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FULL PAPER

Ruthenium Catalyzed *N*-Alkylation of Cyclic Amines with Primary Alcohols

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Abstract: A robust alcohol amination protocol using common saturated amines and primary alcohols as starting materials is described. The reactions are catalyzed by combination of dichloro(*p*-cymene)ruthenium(II) dimer precatalyst with triphenylphosphine ligand, with the excess alcohol substrate or toluene functioning as the solvent. The catalyst and ligand residues can be precipitated from the reaction media by addition of hexane or cold diethyl ether, followed by precipitation and isolation of the product as a hydrochloride salt.

Introduction

Cyclic amines are common structural elements in agrochemicals,[1] as well as in naturally occurring and synthetic pharmaceutically relevant compounds,[2] including antibiotics, anticancer, analgesic, antidepressant, anti-HIV and anti-HCV agents. Many such compounds are in regular clinical use, with selected examples illustrated in Figure 1. Especially piperidine,[3] piperazine,[4] morpholine,[5] and pyrrolidine[6] moieties and their close analogues are frequently occurring motifs in these structures.[2d]

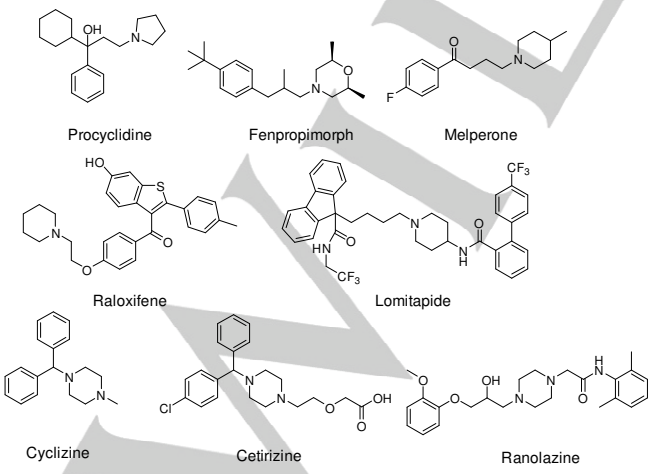
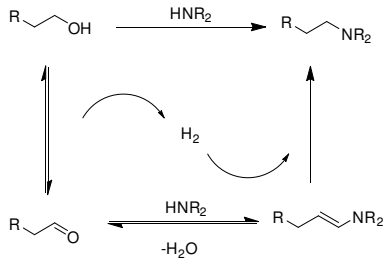


Figure 1. Pharmaceutically active compounds containing saturated cyclic amine motifs.

One of the most common ways to form carbon-nitrogen bonds is by reaction between an organic halide and an amine, in the presence of an inorganic or organic base. While this reaction often is both highly efficient and convenient to operate, it also generates significant amounts of waste. In contrast, the application of catalytic *borrowing hydrogen*[7] (or hydrogen shuttling) for *N*-alkylation using alcohols only produces water as the byproduct, although typically suffers from high reaction temperatures or sensitive catalysts. The borrowing hydrogen reaction of a model primary alcohol followed by amination with secondary amine via enamine to a tertiary amine is illustrated in Scheme 1.

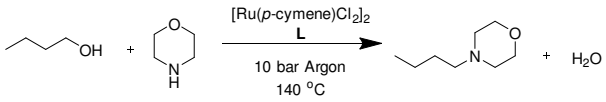


Scheme 1. Amination of primary alcohols with secondary amines under borrowing hydrogen conditions.

In recent years, various homogeneous and heterogeneous[8] catalytic methods have emerged in the borrowing hydrogen field. For homogenous applications, different transition metal catalysts based on iridium,[9] copper,[10] nickel,[11] iron,[12] cobalt,[13] manganese,[14] rhodium[15] and ruthenium[16-19] have been employed. Especially the ruthenium-based systems have been widely and successfully applied to a large variety of amines[16-18] and nitriles.[19] The primary aim of this investigation was to develop a borrowing hydrogen method utilizing a variety of saturated cyclic amines. An important secondary goal was to minimize the waste produced in the purification of the products, i.e., simple removal of catalyst complex and purification of products without the need of chromatographic separation. Here, we describe a robust triphenylphosphine ligated dichloro(*p*-cymene)ruthenium(II) dimer catalyzed methodology for alkylation of cyclic amines with

primary alcohols, while simultaneously minimizing the necessary purification operations.

Results and Discussion



Scheme 2. *N*-Alkylation of morpholine with 1-butanol using dichloro(*p*-cymene)ruthenium(II) dimer precatalyst in combination with phosphine ligands

The *N*-alkylation of morpholine with 1-butanol, illustrated in Scheme 2, was selected as a model reaction, based on the good availability of the reactants. This allowed the reactions to be performed at close to one gram scale in the preliminary screening, carried out in stainless steel reactors at elevated pressure and temperature.

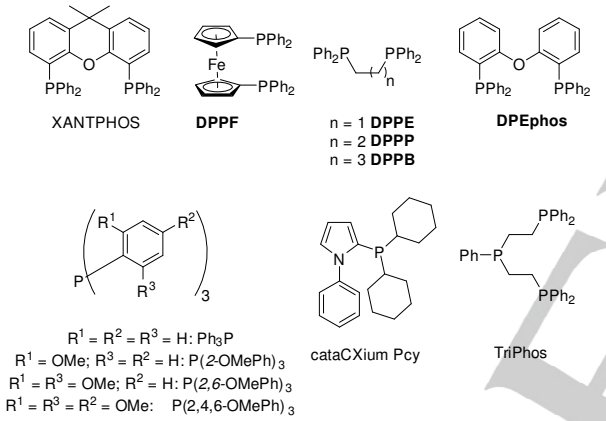


Figure 2. Ligands used in the reaction screening.

Based on prior art,[16-18] a selection of phosphine ligands illustrated in Figure 2 were tested. Results from the ligand screening are summarized in Table 1. As expected, the bidentate ligands **DPPF**, **DPPB** and **DPEphos** in combination with dichloro(*p*-cymene)ruthenium(II) dimer provided good results even at 0.13 mol-% catalyst loading within 21 hours (Table 1, Entries 4, 15 and 17). Tridentate Triphos ligand provided acceptable results in the same reaction setting (Table 1, Entry 21). Also, a number of monodentate ligands, cataCXium®PCy, triphenylphosphine (Ph_3P) and methoxy derivatized triphenylphosphines were investigated. All monodentate ligands resulted in relatively poor GC-based yields for *N*-butyl morpholine, or in no reaction at all. In cases of bidentate ligands, having excess of ligand to ruthenium center (above 1:1 ratio) had minimal to no benefits with respect to the overall yield of *N*-butyl morpholine. Furthermore, under these conditions, in the absence of ligand, some alkylation was observed albeit in low GC-based yield (Table 1, Entry 22). Unfortunately, the absence of ligand resulted in heterogenous mixture interfering with the work-up procedures.

Table 1. Screening of ligands for *N*-alkylation of morpholine with 1-butanol under 10 bar of argon[a]

Entry	Ligand(**L**)	**L** (mol-%)	Yield[b] (%)
1	XANTPHOS	0.52	17
2	XANTPHOS	0.26	16
3	**DPPF**	0.52	53
4	**DPPF**	0.26	54
5	Ph_3P	1.04	30
6	Ph_3P	0.52	20
7	$P(2\text{-}OMePh)_3$	1.04	-[c]
8	$P(2,6\text{-}OMePh)_3$	1.04	-[c]
9	$P(2,4,6\text{-}OMePh)_3$	1.04	-[c]
10	**DPPE**	0.52	-[c]
11	**DPPE**	0.26	38
12	**DPPP**	0.52	44
13	**DPPP**	0.26	53
14	**DPPB**	0.52	51
15	**DPPB**	0.26	57
16	**DPEphos**	0.52	58
17	**DPEphos**	0.26	52
18	cataCXium® PCy	0.52	12
19	cataCXium® PCy	0.26	10
20	Triphos	0.52	-[c]
21	Triphos	0.26	48
22	-	-	18

[a] General Conditions: At 140 °C for ~ 21 h, Morpholine 0.7 mL (8.0 mmol), 1-Butanol 4 mL, $[RuCl_2(p\text{-cymene})]_2$ 6 mg (0.01 mmol; 0.13 mol-%), 10 bar of argon. [b] GC-Yield against tetradecane internal standard. [c] Product barely detectable from the baseline.

Following the initial ligand screening under 10 bar of argon, the reactions with **DPPB**, **DPPF**, **DPEphos,** Triphos and Ph_3P ligands were repeated under atmospheric argon pressure. The results are collected in Table 2. For reaching similar GC-yield of *N*-butyl morpholine as obtained under 10 bar, a four-fold increase in catalyst loading was required with the same reaction time. Surprisingly, unlike the reactions carried out under 10 bar of argon, the Ph_3P ligand here yielded very similar results as compared to the other ligands. Both the Triphos and **DPPF** ligands were excluded from further investigation due to their high cost and minimal benefits over the more common ligands such as **DPEphos** and Ph_3P.

Table 2. *N*-butylation of morpholine under atmospheric pressure.[a]

Entry	Ligand	Yield[b] (%)
1	Triphos	52
2	**DPPB**	43

3	**DPPF**	48
4	**DPEphos**	55
5	Ph_3P	48

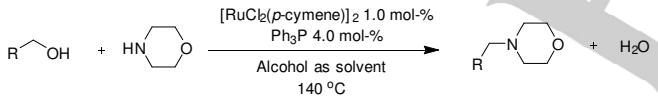
[a] General Conditions: At 140 °C in closed 10 mL stainless steel reactor for ~ 21 h; Morpholine 0.7 mL (8.0 mmol), 1-Butanol 4 mL, $[RuCl_2(p\text{-cymene})]_2$ 24.5 mg (0.04 mmol; 0.5 mol-%), Ligand 0.08 mmol (Ph_3P 0.32 mmol). [b] GC-yield against tetradecane as internal standard.

For purification purposes, after removal of Ph_3P-ligated ruthenium complex with hexane, the *N*-butyl morpholine was precipitated from butanol/hexane solution as a hydrochloride salt by addition of trimethyl silyl chloride to the reaction mixture. The obtained powderous *N*-butyl morpholine hydrochloride was essentially free of catalyst traces (verified by ^{1}H-NMR spectroscopy) after washing with hexane. In comparison, the hydrochloride salt of the product obtained from the reaction using **DPEphos**-ligated ruthenium complex was visibly contaminated with catalyst traces after washing of the powderous product with hexane. The optimized conditions used for substrate scope screening are illustrated in Scheme 3.

