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Ru-catalyzed deoxydehydration (DODH) with hydrazine

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A novel method for the deoxydehydration (DODH) of diols to alkenes has been developed by using hydrazine as a reductant *via* HOME (hydrazone as an organometallic equivalent) chemistry catalyzed by Ru-PNP complexes. This process avoids harsh reaction conditions, minimizes waste, and can be applied to a variety of diol compounds.
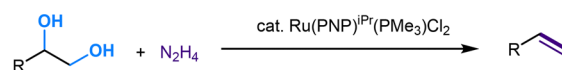
Diol and polyol structures are prevalent in natural compounds and biomolecules.[1] As renewable feedstocks, biomass-derived diols and polyols have become attractive alternatives to fossil fuels in the production of value-added chemicals. Dehydration, hydrogenation, and hydrogenolysis have received great attention for the conversion of polyols.[2–4] On the other hand, olefin serves as a fundamental building block in organic synthesis.[5,6] However, methods for directly converting diols into alkenes are very limited. Thus, the selective and efficient conversion of diols into olefins *via* a deoxydehydration (DODH) process holds the potential to facilitate a wide range of transformations in synthetic chemistry. Compared to traditional, well-developed strategies starting from alkene or carbonyl compounds,[7–10] the olefination derived from abundantly available alcohols *via* DODH offers a cost-effective pathway to achieve C=C linkage from an economic perspective. Currently, DODH methods are quite limited, and existing techniques require toxic and hazardous chemicals (phosphite or phosphine) and harsh reaction conditions.[11–14] Deoxydehydration (DODH) of diols toward alkenes with the extrusion of one oxygen atom and one equivalent of water molecule was exploited first by Corey *et al.*, in a reaction known as the Corey–Winter reaction.[15] However, the well-established Corey–Winter reaction usually involves prolonged heating at elevated temperatures and the use of phosphorylated reductive reagents (Scheme 1a).[16] In addition to the Corey–Winter reaction, the DODH of vicinal diols and polyols is typically performed using Re,[17] V,[18] or Mo[19] in combination

with phosphine, secondary alcohols including 3-octanol, or H_2 (for certain solid catalysts) as reductants.[17–19] This process often necessitates rigorous reaction conditions. Furthermore, they exhibit inefficacy in facilitating the DODH of substrates with complex structures (Scheme 1a).[13] According to HOME-chemistry (hydrazones as organometallic equivalents) and "borrowing hydrogen" strategies,[20–22] our group has developed a HOME-chemistry-based olefination strategy from two carbonyl compounds, which experienced an E1cb process.[23] Likewise, in 2018, Milstein's lab revealed a manganese-catalyzed dehydrogenative coupling of alcohols with hydrazine/hydrazone accompanied by a hydrogen transfer process to produce alkenes,[24] following the example of the Wittig-type and Julia-type olefination of alcohols.[25,26] Besides manganese, ruthenium enabled alcohols as carbonyl surrogates.[27] Moreover, both ruthenium and titanium demonstrated high activity in the conversion of alcohols to alkenes and alkanes as well.[28] Inspired by these works, we proposed that Ru could be a
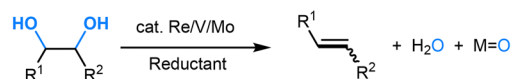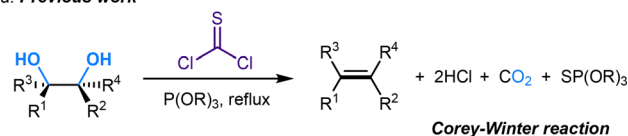
Department of Chemistry, and FRQNT Centre for Green Chemistry and Catalysis, McGill University, Montreal, Quebec H3A 0B8, Canada. E-mail: cj.li@mcgill.ca
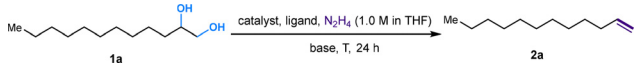† Siyi Luo, Chen-Chen Li, and Zihang Qiu contributed equally.

