

-Supporting Information-

Liquid Ammonia as a Dipolar Aprotic Solvent for Aliphatic Nucleophilic Substitution Reaction

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1. Analysis of chiral starting materials and products.

GC condition for the analysis of (R, S)- α -methyl benzyl alcohol:

Inlet temperature: 150°C; detector temperature: 150°C;

Column: Varian Chrompack CP-Chiral-Dex CB (25.0m $\times$ 250 μ m $\times$ 0.25 μ m);

Oven temperature: Isothermal temperature fixed at 120 °C for 35mins;

Inlet pressure: 14 psig;

Retention time of alcohol enantiomers:

(S)- α -methyl benzyl alcohol: 20.6mins;

(R)- α -methyl benzyl alcohol: 23.6mins.

GC condition for the analysis of (R, S)- α -methyl benzyl chloride:

Inlet temperature: 120°C; detector temperature: 120°C;

Column: Varian Chrompack CP-Chiral-Dex CB (25.0m $\times$ 250 μ m $\times$ 0.25 μ m);

Oven Temperature: Isothermal temperature fixed at 100 °C for 20 mins;

Inlet pressure: 14 psig;

Retention time of the chloride enantiomers:

(S)- α -methyl benzyl chloride: 12.1mins;

(R)- α -methyl benzyl chloride: 11.5mins.

GC condition for the analysis of (R, S)- α -methyl benzylamine:

Inlet temperature: 100°C; detector temperature: 100°C;

Column: Varian Chrompack CP-Chiral-Dex CB (25.0m $\times$ 250 μ m $\times$ 0.25 μ m);

Oven Temperature: Isothermal temperature fixed at 100 °C for 35 mins;

Inlet pressure: 10 psig;

Retention time of the amine enantiomers:

(S)- α -methyl benzylamine: 29.16mins;

(R)- α -methyl benzylamine: 30.02mins.

The structures of amines were confirmed by authenticated samples and GC-MS.

2. Ionisation of phenols and aminium ions in liquid ammonia

2.1 Ionisation of phenols

Table S1 Molar extinction coefficient ($\epsilon_{\max}$) and maximum absorbance wavelength ($\lambda_{\max}$) of phenols in liquid ammonia (LNH₃) at room temperature

phenol	pK _a	$\lambda_{\max}$ (nm)				$\epsilon_{\max}$ (M ⁻¹ ·cm ⁻¹)			
		Et ₂ O	H ₂ O pH=1	H ₂ O pH=13	LNH ₃	Et ₂ O	H ₂ O pH=1	H ₂ O pH=13	LNH ₃
4-methoxyphenol	10.21	290	287	306	296	2650	2800	2780	3530
phenol	9.99	274	270	287	275	1980	1370	2600	2340
4-chlorophenol	9.20	283	285	294	287	1833	1890	2150	1885
3-chlorophenol	9.02	276	274	292	279	2215	1850	2835	2440
4-carboxymethylphenol	8.47	251	255	295	319	25050	20360	28010	28200
3-nitrophenol	8.35	346	340	398	440	2320	2210	3930	4210
4-cyanophenol	7.95	244	243	274	298	16450	17220	22710	35200
2,4-dibromophenol	7.79	287	285	307	331	4240	3360	5670	4260
2,4-dichlorophenol	7.65	286	283	305	325	4880	3120	4850	6240
3,5-dichlorophenol	7.51	282	279	297	320	3265	2295	4425	5470
5-methyl-2-nitrophenol	7.41	282	295	417	441	8765	4275	6004	9640
2-nitrophenol	7.23	272	278	418	444	7410	5985	4620	9140
4-nitrophenol	7.14	302	316	399	434	13165	9155	15990	39060