Table 3. *N*-butylation of morpholine in a glass reactor.[a]

Entry	$[RuCl_2(p\text{-cymene})]_2$ (mol-%)[b]	Ligand(**L**)	**L** (mol-%)	Yield[c] (%)
1	1	Ph_3P	4	> 95
2	1	Ph_3P	2	> 95
3	0.5	Ph_3P	2	86
4	0.25	Ph_3P	1	39
5	1	**DPEphos**	2	> 95
6	0.5	**DPEphos**	1	> 95

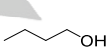
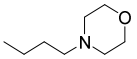
[a] [a] General Conditions: At 140 °C in closed 9 mL sealed thick walled glass reactor for ~ 24 h; Morpholine 0.7 mL (8.0 mmol), 1-Butanol 4 mL. [b] $[RuCl_2(p\text{-cymene})]_2$; 2.0 mol-%: 98 mg, 1.0 mol-%: 49 mg, 0.5 mol-%: 25 mg, 0.25 mol-%: 13 mg. [c] GC-Yield against tetradecane as internal standard.

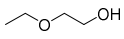
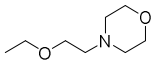
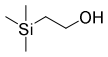
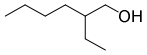
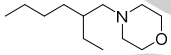
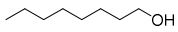
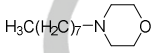
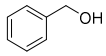
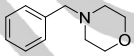
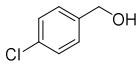
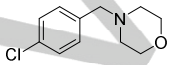
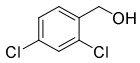
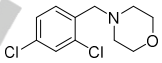
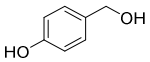
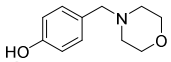
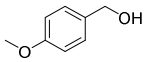
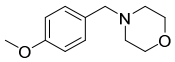
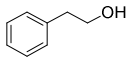
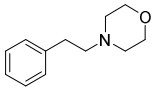
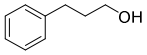
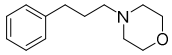
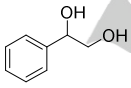
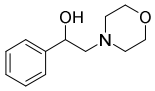
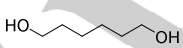
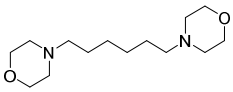
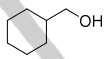
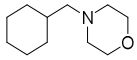
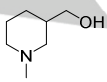
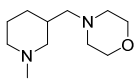
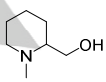
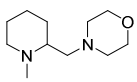


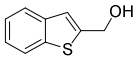
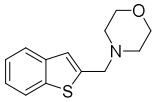
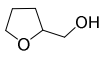
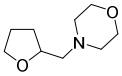
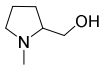
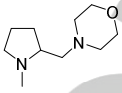
Scheme 3. Optimized reaction conditions obtained from screening.

After the initial screening of reaction conditions, utility of the method was investigated also with other alcohols. Typically, simple unbranched primary alcohols yielded *N*-alkylated morpholines in 60-80% isolated yields (Table 4, Entries 1, 2, 5 and 12), while β-substituted primary alcohols (Table 4, Entries 4, 11, 15-25) resulted in 20-80% isolated yield of the *N*-alkylated product. The β-trimethyl silyl substituent was labile under the investigated conditions, producing the corresponding alkane most likely by hydrolysis of the Si-C bond (Table 4, Entry 3). Unsaturated substrates, such as citronellol, yielded complex unseparable product mixtures. Benzylic 1-phenyl ethanol only gave minor amounts of the *N*-alkylated morpholine derivative, as detected by gas chromatography utilizing both flame ionization detector and mass spectrometry. In contrast, the reactions with benzyl alcohol derivatives as substrates resulted in 32 to 93% isolated yields of the corresponding *N*-benzylated morpholines (Table 4, Entries 6-10). The amination of anisyl alcohol with morpholine was also upscaled to 40 mmol scale to yield 4-[(4-methoxyphenyl)methyl]morpholine hydrochloride in comparable yield and purity as in 8 mmol scale. In cases where conjugated systems could be formed, for example with 2-phenyl ethanol as the substrate, small amounts of unsaturated enamine derivative was detected in the product (Table 4, Entry 11). Secondary alcohols, such as 2-octanol and 1,2-tetradecanediol, reacted in approx. 30% conversion of the starting material with prolonged reaction times not improving the conversion. Also these substrates resulted in heterogeneous mixtures and were, consequently, not investigated further. While the use of 1,2-tetradecanediol as starting material failed, 1-phenyl-1,2-ethanediol was successfully and selectively aminated with morpholine, resulting in 50% isolated yield of compound **13** by crystallization of the product from the crude mixture (Table 4, Entry 13). The use of 1,4-butanediol under these conditions resulted in an unseparable mixture of 1,4-di(morpholin-1-yl)butane with the corresponding conjugated diene. By extending the distance between the two primary alcohol groups, diamination of the terminal diol was achieved in 70% isolated yield for the 1,6-hexanediol substrate (Table 4, Entry 14). Substrates containing tertiary amine functionalities reacted in full conversion of the starting material in 24 hours, but only mediocre (20-38%) isolated yields were obtained (Table 4, Entries 16, 17 and 20). The reaction should be further optimized if these types of substrates are desired, for example, compound **20** was only obtained in 50% GC-based yield with almost full conversion of the alcohol used. Also, the general purification protocol is not fully suitable for all of the compounds investigated. Both sulfur and oxygen containing heterocycles were also investigated as substrates. While the benzothiophene based substrate resulted in 92% isolated yield of the compound **18** as hydrochloride (Table 4, Entry 18), the tetrahydrofurfuryl alcohol starting material gave compound **19** in a significantly lower isolated yield of 45% (Table 4, Entry 19) and furfuryl alcohol produced a very thick, black fluid-like mixture making purification impossible. Finally, fluorene-based substrates were also tested. Similar to 1-phenyl ethanol, the secondary alcohol fluorenol only showed a minute amount of the aminated product by GC analysis. 9-Fluorenemethanol, in turn, gave a significant amount of side products with barely detectable amount of the corresponding aminated compound after 24 hours at 140 ºC.

Table 4. Substrate scope for *N*-alkylation of morpholine with Ph_3P ligated ruthenium catalyst.[a]

Entry	Substrate	Solvent	Product		Yield (%)[b]
1		-		**1**	81[c]

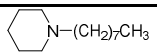
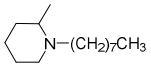
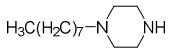
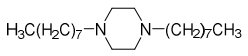
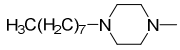
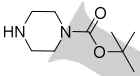
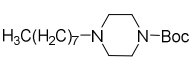
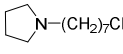
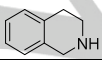
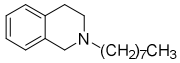
2		Tol[d]		**2**	66[c]
3		Tol[d]		**3**	87[c]
4		-		**4**	65
5		-		**5**	79[c]
6		-		**6**	91[c]
7		Tol[d]		**7**	86[c]
8		Tol[d]		**8**	85[c]
9		Tol[d]		**9**	32[g]
10		-		**10**	92(99)[c],[h]
11		-		**11**	86[c]
12		-		**12**	80[c]
13		Tol[d]		**13**	50[f]
14		Tol[e]		**14**	70
15		-		**15**	78
16		Tol[d]		**16**	38
17		Tol[d]		**17**	30

18		Tol[d]		**18**	92[c]
19		Tol[d]		**19**	45
20		Tol[d]		**20**	20

[a] General Conditions: 4 mL alcohol, 8 mmol morpholine, $[RuCl_2(p\text{-cymene})]_2$ 49 mg (0.08 mmol; 1.0 mol-%), Ph_3P (2eq/Ru, 84 mg) at 140 °C for 24 hour. [b] Isolated yield. [c] Purified as HCl salt. [d] 8 mmol of alcohol and 2.7 mL of toluene [e] 4 mmol of diol and 2.7 mL of toluene. [f] 2 mol-% of catalyst. [g] Purified using flash chromatography. [h] Isolated yield in parentheses for reaction done at 40 mmol scale.

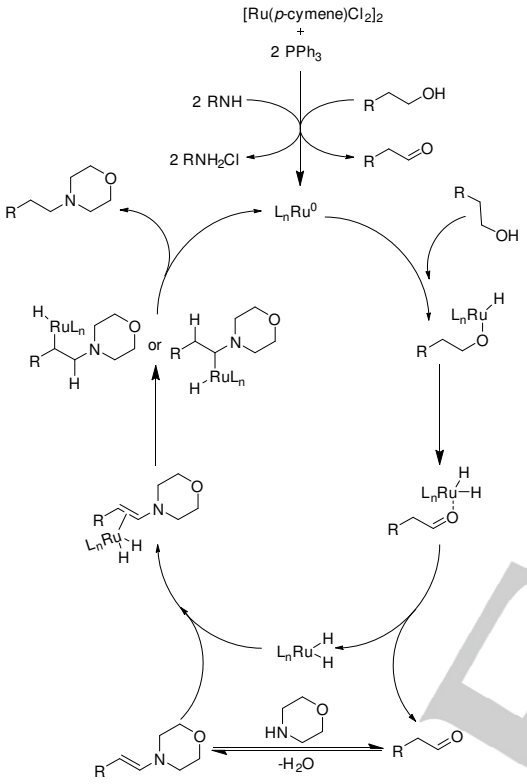
Following the alcohol substrate screening, also different cyclic amines were tested. Simple unhindered compounds, such as piperidine and pyrrolidine, produced the corresponding tertiary amines in high yields (Table 5, Entries 1 and 7). The addition of one α-methyl group as steric hindrance around the amine moiety had minimal effect on the reaction outcome according to GC-analysis of the crude mixture; yielding 75% GC-based yield, but only 51% isolated yield of compound **22** was obtained. (Table 5, Entry 2). Significant steric hindrance around the amine moiety, such as in 2,2,6,6-tetramethyl piperidine, resulted only in barely detectable amounts of the corresponding aminated product by GC analysis. Under slightly modified conditions, selective monoalkylation of piperazine was achieved. Based on GC-analysis of the crude mixture, full conversion of piperazine was achieved without any detectable side products but the monoalkylated piperazine **23** was only obtained in 26% isolated yield (Table 5, Entry 3). By increasing the catalyst loading and extending the reaction time, dialkylation of piperazine could be achieved in 48% isolated yield (Table 5, Entry 4). In contrast, pre *N*-derivatized pipezarines, *N*-methyl piperazine and *N*-Boc-piperazine, yielded the corresponding alkylated piperazines in excellent yields (Table 5, Entries 5 and 6). Also, both indoline and 1,2,3,4-tetrahydroisoquinoline gave the expected alkylated products in 50-80% yields (Table 5, Entries 8 and 9). In case of indoline, both alkylated indole and indoline were detected after the reaction, with the alkylated indoline obtained in 52% isolated yield and the alkylated indole in 23% isolated yield after chromatographic purification.

