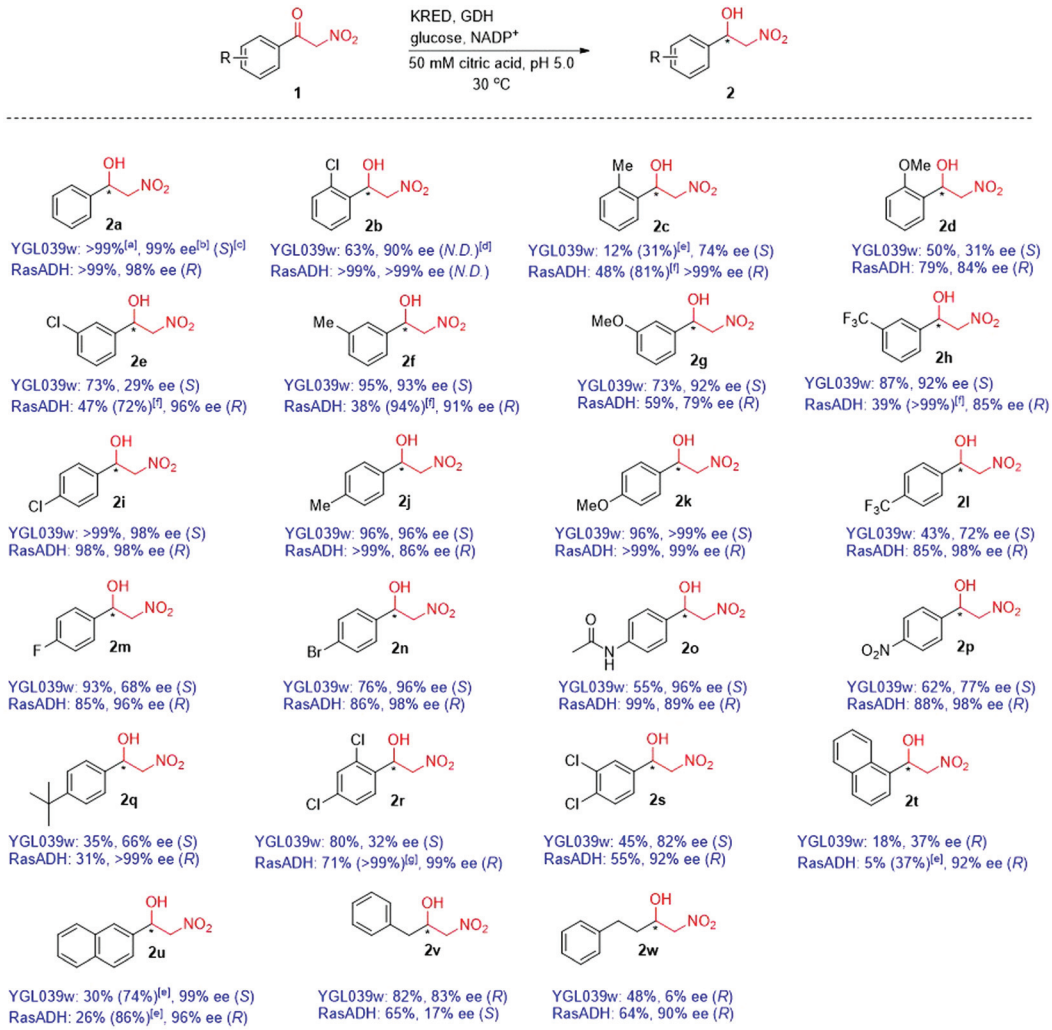
duction of α-nitro ketones using isolated KREDs. Very recently, Brenna and co-workers reported an elegant study using commercial KREDs for the stereoselective reduction of α-nitro ketones (class I, Scheme 1), affording both enantiomers of β-nitro alcohols with good-to-excellent ee values in most cases.[9] Although the use of commercial KREDs is convenient, genome mining or genetic manipulation with these KREDs becomes difficult for most researchers, given that the gene/protein sequences of most of commercial KREDs are not publicly available.[10] Herein, we report the stereoselective bioreduction of α-nitro ketones (both class I and class II, Scheme 1), using isolated KREDs with publicly known sequences, to β-nitro alcohols with good-to-excellent conversions (up to >99%) and stereoselectivities (up to >99% ee) in most cases. We also succeeded in the preparative scale synthesis of several important β-nitro alcohols, including the synthetic intermediates of bioactive molecules (*R*)-tembamide, (*S*)-tembamide, (*S*)-moprolol, (*S*)-toliprolol and (*S*)-propanolol. Moreover, using whole cells of an *E. coli* strain recombinantly coexpressing RasADH and GDH as the biocatalyst, alcohol (*R*)-**2k** was synthesized in a highly stereoselective fashion with a space–time yield of 178 g $L^{-1}$ $d^{-1}$, underscoring the superior applicability of KREDs with publicly known sequence.

