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Rh-Catalyzed Asymmetric Hydrogenation of 1,2-Dicyanoalkenes

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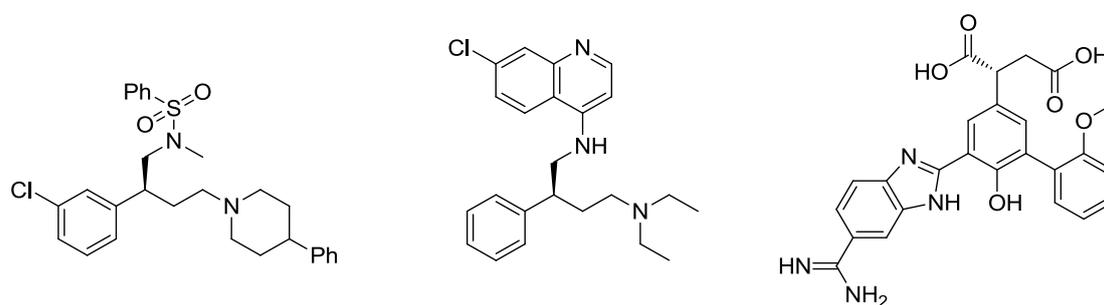


Abstract: A highly efficient enantioselective hydrogenation of 1,2-dicyanoalkenes catalyzed by the complex of rhodium and f-spiroPhos has been developed. A series of 1,2-dicyanoalkenes were successfully hydrogenated to the corresponding chiral 1,2-dicyanoalkanes under mild conditions with excellent enantioselectivities (up to 98% ee). This methodology provides efficient access to the asymmetric synthesis of chiral diamines.

Introduction

Chiral 1,2-dicyanoalkanes are an important class of compounds in organic synthesis and high valuable intermediates for synthesis of many biologically active compounds and pharmaceuticals (Figure 1).¹ They have been regarded as versatile synthetic intermediates due to their readily conversions to other useful chiral building blocks, such as chiral diamines,² dicarboxylic acids,³ diamides⁴ and various heterocycles (pyrrolidines, succinimides, and pyrroles),⁵ which are highly valuable structures for natural and biologically active molecules. Although some significant approaches have been developed in the synthesis of racemic 1,2-dicyanoalkanes, such as the

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4 Michael addition of lithium cyanide to vinyl sulfones,⁶ 1,2-dicyanation of alkynes followed by the
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7 reduction of the corresponding dicyanoalkenes,⁷ and the tandem double Michael addition of
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10 trimethylsilyl cyanide to nitroalkenes,⁸ there is no asymmetric synthesis of chiral
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13 1,2-dicyanoalkanes reported up to now. Therefore, development of an efficient method for
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16 asymmetric catalytic synthesis of chiral 1,2-dicyanoalkanes is of importance and remains
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19 challenging.

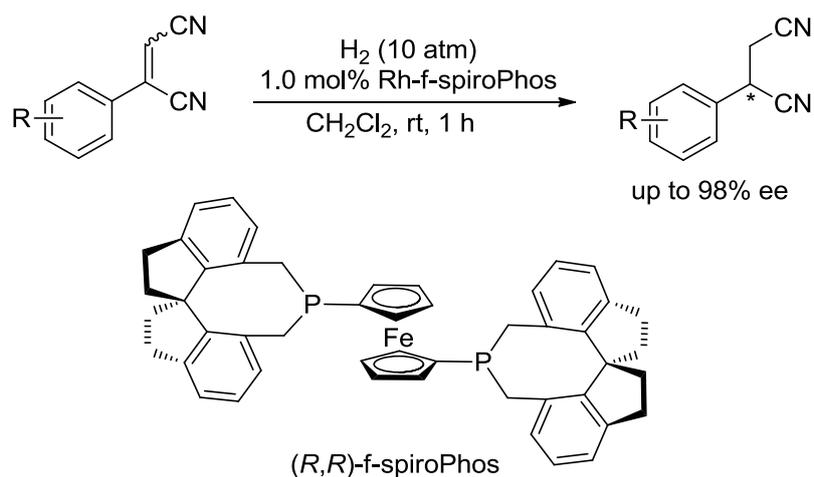


31 **Figure 1.** Key Structural Elements in Chiral Pharmaceuticals and Biologically Active Compounds
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33 Derived from Chiral 1,2-Dicyanoalkanes.
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36 Asymmetric catalytic hydrogenation has been developed as one of the most efficient,
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38 environmentally friendly, atom-economic approaches to generate enantiomerically enriched
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40 products from prochiral substrates,⁹ and great progress on its application in industry has also been
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42 made.¹⁰ Many transition-metal catalysts were developed and exhibited high activity and
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44 enantioselectivity in the asymmetric hydrogenation of various prochiral substrates including
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46 olefins, ketones and imines.⁹ However, to the best of our knowledge, the asymmetric
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48 hydrogenation of 1,2-dicyanoalkenes for straightforward synthesis of the corresponding chiral
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50 1,2-dicyanoalkanes has not yet been explored so far.¹¹ The challenges imposed by both the linear
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60 geometry of the cyano group, which keeps a coordinated catalyst away from the C=C bond, and
the strong binding affinity to transition-metal complexes resulting in catalyst deactivation.^{11c, 12}

Thus, the asymmetric hydrogenation of 1,2-dicyanoalkenes remains challenging and efficient catalysts suitable for this class of substrates are scarce and highly desirable.

Recently, we reported the asymmetric hydrogenation of nitroolefins, imines, unsaturated nitriles and carboxylic acids using f-spiroPhos, a chiral ferrocenyl diphosphine ligand containing the privileged spirobiindane skeleton developed by Zhou and coworkers,¹³ and excellent enantioselectivity and activity were achieved.¹⁴ Herein, we wish to tackle the challenging 1,2-dicyanoalkene substrates in asymmetric hydrogenation and report the first, highly efficient and enantioselective hydrogenation of 1,2-dicyanoalkenes, which provides a straightforward route to prepare chiral 1,2-dicyanoalkanes (Scheme 1).



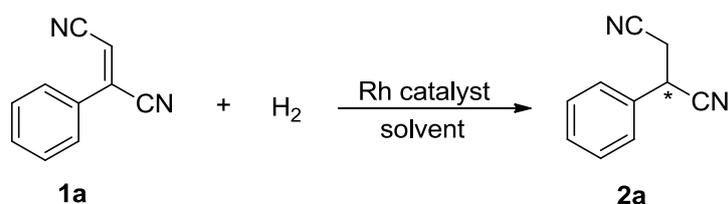
Scheme 1. Rh-Catalyzed Asymmetric Hydrogenation of 2-Aryl-1,2-dicyanoalkenes.

Results and Discussion

The investigation initially began with the hydrogenation of (*E*)-2-phenyl-1,2-dicyanoalkene **1a** as the model substrate under 10 atm of H₂ in CH₂Cl₂ at 40 °C for 1 hour using the catalyst generated in situ by [Rh(COD)Cl]₂ and (*R,R*)-f-spiroPhos. Although a full conversion was observed, only moderate enantioselectivity, 77% ee was achieved. To our delight, by decreasing the reaction temperature to 25 °C the enantioselectivity could be dramatically increased to 90% ee

without any erosion of conversion (Table 1, entries 1 and 2). However, a lower temperature would result in an incomplete conversion and decreased enantioselectivity (entry 3). Subsequently, several other chiral diphosphorus ligands illustrated in figure 2 including (*S*)-BINAP, (*S,R*)-DuanPhos, (*R*)-JosiPhos, (*S*)-f-Binaphane and (*R*)-DM-SegPhos were evaluated and the results revealed that all of them exhibited extremely lower activities and moderate enantioselectivities in this reaction (entries 4–8). The solvent effect was also investigated and it had significant influence on the conversion and enantioselectivity. While in THF this hydrogenation could accomplish with moderate enantioselectivity (entry 9), in some other solvents such as DME, 1,4-dioxane and toluene both incomplete conversions and lower enantioselectivities were provided (entries 10–12). The polar solvent MeOH was not suitable for this transformation and extremely low activity was observed (entry 13).