Table 5. *N*-alkylation of saturated cyclic amines with 1-octanol.[a]

Entry	Substare	Solvent	Product		Yield (%)[b]
1		-		**21**	80[c]
2		-		**22**	51
3		-		**23**	26[d]
4		-		**24**	48[e]
5		-		**25**	91
6		Tol[f]		**26**	80[g]
7		-		**27**	92
8		Tol[f]		**28**	52[g],[h],[i]
9		-		**29**	79[i]

[a] General Conditions: 4 mL 1-octanol, 8 mmol cyclic amine, $[RuCl_2(p\text{-cymene})]_2$ 49 mg (0.08 mmol; 1.0 mol-%), Ph_3P 84 mg (0.32 mmol, 4 mol-%) at 140 °C for 24 hour. [b] Isolated yield. [c] Purified as HCl salt. [d] 6 mmol of piperazine used. [e] 48 hour reaction time with $[RuCl_2(p\text{-cymene})]_2$ 98 mg (0.16 mmol; 2.0 mol-%), Ph_3P 164 mg (0.64 mmol, 8.0 mol-%). [f] 8 mmol of octanol in 2.7 mL of toluene. [g] Purified using flash chromatography. [h] Additional 1.9 mmol of respective indole (Yield: 23 %). [i] 48 hour reaction.

Based on previously reported mechanisms for similar catalyst ligand combinations,[16b,28] it is very likely that the reaction proceeds via formation of a catalytically active ruthenium(0) species by chloride abstraction and dissociation of *p*-cymene. Also, a half-sandwich type [Ru(PPh_3)$_2$(*p*-cymene)Cl]Cl would require an additional inorganic base in order to generate a free coordination site to become catalytically active. Thus, a tentative catalytic cycle is presented in Scheme 4, where L_n symbolizes triphenylphosphine and/or possible amine ligands.



Scheme 4. Proposed catalytic cycle for ruthenium catalyzed borrowing hydrogen reaction.

Conclusion

To conclude, we have developed a simple to operate *N*-alkylation protocol applicable to a variety of cyclic amines with primary alcohols via borrowing hydrogen reaction. Significant advantages of the presented method are the absence of external inorganic base and the concentration ranges close to those commonly required for industrial fine chemical processes. Also, the waste associated with purification procedures was minimized by use of triphenylphosphine ligated ruthenium precatalyst. The in-situ generated catalyst can be mostly precipitated from the reaction mixture followed by simple washing procedures to achieve the pure product. For example this could not be done when utilizing **DPEphos** as ligand. The methodology can be applied to a number of commercially available cyclic amines and primary alcohols. In most cases, the catalyst can be readily precipitated from the reaction media by simple addition of hexane or cold diethyl ether, followed by purification of the product by precipitation as hydrochloride salt followed by toluene trituration or simple acid-base extraction. Limitations arise from sterically hindered amines, secondary alcohols and aliphatic 1,2-diols, as well as from olefin containing compounds. Also, aromatic substituents at β–carbon, such as in 2–phenyl ethanol and indoline, may result in stable enamine derivatives that may be difficult to separate from the product. Currently, our attempts are directed to expansion of the methodology towards possible enantioselective applications, using secondary alcohols and diversely β–substituted primary alcohols as substrates.

Experimental Section

General Considerations: Chemicals, solvents, ruthenium complex and ligands were bought from Merck, TCI or ABCR and used as such unless otherwise noted. 99.996 % Argon was used in ligand and pressure screening, combined liquids were degassed by argon bubbling. Solvents and liquid reagents used in experiments involving glass reactors were dried and degassed and stored in a glovebox. The reaction was followed utilizing GC-Fid, equipped with HP-1 column: (30m × 320 µm × 0.25 µm), and H_2 as carrier gas, using the following temperature program: injector 220 °C, oven T initial = 50 °C (4 min), rate 20 °C/min, T final = 300 °C, hold 5 min. The NMR spectra were recorded using a 500 MHz NMR spectrometer. The measured NMR spectra were calibrated using residual solvent signal as internal standard.[21] The NMR signals assignments were based on 2D NMR (COSY, HSQC, H2BC, INADEQUATE and HMBC) and 1D-TOCSY. Elemental analysis was performed with FLASH 2000 CHNS-analyzer. Infrared spectra were recorded on a FTIR Fourier Transform Infrared Spectrometer. High resolution mass spectroscopy (HRMS) was carried out with micrOTOF spectrometer (Electrospray (ESI)), with a time of flight (TOF) mass analyser. Flash column chromatography was carried out on automated purification system using Redi*Sep* Rf Gold columns with 20-40 µm silica particle size.

Ligand screening: Into ~ 10 mL stainless steel reactor with magnetic stirrer was measured dichloro(*p*-cymene)ruthenium(II) dimer (6 mg, 0.01 mmol) and respective amount of desired (di)phosphine ligand. Reactor was closed and placed under argon atmosphere. Into the reactor was added *n*-butanol (4 mL, 44 mmol), morpholine (0.70 mL, 8 mmol) and tetradecane (0.05 mL, 0.2 mmol). Reactor was pressurized with argon to 10 bar and then set to 140 °C in an aluminum heating block for ~ 21 hours. After cooling down to r.t. the gained solution was analyzed by GC-Fid.

Low pressure experiments: Into ~ 10 mL stainless steel reactor with magnetic stirrer was measured dichloro(*p*-cymene)ruthenium(II) dimer (25 mg, 0.04 mmol) and respective amount of desired (di)phosphine ligand (Ph_3P 0.32 mmol, 84 mg; Triphos 0.08 mmol 43 mg; **DPPB** 0.08 mmol 34 mg; **DPPF** 0.08 mmol 44.5 mg; **DPEphos** 0.08 mmol 44 mg). Reactor was closed and placed under argon atmosphere. Into the reactor was added *n*-butanol (4 mL, 44 mmol), morpholine (0.70 mL, 8 mmol) and tetradecane (0.05 mL, 0.2 mmol). Reactor was set to 140 °C in an aluminum heating block for ~ 21 hours. After cooling down to r.t. the gained solution was analyzed by GC-Fid.

Glass reactor experiments: Into 9 mL thick walled glass reactor with magnetic stirrer was measured dichloro(*p*-cymene)ruthenium(II) dimer and respective amount of desired (di)phosphine ligand. The reactor was taken into a glove box followed by addition of n-butanol (4 mL, 44 mmol), morpholine (0.70 mL, 8 mmol) and tetradecane (55 µL , 0.2 mmol). Reactor was sealed with screw cap, taken outside and heated to 140 °C for 24 hours.

General method A: Into 9 mL thick walled glass reactor with magnetic stirrer was measured dichloro(*p*-cymene)ruthenium(II) dimer (49 mg; 0.08 mmol) and Ph_3P (84 mg; 0.32 mmol). The reactor was taken into a glove

box followed by addition suitable alcohol (4 mL) and respective cyclic amine (8.0 mmol). Reactor was sealed with screw cap, taken outside and heated to 140 °C for 24 hours.

General method B: Into 9 mL thick walled glass reactor with magnetic stirrer was measured dichloro(*p*-cymene)ruthenium(II) dimer (49 mg; 0.08 mmol) and Ph_3P (84 mg; 0.32 mmol). The reactor was taken into a glove box followed by addition of toluene, (2.7 mL) suitable alcohol (8 mmol) and respective cyclic amine (8.0 mmol). Reactor was sealed with screw cap, taken outside and heated to 140 °C for 24 hours.

General purification method. After cooling to room temperature, the mixture was poured into hexane (10 mL) and filtered. Chlorotrimethylsilane (1.6 mL) was added slowly and the mixture was stirred for 2 hours, filtered and washed with small amount of hexane. Solid powder was triturated in small amount of toluene; the liquor was placed into freezer for approx. 12 hours, filtered and triturated in small amount of toluene.

General method for removal of hydrochloride salt. Hydrochloride salt of the amine was suspended into 15 mL of saturated aqueous sodium carbonate and 15 mL of diethyl ether followed by vigorous stirring for two hours. Layers were separated and the aqueous phase was extracted with additional 15 mL of diethyl ether. The organics were combined, dried with sodium sulphate.

***N*-butyl morpholine hydrochloride (1)**. General method **A** with general purification method yielding off white powder. Yield: 1.16 g, 81 %. ^{1}H NMR (D_2O, 500.13 MHz, 25 °C): δ 4.13 (bd, *J* = 12.6 Hz, N-CH_2-CH_2-O, 2H), 3.83 (bt, *J* = 12.2 Hz, , N-CH_2-CH_2-O, 2H), 3.55 (bd, *J* = 12.6 , N-CH_2-CH_2-O, Hz, 2H), 3.25-3.11 (m, N-Bu-CH_2-N, N-CH_2-CH_2-O, 4H), 1.76-1.70 (m, CH_3-CH_2-CH_2-CH_2-N, 2H), 1.44-1.36 (m, CH_3-CH_2-$(CH_2)_2$-N, 2H), 0.94 (t, J = 7.4 Hz, CH_3-$(CH_2)_3$-N, 3H). ^{13}C NMR (D_2O, 125.76 MHz, 25 °C): δ 63.8 (N-CH_2-CH_2-O), 57.1 (CH_3-CH_2-CH_2-CH_2-N), 51.6 (N-CH_2-CH_2-O), 25.0 (CH_3-CH_2-CH_2-CH_2-N), 19.1 (CH_3-CH_2-CH_2-CH_2-N), 12.7 (CH_3-CH_2-CH_2-N). ν_{max} (solid)/cm^{-1}: 2967, 2466, 1447, 1413, 1109, 1065, 974, 912, 867, 621, 472. Anal. Calcd. for $C_8H_{18}ClNO$: C, 53.47; H, 10.10; N, 7.80. Found: C, 53.53; H, 10.32; N, 7.99.