A. pK_a calculation of phenols under ionic strength

The molar extinction coefficient of fully ionised species of phenol in liquid ammonia was obtained by adding the salt (KClO₄) until the absorbance of phenol at its $\lambda_{\max}$ shows a saturation. The apparent pK_a of phenol at zero ionic strength was extrapolated from the empirical linear relationship between square root of ionic strength and observed absorbance. The pK_a of phenol under different ionic strength was calculated according the following equation:

$$\text{pK}_a = -\log \frac{[\text{PhO}^-][\text{NH}_4^+]}{[\text{PhOH}]}$$

Table S2, Figure S2 Linear relationship of pK_a of 4-methoxyphenol ($3 \times 10^{-4} M$) with the square root of ionic strength (I , $KClO_4$) in liquid ammonia at room temperature

$I = C_{KClO_4}(M)$	$I^{1/2}(M^{1/2})$	Absorbance	pK_a
0	0.00	0.035	6.59
0.1	0.32	0.063	6.07
0.2	0.45	0.109	5.58
0.3	0.55	0.127	5.44
0.4	0.63	0.168	5.18
0.5	0.71	0.205	4.99
0.8	0.89	0.264	4.74

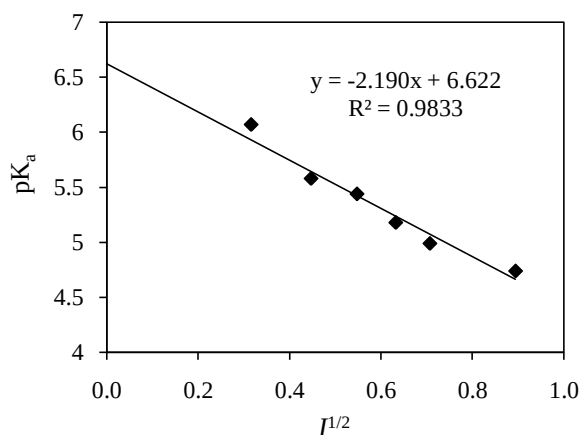


Table S3, Figure S3 Linear relationship of pK_a of phenol ($3 \times 10^{-4} M$) with the square root of ionic strength (I , $KClO_4$) in liquid ammonia at room temperature

$I = C_{KClO_4}(M)$	$I^{1/2}(M^{1/2})$	Absorbance	pK_a
0	0.00	0.000	6.02
0.1	0.07	0.140	5.01
0.2	0.10	0.246	4.66
0.3	0.22	0.321	4.16
0.4	0.45	0.349	4.07
0.5	0.54	0.369	4.00

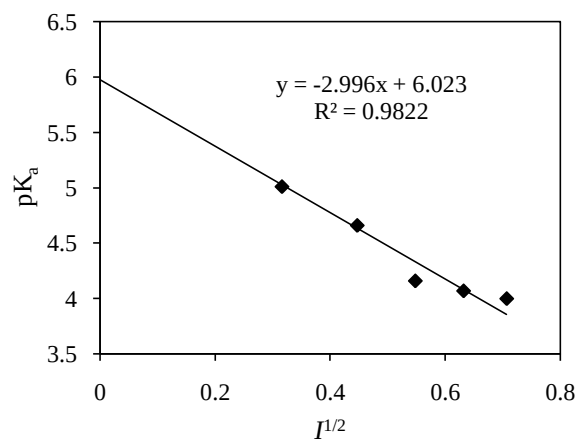


Table S4, Figure S4 Linear relationship of pK_a of 1-naphthol ($1 \times 10^{-4} M$) with the square root of ionic strength (I , $KClO_4$) in liquid ammonia at room temperature

$I = C_{KClO_4}(M)$	$I^{1/2}(M^{1/2})$	Absorbance	pK_a
0	0.00	0.152	6.02
0.005	0.32	0.288	5.01
0.01	0.45	0.431	4.66
0.05	0.55	0.681	4.16
0.2	0.63	0.756	4.07
0.3	0.71	0.833	4.00