Scheme 1 Methods for the direct conversion of diols into olefins.

suitable catalyst for DODH with the assistance of hydrazine due to its versatile applications in coupling processes that involve alcohols. By leveraging the hydrogen transfer process, we developed a Ru-catalyzed DODH reaction enabled by hydrazine. Our approach offers the advantage of being operable under mild conditions with minimal environmental impact. It requires low temperatures and eliminates the need for gas, resulting in only N_2, H_2, and water as byproducts (Scheme 1b). Aromatic-substituted diols and aliphatic diols exhibit good performance within our method. Mechanistically, our approach involves a Ru-catalyzed dehydrogenation, followed by hydrazone formation and an intramolecular E1cb elimination. We started by investigating the reaction conditions of aliphatic diols and hydrazine. A set of ruthenium(II) catalysts was tested first in view of their high activity and good functional group tolerance in hydrazone chemistry involving alcohols as carbonyl surrogates in deoxygenation and Grignard-type reactions.[27,29,30] We utilized 1,2-dodecanediol as our model substrate, attributed to its simple structure and high boiling point. It should be noted that no desired product was detected in the reaction system catalyzed by $Ru(PPh_3)_3Cl_2$ with K_3PO_4 as the base at 100 °C (Table 1, entry 1). The combination of a ruthenium catalyst and an electron-rich phosphine ligand typically resulted in better performance in HOME chemistry.[31] Therefore, after the replacement of $Ru(PPh_3)_3Cl_2$ with more electron-rich $Ru(PMe_3)_4Cl_2$ or more stable $Ru(dppb)PPh_3Cl_2$ as a catalyst, 9% and 7% yields were observed, respectively (Table 1, entries 2 and 3). Then, different bidentate ligands were tested in the presence of [Ru(p-cymene)$Cl_2]_2$ (Table 1, entries 4, 5 and 6). Compared with dppe and DMEDA, the catalyst with more electron-rich and less sterically hindered dmpe showed better activity (Table 1, entry 5). In contrast, ruthenium catalysts with other bidentate ligands proved ineffective in this reaction system (Table 1, entries 7–10). Since the dehydrogenative coupling of alcohols and hydrazine has shown high efficiency with transition-metal pincer catalysts,[24,32,33] we investigated the efficiency of Ru, Mn and Ir-pincer catalysts (Table 1, entries 11–15).[34] The yield was tremendously attenuated with $Ru(PNP-2)Cl_2$ or $Ru(PNP-3)Cl_2$ (Table 1, entries 11 and 12). It was reported that the ruthenium-pincer complex with a monodentate phosphine ligand significantly depressed some potential side reactions, including hydrazone dimerization.[35] Thus, the highest yield was obtained by treating aliphatic diols with $Ru(PNP-3)(PMe_3)Cl_2$ (Table 1, entry 13). Organic bases such as DBU failed to furnish the final product (Table 1, entries 16). In contrast, K_3PO_4 (Table 1, entry 13) was the most effective base (Table 1, entries 17 and 18). Temperature has a significant influence on productivity as well. The yield demonstrated an increasing trend against temperature from 60 to 100 °C (Table 1, entries 13, 19 and 20) but decreased above 100 °C (Table 1, entry 21), probably due to the competing Wolff–Kishner reduction. Notably, when the catalyst loading of $Ru(PNP-3)(PMe_3)Cl_2$ was increased to 10 mol%, an even higher yield was detected at 80 °C (Table 1, entry 23) *versus* 100 °C (Table 1, entry 22). For aromatic diols, an alkyl side product was observed due to the hydrogen transfer ability of the