4-(2-ethoxyethyl)-morpholine hydrochloride (2). General method **B** with modified purification method, utilizing combination of chlorotrimethylsilane and ethanol (2 mL) followed by crystallization from acetone yielding white needles. Yield: 1.04 g, 66 %. m.p. = 127-135 °C. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 4.08-4.00 (b, N(CH''CH'')$_2$O 2H), 3.89-3.83 (b, N(CH'CH')$_2$O, 2H), 3.83-3.79 (m, EtOC$H_2$$CH_2$-N, 2H), 3.59 (q, *J* = 7.0 Hz, CH_3CH_2O, 2H), 3.56-3.49 (b, N(CH''CH'')$_2$O, 2H), 3.41-3.38 (m, EtOCH_2CH_2N, 2H), 3.25-3.22 (b, N(CH'CH')$_2$O, 2H) .1.23 (t, *J* = 7.0 Hz, C$H_3$$CH_2$O, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 67.8 (CH_3CH_2O), 64.8 (N(CH_2CH_2)$_2$O), 64.6 ((EtOC$H_2$$CH_2$-N), 57.9 (EtOC$H_2CH_2$-N), 53.5(N(C$H_2$$CH_2$)$_2$O), 15.3 ($CH_3$$CH_2$O). ν_{max} (solid)/cm^{-1}: 2974, 2868, 2450, 1450, 1403, 1379, 1356, 1287, 1139, 1125, 1083, 1066, 1040, 1011, 954, 917, 860, 599, 461, 409. Anal. Calcd. for $C_8H_{18}ClNO_2$: C, 49.10; H, 9.27; N, 7.16. Found: C, 49.02; H, 9.31; N, 7.33.

Ethyl morpholine hydrochloride (3). General method **B** utilizing 2-trimethyl silyl ethanol, with general purification method yielding pale yellow powder. Yield: 1.05 g, 87 % ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 4.06 (dd, *J* = 3.6 Hz, 13.0 Hz, O-(CH'-CH')$_2$-N, 2H), 3.86-3.80 (m, O-(CH''-CH'')$_2$-N 2H), 3.50 (d, *J* = 13.0 Hz, O-(CH'-CH')$_2$-N, 2H), 3.23 (q, *J* = 7.3 Hz, N-C$H_2$$CH_3$ 2H), 3.12 (dt, *J* = 2.9 Hz, 12.2 Hz, O-(CH''-CH'')$_2$-N, 2H) 1.38 (t, *J* = 7.3 Hz, N-CH_2CH_3, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 65.1 O-(CH_2-CH_2)$_2$-N, 53.6 (N-$CH_2$$CH_3$), 52.6 O-($CH_2$-C$H_2$)$_2$-N, 9.3 (N-$CH_2CH_3$). ν_{max} (solid)/cm^{-1}: 2927, 2462, 1697, 1449, 1255, 1107, 1050, 1022, 922, 860, 822, 601, 450. Anal. Calcd. for $C_6H_{14}ClNO$: C, 47.53; H, 9.31; N, 9.30. Found: C, 47.38; H, 9.31; N, 9.30

4-(2-ethylhexyl)-morpholine (4). General method **A** followed by general purification method and removal of hydrochloride salt. The evaporation of solvents yielded yellow oil. Yield: 1.03 g, 65 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ. 3.69 (t, *J* = 4.6 Hz, O-(CH_2-CH_2)$_2$-N, 4 H), 2.37 (b, O-(CH_2-CH_2)$_2$-N, 4H), 2.17-2.09 (m, CH-CH_2-N, 2H), 1.51-1.42 (m, CH-CH_2-N, 1H), 1.42-1.20 (m, CH_3(CH_2)$_4$- and CH_3CH_2CH, 8H), 0.89 (t, *J* = 6.9 Hz, C$H_3$$(CH_2)_4$-, 3H), 0.85 (t, *J* = 7.5 Hz, C$H_3$$CH_2$CH 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 67.3 (O-(CH_2-CH_2)$_2$-N), 63.6 (CH-CH_2-N), 54.4 (O-(CH_2-CH_2)$_2$-N), 35.9 (CH-CH_2-N), 31.5 (CH_3(CH_2)$_2$CH_2CH), 29.1 (CH_3(CH_2)$_2$$CH_2$CH), 24.7 ($CH_3CH_2$CH), 23.3 ($CH_3$(C$H_2$)$_2$$CH_2$CH), 14.3 (C$H_3$$(CH_2)_4$-), 10.9 (C$H_3$$CH_2$CH). ν_{max} (film)/cm^{-1}: 2926, 1456, 1271, 1118, 1015, 865. HRMS–ESI: m/z [M+H]$^+$ calcd for $C_{12}H_{26}NO$: 200.2009; found: 200.2011.

***N*-octyl morpholine hydrochloride (5).** General method **A** with general purification method yielding white powder. Yield: Crop 1: 1.32 g, Crop 2: 0.18 g; 79 %. ^{1}H NMR (D_2O, 500.13 MHz, 25 °C): δ 4.13 (bd, *J* = 12.6 Hz, N-CH_2-CH_2-O, 2H), 3.83 (bt, *J* = 12.5 Hz, , N-CH_2-CH_2-O, 2H), 3.54 (bd, *J* = 12.8 , N-CH_2-CH_2-O, Hz, 2H), 3.21-3.16 (m, N-Bu-CH_2-N, N-CH_2-CH_2-O, 4H), 1.78-1.71 (m, CH_3-$(CH_2)_5$-CH_2-CH_2-N, 2H), 1.42-1.24 (m, CH_3-$(CH_2)_5$-$(CH_2)_2$-N, 10H), 0.87 (t, J = 7.0 Hz, CH_3-$(CH_2)_7$-N, 3H). ^{13}C NMR (D_2O, 125.76 MHz, 25 °C): δ 63.8 (N-CH_2-CH_2-O), 57.4 (CH_3-$(CH_2)_6$-CH_2-N), 51.5 (N-CH_2-CH_2-O), 31.0 (CH_3-(CH_2)$_4$-$(CH_2)_3$-N), 28.10 (CH_3-(CH_2)$_4$-$(CH_2)_3$-N), 28.07 (CH_3-(CH_2)$_4$-$(CH_2)_3$-N), 25.6 (CH_3-$(CH_2)_4$-CH_2-$(CH_2)_2$-N), 23.0 (CH_3-$(CH_2)_5$-CH_2-CH_2-N), 22.0 (CH_3-(CH_2)$_4$-$(CH_2)_3$-N), 13.4 (CH_3-$(CH_2)_7$-N). ν_{max} (solid)/cm^{-1}: 2931, 2866, 2535, 2432, 1454, 1409, 1381, 1266, 1120, 1088, 1016, 975, 906, 873, 752, 698, 623, 576, 511, 471, 440. Anal. Calcd. for $C_{12}H_{26}ClNO$: C, 61.13; H, 11.11; N, 5.94. Found: C, 61.02; H, 11.29; N, 6.08.

***N*-benzyl morpholine hydrochloride (6).** General method **A** with modified purification method**,** utilizing diethyl ether instead of hexane yielding white powder. Yield: 1.55 g, 91 %. ^{1}H NMR (D_2O, 500.13 MHz, 25 °C): δ 7.59-7.50 (m, 5H), 4.38 (s, 2H), 4.11 (bm, 2H), 3.78 (bm, 2H), 3.44 (bd, *J* = 12.5 Hz, 2H), 3.26 (dt, J = 12.5 Hz; 12.5 Hz; 3.4 Hz, 2H). ^{13}C NMR (D_2O, 125.76 MHz, 25 °C): δ 131.2, 130.3, 129.3, 127.9, 63.6, 60.9, 51.2.

All analytical data were in good accordance with reported data.[22]

4-[(4-chlorophenyl)methyl]-morpholine hydrochloride (7). General method **B** with modified purification method**,** utilizing diethyl ether instead of hexane and addition of 2 mL of ethanol prior to addition of chlorotrimethylsilane. After trituration in toluene the product was crystallized from ethanol at -18 ºC yielding yellow needles. The needles crystallized contained approx. 1 wt-% of ethanol. Yield: 1.72 g, 86 %. m.p.: 190-195 °C, sublimation; 220-225 ºC decomposition. ^{1}H NMR (MeOD, 500.13 MHz, 25 °C): δ 7.60 (d, *J* = 8.4 Hz, Cl-C_{Ar}(C_{Ar}H-C_{Ar}H)$_2$-C_{Ar}-CH_2-N, 2H), 7.50 (d, *J* = 8.4 Hz, Cl-C_{Ar}(C_{Ar}H-C_{Ar}H)$_2$-C_{Ar}-CH_2-N, 2H), 4.39 (s, -CH_2-N-(CH_2-CH_2)$_2$-O, 2H), 4.10-3.75 (b, -N-(CH_2-CH_2)$_2$-O, 4H), 3.40-3.15 (b, -N-(CH_2-CH_2)$_2$-O, 4H). ^{13}C NMR (MeOD, 125.76 MHz, 25 °C): δ 137.4 (Cl-C$_{Ar}$), 134.3 (Cl-C_{Ar}(C_{Ar}H-C$_{Ar}$H)$_2$-C_{Ar}-CH_2-N), 130.4 (Cl-C_{Ar}(C$_{Ar}$H-C_{Ar}H)$_2$-C_{Ar}-CH_2-N), 128.5 (C$_{Ar}$-CH_2-N), 64.8 (-N-(CH_2-CH_2)$_2$-O), 60.9 (-CH_2-N-(CH_2-CH_2)$_2$-O), 52.8 (-N-(CH_2-CH_2)$_2$-O). HRMS–ESI: m/z [M-Cl]$^+$ calcd for $C_{11}H_{15}N_1O_1Cl$: 212.0837; found: 212.038. ν_{max} (solid)/cm^{-1}: 2532, 2474, 1602, 1498, 1450, 1403, 1349, 1262, 1123, 1095, 1083, 1023, 974, 909, 863, 809, 797, 718, 669, 525, 467, 411.