Table 1. Rh-Catalyzed Asymmetric Hydrogenation of (*E*)-2-Phenyl-1,2-dicyanoalkene (1a), Optimizing the Reaction Conditions.^a



entry	ligand	solvent	T (°C)	conv. (%) ^b	ee (%) ^c
1	(<i>R,R</i>)-f-spiroPhos	CH ₂ Cl ₂	40	>99	77
2	(<i>R,R</i>)-f-spiroPhos	CH ₂ Cl ₂	25	>99	90
3	(<i>R,R</i>)-f-spiroPhos	CH ₂ Cl ₂	0	65	82
4	(<i>S</i>)-f-Binaphane	CH ₂ Cl ₂	25	28	52
5	(<i>S</i>)-Binap	CH ₂ Cl ₂	25	trace	ND
6	(<i>R</i>)-DM-SegPhos	CH ₂ Cl ₂	25	3	41

7	(<i>S,R</i>)-DuanPhos	CH ₂ Cl ₂	25	6	27
8	(<i>R</i>)-JosiPhos-1	CH ₂ Cl ₂	25	12	63
9	(<i>R,R</i>)-f-spiroPhos	THF	25	>99	71
10	(<i>R,R</i>)-f-spiroPhos	toluene	25	45	54
11	(<i>R,R</i>)-f-spiroPhos	DME	25	95	71
12	(<i>R,R</i>)-f-spiroPhos	dioxane	25	77	34
13	(<i>R,R</i>)-f-spiroPhos	MeOH	25	trace	ND

^a Unless otherwise mentioned, all reactions were carried out with a [Rh(COD)Cl]₂/(*R,R*)-f-spiroPhos/substrate ratio of 0.5 : 1.1 : 100, 10 atm of H₂, 1 h. ^b Determined by ¹H NMR spectroscopy or GC analysis. ^c Determined by HPLC analysis using a chiral stationary phase or chiral GC analysis.

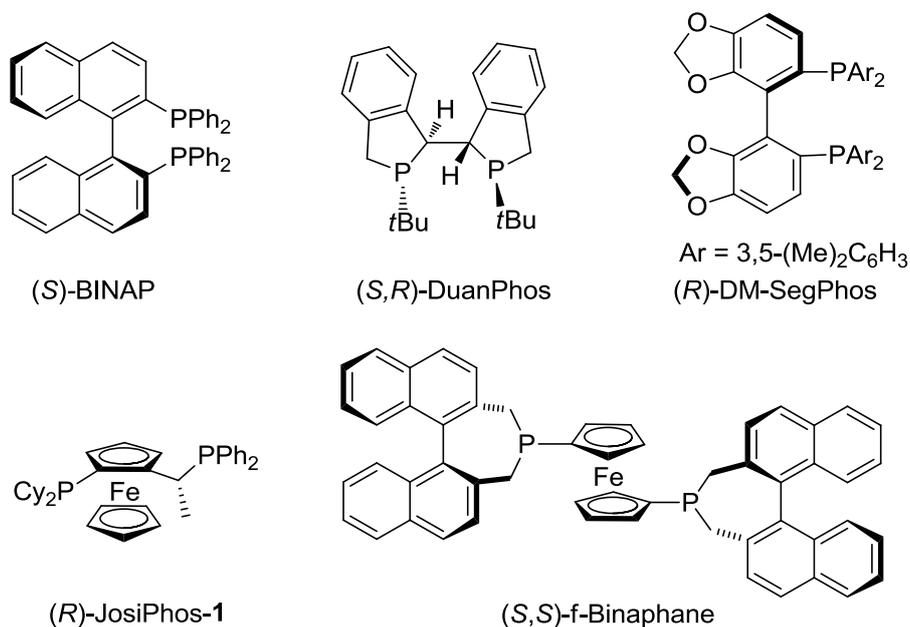
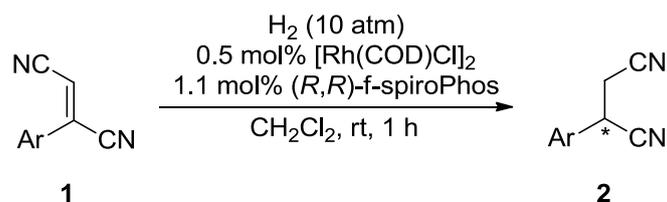


Figure 2. Structures of the Ligands Screened.

Encouraged by the promising result obtained in the hydrogenation of (*E*)-2-phenyl-1,2-dicyanoalkene **1a**, we then prepared a variety of (*E*)-1,2-dicyanoalkene **1** and applied them to the asymmetric hydrogenation under the optimized reaction conditions. As the

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 4 results revealed in table 2, the electronic properties of the substituent at the *meta*- or *para*-position
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 6 of the aromatic ring had no obvious influence on the enantioselectivity. For example, substrates
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 8 bearing regardless of electron-withdrawing substituents (F, **1b** and Br, **1c**) or electron-donating
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 10 substituents (MeO, **1d** and Me, **1e**) at the *para*-position of the aromatic ring could be smoothly
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 12 hydrogenated to produce the corresponding chiral 1,2-dicyanoalkanes with full conversions and
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 14 high enantioselectivities (entries 2–5). Despite a slightly higher hydrogen pressure needed for the
 15
 16 full conversion, substrates with a MeO (**1i**) or Me group (**1j**) at the *ortho*-position as well as the
 17
 18 1-naphthyl substrate **1k** provided much higher enantioselectivities, up to 98% ee, which could
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 20 presumably be attributed to the steric hindrance (entries 9–11). However, electron-withdrawing
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 22 substituents at the *ortho*-position, such as F or Cl group, resulted in lower enantioselectivities, 88%
 23
 24 ee (entry 7–8). Notably, the alkyl substrate **1l** could be smoothly hydrogenated to provide the
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 26 corresponding product **2l** with 96% ee (entry 12).
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36 **Table 2. Rh-Catalyzed Asymmetric Hydrogenation of (*E*)-2-Aryl-1,2-dicyanoalkene **1**.^a**



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entry	R	product	con (%) ^b	ee (%) ^c
1	(<i>E</i>)-C ₆ H ₅ (1a)	2a	>99(98%)	90
2 ^d	(<i>E</i>)-4-FC ₆ H ₄ (1b)	2b	>99(99%)	89
3 ^e	(<i>E</i>)-4-BrC ₆ H ₄ (1c)	2c	>99(98%)	88
4 ^d	(<i>E</i>)-4-MeOC ₆ H ₄ (1d)	2d	>99(97%)	86
5	(<i>E</i>)-4-MeC ₆ H ₄ (1e)	2e	>99(99%)	93
6 ^d	(<i>E</i>)-3-MeC ₆ H ₄ (1f)	2f	>99(97%)	90
7 ^f	(<i>E</i>)-2-ClC ₆ H ₄ (1g)	2g	>99(98%)	88

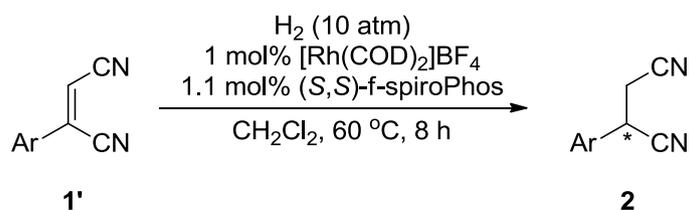
8 ^f	(<i>E</i>)-2-FC ₆ H ₄ (1h)	2h	>99(97%)	89
9 ^d	(<i>E</i>)-2-MeOC ₆ H ₄ (1i)	2i	>99(96%)	96
10 ^d	(<i>E</i>)-2-MeC ₆ H ₄ (1j)	2j	>99(96%)	98
11 ^d	(<i>E</i>)-1-naphthyl (1k)	2k	>99(99%)	93
12	(<i>E</i>)- ⁿ Hexyl (1l)	2l	>99(98%)	96

^a Unless otherwise mentioned, all reactions were carried out at a [Rh(COD)Cl]₂/(*R,R*)-f-spiroPhos/substrate ratio of 0.5:1.1:100 in CH₂Cl₂ at 10 atm of H₂ and 25 °C for 1 h. ^b Conversion, determined by ¹H NMR spectroscopy or GC analysis; data in parentheses are isolated yields. ^c Determined by chiral GC analysis or HPLC analysis. ^d 7 h, 30 atm of H₂. ^e 24 h, 30 atm of H₂. ^f 12 h, 50 atm of H₂.

It was found that the *Z*-isomers of 1,2-dicyanoalkenes were also obtained in high yields together with the *E*-isomers in the synthesis of the substrates. We further investigated the asymmetric hydrogenation of (*Z*)-2-phenyl-1,2-dicyanoalkene **1a'** using Rh/(*R,R*)-f-spiroPhos catalyst under the optimized reaction conditions. However, only moderate enantioselectivity, 73% ee, was obtained with an opposite configuration, which indicated the geometric structure of the substrate had an obvious effect on the coordination of the C=C double bond to the metal center. (*Z*)- and (*E*)-Substrates coordinated to the catalyst from the opposite enantioface, which resulted in the hydrogenation products with opposite configuration.^{11d,14e-g} According to the research of halide effects in rhodium catalysts by Lautens and Fagnou,¹⁵ we changed the metal precursor with the [Rh(COD)₂]BF₄. Gratifyingly, the ee value of the hydrogenation product **2a'** was increased to 90 % still with a complete conversion (table 3, entry 1). Based on this promising result, a series of (*Z*)-1,2-dicyanoalkene **1'** were successfully hydrogenated to afford the desired products with comparable results with those obtained from (*E*)-substrates. As the results showed in table 3, the