Table 1 Investigation of the reaction conditions on aliphatic diols

Entry	Catalyst	Ligand	Catalyst loading (mol%)	Base	T (°C)	2a (%)
1	$Ru(PPh_3)_3Cl_2$	—	5	K_3PO_4	100	0
2	$Ru(PMe_3)_4Cl_2$	—	5	K_3PO_4	100	9
3	$Ru(dppb)PPh_3Cl_2$	—	5	K_3PO_4	100	7
4	[Ru(p-cymene)$Cl_2]_2$	dppe	5	K_3PO_4	100	0
5	[Ru(p-cymene)$Cl_2]_2$	dmpe	5	K_3PO_4	100	36
6	[Ru(p-cymene)$Cl_2]_2$	DMEDA	5	K_3PO_4	100	0
7	Ru1	—	5	K_3PO_4	100	7
8	Ru2	—	5	K_3PO_4	100	0
9	Ru2	dmpe	5	K_3PO_4	100	20
10	$Ru(dppf)(en)Cl_2$	—	5	K_3PO_4	100	7
11	$Ru(PNP-2)Cl_2$	—	5	K_3PO_4	100	11
12	$Ru(PNP-3)Cl_2$	—	5	K_3PO_4	100	18
13	$Ru(PNP-3)(PMe_3)Cl_2$	—	5	K_3PO_4	100	64
14	$Mn(CO)_2(PNP-3)Br$	—	5	K_3PO_4	100	28
15	$Ir(PNP-3)H_2Cl$	—	5	K_3PO_4	100	6
16	$Ru(PNP-3)(PMe_3)Cl_2$	—	5	DBU	100	0
17	$Ru(PNP-3)(PMe_3)Cl_2$	—	5	K_2PO_3	100	49
18	$Ru(PNP-3)(PMe_3)Cl_2$	—	5	KO^{t}Bu	100	20
19	$Ru(PNP-3)(PMe_3)Cl_2$	—	5	K_3PO_4	60	42
20	$Ru(PNP-3)(PMe_3)Cl_2$	—	5	K_3PO_4	80	61
21	$Ru(PNP-3)(PMe_3)Cl_2$	—	5	K_3PO_4	120	51
22	$Ru(PNP-3)(PMe_3)Cl_2$	—	10	K_3PO_4	100	58
23	$Ru(PNP-3)(PMe_3)Cl_2$	—	10	K_3PO_4	80	71
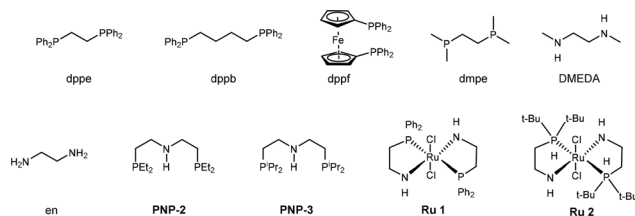
Reaction conditions: **1a** (40.5 mg, 0.2 mmol), $Ru(PNP-3)(PMe_3)Cl_2$ (11.1 mg, 0.02 mmol, 10 mol%), K_3PO_4 (31.8 mg, 0.15 mmol, 75 mol%), 1 M N_2H_4 solution in THF (0.5 mL, 0.5 mmol, 2.5 equiv.), 24 h at 80 °C, under N_2.

Ru catalyst. Thus, further investigation into the reaction conditions was necessary, and 1-phenyl-1,2-ethanediol was chosen as the model substrate. It should be noted that an 88% yield was detected at 70 °C when we shortened the reaction time to 16 h, decreased the catalyst loading to 5 mol% and the amount of base to 25 mol%, and added 5 μL DMSO as an additive (Table 2, entry 7). When the reaction was charged with the identical catalyst loading and base quantity used for aliphatic diols, the resulting yield was diminished in comparison (Table 2, entries 1 and 2). In addition, a decreased yield was noted when the reaction was carried out at temperatures either above or below 70 °C. (Table 2, entries 5 and 8). With other conditions unchanged, a control experiment was performed without DMSO, leading to a diminished yield (Table 2, entry 9).[30] We then applied the optimized reaction conditions to various compounds containing diols, giving rise to moderate to high yields in most cases. In the scope of aliphatic diols, aside from 1,2-dodecanediol affording a satisfactory 70% isolated yield (Table 3, **2a**), a phenyl ring (Table 3, **2b**), morpholine

