-Supporting Information-

Hydrogenolysis-hydrogenation of aryl ethers: selectivity pattern

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S1. Materials. Nickel(II) acetylacetonate, tricyclohexylphosphine ligand, NaOtBu, Lithium tri-tert-butoxyaluminum hydride, diphenyl ether, DIBALH, Et_3SiH and all substrates from Table 2 were purchased from Aldrich Co. Nitroscanate was obtained as a gift from Marvel industries. Anhydrous toluene (with molecular sieves and septum), Sodium dodecyl sulphate (SDS) (electrophoretic grade) and cetyltrimethylammonium bromide (CTAB) (electrophoretic grade) were obtained from Sigma-Aldrich Co. The purity of these surfactants was ascertained tensiometrically. All the products are known compounds and were purchased from Aldrich Co. All other reagents from commercial sources were used as received. Flash chromatography was performed with Merck silica gel 60 (230-400 mesh ASTM).

S2. General procedure for hydrogenolysis-hydrogenation. Nickel(II) acetylacetonate (0.052 g, 0.20 mmol, 20%), tricyclohexylphosphine ligand (0.112 g, 0.40 mmol 40%), NaO^tBu (0.036 g, 0.375 mmol 2.5 eq), Lithium tri-*tert*-butoxyaluminum hydride (0.0953 g 0.375 mmol, 2.5 eq) with diphenyl ether (0.025 g, 0.15 mmol) were added to a CTAB (0.60 mmol) toluene (10 mL) solution; the mixture was stirred for 5 hours in tightly capped, 9 cm long and 1.5 cm internal diameter glass tubes fitted with teflon-lined caps (1.5 cm internal diameter; supplied by United Scientific Pty Ltd) with cylindrical shape containing 1 cm long teflon-coated magnetic stir bars (supplied by United Scientific Pty Ltd). The speed of agitation was maintained at 1.67 Hz. Isothermal conditions were maintained at 70 °C. At the start, the reaction mixture appears dark brown in colour which changes to light green in due course and, at the end of the reaction, becomes dark green. After cooling to room temperature, a solution of SDS (60 mmol) in toluene (5 mL) was added to the reaction mixture which was agitated for an additional 2 min. After cooling to room temperature, the reaction mixture was diluted with ether (1 mL) and carefully quenched at 0 °C with 1 mL of 1.5 M aqueous hydrochloric acid. The organic layer was separated, the aqueous layer was extracted with ether (1 mL), and the combined organic layers were filtered through a plug of Celite. The filtrate was concentrated under reduced pressure and then purified by flash chromatography on silica gel using hexane to give the cyclohexane (0.007 g, 99% yield) and cyclohexanol (0.009 g, 99% yield) as products along with unreacted diphenyl ether (0.01 g).

S3. General analytical information. Percent conversion was determined using a gas chromatograph (Chemito 8610) with a flame ionization detector. A 4 m. long and 0.37 cm internal diameter S.S. column packed with 10% SE-30 on chromosorb WHP was employed for the analysis. Nitrogen at the flow rate of 0.5×10^{-7} m^3 sec^{-1} was used as carrier gas. All the products were known compounds and were identified and confirmed using GC by comparison of retention times of the products with those of authentic compounds. The experiments were performed in replicates of three. The variation in the results from the reported average values was within ± 0.75 %.

S4. Research background. The pharmaceutical research is highly influence by the fragment based drug development (total synthesis of complex drug molecule by joining simple fragments). However, some times the fragmentation study of the particular drugs (breaking complex drug molecule in to simple small molecules) is also very important, for example nitroscanate (1-(4-Isothiocyanatophenoxy)-4-nitrobenzene), which is an anthelmintic drug (Fig S1).

Fig. S1. Nitroscanate.