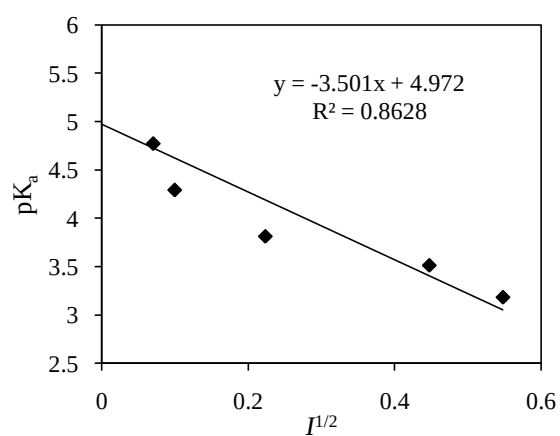


Table S5, Figure S5 Linear relationship of pK_a of 4-chlorophenol ($1 \times 10^{-4} M$) with the square root of ionic strength (I , $KClO_4$) in liquid ammonia at room temperature

$I = C_{KClO_4}(M)$	$I^{1/2}(M^{1/2})$	Absorbance	pK_a
0	0.00	0.056	4.49
0.05	0.07	0.155	3.91
0.1	0.10	0.220	3.48
0.2	0.22	0.281	2.86
0.3	0.32	0.304	2.05

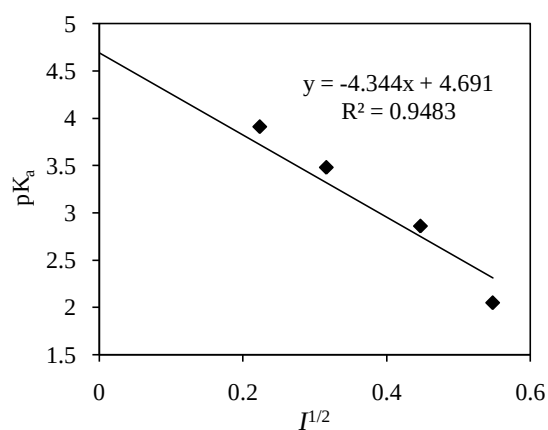


Table S6, Figure S6 Linear relationship of pK_a of 3-chlorophenol ($1 \times 10^{-4} M$) with the square root of ionic strength (I , $KClO_4$) in liquid ammonia at room temperature

$I = C_{KClO_4}(M)$	$I^{1/2}(M^{1/2})$	Absorbance	pK_a
0	0.00	0.053	4.56
0.005	0.07	0.150	4.12
0.01	0.10	0.239	3.72
0.05	0.22	0.360	2.87
0.1	0.32	0.379	2.56

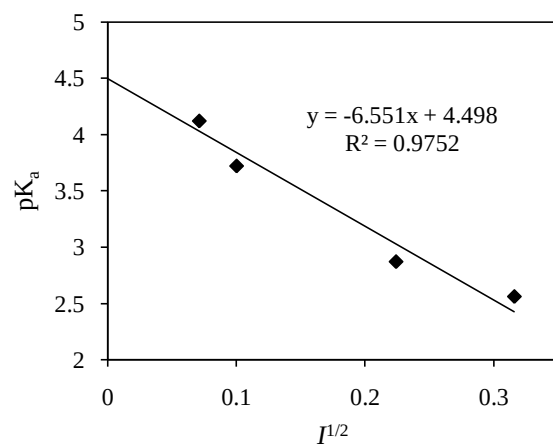


Table S7, Figure S7 Linear relationship of pK_a of 4-carbomethoxy phenol ($5 \times 10^{-5} M$) with the square root of ionic strength (I , $KClO_4$) in liquid ammonia at room temperature

$I = C_{KClO_4}(M)$	$I^{1/2}(M^{1/2})$	Absorbance	$pK_{a,I}$
0	0.00	1.41	4.04
0.01	0.10	1.57	3.84
0.05	0.22	1.71	3.56
0.1	0.32	1.78	3.40