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4 electronic properties of substituents on the phenyl ring of the substrate had a very little effect on
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7 the enantioselectivities. Electron-donating substituents at the identical position of phenyl ring
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10 generally could give a little higher enantioselectivity than electron-withdrawing ones. For instance,
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12 the substrates with a Me or MeO at *para*-position of the phenyl ring provided 91% ee, whereas the
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14 substrates bearing an electron-withdrawing F or Br substituent afforded the corresponding
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16 products with 89% and 88% ee, respectively (entries 2–5). The sterically hindered
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18 *ortho*-substituted substrates, **1h'**–**1k'**, could also be completely hydrogenated with higher
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20 enantioselectivities of up to 95% ee (entries 8, 10 and 11), compared with those provided by the
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22 corresponding *meta*- or *para*-substituted substrates. Both the 1-naphthyl and 2-naphthyl substrate
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24 **1l'** and **1m'** afforded the products **2l'** and **2m'** with high ee values. However, the 2-furyl and
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26 2-thienyl substrates **1n'** and **1o'** only provided moderate enantioselectivities, 65% and 57% ee,
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28 respectively (entries 14 and 15).
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36 **Table 3. Rh-Catalyzed Asymmetric Hydrogenation of (Z)-2-Aryl-1,2-dicyanoalkene 1'.**^a



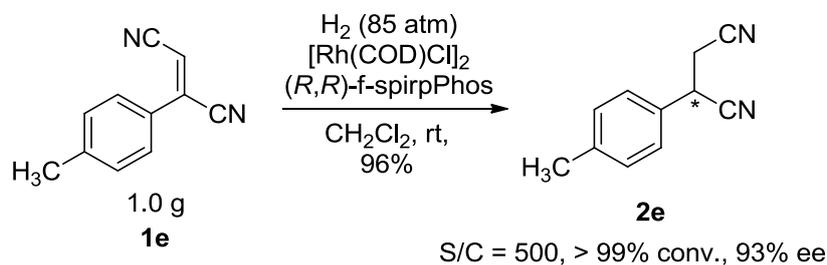
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entry	R	product	con (%) ^b	ee (%) ^c
1	(Z)-C ₆ H ₅ (1a')	2a'	>99(98%)	90
2	(Z)-4-FC ₆ H ₄ (1b')	2b'	>99(97%)	89
3	(Z)-4-BrC ₆ H ₄ (1c')	2c'	>99(99%)	88
4	(Z)-4-MeOC ₆ H ₄ (1d')	2d'	>99(98%)	91
5	(Z)-4-MeC ₆ H ₄ (1e')	2e'	>99(98%)	91
6	(Z)-3-MeC ₆ H ₄ (1f')	2f'	>99(99%)	88
7	(Z)-3-MeOC ₆ H ₄ (1g')	2g'	>99(99%)	87

8	(<i>Z</i>)-2-MeOC ₆ H ₄ (1h')	2h'	>99(98%)	92
9 ^d	(<i>Z</i>)-2-ClC ₆ H ₄ (1i')	2i'	>99(99%)	85
10 ^e	(<i>Z</i>)-2-MeC ₆ H ₄ (1j')	2j'	>99(98%)	95
11	(<i>Z</i>)-2-FC ₆ H ₄ (1k')	2k'	>99(98%)	90
12 ^e	(<i>Z</i>)-1-naphthyl (1l')	2l'	>99(99%)	86
13	(<i>Z</i>)-2-naphthyl (1m')	2m'	>99(98%)	92
14 ^e	(<i>Z</i>)-2-furyl (1n')	2n'	>99(98%)	65
15 ^e	(<i>Z</i>)-2-thienyl (1o')	2o'	>99(96%)	57

^a Unless otherwise mentioned, all reactions were carried out at a [Rh(COD)₂]BF₄/(*S,S*)-f-spiroPhos/substrate ratio of 1.0:1.1:100 in CH₂Cl₂ at 10 atm of H₂ and 60 °C for 8 h. ^b Conversion, determined by ¹H NMR spectroscopy or GC analysis; data in parentheses are isolated yields. ^c Determined by chiral GC analysis or HPLC analysis. ^d 36 h, 50 atm of H₂, 60 °C. ^e 24 h, 50 atm of H₂, 60 °C.

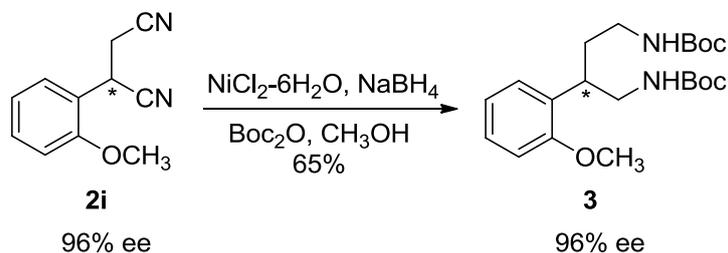
In addition, the hydrogenation on a gram scale using a lower catalyst loading was also explored. Using a loading of 0.2 mol% Rh-(*R,R*)-f-spiroPhos catalyst the asymmetric hydrogenation of (*E*)-**1e** could still be accomplished to produce the product **2e** with maintained enantioselectivity, 93% ee (Scheme 2).



Scheme 2. Asymmetric Hydrogenation of the Substrate **1e** under Lower Catalyst Loading.

Finally, we attempted to apply this method to the asymmetric synthesis of chiral 1,4-diamines, which was regarded as a very important class of building blocks in pharmaceutical synthesis and used extensively as chiral auxiliaries and catalysts.¹⁶ The hydrogenation product **2i** with 96% ee

value could be readily further reduced to afford the chiral 1,4-diamine with unchanged excellent enantioselectivity (Schem 3).¹⁷



Scheme 3. Synthesis of 1,4-Diamine **3** from the Hydrogenation Product **2i**.

Conclusions

In conclusion, we have developed a highly enantioselective hydrogenation of a series of 1,2-dicyanoalkenes including both *E* and *Z*-isomers to produce chiral 1,2-dicyanoalkanes with excellent enantioselectivities (up to 98% ee) and good activity (TON up to 500) using the complex of rhodium and *f*-spiroPhos as catalyst under mild reaction conditions. Moreover, this method is also successfully applied to the synthesis of a chiral 1,4-diamine with an excellent enantioselectivity.

Experimental Section

General Information: All the air or moisture sensitive reactions and manipulations were performed by using standard Schlenk techniques and in a nitrogen-filled glovebox. DME, THF, 1,4-dioxane and toluene were distilled from sodium benzophenone ketyl. CH_2Cl_2 was distilled from calcium hydride. Anhydrous MeOH was distilled from magnesium. ^1H NMR spectra were recorded on a 400 MHz spectrometer. ^{13}C NMR (proton-decoupled) spectra were obtained at 100 MHz. CDCl_3 was the solvent used for the NMR analysis, with tetramethylsilane as the internal standard. Chemical shifts were reported upfield to TMS (0.00 ppm) for ^1H NMR. Optical rotation

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4 was determined using a polarimeter. HRMS were recorded on a mass spectrometer with APCI or
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7 ESI.

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10 **General procedure for the synthesis of compound 1:** Under a nitrogen atmosphere benzoyl
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12 chloride (25.0 mmol, 1.0 equiv) was slowly added at room temperature to a stirred suspension of
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14 copper (I) cyanide (50.0 mmol 2.0 equiv) in dry acetonitrile (80 mL). After about 4 hours of
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16 refluxing the resulting clear solution was cooled to room temperature and concentrated in vacuo.
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18 The residue was washed with ether, filtrated and concentrated in vacuo again. After additional
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20 distillation (0.12 mbar, 65 – 80 °C) the product benzoyl cyanide was obtained as a colorless
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22 solid.¹⁸ The corresponding benzoyl cyanide (9.1 mmol) was placed in a 100 mL round bottom flask,
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24 then Ph₃P=CHCN (13.59 mmol, 1.5 equiv) and toluene (20 mL) was added. The reaction mixture
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26 was stirred at 80 °C until no starting material was detected by TLC. Then the reaction mixture was
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28 cooled to room temperature and concentrated in vacuo. The residue was purified by
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30 chromatography on silica gel (PE:EA = 50:1 – 5:1) to give compound **1**.¹⁷

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39 **2-Phenylfumaronitrile (1a):** Purification by column chromatography (PE:EA = 10:1) afforded the
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41 product as a white solid; MP: 48-50 °C; 0.98 g, yield: 28%; ¹H NMR (400 MHz, CDCl₃) δ =
42
43 7.94-7.91 (m, 2H), 7.59-7.52 (m, 3H), 6.14 (s, 1H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 133.7,
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45 133.3, 130.3, 128.8, 116.9, 115.2, 108.0; TOF-HRMS Calcd. for C₁₀H₅N₂ [M-H⁺]: 153.0458,
46
47 found 153.0458.^{7a}

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52 **2-(4-Fluorophenyl)fumaronitrile (1b):** Purification by column chromatography (PE:EA = 10:1)
53
54 afforded the product as a white solid; MP: 64-66 °C; 0.91 g, yield: 30%; ¹H NMR (400 MHz,
55
56 CDCl₃) δ = 7.89-7.86 (m, 2H), 7.18-7.13 (m, 2H), 6.05 (s, 1H). ¹³C{¹H}NMR (CDCl₃, 100 MHz)
57
58 δ: 164.9 (d, ¹J_{C-F} = 255.0 Hz), 131.8, 130.7, 130.6, 126.0, 125.9, 116.9, 116.7, 116.0, 114.5, 107.1.
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4 TOF-HRMS Calcd. for $C_{10}H_6N_2F$ [$M+H^+$]: 173.0509, found 173.0511.