In 2011, due to high production of this drug and successful use of multiple drugs to control parasitic diseases, the demand for the nitroscanate in the veterinary medicine market went down. Many small scale pharmaceutical industries in Asia were looking for comercial products that could be prepared from nitroscanate. There are very strict rules for the commercialisation of the nitroscanate, hence industries are trying to break down nitroscanate to simple chemicals. Another important concept which came forth was promoting animal health marketed products as potential drug development candidates for human use. Already registered veterinary products like nitroscanate offer advantages such as being extensively and rigorously tested in animals, which reduces the risk, cost, and time required for approval for human trials. However, more intense study is required on the mechanism of action and reduction of cytotoxicity (side effects) for this compound. All these applications and studies of nitroscanate will involve its fragmentation study. Hence, there is a great demand for the easily avail reaction process to cleave C-O bond in the nitroscanate. This demand was the main reason for developing research on the C-O bond cleavage in diphenyl ethers.

S4. Stirring effect.

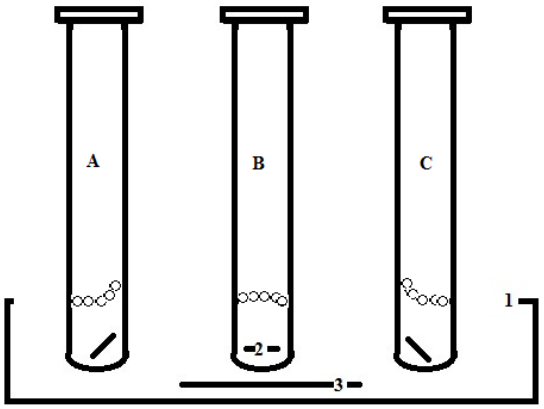

Fig. S2. Position of reaction tubes in heating bath. 1= Heating bath, 2= maganetic stirrer, 3= magnatic stirrer for heating bath. Diagram is not to measure.

Disscussion.

The presence of surfactant in the reaction media causes foam formation. In hydrogenolysis-hydrogenation reactions, the use of 0.60 mmol surfactant produced a very thin layer of foam in the reaction media. This layer does appear toaffect the yield of the reaction. The surfactant concentration in toluene is very important to avoid formation of excessive foam. Foam formation is also dependent on the stirring rate, direction of stirring, and the position of the magnetic stirrer in the reaction media. We performed extensive studies to check the effect of stirring on the yield of the hydrogenolysis by using cylindrical shape (1 cm long) teflon-coated magnetic stir bars (supplied by United Scientific Pty Ltd).

Effect of stirring rate. No stirring (Table S1, No. 1), slow stirring rate (s. r.) (Table S1, No. 2), and high s. r. (Table S1, No. 3) in the reaction causes decreased yield of the product (Table S1, No. 1). In the case of slow s. r., lower yields might be due to the lack of good contact between the reactants. We also observed decantation of solid reagent in the reaction media. In case of high s. r., the formation of foam was observed. Hence, we decided to maintain 1.67 Hz s. r. for the reaction.

Effect of stirring direction and position of bar. Figure S1 shows the possible positions of the magnetic bar in the reaction tube. Due to the presence of heating bath stirrer the position of bar in tube A and C is disturbed, however, when the tube was exactly above heating bath stirrer, the position of the magnetic bar was perfect. Due to this disturbance, in some of the experiments when the tube was in position A or C, we observed formation of uneven layer of foam at the surface of the reaction media as shown in Figure S1. However, when the s. r. was maintain at 1.67 Hz, there was no flotation of reagent particles observed on glass surface or on media surface due to foam. On the other hand, in position B there was a thin layer of foam, (which we cannot measure) however, at all positions (A, B and C) there was no affect of foam formation on the yield or selectivity of the reaction.

Since benzene, which is low boiling product was expected in the reaction; we did not try the over head stirrer for this reaction optimization study.

Table S1. The effect of stirring on the hydrogenolysis–hydrogenation of diphenyl ether.

No.	Reaction conditions Ni (5 mol%), L (10 mol%), $LiAl(O^tBu)_3H$ (2.5 eq), NaO^tBu (2.5 eq), Toluene (1.5 mL), CTAB (0.60 mmol), 5 h, 70 ^OC	Conversion[a] (%)
1	s. r.[b] 0 Hz	42, **1a** (50), **1b** (50)
2	s. r. 0.2 Hz	40, **1a** (50), **1b** (50)
3	s. r. 10 Hz	30, **1a** (50), **1b** (50)

[a]Conversion was determined by gas chromatography; [b]stirring rate. Each experiment was done three times independently

Table S2. The effect of temperature, L, Ni and hydride source on the hydrogenolysis–hydrogenation of diphenyl ether.