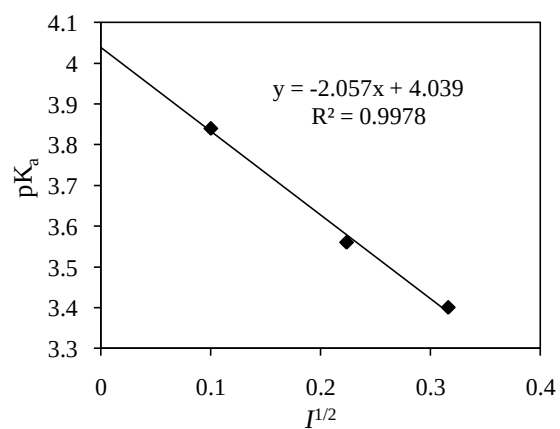
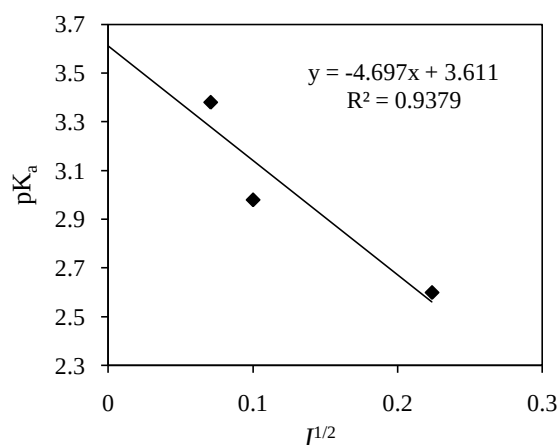


Table S8, Figure S8 Linear relationship of pK_a of 3-nitrophenol ($1 \times 10^{-4} M$) with the square root of ionic strength (I , $KClO_4$) in liquid ammonia at room temperature

$I = C_{KClO_4}(M)$	$I^{1/2}(M^{1/2})$	Absorbance	$pK_{a,I}$
0	0.00	0.123	3.63
0.005	0.07	0.136	3.38
0.01	0.10	0.150	2.98
0.05	0.22	0.157	2.60



B. Modeling the influence of added ammonium ion on the ionisation and ion-pairing behaviour of phenols in liquid ammonia

Two simultaneous equilibria need to be considered: deprotonation of the phenol by ammonia to give the ion pair, and dissociation of the ion pair to give the free phenolate and ammonium ions.



These equilibria can be defined by the equilibrium constants K_i and K_d .

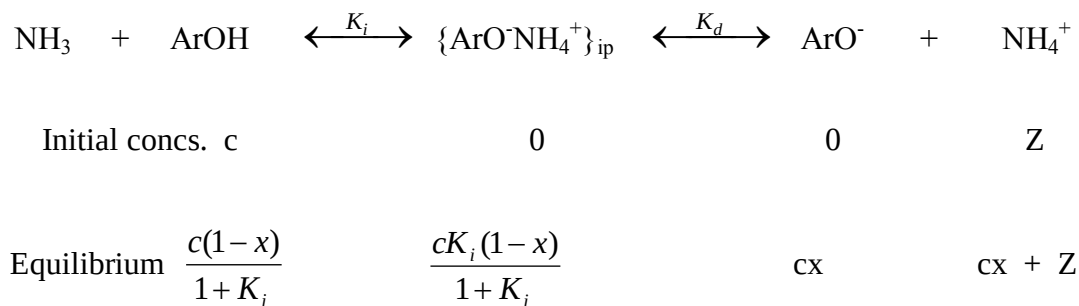
$$K_i = \frac{[ArO^-NH_4^+]_{ip}}{[ArOH]} \quad K_d = \frac{[ArO^-][NH_4^+]}{[ArO^-NH_4^+]_{ip}}$$

We require a smooth function that describes the ionisation process at low (spectroscopic) concentration, where the only ammonium ion present is that produced by dissociation of the ion pair, through to conditions where ammonium ion is added to the solution. Solutions containing stoichiometric initial

concentrations of phenol (c) and ammonium ion (Z) (added as ammonium chloride) are made up. Both equilibria must be satisfied, and from the mass balance across the phenol/ion pair equilibrium alone.

$$[\text{ArOH}]_T = [\text{ArOH}] + [\text{IP}], \text{ so } \frac{[\text{ArOH}]}{[\text{ArOH}]_T} = \frac{1}{1 + K_i} \text{ and } \frac{[\text{IP}]}{[\text{ArOH}]_T} = \frac{K_i}{1 + K_i}$$

Proceeding as usual for a dissociation process:



$$\text{Whence } K_d = \frac{(cx)(cx + Z)}{\frac{cK_i(1-x)}{1 + K_i}} = \frac{x(cx + Z)(1 + K_i)}{K_i(1-x)}$$

This transforms to the quadratic:

$c(1 + K_i)x^2 + x(Z + K_iZ + K_iK_d) - K_iK_d = 0$, which can be implemented on Excel with Z as the variable.