## Results and discussion

We first examined the ability of YGL039w, a KRED originating from *Saccharomyces cerevisiae*, in the reduction of the model substrate α-nitro acetophenone **1a**, since this enzyme was previously shown to be capable of stereoselectively reducing α-nitrile ketones.[4c] To our delight, YGL039w indeed was able to convert **1a** to the desired alcohol **2a** (Fig. S3 and Table S4†). We found that citric acid buffer of pH 5 was the best buffer, in which **2a** was formed in 83% conversion as measured by $^1$H NMR, alongside with 9% **1a** and 8% benzoic acid (**3a**) (see Fig. S3 and S4† for a detailed discussion of calculating $^1$H NMR conversions). The formation of benzoic acid presumably arises from the instability of **1a** under the reaction conditions.[9,11] Due to the strong acidity of its α-proton, **1a** likely exists predominantly as its enol(ate) form under higher pHs, accounting for the relatively slow reactions observed at pHs 6, 7, and 8. On the other hand, YGL039w and/or glucose dehydrogenase used for NADPH regeneration might have decreased catalytic abilities at pH 4, which again would result in lower conversions. We were pleased to find that the complete conversion of **1a** to **2a** could be realized by increasing the enzyme loading and reaction time, and importantly no benzoic acid was detected under such conditions (entry 6, Table S4†). Moreover, the biosynthesized **2a** possessed excellent enantiomeric purity (99% ee, (*S*)-configuration). Aiming to uncover an stereocomplementary enzyme, an in-house collection of 13 KREDs with publicly known sequences were further evaluated on the bioreduction of **1a** under the optimal reaction conditions (Table S5†). Gratifyingly, RasADH, a KRED originating from *Ralstonia* species,[12] produced the desired (*R*)-**2a** with 98% ee.

With a pair of stereocomplementary KREDs identified, we next evaluated the performance of these two enzymes in reducing 23 class I α-nitro ketones: 1-aryl-2-nitro-1-ethanone (**1**) (Scheme 2). In YGL039w-catalyzed reductions of ketones with a mono-substituted phenyl ring (**1a** to **1q**), the desired alcohols (**2a** to **2q**) were generated in moderate-to-excellent conversions (up to >99%), with good-to-excellent enantiomeric purities in most cases (up to >99% ee). Apparently, steric effect played an important role with regard to reaction conversion. For example, moderate conversions (55% and 35%) were seen for substrates **1o** and **1q** which bear bulky *p*-NHC(O)$CH_3$ and *p*-*t*Bu groups, respectively. In contrast, >95% conversions were achieved for substrates **1j** and **1k** with a *p*-Me and a *p*-OMe group, respectively. Steric effects were also reflected in the reduction of substrates with the same substituents, located at different positions. For instance, while ketone **1i** with a *p*-chloro group was transformed to alcohol **2i** in >99% conversion, its positional isomers **1e** (*m*-chloro) and **1b** (*o*-chloro) were reduced in 73% and 63% conversions, respectively. Electronic effect also has a strong influence on the reactivity, as evidenced by the superior conversions observed for ketones with electron-donating groups (EDGs) (*e.g.*, **1j** and **1k**) over those with electron-withdrawing groups (EWGs) (*e.g.*, **1l** and **1p**). Bis-substituted ketones **1r** and **1s** are also substrates of YGL039w, affording the corresponding alcohols **2r** and **2s** in 80% and 45% conversions, respectively. Replacement of the phenyl ring with a naphthalenyl ring probably rendered the carbonyl group less accessible, which resulted in poor conversions observed for **1t** and **1u**. Nevertheless, thus formed