4-[(2,4-dichlorophenyl)methyl]-morpholine hydrochloride (8). General method **B** with modified purification method**,** utilizing diethyl ether instead of hexane and addition of 2 mL of ethanol prior to addition of chlorotrimethylsilane. Yielding title compound as pale yellow powder after trituration in toluene. Yield: 1.91 g; 85 %. ^{1}H NMR (MeOD, 500.13 MHz, 25 °C): δ 7.80 (d, *J* = 8.4 Hz, ClC_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}-, 1H), 7.67 (d, *J* = 2.0 Hz, C_{Ar}(Cl)-C_{Ar}H-C_{Ar}(Cl), 1H), 7.51 (dd, *J* = 2.0 Hz, 8.4 Hz, ClC_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}-, 1H), 4.56 (s, -CH_2-N-(CH_2-CH_2)$_2$-O, 2H), 4.10-3.80 (b, (-N-(CH_2-CH_2)$_2$-O, 4H), 3.40 (b, (-N-(CH_2-CH_2)$_2$-O, 4H). ^{13}C NMR (MeOD, 125.76 MHz, 25 °C): δ 138.4 (-C_{Ar}H-C$_{Ar}$(Cl)-C_{Ar}-), 137.9 (ClC_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}-), 136.2 (ClC_{Ar}-C_{Ar}H-C$_{Ar}$H-C_{Ar}-), 131.1 (C_{Ar}(Cl)-C$_{Ar}$H-C_{Ar}(Cl)), 129.3 (ClC_{Ar}-C$_{Ar}$H-C_{Ar}H-C_{Ar}-), 126.9 ClC_{Ar}-C_{Ar}H-C_{Ar}H-C$_{Ar}$-, 64.8 (-N-(CH_2-CH_2)$_2$-O), 57.9 (-CH_2-N-(CH_2-CH_2)$_2$-O), 43.2 (-N-(CH_2-CH_2)$_2$-O). ν_{max} (solid)/cm^{-1}:

2309, 1588, 1479, 1437, 1405, 1261, 1117, 1082, 1054, 976, 907, 865, 821, 800, 746, 699, 659, 613, 562, 493, 459, 419. Anal. Calcd. for $C_{11}H_{14}Cl_3NO$: C, 46.75; H, 4.99; N, 4.96. Found: C, 46.92; H, 5.20; N, 5.02.

4-(4-morpholinylmethyl)-phenol (9). General method **B**. The gained crude mixture was poured onto cold diethyl ether and filtered. After evaporation of solvents the crude mixure was purified using flash chromatography (gradient: hexane:EtOAc 0-100 %) yielding pale yellow solid containing minor impurities. Yield: 0.50 g, 32 %. R_f: 0.11, (1:1 hexane:ethyl acetate). ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 3.73 (t, *J* = 4.7 Hz, 4H), 3.45 (s, 2H), 2.49 (b, 4H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 155.6, 131.1, 128.2, 128.2, 115.6, 66.8, 63.0, 53.5.

All analytical data were in good accordance with reported data.[23]

4-[(4-methoxyphenyl)methyl]-morpholine hydrochloride (10). General method **A** with modified purification method**,** utilizing diethyl ether instead of hexane. A pure white powder was obtained directly by washing of the formed hydrochloride salt few times with cold diethyl. Yield: 1.76 g, 92 %. ^{1}H NMR (MeOD, 500.13 MHz, 25 °C): δ 7.50 (d, *J* = 8.7 Hz, H_3CO-C_{Ar}(C_{Ar}H-C_{Ar}H)$_2$-C_{Ar}-, 2H), 7.02 (d, *J* = 8.7 Hz, H_3CO-C_{Ar}(C_{Ar}H-C_{Ar}H)$_2$-C_{Ar}-, 2H), 4.31 (s, -C$\underline{H}_2$-N-(CH_2-CH_2)$_2$-O, 2H), 4.10-3.70 (m, -N-(CH_2-C$\underline{H}_2$)$_2$-O and OC$\underline{H}_3$, 7H), 3.40-3.10 (b, -N-(C$\underline{H}_2$-CH_2)$_2$-O, 4H). ^{13}C NMR (MeOD, 125.76 MHz, 25 °C): δ 162.6 (H_3CO-$\underline{C}_{Ar}$-), 134.1 (H_3CO-C_{Ar}(C_{Ar}H-$\underline{C}_{Ar}$H)$_2$-C_{Ar}-, 121.4 (H_3CO-C_{Ar}(C_{Ar}H-C_{Ar}H)$_2$-$\underline{C}_{Ar}$-), 115.6 (H_3CO-C_{Ar}($\underline{C}_{Ar}$H-C_{Ar}H)$_2$-C_{Ar}-), 64.9 (-N-(CH_2-$\underline{C}H_2$)$_2$-O), 61.5 (-$\underline{C}H_2$-N-(CH_2-CH_2)$_2$-O), 55.9 (O$\underline{C}H_3$), 52.5 (-N-($\underline{C}H_2$-CH_2)$_2$-O). ν_{max} (solid)/cm^{-1}: 2450, 1611, 1516, 1437, 1404, 1302, 1252, 1185, 1122, 1081, 1059, 1031, 960, 944, 907, 866, 854, 835, 822, 795, 759, 569, 516, 461, 432. Anal. Calcd. for $C_{12}H_{18}ClNO_2$: C, 59.14; H, 7.44; N, 5.75. Found: C, 59.09; H, 7.56; N, 5.73.

4-[(4-methoxyphenyl)methyl]-morpholine hydrochloride (10). Into 30 mL thick walled glass reactor with magnetic stirrer was measured dichloro(*p*-cymene)ruthenium(II) dimer (245 mg; 0.4 mmol) and Ph_3P (420 mg; 1.6 mmol). The reactor was taken into a glove box followed by addition 4-methoxybenzyl alcohol (10 mL) and morpholine (3.50 mL, 40.0 mmol). Reactor was sealed with screw cap, taken outside and heated to 140 °C for 24 hours. After cooling to room temperature, the mixture was poured into cold diethyl ether (30 mL) and filtered. Ethanol (2 mL) was added to the mixture followed by slow addition of chlorotrimethylsilane (8.0 mL), the mixture was stirred for 2 hours, filtered and washed with small amount of diethyl ether. The off white powder was triturated toluene (30 mL) for approx. 1.5 h; filtered and washed with diethyl ether to yield white powder after drying under vacuum. Yield: 9.70 g, 99 %. All analytical data were in good accordance with the previous experiment, *vide supra*.

4-(2-phenylethyl)-morpholine hydrochloride (11). General method **A** with general purification method yielding off white powder containing tiny amount of the styrene derivative (by NMR-analysis). Yield: Crop 1: 1.42 g, Crop 2: 0.14 g, 86 %. ^{1}H NMR (MeOD, 500.13 MHz, 25 °C): δ. 7.37-7.31 (m, -C_{ar}H-(C_{ar}H)$_2$-(C_{ar}H)$_2$-C_{ar}-, 4H), 7.29-2.24 (m, -C_{ar}H-(C_{ar}H)$_2$-(C_{ar}H)$_2$-C_{ar}-, 1H), 4.06 (dd, *J* = 3.5 Hz, 13.0 Hz, -N-(C$\underline{H}$')$_2$-(CH')$_2$-O, 2H), 3.89-3.54 (m, N-(C$\underline{H}$'')$_2$-(CH'')$_2$-O, 2H), 3.57 (d, *J* = 13.0 Hz, N-(CH')$_2$-(C$\underline{H}$')$_2$-O, 2H), 3.41-3.35 (m, Ph-CH_2-C$\underline{H}_2$-N-, 2H), 3.21 (dt, *J* = 3.5 Hz, 12.3, -N-(CH'')$_2$-(C$\underline{H}$'')$_2$-O, Hz, 2H), 3.15-3.11 (m, Ph-C$\underline{H}_2$-CH_2-N-, 2H). ^{13}C NMR (MeOD, 125.76 MHz, 25 °C): δ 137.5 (C_{ar}H-(C_{ar}H)$_2$-(C_{ar}H)$_2$-$\underline{C}_{ar}$-), 130.0 (C_{ar}H-($\underline{C}_{ar}$H)$_2$-(C_{ar}H)$_2$-C_{ar}-), 129.9 (C_{ar}H-(C_{ar}H)$_2$-($\underline{C}_{ar}$H)$_2$-C_{ar}-), 128.2 ($\underline{C}_{ar}$H-(C_{ar}H)$_2$-(C_{ar}H)$_2$-C_{ar}-), 65.0 (-N-($\underline{C}$H)$_2$-(CH)$_2$-O), 59.3 (Ph-CH_2-$\underline{C}H_2$-N-), 53.2 (-N-(CH)$_2$-($\underline{C}$H)$_2$-O), 30.9 (Ph-$\underline{C}H_2$-CH_2-N-). ν_{max} (solid)/cm^{-1}: 2430, 1454, 1266, 1128, 1091, 980, 906, 871, 753, 698, 630, 576, 511, 469, 440. HRMS–ESI: m/z [M-Cl]$^+$ calcd for $C_{17}H_{35}N_2O_2$: 192.1383; found: 192.1410.

4-(3-phenylpropyl)-morpholine hydrochloride (12). General method **A** with modified purification method**,** utilizing diethyl ether instead of hexane, yielding white powder. Yield: 1.54 g, 80 %. ^{1}H NMR (MeOD, 500.13 MHz, 25 °C): δ 7.31-7.24 (m, 4H), 7.23-7.18 (m, 1H), 4.02 (dd, *J* = 3.3 Hz, 13.1 Hz, 2H) 3.84-3.78 (m, 2H), 3.48 (d, J = 12.8 Hz, 2H), 3.18-3.08 (m, 4H), 2.73 (t, *J* = 7.6 Hz, 2H), 2.14-2.07 (m, 2H). ^{13}C NMR (MeOD, 125.76 MHz, 25 °C): δ 141.4, 129.7, 129.4, 127.5, 65.0, 58.0, 53.1, 33.4, 26.4.

All analytical data were in good accordance with reported data.[24]

1-Phenyl-2-morpholinoethanol (13). General method **A** utilizing double amount of catalyst and ligand. The gained mixture was transferred to round bottom flask with diethyl ether and placed cooled to -18 °C. Gained precipitate was crystallized from 2-propanol followed by extraction into hot hexane, decantation, evaporation and finally recrystallized from 2-propanol to afford white needles. The purification cycle was repeated to yield additional crops. Yield: Crop 1: 0.69 g, Crop 2: 0.14 g, 50 %. m.p.: 80-82 °C (lit: 85 °C).[25] ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 7.41-7.36 (m, 4H), 7.32-7.28 (m, 1H) 4.77 (dd, *J* = 10.5 Hz, 3.5 Hz, 1H), 3.90-4.00 (b, 1H), 3.82-3.74 (m, 4H), 2.82-2.72 (b, 2H), 2.60-2.45 (m, 4H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 142.0, 128.5, 127.7, 126.0, 68.7, 67.2, 66.8, 53.6.