For the modeling the influence of added ammonium ion on the ionisation and ion-pairing behaviour of phenols in liquid ammonia under constant ionic strength (NaCl), the modeling was based on the approximation that the extinction coefficient of ion pair for ionised phenol does not change with the nature of counter-ion.

Table S9, Figure S9 Titration of 4-carbomethoxy phenol ($5 \times 10^{-5} \text{M}$) with NH_4Cl salt in liquid ammonia at room temperature

$[\text{NH}_4\text{Cl}]/\text{M}$	Absorbance
0	1.500
1.00×10^{-5}	1.420
2.50×10^{-5}	1.318
5.00×10^{-5}	1.176
1.25×10^{-3}	0.927
2.50×10^{-3}	0.846
3.75×10^{-3}	0.757
5.00×10^{-3}	0.734
1.00×10^{-2}	0.781
5.00×10^{-2}	0.782

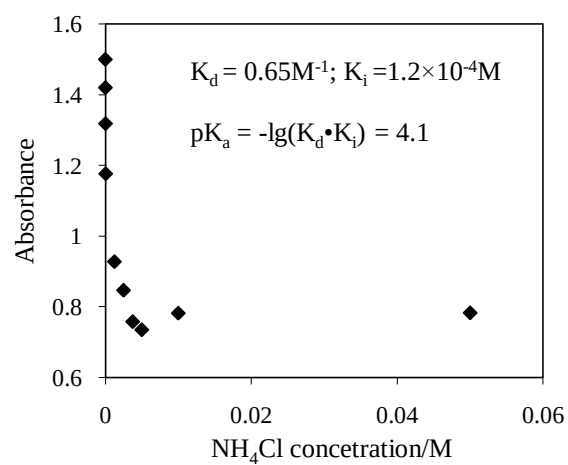


Table S10, Figure S10 Titration of 4-carbomethoxy phenol ($5 \times 10^{-5} \text{M}$) with NH_4Cl salt ($I=0.2 \text{M}$, NaCl) in liquid ammonia at room temperature

$[\text{NH}_4\text{Cl}]/\text{M}$	$[\text{NaCl}]/\text{M}$	Absorbance
0	0.20	1.89
0.01	0.19	1.41
0.03	0.17	1.29
0.04	0.16	1.10
0.05	0.15	1.03
0.10	0.10	0.914
0.15	0.05	0.872
0.20	0	0.874

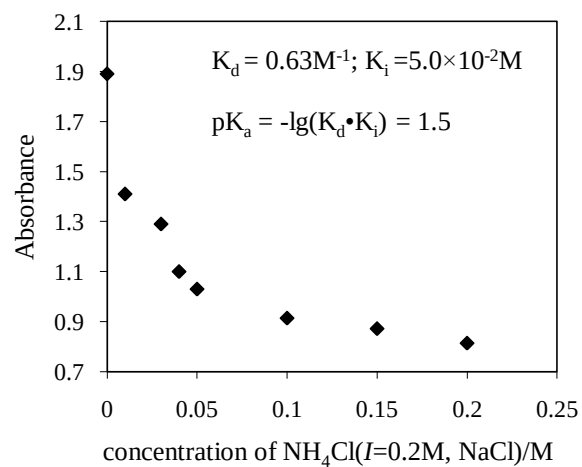


Table S11, Figure S11 Titration of 4-nitrophenol ($2.5 \times 10^{-5} \text{M}$) with NH_4Cl salt in liquid ammonia at room temperature