**Scheme 2** KRED-catalyzed stereocomplementary synthesis of β-nitro alcohols **2**. Unless otherwise stated, the reaction was carried out with 10 mM ketone substrate, 20 mM glucose, 0.2 mM $NADP^+$, 1 mg $mL^{-1}$ KRED (24.7 μM YGL039w or 34.6 μM RasADH) and 1 mg $mL^{-1}$ glucose dehydrogenase (GDH) (24.3 μM) in 1 mL of 50 mM citric acid, pH 5.0 at 30 °C and 180 rpm for 1 h. [a] The reaction conversion was determined using $^1H$ NMR (see Table S6† for details). [b] The ee was determined using chiral HPLC. [c] The absolute configuration was determined by comparing the elution order in chiral HPLC with known data. [d] The absolute configuration was not determined (N.D.). [e] The reaction was performed with 5 mg $mL^{-1}$ KRED (123.7 μM YGL039w or 173.1 μM RasADH) and 1 mg $mL^{-1}$ GDH (24.3 μM) for 2 h. [f] The reaction was performed with 3 mg $mL^{-1}$ KRED (74.2 μM YGL039w or 103.8 μM RasADH) and 1 mg $mL^{-1}$ GDH (24.3 μM) for 2 h. [g] The reaction was performed with 1 mg $mL^{-1}$ KRED (24.7 μM YGL039w or 34.6 μM RasADH) and 1 mg $mL^{-1}$ GDH (24.3 μM) for 2 h.

alcohol **2u** possessed remarkably high enantiomeric purity (99% ee). α-Nitro ketones **1v** and **1w**, containing one and two carbons, respectively, between the phenyl ring and the carbonyl group, were subjected to YGL039w-catalyzed reduction, furnishing the desired alcohols **2v** and **2w** in 82% and 48% conversions, respectively. Interestingly, the configuration of product **2v** was identified as (*R*), opposite to that of **2a**, suggesting multiple enzyme–substrate binding modes exist. Due to the instability of the α-nitro ketones under reaction conditions, variable amounts (4% to 40%) of benzoic acid derivatives **3** appeared as side products in nine out of 23 bioreduction reactions (see Table S6† for details).

The majority of the examined substrates were reduced by RasADH in excellent stereoselectivities (up to >99% ee). Contrary to YGL039w, RasADH transformed α-nitro ketones equipped with substituents at the *ortho*-position more readily than those bearing substituents at the *meta*-position (**1b**, **1c**, **1d** *versus* **1e**, **1f**, **1g**). With the exception of ketone **1q** (bearing a *p*-*t*Bu substituent), all the mono-*para*-substituted ketones turned out to be excellent substrates for RasADH, and the desired alcohols were generated in 85%-to->99% conversions. Similar to YGL039w, RasADH reduced bis-substituted ketones (**1r** and **1s**) and ketones with a naphthalenyl ring (**1t** and **1u**) with diminished efficiency, probably due to steric hindrance. Having one and two carbons, respectively, between the phenyl ring and the carbonyl group, ketone **1v** and **1w** were both reduced by RasADH in moderate conversions but with fairly different stereoselectivities (17% *versus* 90% ee). Finally, reac-

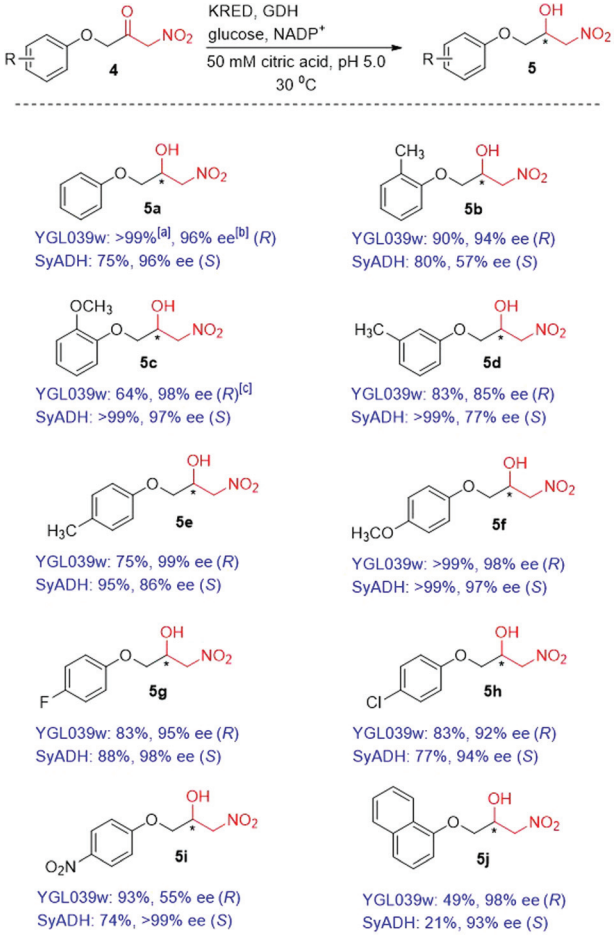
tion conversions could be improved by increasing enzyme loadings or prolonging reaction time (*e.g.*, **1c** and **1u**).