All analytical data were in good accordance with reported data.[26]

1,6-di(morpholin-1-yl)hexane (14). General method **B** utilizing 1,6-hexabediol (0.75 g, 4 mmol). **P**urification by general method, followed by removal of hydrochloride salt. The solvent was evaporated to afford yellow oil containing minor impurities Yield: 0.72 g, 70 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 3.70 (t, *J* = 4.7 Hz, 8H), 2.41 (b, 8H), 2.33-2.29 (m, 4H), 1.53-1.42 (m, 4H), 1.32-1.29 (m, 4H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 67.1, 59.3, 53.9, 27.6, 26.7.

All analytical data were in good accordance with reported data. [27]

***N*-(Cyclohexylmethyl)morpholine (15).** General method **A** followed by general purification method and removal of hydrochloride salt. The evaporation of solvents yielded pale brown liquid. Yield: 1.16 g, 78 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 3.69 (t, *J* = 4.7 Hz, 4H), 2.37 (b, 4H), 2.10 (d, *J* = 7.2 Hz, 2H), 1.77-1.73 (m, 2H), 1.72-1.63 (m, 3H), 1.52-1.42 (m, 1H), 1.26-1.09 (m, 3H), 0.90-0.81 (m, 2H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 67.2, 66.3, 54.3, 34.8, 32.0, 26.9, 26.3.

All analytical data were in good accordance with reported data.[28]

4-[(1-methyl-3-piperidinyl)methyl]morpholine (16). General method **B**. Ethanol (2 mL) and chlorotrimethylsilane (1.6 mL) were added slowly and the mixture was stirred for 2 hours. Water (~ 10 mL) was added to the mixture and stirred until two clear layers formed (~1 h). Layers were separated and the organic layer extracted with H_2O (~ 10 mL). Combined aqueous fractions were extracted twice with toluene (2x 10 mL). To the aqueous fraction were added 10 mL of saturated Na_2CO_3 and 15 mL of diethyl ether. The biphasic system was stirred vigorously until two clear layers could be separated (~ 1-2 h). Layers were separated and aqueous fraction extracted with addition diethyl ether (10 mL). Organics were combined, dried with sodium sulfate and evaporated to dryness yielding red brown liquid containing minor impurities. Yield: 0.59 g, 38 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 3.70-3.63 (m, N-(CH_2C$\underline{H}_2$)$_2$-O, 4H), 2.90 (bd, *J* = 10.7 Hz, -CH_2-N(Me)-C$\underline{H}$'CH-, 1H), 2.75 (bd, *J* = 10.7 Hz, (-C$\underline{H}$'-N(Me)-CH_2CH-, 1H), 2.44-2.28 (bm, N-(C$\underline{H}_2$$CH_2$)$_2$-O, 4H), 2.23 (s, N-C$\underline{H}_3$, 3H), 2.13 (d, *J* = 7.3 Hz, -C$\underline{H}_2$-N-($CH_2$$CH_2$)$_2$-O, 2H), 1.88-1.77 (m, -C$\underline{H}$''-N(Me)-CH_2CH- and -CH_2-N(Me)-CH_2C$\underline{H}$- 2H), 1.73-1.61 (m, -C$\underline{H}$'-CH_2-CH_2-N(Me)- and -CH_2-C$\underline{H}$'-CH_2-N(Me)-, 2H), 1.60-1.50 (m, -CH_2-N(Me)-C$\underline{H}$''CH- and -CH_2-C$\underline{H}$''-CH_2-N(Me)-, 2H), 0.88-0.78 (m, -C$\underline{H}$''-CH_2-CH_2-N(Me)-, 1H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 67.1 (N-(CH_2C$\underline{H}_2$)$_2$-O), 63.6 (-C$\underline{H}_2$-N-($CH_2$$CH_2$)$_2$-O), 61.2 (-$CH_2$-N(Me)-C$\underline{H}_2$CH-), 56.6 (-C$\underline{H}_2$-N(Me)-$CH_2$CH-), 54.3 (N-(C$\underline{H}_2$$CH_2$)$_2$-O), 46.9 (N-C$\underline{H}_3$), 33.4 (-$CH_2$-N(Me)-$CH_2C\underline{H}$-), 29.1 (-C$\underline{H}_2$-$CH_2$-$CH_2$-N(Me)-), 25.4 (-$CH_2$-C$\underline{H}_2$-$CH_2$-N(Me)-). HRMS–ESI: m/z [M+H]$^+$ calcd for $C_{11}H_{12}N_2O_1$: 199.1805; found: 199.1809. ν_{max} (film)/cm^{-1}: 2930, 2849, 2773, 1444, 1374, 1272, 1202, 1117, 1059, 1007, 909, 863, 835, 799, 778, 696, 629, 477.

4-[(1-methyl-2-piperidinyl)methyl]-morpholine (17). General method **B.** Ethanol (2 mL) and chlorotrimethylsilane (1.6 mL) were added slowly and the mixture was stirred for 2 hours. Water (~ 10 mL) was added to the mixture and stirred until two clear layers formed (~1 h). Layers were separated and the organic layer extracted with H_2O (~ 10 mL). Combined aqueous fractions were extracted twice with toluene (2x 10 mL). To the aqueous fraction were added 10 mL of saturated Na_2CO_3 and 15 mL of diethyl ether. The biphasic system was stirred vigorously until two clear layers could be separated (~ 1-2 h). Layers were separated and aqueous fraction extracted with addition diethyl ether (10 mL). Organics were combined, dried with sodium sulfate and evaporated to dryness yielding dark yellow oil with minor impurities of the respective enamine. Yield: 0.46 g, 30 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 3.69-3.62 (m, N-(CH_2CH_2)$_2$-O, 4H), 2.82-2.76 (m, -CH''-N(Me)-CH-, 1H), 2.54 (dd, *J* = 4.8 Hz 12.0 Hz, -CH'-N-(CH_2CH_2)$_2$-O, 1H), 2.39 (b, -N-(CH_2CH_2)$_2$-O, 4H), 2.29 (m, N-CH_3, 3H), 2.14 (dd, *J* = 12.0 Hz 18.4 Hz, -CH''-N-(CH_2CH_2)$_2$-O, 1H), 2.04 (dt, *J* = 3.5 Hz, 11.4 Hz, -CH-N(Me)-CH-, 1H), 2.01-1.95 (m, -CH_2-N(Me)-CH-, 1H), 1.84-1.77 (m, CH_2-N(Me)CH-CH'-CH_2, 1H), 1.72-1.66 (m, -CH'-CH_2CH_2-N(Me), 1H), 1.60-1.46 (m, -CH_2CH_2-N(Me)-, 2H), 1.27-1.15 (m, -CH''-CH_2CH_2-N(Me) and CH_2-N(Me)CH-CH''-CH_2, 2H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 67.2 (N-(CH_2CH_2)$_2$-O), 63.1 (-CH_2-N-(CH_2CH_2)$_2$-O), 61.1 (-CH_2-N(Me)-CH-), 57.6 (-CH_2-N(Me)-CH-), 54.7 (N-(CH_2CH_2)$_2$-O), 43.7 (N-CH_3), 31.1 (CH_2-N(Me)CH-CH_2-CH_2), 25.9 (-CH_2CH_2-N(Me)-), 24.2 (-CH_2-CH_2CH_2-N(Me)). HRMS–ESI: m/z $[M+H]^+$ calcd for $C_{11}H_{12}N_2O_1$: 199.1805; found: 199.1799. ν_{max} (film)/cm^{-1}: 2929, 2581, 2778, 1445, 1372, 1276, 1204, 1116, 1070, 1031, 1008, 866, 801, 762, 634, 498.

4-(benzothiophene-2-ylmethyl)morpholine hydrochloride (18). General method **B** with modified purification method**,** utilizing diethyl ether instead of hexane and addition of ethanol (2 mL) prior to addition of chlorotrimethylsilane (1.6 mL). Yielding title compounds as light brown powder after trituration in toluene. Yield: 1.99 g, 92 %. ^{1}H NMR (MeOD, 500.13 MHz, 25 °C): δ 7.85-7.95 (m, C_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}-S, 2H), 7.70 (s, -C_{Ar}-CH-C(CH_2-)-S-C_{Ar}-, 1H), 7.40-7.45 (m, C_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}-S, 2H), 4.73 (s, -CH_2-N-(CH_2-CH_2)$_2$-O, 2H) 4.10-3.90 (bm, -CH_2-N-(CH_2-CH_2)$_2$-O, 4H), 3.53-3.23 (bm, -CH_2-N-(CH_2-CH_2)$_2$-O, 4H). ^{13}C NMR (MeOD, 125.76 MHz, 25 °C): δ 142.5 (-C_{Ar}-CH-C(CH_2-)-S-C_{Ar}-), 140.5 (-C_{Ar}-CH-C(CH_2-)-S-C_{Ar}-), 131.2 (-C_{Ar}-CH-C(CH_2-)-S-C_{Ar}-), 131.0 (-C_{Ar}-CH-C(CH_2-)-S-C_{Ar}-), 127.0 (C_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}-S), 126.2 (C_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}-S), 125.5 (C_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}-S), 123.4 (C_{Ar}-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}H-C_{Ar}-S), 64.9 (-CH_2-N-(CH_2-CH_2)$_2$-O), 56.0 (-CH_2-N-(CH_2-CH_2)$_2$-O), 52.7 (-CH_2-N-(CH_2-CH_2)$_2$-O). ν_{max} (solid)/cm^{-1}: 2961, 2529, 2451, 1532, 1457, 1433, 1409, 1346, 1303, 1258, 1198, 1146, 1124, 1079, 1060, 1016, 986, 956, 903, 867, 831, 743, 725, 707, 621, 567, 500, 443, 416. Anal. Calcd. for $C_{13}H_{16}ClNOS$: C, 57.88; H, 5.98; N, 5.19; S, 11.88. Found: C, 57.70 H, 6.03; N, 5.06; S, 11.64.