$[\text{NH}_4\text{Cl}]/\text{M}$	Absorbance
0	0.942
0.01	0.889
0.02	0.875
0.05	0.815
0.10	0.796
0.50	0.792
1.00	0.790
2.00	0.799

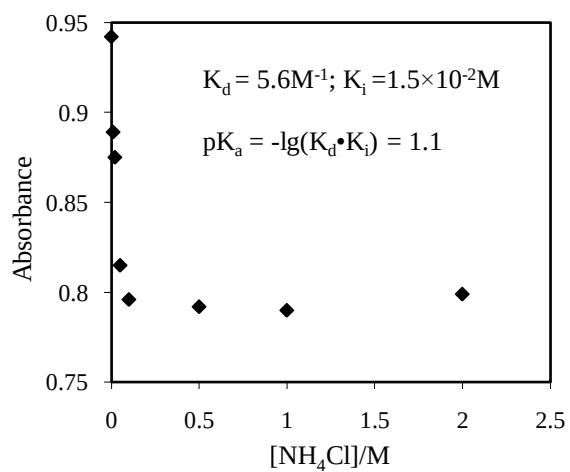
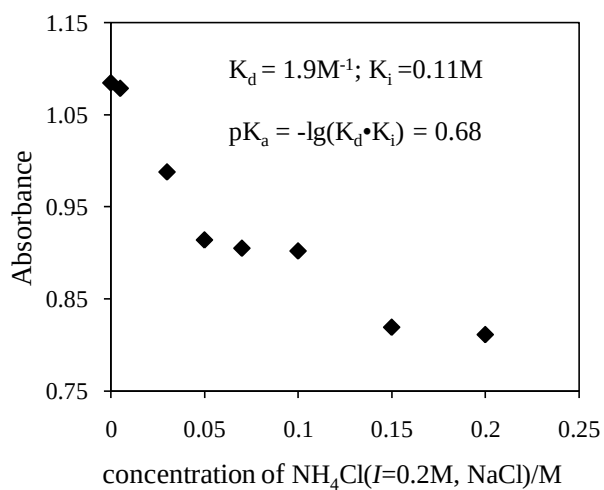


Table S12, Figure S12 Titration of 4-nitrophenol ($2.5 \times 10^{-5} \text{M}$) with NH_4Cl salt ($I=0.2\text{M}$, NaCl) in liquid ammonia at room temperature

$[\text{NH}_4\text{Cl}]/\text{M}$	$[\text{NaCl}]/\text{M}$	Absorbance
0	0.20	1.085
0.005	0.195	1.079
0.03	0.17	0.988
0.05	0.15	0.914
0.07	0.13	0.905
0.10	0.10	0.902
0.15	0.05	0.819
0.20	0	0.811



2.2 Ionisation of aminium ions

Table S13 ^1H NMR shift of trifluoroethylamine and trifluoroethylamine hydrochloride in DMSO- d_6 and in liquid ammonia at 25°C

	trifluoroethylamine	trifluoroethylamine hydrochloride
DMSO- d_6	δ 3.13(q, 2H)	δ 3.17(q, 2H)
LNH_3	δ 3.15(q, 2H)	δ 3.18(q, 2H)

Table S14 ^1H NMR shift of benzylamine, benzylamine hydrochloride and triethylbenzylammonium chloride in DMSO- d_6 and in liquid ammonia at 25°C

	benzylamine	benzylamine hydrochloride	triethylbenzylammonium chloride
DMSO- d_6	δ 3.71(s, 2H), 7.11-7.37(m, 5H)	δ 4.00(s, 2H), 7.32-7.53(m, 5H)	δ 1.30(t, 9H), 3.20(q, 6H), 4.59(s, 2H), 7.47-7.58(m, 5H)
LNH_3	δ 3.69(s, 2H), 7.12-7.26(m, 5H)	δ 3.69(s, 2H), 7.14-7.29(m, 5H)	δ 1.36(t, 9H), 3.20(q, 6H), 4.69(s, 2H), 7.49-7.62(m, 5H)