Given that enantioenriched 1-aryloxy-3-nitro-2-propanol derivatives (**5**) are key synthetic intermediates to β-adrenergic receptor blocking agents,[6b] we were keen to find out that if they could be prepared through KRED-catalyzed stereoselective reduction of their ketone precursors: 1-aryloxy-3-nitro-2-propanone (**4**). We first re-examined the same library of KREDs used for the above reduction of **1** for the reduction of the model substrate **4a** (Table S8†). Again, YGL039w and RasADH stood out as the most selective enzymes with opposite stereochemical preferences, affording **5a** in 96% ee and 58% ee, respectively. To find an enzyme with the same stereochemical preference as RasADH but with improved stereoselectivity in reducing **4a**, we screened 10 more KREDs. Out of these enzymes, SyADH performed the best, yielding the intended isomer of **5a** in 96% ee. Originating from *Sphingobium yanoikuyae*,[13] SyADH was previously used in the stereoselective reduction of α-chloro ketones to β-chloro alcohols.

Ten α-nitro ketones of this second class were then chosen for the study of substrate scope (Scheme 3). In general, steric and electronic effects exhibited by the phenyl ring R group were less significant here than in the bioreduction of class I α-nitro ketones, probably because the phenyl ring is not directly connected to the carbonyl group. Except ketone **4j**, all the ketones were readily reduced by YGL039w and SyADH to give the desired alcohols in good-to-excellent conversions (up to >99%), along with excellent stereoselectivities (up to 99% ee) being achieved in most cases. Similar as in the above discussion, the steric hindrance introduced by the naphthalenyl ring likely caused the low conversions observed for ketone **4j**. Nevertheless, the bioreduction of **4j** catalyzed by YGL039w yielded the corresponding alcohol (*S*)-**5j** with 98% ee. As a result of the instability of α-nitro ketones, α-aryloxy acetic acid (**6**) was detected as side products in about half of the bioreduction reactions in amounts ranging from 5% to 41% (see Table S9† for details).

To demonstrate the synthetic potential of our developed system, the bioreduction of select α-nitro ketones (**1a**, **1i**, **1k**, **4a** to **4j**) was carried out in preparative scale (250 mg ketone substrates, 5 g $L^{-1}$ concentration). DMSO was added to 10% (v/v) to help dissolve the hydrophobic substrates. Using cell-free extracts (CFE) of KREDs as biocatalysts, ketone substrates were completely consumed, and the desired β-nitro alcohols were isolated in 42%-to-90% yields with 32% ee-to-99% ee (Tables S12–S14†). Notably, enantioenriched alcohols (*R*)-**2k**, (*S*)-**2k**, (*S*)-**5c**, (*S*)-**5d**, and (*S*)-**5j** thus prepared are key synthetic intermediates to the hypoglycemic natural product (*R*)-tembamide, the antiviral natural product (*S*)-tembamide, and the β-adrenergic receptor blocking agents (*S*)-moprolol, (*S*)-toliprolol, and (*S*)-propanolol (Fig. 1).[6b,14]

In order to further demonstrate the practical utility of these KRED-catalyzed bioreductions, we sought to increase the substrate loadings of the above processes. At a substrate concentration of 10 g $L^{-1}$ (ketone **1k**), 89% and >99% conversions were achieved for YGL039w- and RasADH-catalyzed reactions,




**Scheme 3** KRED-catalyzed stereocomplementary synthesis of β-nitro alcohols **5**. The reaction was carried out with 10 mM ketone substrate, 20 mM glucose, 0.2 mM $NADP^+$, 1 mg $mL^{-1}$ KRED (24.7 μM YGL039w or 33.2 μM SyADH) and 1 mg $mL^{-1}$ glucose dehydrogenase (GDH) (24.3 μM) in 1 mL of 50 mM citric acid, pH 5.0 at 30 °C and 180 rpm for 1 h. [a] The reaction conversion was determined using $^1$H NMR. [b] The ee was determined using chiral HPLC. [c] The absolute configuration of **5c** was determined by $^1$H NMR spectroscopy using Mosher's reagent (see Fig. S5 and S6, and the associated discussion in ESI† for details); the absolute configuration of the rest of compounds (**5a**, **5b**, **5d** to **5j**) was assigned by analogy.

respectively (entry 1, Table S15†). In contrast, substantially decreased conversions were seen in reactions with higher substrate loadings (<71% and <21% for 20 and 50 g $L^{-1}$, respectively). We conjectured that using other organic solvents might combat potential substrate or product inhibition;[15] 16 additional organic solvents (10% v/v), both water-miscible and water-immiscible, were examined in bioreduction reactions carried out at a substrate concentration of 50 g $L^{-1}$ (Table S16†). Disappointingly, only limited improvement was realized, with the highest conversion being 47% (entry 5, Table S16†).