5
6
7 **2-(4-Bromophenyl)fumaronitrile (1c)**: Purification by column chromatography (PE:EA = 50:1)

8
9 afforded the product as a white solid; MP: 62-64 °C; 1.05 g, yield: 30%; 1H NMR (400 MHz,

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11 $CDCl_3$) δ = 7.79-7.77 (d, J = 8.8 Hz, 2H), 7.68-7.66 (d, J = 8.8 Hz, 2H), 6.17(s, 1H).

12
13 $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ : 132.8, 131.9, 129.5, 128.6, 127.7, 115.9, 114.4, 107.9.

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16
17 TOF-HRMS Calcd. for $C_{10}H_4N_2Br$ [$M-H^+$]: 230.9563, found 230.9564.^{7b}

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19
20 **2-(4-Methoxyphenyl)fumaronitrile (1d)**: Purification by column chromatography (PE:EA = 10:1)

21
22 afforded the product as a white solid; MP: 82-86 °C; 1.05 g, yield: 35%; 1H NMR (400 MHz,

23
24 $CDCl_3$) δ = 7.93-7.91 (m, 2H), 7.00-6.98 (m, 2H), 5.94 (s, 1H), 3.87 (s, 3H). $^{13}C\{^1H\}$ NMR

25
26
27 ($CDCl_3$, 100 MHz) δ : 163.6, 132.7, 130.8, 122.9, 117.1, 115.9, 115.4, 104.3, 56.2. TOF-HRMS

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31 Calcd. for $C_{11}H_9N_2O$ [$M+H^+$]: 185.0709, found 185.0709.^{7b}

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33 **2-(*p*-Tolyl)fumaronitrile (1e)**: Purification by column chromatography (PE:EA = 20:1) afforded

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35 the product as light yellow solid; MP: 94-97 °C; 0.81 g, yield: 27%; 1H NMR (400 MHz, $CDCl_3$) δ

36
37 = 7.83 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 6.06 (s, 1H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR

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40 ($CDCl_3$, 100 MHz) δ : 143.8, 132.8, 130.0, 128.1, 127.1, 116.4, 114.9, 106.0, 105.9, 21.6.

41
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44 TOF-HRMS Calcd. for $C_{11}H_9N_2$ [$M+H^+$]: 169.0760, found 169.0759.

45
46
47 **2-(*m*-Tolyl)fumaronitrile (1f)**: Purification by column chromatography (PE:EA = 10:1) afforded

48
49 the product as a light yellow solid; MP: 75-79 °C; 0.84 g, yield: 28%; 1H NMR (400 MHz, $CDCl_3$)

50
51 δ = 7.74-7.69 (m, 2H), 7.44-7.37 (m, 2H), 6.10 (s, 1H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100

52
53
54 MHz) δ : 140.4, 134.3, 134.2, 130.4, 130.1, 127.9, 124.4, 115.3, 114.8, 107.6, 21.9. TOF-HRMS

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56
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58 Calcd. for $C_{11}H_9N_2$ [$M+H^+$]: 169.0760, found 169.0758.

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60 **2-(2-Chlorophenyl)fumaronitrile (1g)**: Purification by column chromatography (PE:EA = 20:1)

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2
3
4 afforded the product as light yellow liquid; 0.78 g, yield: 26%; ^1H NMR (400 MHz, CDCl_3) δ =
5
6 7.55-7.42 (m, 4H), 6.36 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 132.9, 132.8, 131.9, 130.7,
7
8 130.5, 129.0, 127.7, 115.1, 114.8, 113.2. TOF-HRMS Calcd. for $\text{C}_{10}\text{H}_6\text{N}_2\text{Cl}$ [$\text{M}+\text{H}^+$]: 189.0214,
9
10 found 189.0215.
11

12
13
14 **2-(2-Fluorophenyl)fumaronitrile (1h)**: Purification by column chromatography (PE:EA = 30:1)
15
16 afforded the product as a white solid; MP: 88-90 °C; 0.63 g, yield: 21%; ^1H NMR (400 MHz,
17
18 CDCl_3) δ = 7.54-7.46 (m, 2H), 7.25-7.14 (m, 2H), 6.24-6.23 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100
19
20 MHz) δ : 160.8 (d, $^1J_{\text{C-F}} = 255.0$ Hz), 134.3, 134.2, 130.8, 128.4, 125.4, 118.2, 118.1, 117.3, 117.1,
21
22 114.6, 113.9, 112.6, 112.4. TOF-HRMS Calcd. for $\text{C}_{10}\text{H}_6\text{N}_2\text{F}$ [$\text{M}+\text{H}^+$]: 173.0509, found 173.0511.
23
24
25

26
27
28 **2-(2-Methoxyphenyl)fumaronitrile (1i)**: Purification by column chromatography (PE:EA = 10:1)
29
30 afforded the product as a white solid; MP: 58-60 °C; 1.14 g, yield: 38%; ^1H NMR (400 MHz,
31
32 CDCl_3) δ = 7.53-7.48 (m, 2H), 7.09-7.00 (m, 2H), 6.17 (s, 1H), 3.94 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR
33
34 (CDCl_3 , 100 MHz) δ : 157.0, 133.7, 131.1, 130.1, 121.1, 119.3, 116.1, 114.2, 111.9, 111.8, 55.7.
35
36 TOF-HRMS Calcd. for $\text{C}_{11}\text{H}_9\text{N}_2\text{O}$ [$\text{M}+\text{H}^+$]: 185.0709, found 185.0708.^{7b}
37
38

39
40
41 **2-(*o*-Tolyl)fumaronitrile (1j)**: Purification by column chromatography (PE:EA = 20:1) afforded
42
43 the product as light yellow liquid; 0.9 g, yield: 30%; ^1H NMR (400 MHz, CDCl_3) δ = 7.43-7.31
44
45 (m, 4H), 6.27 (s, 1H), 2.45 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 136.2, 134.2, 131.5, 131.3,
46
47 129.7, 128.9, 126.7, 115.5, 113.6, 19.6. TOF-HRMS Calcd. for $\text{C}_{11}\text{H}_9\text{N}_2$ [$\text{M}+\text{H}^+$]: 169.0760, found
48
49 169.0759.
50
51

52
53
54 **2-(Naphthalen-1-yl)fumaronitrile (1k)**: Purification by column chromatography (PE:EA = 20:1)
55
56 afforded the product as a light yellow solid; MP: 128-131 °C; 0.78 g, yield: 26%; ^1H NMR (400
57
58 MHz, CDCl_3) δ = 8.06-8.04 (m, 1H), 7.96-7.94 (m, 2H), 7.66-7.57 (m, 4H), 6.45 (s, 1H),
59
60

¹³C{¹H}NMR (CDCl₃, 100 MHz) δ : 133.7, 133.5, 132.6, 129.6, 129.1, 128.3, 128.0, 127.6, 127.3, 125.2, 123.6, 116.1, 114.3, 113.7. TOF-HRMS Calcd. for C₁₄H₉N₂ [M+H⁺]: 205.0760, found 205.0760.

2-Hexylfumaronitrile (11): Purification by column chromatography (PE:EA = 20:1) afforded the product as light yellow liquid; 0.25 g, yield: 21%; ¹H NMR (400 MHz, CDCl₃) δ = 5.96 (s, 1H), 2.59 (t, *J* = 7.44 Hz, 2H), 1.62-1.69 (m, 2H), 1.33-1.39 (m, 6H), 0.88-0.91 (m, 3H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ : 137.6, 116.7, 114.0, 112.7, 34.2, 31.8, 28.8, 28.0, 22.9, 14.5. The analytical data are consistent with the literature.^{7a}

2-Phenylmaleonitrile (1a'): Purification by column chromatography (PE:EA = 5:1) afforded the product as a white solid; MP: 90-92 °C; 2.03 g, yield: 58%; ¹H NMR (400 MHz, CDCl₃) δ = 7.67-7.65 (m, 2H), 7.58-7.53 (m, 1H), 7.51-7.50 (m, 2H), 6.39 (s, 1H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ : 133.5, 132.9, 129.9, 129.7, 126.7, 114.7, 114.2, 107.4. TOF-HRMS Calcd. for C₁₀H₅N₂ [M-H⁺]: 153.0458, found 153.0458.^{7a}

2-(4-Fluorophenyl)maleonitrile (1b'): Purification by column chromatography (PE:EA = 5:1) afforded the product as a white solid; MP: 112-115 °C; 1.89 g, yield: 63%; ¹H NMR (400 MHz, CDCl₃) δ = 7.62-7.59 (m, 2H), 7.15-7.11 (m, 2H), 6.27 (s, 1H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ : 165.3 (d, ¹*J*_{C-F} = 255.0 Hz), 132.2, 129.1, 129.0, 126.2, 126.1, 117.2, 117.0, 114.6, 114.0, 107.3. TOF-HRMS Calcd. for C₁₀H₆N₂F [M+H⁺]: 173.0509, found 173.0510.