Table S15 ^1H NMR shift of piperidine and piperidine hydrochloride in DMSO- d_6 and in liquid ammonia at 25°C

	piperidine	piperidine hydrochloride
DMSO- d_6	δ 2.64(t, 4H), 1.36-1.54(m, 6H)	δ 2.96(t, 4H), 1.52-1.71(m, 6H)
LNH_3	^a δ 2.61(t, 4H), 1.35-1.41(m, 6H)	^a δ 2.59(t, 4H), 1.34-1.41(m, 6H)
LNH_3	^b δ 2.61(t, 4H), 1.35-1.43(m, 6H)	^b δ 2.57(t, 4H), 1.31-1.38(m, 6H)

^a 0.1M. ^b 1M.

3. Solvolysis and nucleophilic substitution reactions of benzyl chlorides in liquid ammonia at 25°C

3.1 Solvolysis of benzyl chlorides

Table S16 Solvolysis rate of benzyl chloride in liquid ammonia at different temperature

temperature(K)	$10^4 k_{\text{obs}}(\text{s}^{-1})$	$10^5 k_2(\text{M}^{-1}\text{s}^{-1})$
268.2	1.28	0.338
283.2	3.25	0.881
298.2	8.89	2.48
308.2	13.3	3.79

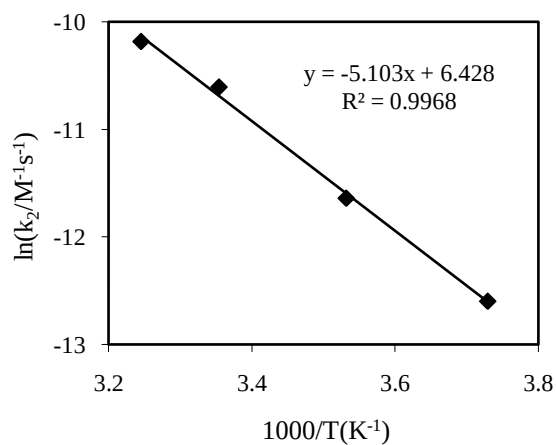


Figure S13 Arrhenius plot for the solvolysis of benzyl chloride

Table S17 Solvolysis rate of 4-chlorobenzyl chloride in liquid ammonia at different temperature

temperature(K)	$10^4 k_{\text{obs}}(\text{s}^{-1})$	$10^5 k_2(\text{M}^{-1}\text{s}^{-1})$
268.2	1.48	0.391
283.2	4.36	1.18
298.2	9.81	2.74
308.2	16.8	4.78

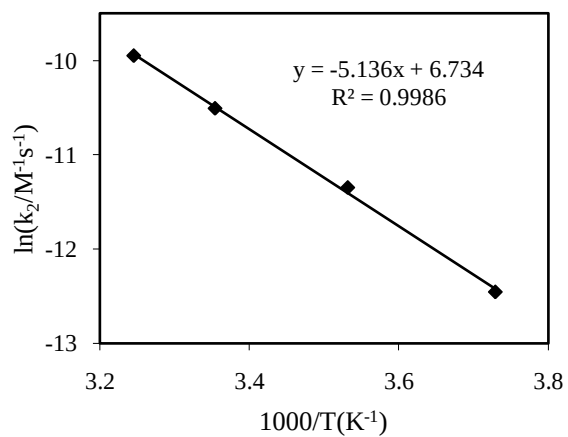


Figure S14 Arrhenius plot for the solvolysis of 4-chlorobenzyl chloride

Table S18 Solvolysis rate of 4-nitrobenzyl chloride in liquid ammonia at different temperature

temperature(K)	$10^4 k_{\text{obs}}(\text{s}^{-1})$	$10^5 k_2(\text{M}^{-1}\text{s}^{-1})$
268.2	2.42	0.636
283.2	6.71	1.82
298.2	15.3	4.27
308.2	22.9	6.52