4-[(Tetrahydro-2-furanyl)methyl]morpholine (19). General method **B**. After cooling to room temperature, the mixture was poured into hexane (10 mL) and filtered. Ethanol (2 mL) and chlorotrimethylsilane (1.6 mL) were added to the mixture was stirred for 2 hours at room temperature. The excess solvents were evaporated and the thick black oil was taken into small amount of acetone and allowed to stand at -18 ºC for few days. The white to pale yellow solid was separated and the procedure repeated for the liquor. Hydrochloride salt was removed from combined solids by the general method. The solvent was evaporated to afford pale yellow brown liquid. Yield: 0.62 g; 45 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 4.06-4.01 (m, 1H), 3.90-3.86 (m, 1H), 3.76-3.69 (m, 5H), 2.55-2.38 (m, 6H), 2.02-1.95 (m, 1H), 1.93-1.80 (m, 2H), 1.53-.45 (m, 1H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 76.5, 68.3, 67.0, 63.9, 54.4, 30.4, 25.5.

All analytical data were in good accordance with reported data.[29]

4-[(1-methyl-2-pyrrolidinyl)methyl]morpholine (20). General method **B**. Ethanol (2 mL) and chlorotrimethylsilane (1.6 mL) were added slowly and the mixture was stirred for 2 hours. Water (~ 10 mL) was added to the mixture and stirred until two clear layers formed (~1 h). Layers were separated and the organic layer extracted with H_2O (~ 10 mL). Combined aqueous fractions were extracted twice with toluene (2x 10 mL). To the aqueous fraction were added 10 mL of saturated Na_2CO_3 and 15 mL of diethyl ether. The biphasic system was stirred vigorously until two clear layers could be separated (~ 1-2 h). Layers were separated and aqueous fraction extracted with addition diethyl ether (10 mL). Organics were combined, dried with sodium sulfate and evaporated to dryness yielding red brown liquid containing minor impurities. Yield: 0.29 g, 20 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 3.67 (t, *J* = 4.6 Hz, N-(CH_2CH_2)$_2$-O, 4 H), 3.05-3.01 (m, (-CH'-N(Me)-CH-, 1H), 2.51-2.40 (m, -N-(CH_2CH_2)$_2$-O and -CH'-N-(CH_2CH_2)$_2$-O, 5H) 2.39 (s, N-CH_3, 3H), 2.36-2.20 (m, (-CH_2-N(Me)-CH- and -CH''-N-(CH_2CH_2)$_2$-O, 2H), 2.20- 2.12 (m, -CH''-N(Me)-CH-, 1H), 1.98-1.90 (m, -CH'-CH_2-CH_2-N(Me)-CH-, 1H), 1.79-1.62 (m, -CH_2-CH_2-CH_2-N(Me)-CH-, 2H), 1.56-1.49 (m, -CH''-CH_2-CH_2-N(Me)-CH- 1H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 67.1 (N-(CH_2CH_2)$_2$-O), 64.5 (-CH_2-N-(CH_2CH_2)$_2$-O), 62.6 (-CH_2-N(Me)-CH-), 57.9 ((-CH_2-N(Me)-CH-), 54.5 (N-(CH_2CH_2)$_2$-O), 41.7 (N-CH_3), 30.9 (-CH_2-CH_2-CH_2-N(Me)-CH-), 22.7 (-CH_2-CH_2-CH_2-N(Me)-CH-). HRMS–ESI: m/z $[M+H]^+$ calcd for $C_{10}H_{21}N_2O$: 185.1648 found: 185.1639. ν_{max} (film)/cm^{-1}: 2954, 2769, 1454, 1275, 1206, 1115, 1070, 1035, 1013, 910, 863, 796, 491.

***N*-octyl piperidine hydrochloride (21)**. General method **A** with general purification method yielding white powder. Second crop was triturated first in diethyl ether followed by toluene trituration. Yield: Crop1. 1.14 g, Crop 0.36 g, 80 %. ^{1}H NMR (D_2O, 500.13 MHz, 25 °C): δ 3.52 (bd, N-(CH_2)$_2$-(CH_2)$_2$-CH_2, 2H), 3.09-3.05 (m, , CH_2-N-(CH_2)$_2$- , 2H), 2.94-2.88 (m, N-(CH_2)$_2$-(CH_2)$_2$-CH_2, 2H), 1.99-1.90 (m, N-(CH_2)$_2$-(CH_2)$_2$-CH_2, 2H), 1.85-1.79 (m, N-(CH_2)$_2$-(CH_2)$_2$-CH_2, 1H), 1.77-1.66 (m, N-(CH_2)$_2$-(CH_2)$_2$-CH_2, CH_2-CH_2-N-(CH_2)$_2$-(CH_2)$_2$-CH_2, 4H), 1.52-1.44 (m, N-(CH_2)$_2$-(CH_2)$_2$-CH_2, 1H), 1.39-1.26 (m, CH_3-(CH_2)$_5$-(CH_2)$_2$-N, 10H) 0.87 (t, J = 7.1 Hz, CH_3-(CH_2)$_7$-N, 3H). ^{13}C NMR (D_2O, 125.76 MHz, 25 °C): δ 57.0 (CH_2-N-(CH_2)$_2$-), 53.1 (N-(CH_2)$_2$-(CH_2)$_2$-CH_2), 31.0 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 28.13 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 28.11 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 25.8 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 23.3 (-CH_2-CH_2-N-(CH_2)$_2$-(CH_2)$_2$-CH_2), 22.8 (N-(CH_2)$_2$-(CH_2)$_2$-CH_2), 22.0 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 21.2 (N-(CH_2)$_2$-(CH_2)$_2$-CH_2), 13.4 (CH_3-(CH_2)$_7$-N). ν_{max} (solid)/cm^{-1}: 2430, 1454, 1265, 1127, 1091, 979, 906, 871, 752. Anal. Calcd. for $C_{13}H_{28}ClN$: C, 66.78; H, 12.07; N, 5.99. Found: C, 66.39; H, 12.05; N, 5.90.

***N*-octyl 2-methyl piperidine (22).** General method **A** with modified purification method**,** using 4 hours of stirring after addition of chlorotrimethylsilane, yielding white solid in two crops. The crops were combined and the hydrochloride salt removed according to the general method. The solvent was evaporated to afford yellow oil. Yield: 0.86 g, 51 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 2.86-2.82 (m, -(CH(CH_3)-N-CH'-CH_2-CH_2-, 1H), 2.64-2.60 (m, CH_3-(CH_2)$_6$-CH'-N, 1H), 2.34-2.28 (m, CH_3-(CH_2)$_6$-CH''-N 1H), 2.26-2.20 (m, N-CH(CH_3)-CH_2, 1H), 2.14-2.09 (m, -(CH(CH_3)-N-CH''-CH_2-CH_2-, 1H), 1.67-1.49 (m, N-CH(CH_3)-CH', -(CH(CH_3)-N-CH_2-CH_2-CH_2-, -(CH(CH_3)-N-CH_2-CH_2-CH'-, 4H), 1.49-1.36 (m, N-CH_2-CH_2-(CH_2)$_5$-CH_3, 2H) 1.32-1.16 (m, N-CH(CH_3)-CH'', -(CH(CH_3)-N-CH_2-CH_2-CH''-, -N-(CH_2)$_2$-(CH_2)$_5$-CH_3, 12H), 1.04 (d, *J* = 6.3 Hz, piperidine-CH_3, 3H), 0.87 (t, J = 7.0 Hz, CH_3-(CH_2)$_7$-N, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 55.9 (N-CH(CH_3)-CH_2), 54.4 (CH_3-(CH_2)$_6$-CH_2-N), 52.4 (-(CH(CH_3)-N-CH_2-CH_2-CH_2-), 34.9 (N-CH(CH_3)-CH_2), 31.9 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 29.8 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 29.4 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 28.0 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 26.4 (-(CH(CH_3)-N-CH_2-CH_2-CH_2-), 25.3 (N-CH_2-CH_2-(CH_2)$_5$-CH_3), 24.3 (-(CH(CH_3)-N-CH_2-CH_2-CH_2-), 22.8 (CH_3-(CH_2)$_5$-(CH_2)$_2$-N), 19.4 (piperidine-CH_3), 14.2 (CH_3-(CH_2)$_7$-N). ν_{max} (film)/cm^{-1}: 2923, 2853, 1466, 1371, 1076. HRMS–ESI: m/z $[M+H]^+$ calcd for $C_{14}H_{30}N$: 212.2373; found: 212.2405.

***N*-octyl piperazine (23)**. General method **A,** utilizing piperazine (0.53 g; 6 mmol), followed by general purification method. Gained red brown paste was extracted with hot acetone and the whole mixture was placed in freezer after cooling to rt, precipitating white to pale red solid. The hydrochloride was removed with the general method .The solvent was evaporated to afford red brown liquid. Yield: 0.31 g, 26%. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 2.87 (t, *J* = 4.9 Hz, 4H), 2.38 (b, 4H), 2.29-2.26 (m,

2H), 1.58 (b, 1H), 1.49-1.44 (m, 2H), 1.30-1.25 (m, 10H), 0.86 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 59.7, 54.9, 46.3, 32.0, 29.7, 29.4, 27.8, 26.8, 22.8, 14.2.

All analytical data were in good accordance with reported data. [30]

***N,N*-dioctylpiperazine (24).** Into 9 mL thick walled glass reactor with magnetic stirrer was measured dichloro(*p*-cymene)ruthenium(II) dimer (98 mg; 0.16 mmol), Ph_3P (168 mg; 0.64 mmol) and piperazine (0.35 g, 4 mmol). The reactor was taken into glove box followed by addition octanol (4 mL). Reactor was sealed with screw cap, taken outside and heated to 140 °C for 48 hours. After cooling to room temperature the mixture was purified following the general purification method and removal of the hydrochloride salt. The solvent was evaporated to afford red brown liquid. Yield: 0.60 g, 48%. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 2.47 (b, N-[(C$\underline{H}_2$)$_2$-]$_2$-N, 8H), 2.23-2.28 (m, N-C$\underline{H}_2$-(CH$_2$)$_6$CH$_3$, 4H), 1.50-1.45 (m, N-CH$_2$-C$\underline{H}_2$-(CH$_2$)$_5$CH$_3$, 4H), 1.31-1.19 (m, N-(CH$_2$)$_2$(C$\underline{H}_2$)$_5$CH$_3$, 20H), 0.87 (t, *J* = 7.0 Hz, N-(CH$_2$)$_7$C$\underline{H}_3$, 6H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 59.1 (N-$\underline{C}$H$_2$-(CH$_2$)$_6$CH$_3$), 53.5 (N-[($\underline{C}$H$_2$)$_2$-]$_2$-N), 32.0 (N-(CH$_2$)$_2$($\underline{C}$H$_2$)$_5$CH$_3$), 29.7 (N-(CH$_2$)$_2$($\underline{C}$H$_2$)$_5$CH$_3$), 29.4 (N-(CH$_2$)$_2$($\underline{C}$H$_2$)$_5$CH$_3$), 27.8 (N-(CH$_2$)$_2$($\underline{C}$H$_2$)$_5$CH$_3$), 27.1 (N-CH$_2$-$\underline{C}$H$_2$-(CH$_2$)$_5$CH$_3$), 23.0 (N-(CH$_2$)$_2$($\underline{C}$H$_2$)$_5$CH$_3$), 14.2 (N-(CH$_2$)$_7$$\underline{C}H_3$). ν_{max} (film)/cm^{-1}: 2922, 2853, 2806, 1464, 1375, 1270, 1159, 1117, 1012, 825, 721. HRMS–ESI: m/z [M+H]$^+$ calcd for $C_{20}H_{43}N_2$: 311.3421; found: 311.3511.