No.	Reaction conditions	Conversion[a] (%) (% Selectivity)	Yield[b] (%)
1	Ni (20 mol%), L (40 mol%), $LiAl(O^tBu)_3H$ (12 eq), toluene (1.5 mL), 56 h, 120 ^OC, under nitrogen atmosphere	~10, cyclohexane, cyclohexene	-
2	Ni (5 mol%), L (10 mol%), $LiAl(O^tBu)_3H$ (2.5 eq), toluene (1.5 mL), CTAB (0.60 mmol), 16 h, 70 ^OC, under nitrogen atmosphere	85, **1a** (50), **1b** (50)	**1a** (90), **1b** (95)
3	Ni (5 mol%), L (10 mol%), $LiAl(O^tBu)_3H$ (2.5 eq), toluene (1.5 mL), CTAB (0.60 mmol), 16 h, 70 ^OC, no inert atmosphere	85, **1a** (50), **1b** (50)	-
4	Ni (5 mol%), L (10 mol%), $LiAl(O^tBu)_3H$ (2.5 eq), toluene (1.5 mL), CTAB (0.60 mmol), 16 h, 120 ^OC	60, **1a** (50), **1b** (50)	-
5	Ni (20 mol%), L (40 mol%), $LiAl(O^tBu)_3H$ (12 eq), toluene (1.5 mL), SDS (0.60 mmol), 48 h, 120 ^OC	~10, **1a** (50), **1b** (50)	-
6	Ni (5 mol%), L (10 mol%), DIBALH[c] (2.5 eq), toluene (1.5 mL), CTAB (0.60 mmol), 16 h, 70 ^OC	58, **1a** (50), **1b** (50)	-
7	Ni (5 mol%), L (10 mol%), Et_3SiH[d] (2.5 eq), toluene (1.5 mL), CTAB (0.60 mmol), 16 h, 70 ^OC	30, **1a** (50), **1b** (50)	-
8	Ni (5 mol%), Hg (5 mol%), L (10 mol%), $LiAl(O^tBu)_3H$ (2.5 eq), toluene (1.5 mL), CTAB (0.60 mmol), 16 h, 70 ^OC	>5	-

[a]Conversion was determined by gas chromatograph. [b]Isolated yield. [c]Di-isobutylaluminum hydride (conversion is almost similar with $LiAl(O^tBu)_3H$). [d] Reduced conversion with Et_3SiH was due to the milder proton donating nature of Et_3SiH as compared to DIBALH and $LiAl(O^tBu)_3H$.

S5. The effect of surfactant nature and concentration.

The presence of cationic reverse micelles in the reaction media aids thehydrogenolysis-hydrogenation of diphenyl ether to selectively form cyclohexane and cyclohexanol. The % conversion of hydrogenolysis-hydrogenation reaction was found to be dependent on the head-group charges of the surfactant used in the reaction (Figure S3). The difference between the charges of reverse and normal micelles is that in reverse micelles charge is more concentrated compared to the normal micelles. Hence, the charge of reverse micelles appears to play an important role in this reaction. Another interesting observation was, at concentration 0.5 mmol for CTAB and SDS, there is very small but definite increase in the % conversion (from 2% to 4%), which remained constant for SDS and increased gradually for CTAB. The reason for increase in % conversion (in order of 2, for 0 to 0.5 mmol SDS from 2% to 4%) might be due to the hydrophilic-hydrophobic interaction of the regents in the reaction media. We also tried non-ionic surfactant (TritonX-100) and found no significant difference in % conversion from SDS.