An alternative form of biocatalysis,[16] the use of resting *E. coli* whole cells coexpressing RasADH and GDH was also explored for the reduction of **1k** (Table S17†). Both two gene-

two plasmid and two gene-one plasmid approaches were adopted for the construction of the required recombinant *E. coli* strains. We first evaluated the biocatalyst prepared using the former approach. In the presence of 10% DMSO (v/v), the reaction, conducted at a substrate concentration of 50 g $L^{-1}$, reached 54% conversion after 5 h (entry 1, Table S17†). The inclusion of other organic solvents (20% v/v) positively influenced the reaction conversions (up to 80%) (entries 4 to 11, Table S17†). The three best-performing solvents (acetone, diethylene glycol dimethyl ether (DGDE), and dioxane) were then examined at a concentration of 50% (v/v). To our delight, the use of dioxane at 50% (v/v) resulted in further increased conversion (86%) (entry 14, Table S17†). Under such optimized conditions, **1k** (250 mg) was readily converted to (*R*)-**2k** (111 mg, 44% isolated yield) in a 5 mL reaction after 3 h, giving a space–time yield of 178 g $L^{-1}$ $d^{-1}$. Finally, the whole-cell catalysts prepared through the two gene-one plasmid method were subjected to the reduction of **1k** as well. As only moderate conversions were made at substrate concentration of 75 g $L^{-1}$ (entries 15 and 16, Table S17†), no further efforts were attempted. It is worth noting that such coexpression approaches are not applicable to most of commercial KREDs, at least for most researchers, since the associated genetic manipulation requires knowing the gene/protein sequences.

## Conclusions

In summary, YGL039w and RasADH/SyADH were identified as stereocomplementary KREDs through a campaign of screening 24 KREDs with publicly known sequences on the bioreduction of α-nitro ketones. We show that 23 class I ketones (1-aryl-2-nitro-1-ethanone (**1**)) and ten class II ketones (1-aryloxy-3-nitro-2-propanone (**4**)) were successfully bioreduced to generate both enantiomers of the corresponding β-nitro alcohols, with good-to-excellent conversions and stereoselectivities being achieved in most cases. To the best of our knowledge, this is the first report of a ketoreductase-catalyzed reduction of 1-aryloxy-3-nitro-2-propanone (**4**). The synthetic potential of our system was showcased by the highly stereoselective syntheses of key intermediates to (*R*)-tembamide, (*S*)-tembamide, (*S*)-moprolol, (*S*)-toliprolol, and (*S*)-propanolol in preparative scales. Finally, by employing whole cells of a recombinant *E. coli* strain coexpressing RasADH and GDH as the biocatalyst, the β-nitro alcohol (*R*)-**2k**, the key synthetic intermediate to hypoglycemic natural product (*R*)-tembamide, was synthesized with a space–time yield of 178 g $L^{-1}$ $d^{-1}$ as with 95% ee, underscoring the superior applicability of KREDs with publicly known sequences. We believe that our catalytic system will find wide usage in the preparation of valuable chiral β-nitro alcohols.

## Conflicts of interest

There are no conflicts to declare.

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## Notes and references

1 (*a*) F. Qin, B. Qin, T. Mori, Y. Wang, L. Meng, X. Zhang, X. Jia, I. Abe and S. You, *ACS Catal.*, 2016, **6**, 6135–6140; (*b*) W. Kroutil, H. Mang, K. Edegger and K. Faber, *Curr. Opin. Chem. Biol.*, 2004, **8**, 120–126; (*c*) R. Zhang, Y. Xu and R. Xiao, *Biotechnol. Adv.*, 2015, **33**, 1671–1684.