Table 2 Investigation of the reaction conditions on aromatic diols

Entry	Catalyst	Catalyst loading (mol%)	K_3PO_3 (mol%)	T (°C)	DMSO (µL)	4a (%)
1	Ru(PNP-3)(PMe$_3$)Cl$_2$	10	75	80	5	34
2	Ru(PNP-3)(PMe$_3$)Cl$_2$	5	75	80	5	51
3	Ru(PNP-3)(PMe$_3$)Cl$_2$	5	100	80	5	43
4	Ru(PNP-3)(PMe$_3$)Cl$_2$	5	50	80	5	53
5	Ru(PNP-3)(PMe$_3$)Cl$_2$	5	25	80	5	58
6	Ru(PNP-3)(PMe$_3$)Cl$_2$	5	10	80	5	40
7	Ru(PNP-3)(PMe$_3$)Cl$_2$	5	25	70	5	88
8	Ru(PNP-3)(PMe$_3$)Cl$_2$	5	25	50	5	23
9	Ru(PNP-3)(PMe$_3$)Cl$_2$	5	25	70	—	68

Reaction conditions: **3a** (27.6 mg, 0.2 mmol), Ru(PNP-3)(PMe$_3$)Cl$_2$ (5.54 mg, 0.01 mmol, 5 mol%), K$_3$PO$_4$ (10.6 mg, 0.05 mmol, 25 mol%), 1 M N$_2$H$_4$ solution in THF (0.5 mL, 0.5 mmol, 2.5 equiv.), DMSO (5 µL, 0.07 mmol, 35 mol%), 16 h at 70 °C, under N$_2$.

(Table 3, **2c** and **2j**), methoxy group (Table 3, **2d**), alkene (Table 3, **2g**) and carbazole (Table 3, **2i**) were well tolerated. In contrast, lower reactivities were observed on substrates with substituted ethoxy benzenes (Table 3, **2e** and **2f**). Their products, **2e** and **2f**, were mixed with unreacted starting materials. Furthermore, meglumine exhibited a low reactivity, likely attributed to challenges in solubility and the incompatibility of amine functionalities (Table 3, **2h**). It is worth noting that complex mixtures were formed in the presence of an additional terminal hydroxy group or aldehyde functional group, including glyceraldehyde. This could be explained by the possible intermolecular olefination side reaction and other competing reactions. Furthermore, fructose is not suitable for the reaction, indicating that condensation of N$_2$H$_4$ did not occur on the internal carbonyl group, which serves as evidence for the mechanism that dehydrogenation likely takes place at the terminal OH group. As for aromatic diols, apart from the 88% yield detected in the conversion of 1-phenyl-1,2-ethanediol (Table 3, **4a**), the reaction is applicable to naphthalene (Table 3, **4d**) and halo-substituted aromatic rings (Table 3, **4b** and **4c**). Substrates bearing sterically hindered polycyclic aromatic hydrocarbons such as fluorene (Table 3, **4e**) and pyrene (Table 3, **4f**) delivered 40% and 30% yields, respectively. Besides, the reactivity was dramatically attenuated in the presence of the methylenedioxy group (Table 3, **4h**) compared to the alkoxy group (Table 3, **4g**). This likely occurs due to the conflicting electronic effect of *meta* and *para*-oxygen on the aromatic ring, slowing down the E1cB elimination process. An alternative explanation could be that oxygen may coordinate with ruthenium, thereby hindering the reaction pathway. In contrast, the substrate with the *para*-electron-donating benzyloxy and *tert*-butoxy groups exhibited high reactivity due to their weaker electronic effect and higher steric hindrance (Table 3, **4i** and **4j**). Other common functional groups were well tolerated (Table 3, **4m** and **4n**), with the exception of heterocycles

Table 3 Substrate scope of hydrazine-assisted DODH

[a] ^{1}H NMR yields were reported using mesitylene as an internal standard. [b] The reaction was conducted at 100 °C. [c] The reaction was conducted at 120 °C. Reaction conditions A for aliphatic diols: diol (0.2 mmol), Ru(PNP-3)(PMe$_3$)Cl$_2$ (11.1 mg, 0.02 mmol, 10 mol%), K$_3$PO$_4$ (31.8 mg, 0.15 mmol, 75 mol%), 1 M N$_2$H$_4$ solution in THF (0.5 mL, 0.5 mmol, 2.5 equiv.), 24 h at 80 °C, under an N$_2$ atmosphere. Yields of isolated products were reported unless otherwise noted. Reaction conditions B for aromatic diols: diol (0.2 mmol), Ru(PNP-3)(PMe$_3$)Cl$_2$ (5.54 mg, 0.01 mmol, 5.0 mol%), K$_3$PO$_4$ (10.6 mg, 0.05 mmol, 25 mol%), 1 M N$_2$H$_4$ solution in THF (0.5 mL, 0.5 mmol, 2.5 equiv.), DMSO (5 µL, 0.07 mmol, 35 mol%), 16 h at 70 °C, under an N$_2$ atmosphere. Yields of isolated products were reported unless otherwise noted.