2-(4-Bromophenyl)maleonitrile (1c'): Purification by column chromatography (PE:EA = 30:1) afforded the product as a white solid; MP: 107-110 °C; 2.06 g, Yield: 59%; ¹H NMR (400 MHz, CDCl₃) δ = 7.65 (d, *J* = 8.6 Hz, 2H), 7.52 (d, *J* = 8.6 Hz, 2H), 6.39 (s, 1H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ : 133.0, 132.4, 128.8, 128.0, 127.9, 114.4, 113.7, 107.8. TOF-HRMS Calcd. for

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2
3
4 $C_{10}H_4N_2Br$ $[M-H^+]$: 230.9563, found 230.9563.^{7b}
5
6

7 **2-(4-Methoxyphenyl)maleonitrile (1d')**: Purification by column chromatography (PE:EA = 5:1)

8
9 afforded the product as a white solid; MP: 114-117 °C; 1.56 g, yield: 52%; ¹H NMR (400 MHz,

10
11 $CDCl_3$) δ = 7.65 (d, J = 9.0 Hz, 2H), 6.98 (d, J = 8.9 Hz, 2H), 6.21 (s, 1H), 3.88 (s, 3H).

12
13 ¹³C{¹H}NMR ($CDCl_3$, 100 MHz) δ : 163.4, 132.7, 128.6, 122.4, 115.2, 115.1, 114.3, 103.9, 55.7.

14
15
16
17 TOF-HRMS Calcd. for $C_{11}H_9N_2O$ $[M+H^+]$: 185.0709, found 185.0709.^{7b}
18

19
20 **2-(p-Tolyl)maleonitrile (1e')**: Purification by column chromatography (PE:EA = 10:1) afforded

21
22 the product as light yellow solid; MP: 134-136 °C; 1.74 g, yield: 58%; ¹H NMR (400 MHz, $CDCl_3$)

23
24 δ = 7.55 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 6.33 (s, 1H), 2.43 (s, 3H). ¹³C{¹H}NMR

25
26 ($CDCl_3$, 100 MHz) δ : 144.0, 133.2, 130.3, 127.1, 126.6, 114.9, 114.2, 105.9, 21.5. TOF-HRMS

27
28
29
30
31 Calcd. for $C_{11}H_9N_2$ $[M+H^+]$: 169.0760, found 169.0759.
32

33
34 **2-(m-Tolyl)maleonitrile (1f')**: Purification by column chromatography (PE:EA = 5:1) afforded the

35
36 product as a light yellow solid; MP: 127-130 °C; 1.89 g, yield: 63%; ¹H NMR (400 MHz, $CDCl_3$)

37
38 δ = 7.45-7.39 (m, 2H), 7.38-7.37 (m, 2H), 6.35 (s, 1H), 2.42 (s, 3H). ¹³C{¹H}NMR ($CDCl_3$, 100

39
40
41 MHz) δ : 140.1, 134.2, 133.8, 129.9, 129.3, 127.9, 125.9, 124.4, 116.9, 107.7, 21.9. TOF-HRMS

42
43
44
45 Calcd. for $C_{11}H_9N_2$ $[M+H^+]$: 169.0760, found 169.0759.
46

47
48 **2-(3-Methoxyphenyl)maleonitrile (1g')**: Purification by column chromatography (PE:EA = 10:1)

49
50 afforded the product as a light yellow solid; MP: 86-88 °C; 0.75 g, yield: 25%; ¹H NMR (400 MHz,

51
52 $CDCl_3$) δ = 7.36-7.32 (m, 1H), 7.18-7.15 (m, 1H), 7.05-7.03 (m, 2H), 6.30 (s, 1H), 3.78 (s, 3H).

53
54
55 ¹³C{¹H}NMR ($CDCl_3$, 100 MHz) δ : 160.3, 133.3, 131.1, 130.8, 119.0, 118.5, 114.7, 114.1, 112.0,

56
57
58 107.7, 55.6. TOF-HRMS Calcd. for $C_{11}H_9N_2O$ $[M+H^+]$: 185.0709, found 185.0709.
59

60 **2-(2-Methoxyphenyl)maleonitrile (1h')**: Purification by column chromatography (PE:EA = 5:1)

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2
3
4 afforded the product as a light yellow solid; MP: 146-149 °C; 1.44 g, yield: 48%; ¹H NMR (400
5 MHz, CDCl₃) δ = 7.68-7.66 (m, 1H), 7.51-7.47 (m, 1H), 7.04 (t, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.4
6 Hz, 1H), 6.98 (s, 1H), 3.96 (s, 3H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 158.8, 133.7, 131.4, 130.6,
7
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12 121.4, 118.8, 115.6, 114.9, 112.0, 111.2, 56.0. TOF-HRMS Calcd. for C₁₁H₉N₂O [M+H⁺]:
13
14
15 185.0709, found 185.0709.^{7b}
16

17 **2-(2-Chlorophenyl)maleonitrile (1i')**: Purification by column chromatography (PE:EA = 10:1)
18
19 afforded the product as a white solid; MP: 70-74 °C; 1.68 g, yield: 56%; ¹H NMR (400 MHz,
20
21 CDCl₃) δ = 7.53-7.26 (m, 4H), 6.43 (s, 1H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 132.8, 132.6,
22
23
24
25 131.4, 131.3, 130.6, 129.5, 127.9, 115.0, 113.9, 113.8. TOF-HRMS Calcd. for C₁₀H₆N₂Cl [M+H⁺]:
26
27
28 189.0214, found 189.0214.
29

30
31 **2-(*o*-Tolyl)maleonitrile (1j')**: Purification by column chromatography (PE:EA = 10:1) afforded
32
33 the product as a white solid; MP: 63-67 °C; 1.77 g, yield: 59%; ¹H NMR (400 MHz, CDCl₃) δ =
34
35 7.36-7.32 (m, 1H), 7.24-7.18 (m, 3H), 6.02 (s, 1H), 2.42 (s, 3H). ¹³C{¹H}NMR (CDCl₃, 100 MHz)
36
37
38 δ: 136.4, 134.3, 131.7, 131.6, 130.8, 128.9, 127.0, 114.3, 114.1, 113.3, 20.3. TOF-HRMS Calcd.
39
40
41 for C₁₁H₉N₂ [M+H⁺]: 169.0760, found 169.0759.
42

43
44 **2-(2-Fluorophenyl)maleonitrile (1k')**: Purification by column chromatography (PE:EA = 20:1)
45
46 afforded the product as a white solid; MP: 105-108 °C; 1.71 g, yield: 57%; ¹H NMR (400 MHz,
47
48 CDCl₃) δ = 7.66-7.61 (m, 1H), 7.50-7.45 (m, 1H), 7.28-7.24 (m, 1H), 7.18-7.13 (m, 1H),
49
50
51 6.62-6.61 (m, 1H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 160.8 (d, ¹*J*_{C-F} = 255.0 Hz), 134.3, 134.2,
52
53
54 130.8, 128.4, 125.4, 117.3, 117.1, 114.6, 112.6, 112.4. TOF-HRMS Calcd. for C₁₀H₆N₂F [M+H⁺]:
55
56
57 173.0509, found 173.0511.
58

59
60 **2-(Naphthalen-1-yl)maleonitrile (1l')**: Purification by column chromatography (PE:EA = 10:1)

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2
3
4 afforded the product as a light yellow liquid; 1.62 g, yield: 54%; ^1H NMR (400 MHz, CDCl_3) δ =
5
6 8.09-7.93 (m, 3H), 7.66-7.54 (m, 4H), 6.32 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 133.6,
7
8 133.2, 132.6, 129.4, 129.1, 128.8, 128.2, 128.0, 127.2, 125.2, 123.4, 114.9, 114.3, 114.0.
9
10
11 TOF-HRMS Calcd. for $\text{C}_{14}\text{H}_9\text{N}_2$ [$\text{M}+\text{H}^+$]: 205.0760, found 205.0759.