2 (*a*) S. K. Ma, J. Gruber, C. Davis, L. Newman, D. Gray, A. Wang, J. Grate, G. W. Huisman and R. A. Sheldon, *Green Chem.*, 2010, **12**, 81–86; (*b*) J. Liang, J. Lalonde, B. Borup, V. Mitchell, E. Mundorff, N. Trinh, D. A. Kochrekar, R. N. Cherat and G. G. Pai, *Org. Process Res. Dev.*, 2010, **14**, 193–198.

3 S. Zhang, Y. Li, Y. Xu and Z. Wang, *Chin. Chem. Lett.*, 2018, **29**, 873–883.

4 (*a*) H. Ankati, Y. Yang, D. Zhu, E. R. Biehl and L. Hua, *J. Org. Chem.*, 2008, **73**, 6433–6436; (*b*) G. Xu, H. Yu, Z. Zhang and J. Xu, *Org. Lett.*, 2013, **15**, 5408–5411; (*c*) R. W. Nowill, T. J. Patel, D. L. Beasley, J. A. Alvarez, E. Jackson III, T. J. Hizer, I. Ghiviriga, S. C. Mateer and B. D. Feske, *Tetrahedron Lett.*, 2011, **52**, 2440–2442; (*d*) Y. Geng, R. Zhang, Y. Xu, S. Wang, C. Sha and R. Xiao, *Biocatal. Biotransform.*, 2011, **29**, 172–178; (*e*) G. Xu, H. Yu, X. Zhang and J. Xu, *ACS Catal.*, 2012, **2**, 2566–2571.

5 J. Otevrel and P. Bobal, *J. Org. Chem.*, 2017, **82**, 8342–8358.

6 (*a*) J. H. Schrittwieser, F. Coccia, S. Kara, B. Grischek, W. Kroutil, N. d'Alessandro and F. Hollmann, *Green Chem.*, 2013, **15**, 3318–3331; (*b*) J. D. White and S. Shaw, *Org. Lett.*, 2012, **14**, 6270–6273.

7 D. J. Ager, I. Prakash and D. R. Schaad, *Chem. Rev.*, 1996, **96**, 835–876.

8 (*a*) T. Fujisawa, H. Hayashi and Y. Kishioka, *Chem. Lett.*, 1987, **16**, 129–132; (*b*) E. C. S. Brenelli, M. de Carvalho, M. T. Okubo, M. Marques, P. J. S. Moran, J. A. R. Rodrigues and A. E. P. M. Sorrilha, *Indian J. Chem.*, 1992, **31B**, 821–823; (*c*) S. R. Wallner, I. Lavandera, S. F. Mayer, R. Öhrlein, A. Hafner, K. Edegger, K. Faber and W. Kroutil, *J. Mol. Catal. B: Enzym.*, 2008, **55**, 126–129; (*d*) S. Venkataraman and A. Chadha, *RSC Adv.*, 2015, **5**, 73807–73813.

9 F. Tentori, E. Brenna, D. Colombo, M. Crotti, F. G. Gatti, M. C. Ghezzi and G. Pedrocchi-Fantoni, *Catalysts*, 2018, **8**, 308–318.

10 H. Li, D. Zhu, L. Hua and E. R. Biehl, *Adv. Synth. Catal.*, 2009, **351**, 583–588.

11 R. G. Pearson, D. H. Anderson and L. L. Alt, *J. Am. Chem. Soc.*, 1955, **77**, 527–529.

12 I. Lavandera, A. Kern, B. Ferreira-Silva, A. Glieder, S. de Wildeman and W. Kroutil, *J. Org. Chem.*, 2008, **73**, 6003–6005.
13 A. S. de Miranda, R. C. Simon, B. Grischek, G. C. de Paula, B. A. C. Horta, L. S. M. de Miranda, W. Kroutil, C. O. Kappe and R. O. M. A. de Souza, *ChemCatChem*, 2015, **7**, 984–992.
14 D. J. Buchanan, D. J. Dixon, M. S. Scott and D. I. Lainé, *Tetrahedron: Asymmetry*, 2004, **15**, 195–197.
15 (*a*) M. A. F. Delgove, M. T. Elford, K. V. Bernaerts and S. M. A. De Wildeman, *J. Chem. Technol. Biotechnol.*, 2018, **93**, 2131–2140; (*b*) S. K. Au, B. R. Bommarius and A. S. Bommarius, *ACS Catal.*, 2014, **4**, 4021–4026; (*c*) F. G. Mutti and W. Kroutil, *Adv. Synth. Catal.*, 2012, **354**, 3409–3413.
16 R. A. Sheldon and J. M. Woodley, *Chem. Rev.*, 2018, **118**, 801–838.