(Table 3, **4k** and **4l**). Furthermore, the compound 1-(3-nitrophenyl)ethane-1,2-diol underwent a conversion to vinylaniline alongside a reduction process (Table 3, **4o**). Aromatic diols that featured an ester group (methyl 4-vinylbenzoate), a cyano group (4-vinylbenzonitrile), or an additional simple alkyl group at the 2-position (prop-1-en-2-ylbenzene) were found to be ineffective (see the SI). The reactions involving certain internal diols derived from their respective alkenes also proceeded effectively (Table 3, **4p** and **4q**). The 1-phenylpropane-1,2-diol-derived product **4p** was obtained in an 84% yield with a 93 : 7 *E* : *Z* ratio; however, **4q**, due to its steric hindrance, gave only a 29% yield with poor stereoselectivity.

In conclusion, we have disclosed for the first time a DODH process of terminal diols toward alkenes with hydrazine by using a ruthenium catalyst. Both aromatic and aliphatic diols were efficiently transformed, resulting in the release of benign water, hydrogen gas, and nitrogen gas as by-products. Compared to traditional DODH methodologies, this protocol exhibits high selectivity of terminal diols under mild reaction conditions. From a sustainability perspective, this DODH method sets up a promising avenue for the selective conversion

of biomass-based feedstocks into high-value olefin products. Therefore, further studies of the mechanism and synthetic utilities of this DODH strategy are ongoing.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the SI. Supplementary information: General information, experimental procedures, unsuccessful substrates, spectroscopic data, and copies of ^{1}H and ^{13}C NMR spectra of the products. See DOI: **https://doi.org/10.1039/d5cc04813c**.