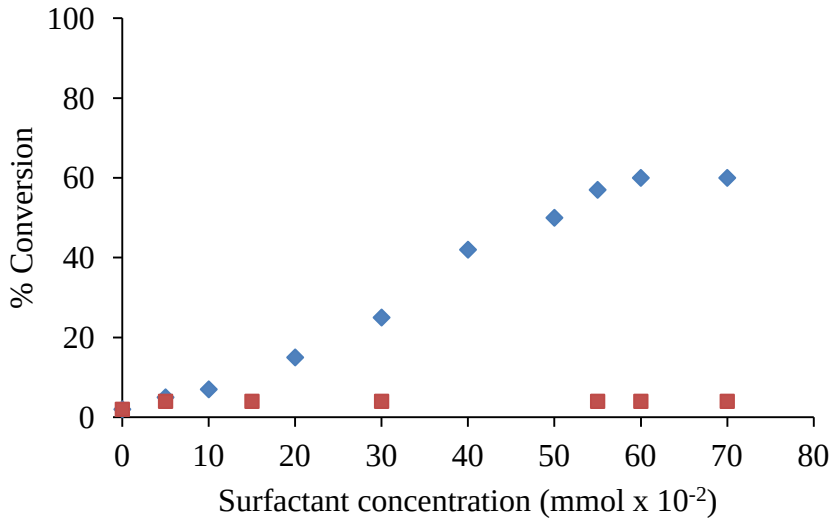

Fig. S3. The effect of surfactant nature and concentration (◆CTAB and ■SDS) on hydrogenolysis-hydrogenation of diphenyl ether in the presence of Ni (5 mol%), L (10 mol%), $LiAl(O^tBu)_3H$ (2.5 eq), toluene (1.5 mL), 5 h, 70 ^OC, stirring rate 1.67 Hz. Each experiment was done three times independently. The variation in the results from the reported average values was within ± 0.75%.

S6. Hypothetical mechanism for H-H reaction.

Scheme S1. Proposed mechanism for the selective arene hydrogenation of DPE in micellar medium.

The exact mechanism for Ni catalyzed H-H in reverse micellar media is still unknown. In micellar medium the formation of L-Ni(II) complex seems to takes place in hydrophobic bulk. The positive effect of strong base NaO^tBu may be due to the formation of an anionic Ni complex which is the main reactive species for hydrogenolysis. The formation of an anionic Ni complex is supported by the very low yield in the presence of anionic surfactant SDS. In this case the anionic Ni complex may be repelled due to concentrated negative charge on the core of anionic micelle. On the other hand, increased yields and shorter reaction times in the presence of CTAB (cationic surfactant) can be explained by considering the attraction between the anionic Ni complex (from bulk) and concentrated positive charge. This may facilitate the contact between anionic Ni complex and the ArOAr (near palisade layer).
After hydrogenolysis of the C-O bond in DPE, benzene and phenol form as products. However, the spatial orientation of phenol in the palisade layer of micelles may be responsible for restricting the further hydrogenolysis of the C-O bond in phenol. Relatively hydrophilic OH group orient towards the reverse micellar core whereas hydrophobic aromatic rings which are orientated towards the bulk solution (containing all reagents) undergoes further reduction. The orientation of the phenol may also keep the phenol intact at the reaction site. Concomitantly, the benzene fragment is further reduced to form cyclohexane. Due to their relative hydrophobic nature (compare to phenol) these final products (cyclohexane and benzene) drift away from the reaction site.

S7. Colloidal Ni species.

The anionic Ni complex is the main reactive species for hydrogenolysis. Micelles seems to protect L-Ni(II) complex (present in hydrophobic bulk) from other reagents like NaO^tBu and $LiAl(O^tBu)_3H$ (present near the anisotropic palisade layer). The separation of catalyst-L from other reagents might protect the catalyst from decomposition and prolongs the activation of the Ni catalyst. This protected colloidal form of Ni may be one of the reasons for the selective arene hydrogenation.
To test the formation of colloidal Ni we added mercury (Hg) with the catalyst system in the reaction medium (Table S2, entry 6). The low % conversion of DPE, shows the inactivity of the Ni catalyst system due to the formation of colloidal nickel amalgamate by the reaction of Hg with the anionic Ni colloidal species in the hydrophobic bulk of micellar medium.