12
13
14 **2-(Naphthalen-2-yl)maleonitrile (1m')**: Purification by column chromatography (PE:EA = 10:1)
15
16 afforded the product as a light yellow solid; MP: 147-151 °C; 1.74 g, yield: 58%; ^1H NMR (400
17
18 MHz, CDCl_3) δ = 8.22 (s, 1H), 7.96-7.88 (m, 3H), 7.64-7.59 (m, 3H), 6.47 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR
19
20 (CDCl₃, 100 MHz) δ : 134.9, 133.3, 132.7, 129.8, 129.4, 129.3, 129.1, 127.9, 127.8, 127.1, 120.8,
21
22 114.9, 114.2, 106.8. TOF-HRMS Calcd. for $\text{C}_{14}\text{H}_9\text{N}_2$ [$\text{M}+\text{H}^+$]: 205.0760, found 205.0760.
23
24
25

26
27
28 **2-(Furan-2-yl)maleonitrile (1n')**: Purification by column chromatography (PE:EA = 10:1)
29
30 afforded the product as a light yellow liquid; 1.62 g, yield: 54%; ^1H NMR (400 MHz, CDCl_3) δ =
31
32 7.70 (s, 1H), 7.22-7.21 (m, 1H), 6.65-6.64 (m, 1H), 5.80 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz)
33
34 δ : 147.4, 146.2, 120.2, 118.4, 114.7, 114.2, 113.4, 100.9. TOF-HRMS Calcd. for $\text{C}_8\text{H}_4\text{N}_2\text{ONa}$
35
36 [$\text{M}+\text{Na}^+$]: 167.0215, found 167.0212.
37
38
39

40
41
42 **2-(Thiophen-2-yl)maleonitrile (1o')**: Purification by column chromatography (PE:EA = 10:1)
43
44 afforded the product as a light yellow liquid; 1.8 g, yield: 60%; ^1H NMR (400 MHz, CDCl_3) δ =
45
46 7.58-7.57 (m, 2H), 7.18-7.17 (m, 1H), 6.11 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 134.9,
47
48 134.7, 133.6, 128.9, 126.5, 115.9, 115.7, 102.1. TOF-HRMS Calcd. for $\text{C}_8\text{H}_4\text{N}_2\text{SNa}$ [$\text{M}+\text{Na}^+$]:
49
50 182.9987, found 182.9988.
51
52
53

54
55 **General procedure for asymmetric hydrogenation of 1:** A stock solution was made by mixing
56
57 $[\text{Rh}(\text{COD})\text{Cl}]_2$ with (*R,R*)-f-spirophos in a 1:2.2 molar ratio in CH_2Cl_2 at room temperature for 20
58
59 min in a nitrogen-filled glovebox. An aliquot of the catalyst solution (1.0 mL, 0.001 mmol) was
60

transferred by syringe into the vials charged with different substrates (0.1 mmol for each) in anhydrous CH_2Cl_2 (2.0 mL). The vials were subsequently transferred into an autoclave which hydrogen gas was charged. The reaction was then stirred under H_2 (10 atm) at room temperature for 7 h for the substrates **1** or 60 °C 8 h for the substrates **1'**. The hydrogen gas was released slowly and carefully. The solution was passed through a short column of silica gel to remove the metal complex. The ee values of products **2** or **2'** were determined by GC analysis on a chiral stationary phase. The crude products **2j**, **2l'**, **2m'** were concentrated and purified by column chromatography and the ee values were determined by HPLC analysis on a chiral stationary phase.

(+)-2-Phenylsuccinonitrile (2a): 19.1 mg, yield 98%; 90% ee; $[\alpha]_{\text{D}}^{20} = +30.2$ (c = 0.5, CH_2Cl_2); GC condition: Supelco gamma DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N_2 1.0 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; $t_{\text{R}} = 77.9$ min (minor), $t_{\text{R}} = 78.3$ min (major).

(2a'): 18.9 mg, yield 97%; 90% ee; $[\alpha]_{\text{D}}^{20} = +30.0$ (c = 0.5, CH_2Cl_2); GC condition: Supelco gamma DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N_2 1.0 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; $t_{\text{R}} = 77.9$ min (minor), $t_{\text{R}} = 78.4$ min (major). ^1H NMR (400 MHz, CDCl_3) $\delta = 7.46$ -7.41 (m, 5H), 4.16 (t, $J = 6.9$ Hz, 1H), 3.03-2.91 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 132.8, 130.3, 130.2, 127.8, 118.3, 115.7, 34.7, 25.3. TOF-HRMS Calcd. for $\text{C}_{10}\text{H}_9\text{N}_2$ $[\text{M}+\text{H}^+]$: 157.0760, found 157.0759.^{7a, 19}

(+)-2-(4-Fluorophenyl)succinonitrile (2b): 21.5 mg, yield 99%; 89% ee; $[\alpha]_{\text{D}}^{20} = +46.0$ (c = 0.5, CH_2Cl_2); GC condition: Supelco alpha DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N_2 1.0 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; $t_{\text{R}} = 67.3$ min (minor), $t_{\text{R}} = 68.2$ min (major). **(2b')**: 21.1 mg, yield 97%; 89% ee; $[\alpha]_{\text{D}}^{20} = +46.2$ (c = 0.5, CH_2Cl_2); GC condition:

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2
3
4 Supelco alpha DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N₂ 1.0 mL/min, programmed 100
5
6 °C - 1 °C/min - 200 °C - 50 min; t_R = 67.2 min (major), t_R = 68.7 min (minor). ¹H NMR (400 MHz,
7
8 CDCl₃) δ = 7.42-7.39 (m, 2H), 7.17-7.13 (m, 2H), 4.16 (t, *J* = 6.8 Hz, 1H), 3.02-2.90 (m, 2H).
9
10 ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 163.1 (d, ¹*J*_{C-F} = 249.0 Hz), 129.2, 129.1, 128.0, 127.9, 117.5,
11
12 116.9, 116.6, 115.0, 33.3, 24.7. TOF-HRMS Calcd. for C₁₀H₆N₂F [M-H⁺]: 173.0520, found
13
14 173.0521.
15
16 (+)-2-(4-Bromophenyl)succinonitrile (**2c**): 28.7 mg, yield 98%; 88% ee; [α]_D²⁰ = +27.6 (c = 0.5,
17
18 CH₂Cl₂); GC condition: Supelco gamma DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N₂ 1.0
19
20 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; t_R = 77.9 min (minor), t_R = 78.3 min
21
22 (major). (**2c'**): 29.0 mg, yield 99%; 88% ee; [α]_D²⁰ = +27.7 (c = 0.5, CH₂Cl₂); GC condition:
23
24 Supelco gamma DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N₂ 1.0 mL/min, programmed
25
26 100 °C - 1 °C/min - 200 °C - 50 min; t_R = 77.9 min (minor), t_R = 78.4 min (major). ¹H NMR (400
27
28 MHz, CDCl₃) δ = 7.61-7.58 (m, 2H), 7.31-7.28 (m, 2H), 4.14 (t, *J* = 6.8 Hz, 1H), 3.01-2.90 (m,
29
30 2H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 132.8, 131.1, 128.9, 123.9, 117.3, 114.9, 33.5, 24.5.
31
32 TOF-HRMS Calcd. for C₁₀H₆N₂Br [M-H⁺]: 232.9719, found 232.9719.
33
34 (+)-2-(4-Methoxyphenyl)succinonitrile (**2d**): 22.5 mg, yield 97%; 86% ee; [α]_D²⁰ = +33.4 (c =
35
36 0.5, CH₂Cl₂); GC condition: Supelco alpha DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N₂
37
38 1.0 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; t_R = 85.5 min (minor), t_R = 86.4
39
40 min (major). (**2d'**): 22.8 mg, yield 98%; 91% ee; [α]_D²⁰ = +35.6 (c = 0.5, CH₂Cl₂); GC condition:
41
42 Supelco alpha DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N₂ 1.0 mL/min, programmed 100
43
44 °C - 1 °C/min - 200 °C - 50 min; t_R = 85.6 min (minor), t_R = 86.7 min (major). ¹H NMR (400 MHz,
45
46 CDCl₃) δ = 7.31 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 4.12 (t, *J* = 6.9 Hz, 1H), 3.82 (s, 3H),
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2.99-2.87 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 160.4, 128.5, 124.1, 118.1, 115.4, 115.0, 55.4, 33.3, 24.9. TOF-HRMS Calcd. for $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}$ [$\text{M}+\text{H}^+$]: 187.0865, found 187.0867.

(+)-2-(p-Tolyl)succinonitrile (2e): 21.0 mg, yield 99%; 93% ee; $[\alpha]_{\text{D}}^{20} = +36.9$ ($c = 0.5$, CH_2Cl_2);

GC condition: Supelco alpha DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2 1.0 mL/min, programmed 100 $^\circ\text{C}$ - 1 $^\circ\text{C}/\text{min}$ - 200 $^\circ\text{C}$ - 50 min; $t_{\text{R}} = 68.7$ min (minor), $t_{\text{R}} = 69.6$ min (major).

(2e'): 20.8 mg, yield 98%; 91% ee; $[\alpha]_{\text{D}}^{20} = +36.2$ ($c = 0.5$, CH_2Cl_2); GC condition: Supelco alpha

DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2 1.0 mL/min, programmed 100 $^\circ\text{C}$ - 1 $^\circ\text{C}/\text{min}$

- 200 $^\circ\text{C}$ - 50 min; $t_{\text{R}} = 68.8$ min (minor), $t_{\text{R}} = 69.8$ min (major). ^1H NMR (400 MHz, CDCl_3) $\delta =$

7.23-7.16 (m, 4H), 4.05 (t, $J = 6.9$ Hz, 1H), 2.93-2.81 (m, 2H), 2.30 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 ,

100 MHz) δ : 139.6, 130.3, 129.2, 127.0, 117.9, 115.3, 33.7, 24.7, 21.1. TOF-HRMS Calcd. for

$\text{C}_{11}\text{H}_9\text{N}_2$ [$\text{M}-\text{H}^+$]: 169.0771, found 169.0772.