1-Methyl-4-octyl-piperazine (25). General method **A.** After cooling to room temperature, the mixture was poured into hexane (10 mL) and filtered. Chlorotrimethylsilane (1.6 mL) was added slowly and the mixture was stirred for 2 hours. To the mixture was added water (~ 10 mL) and stirred until two clear layers formed (~1 h). Layers were separated and the organic layer extracted with H_2O (~ 10 mL). Combined aqueous fractions were extracted twice with toluene (2x 10 mL). Into the aqueous fraction were added 10 mL of saturated Na_2CO_3 and 15 mL of diethyl ether. The biphasic system was stirred vigorously until two clear layers could be separated (~ 1-2 h). Layers were separated and aqueous was extracted with addition diethyl ether (10 mL). Organics were combined, dried with sodium sulfate and evaporated to dryness. The gained cloudy yellowish oil was further taken into hexane and kept at -18 °C for 1 hour before filtering thru thin pad of cellite and evaporated to yield colorless oil. Yield: 1.55 g, 91 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 2.80-2.32 (b, 8H), 2.31-2.28 (m, 2H), 2.26 (s, 3H), 1.49-1.44 (m, 2H), 1.30-1.17 (m, 10H), 0.85 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 59.0, 55.3, 53.4, 46.2, 31.9, 29.7, 29.4, 27.8, 27.1, 22.8, 14.2.

All analytical data were in good accordance with reported data.[31]

4-Octyl-1-(*tert*-butoxycarbonyl)piperazine (26). General method **B**. After cooling to room temperature, the mixture was poured into hexane (10 mL) and filtered. Solvents were evaporated followed by flash purification (Gradient: Petrol ether:EtOAc 0-100 %) yielding red brown oil. Yield: 1.91 g, 80 %. R_f = 0.33 (Hexane:EtOAc 3:1). ^{1}H NMR (MeOD, 500.13 MHz, 25 °C): δ 3.43 (b, (C$\underline{H}_2$)$_2$-N-Boc ,4H), 2.42 (t, (C$\underline{H}_2$)$_2$-N-octyl ,4H), 2.35 (m, CH$_3$(CH$_2$)$_5$CH$_2$C$\underline{H}_2$-N ,2H), 1.55-1.50 (m, CH$_3$(CH$_2$)$_5$C$\underline{H}_2$CH$_2$-N, 2H), 1.45 (s, OC(C$\underline{H}_3$)$_3$, 9H), 1.36-1.10 (m, CH$_3$(C$\underline{H}_2$)$_5$CH$_2$CH$_2$-N, 10H), 0.90 (t, J = 7.0 Hz, C$\underline{H}_3$(CH$_2$)$_5$CH$_2$CH$_2$-N, 3H). ^{13}C NMR (MeOD, 125.76 MHz, 25 °C): δ 156.4 (-$\underline{C}$O$_2$-C(CH$_3$)$_3$), 81.2 (-CO$_2$-$\underline{C}$(CH$_3$)$_3$), 59.8 (CH$_3$(CH$_2$)$_5$CH$_2$$\underline{C}H_2$-N), 54.0 ((C$\underline{H}_2$)$_2$-N-octyl) 44.8-43.8 ((C$\underline{H}_2$)$_2$-N-Boc), 33.0 ((CH$_3$(C$\underline{H}_2$)$_5CH_2CH_2$-N)), 30.6 (CH$_3$(C$\underline{H}_2$)$_5CH_2CH_2$-N), 30.4 (CH$_3$(C$\underline{H}_2$)$_5CH_2CH_2$-N), 28.6 (CO$_2$C(C$\underline{H}_3$)$_3$, CH$_3$(C$\underline{H}_2$)$_5CH_2CH_2$-N), 27.5 (CH$_3$(CH$_2$)$_5C\underline{H}_2CH_2$-N), 23.7 (CH$_3$(C$\underline{H}_2$)$_5CH_2CH_2$-N), 14.4 (C$\underline{H}_3$(CH$_2$)$_5CH_2CH_2$-N). ν_{max} (film)/cm^{-1}: 2925, 1697, 1416, 1364, 1242, 1170, 1004, 867, 768. HRMS–ESI: m/z [M+H]$^+$ calcd for $C_{17}H_{35}N_2O_2$: 299.2693; found: 299.2695.

***N*-octyl pyrrolidine (27).** General method **A.** After cooling to room temperature, the mixture was poured into hexane (10 mL) and filtered. Chlorotrimethylsilane (1.6 mL) was added slowly and the mixture was stirred for 2 hours. Water (~ 10 mL) was added to the mixture and stirred until two clear layers formed (~1 h). Layers were separated and the organic layer extracted with H_2O (~ 10 mL). Combined aqueous fractions were extracted twice with toluene (2x 10 mL). To the aqueous fraction were added 10 mL of saturated Na_2CO_3 and 15 mL of diethyl ether. The biphasic system was stirred vigorously until two clear layers could be separated (~ 1-2 h). Layers were separated and aqueous fraction extracted with addition diethyl ether (10 mL). Organics were combined, dried with sodium sulfate and evaporated to dryness yielding colorless oil with minor solvent impurities. Yield: 1.35 g, 92 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ. 2.50-2.43 (m, 4H), 2.42-2.36 (m, 2H), 1.78-1.71 (m, 4H), 1.56-1.45 (m, 2H), 1.35-1.17 (m, 10H), 0.86 (t, *J* = 9.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ. 56.9, 54.4, 32.0, 29.7, 29.4, 29.3, 27.9, 23.5, 22.8, 14.2.

All analytical data were in good accordance with reported data.[32]

***N*-octyl-Indoline (28).** General method **B** with 48 hour reaction time. After cooling to room temperature, the mixture was poured into hexane (10 mL) and filtered. Solvents were evaporated followed by two subsequent purifications by flash chromatography (gradient: petrol ether:EtOAc 0-100 %) yielding two products: Indoline derivative as pale yellow liquid. Yield: 0.96 g, 52 %, R_f: 0.67 (Toluene); Indole derivative as pale green liquid. Yield: 0.43 g, 23 %, R_f: 0.88 (Toluene).

***N*-octyl-Indoline:** ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ 7.09-7.04 (m, 2H), 6.63 (t, *J* = 7.3, Hz, 1H), 6.47 (d, *J* = 7.7 Hz, 1H), 3.34 (t, *J* = 8.3 Hz, 2H), 3.05 (t, *J* = 7.4 Hz, 2H), 2.96 (t, *J* = 8.3 Hz, 2H), 1.64-1.56 (m, 2H), 1.39-1.29 (m, 10H), 0.91 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ 152.9, 130.1, 127.4, 124.5, 117.3, 107.0, 53.2, 49.5, 32.0, 29.6, 29.5, 28.7, 27.5, 27.4, 22.8, 14.3.

All analytical data were in good accordance with reported data.[33]

***N*-octyl-Indole:** ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ. 7.65 (d, *J* = 7.9 Hz, 1H), 7.38-7.35 (m, 1H), 7.24-7.21 (m, 1H), 7.14-7.08 (m, 2H), 6.51 (dd, *J* = 3.1 Hz, 0.7 Hz, 1H), 4.13 (t, *J* = 7.2 Hz, 2H), 1.89-1.82 (m, 2H), 1.38-1.21 (m, 10H) 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ. 136.1, 128.7, 127.9, 121.4, 121.1, 119.3, 109.5, 100.9, 46.6, 31.9, 30.4, 29.4, 29.3, 27.2, 22.8, 14.2.

All analytical data were in good accordance with reported data.[34]

***N*-octyl Tetrahydroquinoline (29).** General method **A,** using 48 hour reaction time, followed by general purification method and removal of hydrochloride salt. Evaporation of solvent yielded a red brown liquid. Yield: 1.55 g, 79 %. ^{1}H NMR ($CDCl_3$, 500.13 MHz, 25 °C): δ. 7.14-7.08 (m, 3H), 7.03-7.01 (m, 1H), 3.63 (s, 2H), 2.91 (t, J = 5.9 Hz, 2H), 2.73 (t, J = 5.9 Hz, 2H), 2.50, (t, J = 7.7 Hz, 2H), 1.64-1.57 (m, 2H), 1.34-1.28 (m, 10H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125.76 MHz, 25 °C): δ. 135.1, 134.5, 128.8, 126.7, 126.1, 125.6, 58.8, 56.4, 51.2, 32.0, 29.7, 29.4, 29.3, 27.8, 27.4, 22.8, 14.3.

All analytical data were in good accordance with reported data. [35]

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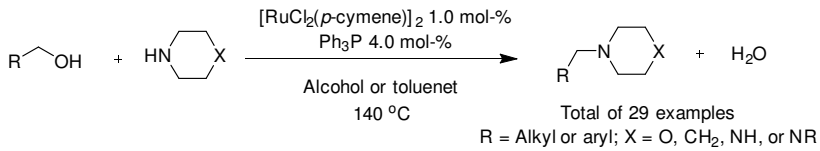
FULL PAPER

Borrowing hydrogen



A robust alcohol amination protocol using common saturated amines and primary alcohols as starting material is described with total of 29 examples. The reactions are catalyzed by combination of dichloro(*p*-cymene)ruthenium(II) dimer precatalyst with triphenylphosphine ligand. The catalyst residues can be precipitated from the reaction media by addition of hexane or cold diethyl ether, followed by precipitation and isolation of the product as a hydrochloride salt without the need of chromatographic purification in most cases.