Notes and references

1 K. Yamatsugu and M. Kanai, *Chem. Rev.*, 2023, **123**, 6793–6838.
2 P. Gallezot, *Chem. Soc. Rev.*, 2012, **41**, 1538–1558.
3 C. Xu, E. Paone, D. Rodríguez-Padrón, R. Luque and F. Mauriello, *Renewable Sustainable Energy Rev.*, 2020, **127**, 109852.
4 M. J. Climent, A. Corma and S. Iborra, *Green Chem.*, 2014, **16**, 516–547.
5 M. Schuster and S. Blechert, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2036–2056.
6 Z. Wu, M. Hu, J. Li, W. Wu and H. Jiang, *Org. Biomol. Chem.*, 2021, **19**, 3036–3054.
7 A. Maercker, *Org. React.*, 2004, **14**, 270–490.
8 R. H. Grubbs, *Angew. Chem., Int. Ed.*, 2006, **45**, 3760–3765.
9 L. F. Van Staden, D. Gravestock and D. J. Ager, *Chem. Soc. Rev.*, 2002, **31**, 195–200.
10 P. R. Blakemore, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2563–2585.
11 C. Boucher-Jacobs and K. M. Nicholas, *Deoxydehydration of polyols, Selective catalysis for renewable feedstocks and chemicals*, 2014, pp. 163–184.
12 A. R. Petersen and P. Fristrup, *Chem. – Eur. J.*, 2017, **23**, 10235–10243.
13 L. J. Donnelly, S. P. Thomas and J. B. Love, *Chem. – Asian J.*, 2019, **14**, 3782–3790.
14 N. N. Tshibalonza and J.-C. M. Monbaliu, *Green Chem.*, 2020, **22**, 4801–4848.
15 E. Block, *Org. React.*, 1984, **30**, 457–566.
16 E. E. López-López, J. A. Pérez-Bautista, F. Sartillo-Piscil and B. A. Frontana-Uribe, *Beilstein J. Org. Chem.*, 2018, **14**, 547–552.
17 (*a*) L. Sandbrink, E. Klindtworth, H.-U. Islam, A. M. Beale and R. Palkovits, *ACS Catal.*, 2016, **6**, 677–680; (*b*) Y. Nakagawa, S. Tazawa, T. Wang, M. Tamura, N. Hiyoshi, K. Okumura and K. Tomishige, *ACS Catal.*, 2018, **8**, 584–595; (*c*) K. Yamaguchi, J. Cao, M. Betchaku, Y. Nakagawa, M. Tamura, A. Nakayama, M. Yabushita and K. Tomishige, *ChemSusChem.*, 2022, **15**, e202102663.
18 A. R. Petersen, L. B. Nielsen, J. R. Dethlefsen and P. Fristrup, *ChemCatChem*, 2018, **10**, 769–778.
19 J. R. Dethlefsen, D. Lupp, B. C. Oh and P. Fristrup, *ChemSusChem*, 2014, **7**, 425–428.
20 C.-J. Li, *Pure Appl. Chem.*, 2023, **95**, 465–474.
21 X.-J. Dai, C.-C. Li and C.-J. Li, *Chem. Soc. Rev.*, 2021, **50**, 10733–10742.
22 C.-J. Li, J. Huang, X.-J. Dai, H. Wang, N. Chen, W. Wei, H. Zeng, J. Tang, C. Li and D. Zhu, *Synlett*, 2019, 1508–1524.
23 W. Wei, X.-J. Dai, H. Wang, C. Li, X. Yang and C.-J. Li, *Chem. Sci.*, 2017, **8**, 8193–8197.
24 U. K. Das, S. Chakraborty, Y. Diskin-Posner and D. Milstein, *Angew. Chem., Int. Ed.*, 2018, **57**, 13444–13448.
25 D. Srimani, G. Leitus, Y. Ben-David and D. Milstein, *Angew. Chem., Int. Ed.*, 2014, **53**, 11092–11095.
26 E. Khaskin and D. Milstein, *Chem. Commun.*, 2015, **51**, 9002–9005.
27 C.-C. Li, H. Wang, M. M. Sim, Z. Qiu, Z.-P. Chen, R. Z. Khaliullin and C.-J. Li, *Nat. Commun.*, 2020, **11**, 1–9.
28 (*a*) B. Sardar, N. Biswas and D. Srimani, *Organometallics*, 2023, **42**, 55–61; (*b*) D. Cao, S. Xia, L.-J. Li, H. Zeng and C.-J. Li, *ACS Catal.*, 2024, **14**, 14966–14973; (*c*) S. Stanowski, K. M. Nicholas and R. S. Srivastava, *Organometallics*, 2012, **31**, 515–518; (*d*) S. Murru, K. M. Nicholas and R. S. Srivastava, *J. Mol. Catal., A*, 2012, **363**, 460–464; (*e*) H. R. Dieguez, A. Lopez, V. Domingo, J. F. Arteaga, J. A. Dobado, M. M. Herrador, J. F. Quilez del Moral and A. F. Barrero, *J. Am. Chem. Soc.*, 2010, **132**, 254–259.
29 C.-C. Li, J. Kan, Z. Qiu, J. Li, L. Lv and C.-J. Li, *Angew. Chem., Int. Ed.*, 2020, **59**, 4544–4549.
30 X.-J. Dai and C.-J. Li, *J. Am. Chem. Soc.*, 2016, **138**, 5433–5440.
31 X.-J. Dai, H. Wang and C.-J. Li, *Angew. Chem., Int. Ed.*, 2017, **56**, 6302–6306.
32 U. K. Das, Y. Ben-David, Y. Diskin-Posner and D. Milstein, *Angew. Chem., Int. Ed.*, 2018, **57**, 2179–2182.
33 J. O. Bauer, G. Leitus, Y. Ben-David and D. Milstein, *ACS Catal.*, 2016, **6**, 8415–8419.
34 J.-L. Huang, X.-J. Dai and C.-J. Li, *Eur. J. Org. Chem.*, 2013, 6496–6500.
35 S. Luo, H. D. M. Pham, C.-C. Li, Z. Qiu, R. Cheng, R. Z. Khaliullin and C.-J. Li, *Org. Lett.*, 2024, **26**, 3004–3009.