(+)-2-(m-Tolyl)succinonitrile (2f): 20.6 mg, yield 97%; 90% ee; $[\alpha]_{\text{D}}^{20} = +45.9$ ($c = 0.5$, CH_2Cl_2);

GC condition: Supelco gamma DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2 1.0 mL/min, programmed 100 $^\circ\text{C}$ - 1 $^\circ\text{C}/\text{min}$ - 200 $^\circ\text{C}$ - 50 min; $t_{\text{R}} = 77.0$ min (minor), $t_{\text{R}} = 77.3$ min (major).

(2f'): 21.0 mg, yield 99%; 88% ee; $[\alpha]_{\text{D}}^{20} = +45.0$ ($c = 0.5$, CH_2Cl_2); GC condition: Supelco

gamma DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2 1.0 mL/min, programmed 100 $^\circ\text{C}$ - 1

$^\circ\text{C}/\text{min}$ - 200 $^\circ\text{C}$ - 50 min; $t_{\text{R}} = 77.5$ min (minor), $t_{\text{R}} = 77.9$ min (major). ^1H NMR (400 MHz,

CDCl_3) $\delta = 7.25$ -7.12 (m, 4H), 4.04 (t, $J = 6.9$ Hz, 1H), 2.93-2.82 (m, 2H), 2.31 (s, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 139.7, 132.1, 130.3, 129.6, 127.8, 124.3, 117.9, 115.3, 34.0,

24.8, 21.4. TOF-HRMS Calcd. for $\text{C}_{11}\text{H}_9\text{N}_2$ [$\text{M}-\text{H}^+$]: 169.0771, found 169.0771.

(+)-2-(2-Chlorophenyl)succinonitrile (2g): 22.3 mg, yield 98%; 88% ee; $[\alpha]_{\text{D}}^{20} = +96.3$ ($c = 0.5$,

CH_2Cl_2); GC condition: Supelco gamma DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2 1.0

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4 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; $t_R = 84.9$ min (major), $t_R = 86.4$ min
5
6
7 (minor). **(2i')**: 23.5 mg, yield 99%; 85% ee; $[\alpha]_D^{20} = +95.6$ ($c = 0.5$, CH_2Cl_2); GC condition:
8
9
10 Supelco gamma DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2 1.0 mL/min, programmed
11
12 100 °C - 1 °C/min - 200 °C - 50 min; $t_R = 84.9$ min (major), $t_R = 86.3$ min (minor). ^1H NMR (400
13
14 MHz, CDCl_3) $\delta = 7.69$ -7.66 (m, 1H), 7.47-7.38 (m, 3H), 4.66 (t, $J = 5.6$ Hz, 1H), 3.10-2.94 (m,
15
16 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 132.5, 131.1, 130.4, 129.8, 129.4, 128.2, 117.3, 115.1,
17
18 31.6, 22.7. TOF-HRMS Calcd. for $\text{C}_{10}\text{H}_6\text{N}_2\text{Cl}$ [$\text{M}-\text{H}^+$]:189.0224, found 189.0226.
19
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22
23 **(+)-2-(3-Methoxyphenyl)succinonitrile (2g')**: 23.0 mg, yield 99%; 87% ee; $[\alpha]_D^{20} = +45.2$ ($c =$
24
25 0.5, CH_2Cl_2); GC condition: Supelco alpha DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2
26
27 2.0 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; $t_R = 72.8$ min (minor), $t_R = 73.8$
28
29 min (major). ^1H NMR (400 MHz, CDCl_3) $\delta = 7.37$ -7.33 (m, 1H), 6.98-6.93 (m, 3H), 4.14 (t, $J =$
30
31 6.8 Hz, 1H), 3.82 (s, 3H), 2.97-2.95 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ : 160.4, 133.6,
32
33 130.8, 119.3, 117.9, 115.4, 114.9, 113.1, 55.5, 34.0, 24.6. TOF-HRMS Calcd. for $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}$
34
35 [$\text{M}+\text{H}^+$]:187.0865, found 187.0867.²⁰
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41 **(+)-2-(2-Fluorophenyl)succinonitrile (2h)**: 21.1 mg, yield 97%; 89% ee; $[\alpha]_D^{20} = +59.1$ ($c = 0.5,$
42
43 CH_2Cl_2); GC condition: Supelco gamma DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2 1.0
44
45 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; $t_R = 74.2$ min (minor), $t_R = 74.6$ min
46
47 (major). **(2k')**: 21.3 mg, yield 98%; 90% ee; $[\alpha]_D^{20} = +59.8$ ($c = 0.5$, CH_2Cl_2); GC condition:
48
49
50 Supelco gamma DexTM 225 column (30 m \times 0.25 mm \times 0.25 μm), N_2 1.0 mL/min, programmed
51
52 100 °C - 1 °C/min - 200 °C - 50 min; $t_R = 73.6$ min (minor), $t_R = 73.8$ min (major). ^1H NMR (400
53
54 MHz, CDCl_3) $\delta = 7.43$ (t, $J = 7.6$ Hz, 1H), 7.31-7.30 (m, 1H), 7.14 (t, $J = 7.6$ Hz, 1H), 7.03 (t, $J =$
55
56 9.4 Hz, 1H), 4.34 (t, $J = 6.4$ Hz, 1H), 2.94-2.82 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ :
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4 159.6 (d, $^1J_{C-F} = 247.0$ Hz), 129.2, 129.1, 128.0, 127.9, 117.5, 116.9, 116.6, 115.0, 33.3, 24.7.

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6
7 131.8, 131.7, 129.2, 129.1, 125.5, 125.4, 119.5, 119.4, 116.9, 116.4, 116.2, 114.9, 28.5, 28.4, 23.1,

8
9
10 23.0. TOF-HRMS Calcd. for $C_{10}H_6N_2F$ $[M-H^+]$: 173.0520, found 173.0521.

11
12 **(+)-2-(2-Methoxyphenyl)succinonitrile (2i)**: 22.4 mg, yield 96%; 96% ee; $[\alpha]_D^{20} = +106.7$ (c =

13
14 0.5, CH_2Cl_2); GC condition: Supelco gamma DexTM 225 column (30 m \times 0.25 mm \times 0.25 μ m), N_2

15
16
17 1.0 mL/min, programmed 100 $^\circ$ C - 1 $^\circ$ C/min - 200 $^\circ$ C - 50 min; $t_R = 81.2$ min (minor), $t_R = 81.9$

18
19
20 min (major). **(2h')**: 22.8 mg, yield 98%; 92% ee; $[\alpha]_D^{20} = +105.2$ (c = 0.5, CH_2Cl_2); GC condition:

21
22
23 Supelco gamma DexTM 225 column (30 m \times 0.25 mm \times 0.25 μ m), N_2 1.0 mL/min, programmed

24
25
26 100 $^\circ$ C - 1 $^\circ$ C/min - 200 $^\circ$ C - 50 min; $t_R = 81.3$ min (minor), $t_R = 82.1$ min (major). 1H NMR (400

27
28
29 MHz, $CDCl_3$) $\delta = 7.49$ (d, $J = 7.6$ Hz, 1H), 7.40 (t, $J = 7.7$ Hz, 1H), 7.05 (t, $J = 7.7$ Hz, 1H), 6.95

30
31
32 (d, $J = 8.3$ Hz, 1H), 4.51 (t, $J = 6.6$ Hz, 1H), 3.89 (s, 3H), 3.04-2.92 (m, 2H). $^{13}C\{^1H\}$ NMR

33
34
35 ($CDCl_3$, 100 MHz) δ : 155.9, 130.9, 128.7, 121.4, 120.2, 118.0, 115.7, 111.1, 55.6, 29.2, 22.2.

36
37
38 TOF-HRMS Calcd. for $C_{11}H_{11}N_2O$ $[M+H^+]$: 187.0865, found 187.0867.

39
40 **(+)-2-(o-Tolyl)succinonitrile (2j)**: 20.4 mg, yield 96%; 98% ee; $[\alpha]_D^{20} = +132.2$ (c = 0.5, CH_2Cl_2);

41
42
43 GC condition: Supelco alpha DexTM 225 column (30 m \times 0.25 mm \times 0.25 μ m), N_2 1.0 mL/min,

44
45
46 programmed 100 $^\circ$ C - 1 $^\circ$ C/min - 200 $^\circ$ C - 50 min; $t_R = 67.6$ min (major), $t_R = 68.1$ min (minor).

47
48 **(2j')**: 20.8 mg, yield 98%; 95% ee; $[\alpha]_D^{20} = +131.6$ (c = 0.5, CH_2Cl_2); GC condition: Supelco

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50
51 alpha DexTM 225 column (30 m \times 0.25 mm \times 0.25 μ m), N_2 1.0 mL/min, programmed 100 $^\circ$ C - 1

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53
54 $^\circ$ C/min - 200 $^\circ$ C - 50 min; $t_R = 67.4$ min (minor), $t_R = 68.2$ min (major). 1H NMR (400 MHz,

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56
57 $CDCl_3$) $\delta = 7.41$ -7.40 (m, 1H), 7.24-7.18 (m, 3H), 4.28 (t, $J = 6.9$ Hz, 1H), 2.92-2.81 (m, 2H),

58
59
60 2.32 (s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ : 135.6, 132.1, 131.1, 130.2, 128.1, 128.0, 118.7,

115.8, 31.4, 23.9, 19.7. TOF-HRMS Calcd. for $C_{11}H_9N_2$ $[M-H^+]$: 169.0771, found 169.0772.

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4 (+)-**2-(Naphthalen-1-yl)succinonitrile (2k)**: 25.5 mg, yield 99%; 93% ee; $[\alpha]_D^{20} = +52.0$ (c = 0.5,
5
6 CH₂Cl₂); HPLC condition: Lux 5u Cellulose-2 (250 × 4.60mm), ipa : hex = 35:65, 1mL/min, 254
7
8 nm; $t_R = 10.7$ min (major), $t_R = 14.6$ min (minor). (**2l'**): 25.5 mg, yield 99%; 86% ee; $[\alpha]_D^{20} =$
9
10 +45.0 (c = 0.5, CH₂Cl₂); HPLC condition: Lux 5u Cellulose-2 (250 × 4.60mm), ipa : hex = 35:65,
11
12 1mL/min, 254 nm; $t_R = 10.5$ min (minor), $t_R = 14.0$ min (major). ¹H NMR (400 MHz, CDCl₃) $\delta =$
13
14 7.95-7.85 (m, 2H), 7.83-7.79 (m, 2H), 7.67-7.54 (m, 3H), 4.94 (t, *J* = 6.7 Hz, 1H), 3.20-3.06 (m,
15
16 2H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ : 133.7, 130.1, 129.4, 128.8, 127.3, 127.1, 126.2, 125.9,
17
18 125.1, 120.5, 117.5, 114.8, 30.8, 23.1. TOF-HRMS Calcd. for C₁₄H₁₁N₂ [M+H⁺]: 207.0916, found
19
20 207.0914.
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28 (**S**)-**2-Hexylsuccinonitrile (2l)**: 20.1 mg, yield 98%; 96% ee; $[\alpha]_D^{20} = -62.0$ (c = 0.5, EtOH); GC
29
30 condition: Supelco gamma DexTM 225 column (30 m × 0.25 mm × 0.25 μ m), N₂ 3.0 mL/min,
31
32 programmed 100 °C - 2 °C/min - 190 °C - 30 min; $t_R = 35.6$ min (minor), $t_R = 35.7$ min (major). ¹H
33
34 NMR (400 MHz, CDCl₃) $\delta = 2.91$ (s, 1H), 2.72 (s, 2H), 1.76-1.77 (m, 2H), 1.55-1.57 (m, 1H),
35
36 1.46-1.47 (m, 1H), 1.24-1.30 (s, 6H), 0.87-0.89 (m, 3H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ :
37
38 119.5, 116.2, 32.0, 31.9, 29.0, 27.2, 23.0, 21.6, 14.5, 1.56. The analytical data are consistent with
39
40 the literature.²¹
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47 (+)-**2-(Naphthalen-2-yl)succinonitrile (2m')**: 25.2 mg, yield 98%; 92% ee; $[\alpha]_D^{20} = +51.4$ (c =
48
49 0.5, CH₂Cl₂); HPLC condition: Lux 5u Cellulose-2 (250 × 4.60mm), ipa : hex = 35:65, 1mL/min,
50
51 254 nm; $t_R = 9.9$ min (major), $t_R = 11.0$ min (minor). ¹H NMR (400 MHz, CDCl₃) $\delta = 7.94$ -7.87
52
53 (m, 4H), 7.58-7.56 (m, 2H), 7.45-7.43 (m, 1H), 4.32 (t, *J* = 6.8 Hz, 1H), 3.10-2.99 (m, 2H).
54
55 ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ : 132.6, 132.5, 129.2, 128.7, 127.4, 127.1, 126.6, 126.5, 126.3,
56
57 123.2, 117.1, 114.5, 33.6, 24.0. TOF-HRMS Calcd. for C₁₄H₁₁N₂ [M+H⁺]: 207.0916, found
58
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4 207.0915.
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6
7 (+)-2-(Furan-2-yl)succinonitrile (**2n'**): 17.9 mg, yield 98%; 65% ee; $[\alpha]_D^{20} = +37.6$ (c = 0.5,
8
9 CH₂Cl₂); GC condition: Supelco alpha DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N₂ 1.0
10 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; t_R = 43.3 min (minor), t_R = 44.5 min
11
12 (major). ¹H NMR (400 MHz, CDCl₃) δ = 7.46 (s, 1H), 6.52-6.42 (m, 2H), 4.32 (t, J = 6.7 Hz, 1H),
13
14 3.06 (d, J = 6.7 Hz, 2H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 144.8, 144.5, 116.2, 115.5, 111.7,
15
16 28.8, 22.1. TOF-HRMS Calcd. for C₈H₆N₂ONa [M+Na⁺]: 169.0372, found 169.0374.
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23 (+)-2-(Thiophen-2-yl)succinonitrile (**2o'**): 19.4 mg, yield 96%; 57% ee; $[\alpha]_D^{20} = +54.8$ (c = 0.5,
24
25 CH₂Cl₂); GC condition: Supelco alpha DexTM 225 column (30 m × 0.25 mm × 0.25 μm), N₂ 1.0
26 mL/min, programmed 100 °C - 1 °C/min - 200 °C - 50 min; t_R = 63.7 min (minor), t_R = 65.1 min
27
28 (major). ¹H NMR (400 MHz, CDCl₃) δ = 7.37-7.36 (m, 1H), 7.21-7.20 (m, 1H), 7.05-7.02 (m, 1H),
29
30 4.47 (t, J = 6.7 Hz, 1H), 3.04-3.02 (m, 1H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 134.0, 128.2,
31
32 128.1, 127.6, 117.6, 115.6, 29.9, 25.5. TOF-HRMS Calcd. for C₈H₆N₂SNa [M+Na⁺]: 185.0143,
33
34 found 185.0146.
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41 **General procedure for the synthesis of 1,4-diamines:** To a stirring solution of the hydrogenation
42 product (0.2 mmol) in MeOH (3 mL) Boc₂O (0.8 mmol) and NiCl₂·6H₂O (0.8 mmol) were first
43 added, then NaBH₄ (3.2mmol) was added portionwise at 0 °C over 1 h. The mixture was stirred at
44 room temperature until no starting material was detected by TLC and carefully quenched with
45 H₂O. The aqueous layer was extracted with ethyl acetate, dried over MgSO₄. After the solvent was
46 removed in vacuo, the residue was purified by silica gel column chromatography using petroleum
47 ether/ AcOEt as an eluent.¹⁷
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1,4-Bis((*tert*-butoxycarbonyl)amino)-2-(4-methoxyphenyl)butane (**3**): 25.5 mg, yield: 65%; 96%

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4 ee; $[\alpha]_{\text{D}}^{25} = -8.8$ (c = 0.5, CH₂Cl₂); HPLC condition: Lux 5u Cellulose-2 (250 × 4.60mm), ipa :
5
6
7 hex = 10:90, 1mL/min, 254 nm; t_R = 8.4 min (major), t_R = 9.9 min (minor). ¹H NMR (CDCl₃, 400
8
9 MHz) δ: 7.22-6.85 (m, 4H), 4.65 (s, 1H), 4.45 (s, 1H), 3.81(s, 3H), 3.46-3.45 (m, 1H), 3.30-3.25
10
11 (m, 2H), 3.10-3.06 (m, 1H), 2.88-2.83 (m, 1H), 2.03 (s, 1H), 1.86-1.81 (m, 1H), 1.41-1.38(m,
12
13 18H). ¹³C{¹H}NMR (CDCl₃, 100 MHz) δ: 158.1, 156.5, 156.4, 131.4, 130.2, 128.3, 128.2, 121.6,
14
15 111.2, 79.5, 79.4, 55.9, 45.4, 39.1, 36.8, 33.4, 31.5, 28.9, 28.8, 19.7, 1.5. TOF-HRMS Calcd. for
16
17 C₂₁H₃₅N₂O₅ [M+H⁺]: 395.2540, found 395.2539.
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25
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38 SUPPORTING INFORMATION

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41 NMR, GC and HPLC spectra. This material is available free of charge via the Internet at
42
43 <http://pubs.acs.org>.
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