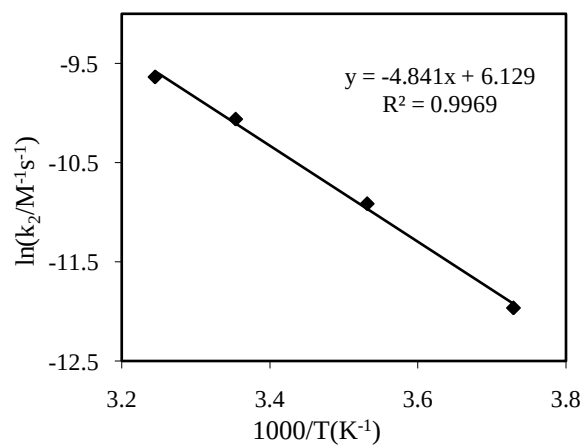
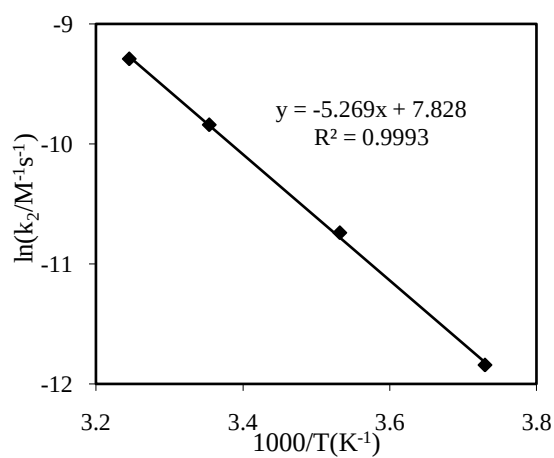


Figure S15 Arrhenius plot for the solvolysis of 4-nitrobenzyl chloride

Table S19 Solvolysis rate of 4-methoxybenzyl chloride in liquid ammonia at different temperature

temperature(K)	$10^4 k_{\text{obs}}(\text{s}^{-1})$	$10^5 k_2(\text{M}^{-1}\text{s}^{-1})$
268.2	2.72	0.717
283.2	7.99	2.16
298.2	19.1	5.33
308.2	32.3	9.23

**Figure S16** Arrhenius plot for the solvolysis of 4-methoxybenzyl chloride**Table S20** Solvolysis rate of α -methyl benzyl chloride in liquid ammonia at different temperature

temperature(K)	$10^5 k_{\text{obs}}(\text{s}^{-1})$	$10^7 k_2(\text{M}^{-1}\text{s}^{-1})$
298.2	0.671	1.87
308.2	1.62	4.53
318.2	3.98	11.1

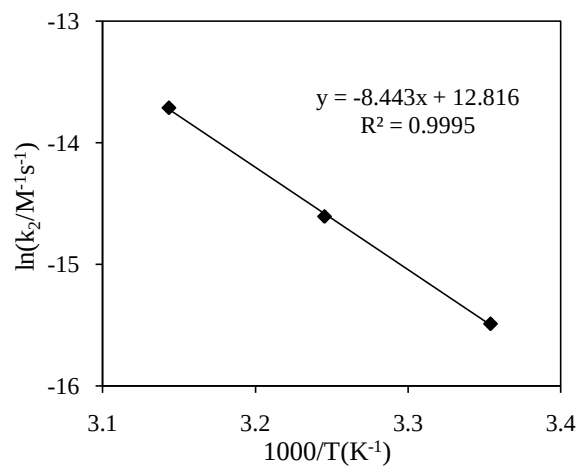


Figure S17 Arrhenius plot for the solvolysis of α -methyl benzyl chloride

Table S21 Solvolysis of enantiomerically rich S- α -methyl benzyl chloride in aqueous ammonia at 25°C

H ₂ O volume fraction	0% H ₂ O	10% H ₂ O	20% H ₂ O	30% H ₂ O
ee% of reactant chloride(S)	37.8	40.8	40.8	40.8
ee% of product amine(R)	37.8	36.6	36.5	35.9

Table 22 The rate for the solvolysis of α -methyl benzyl chloride and product analysis in aqueous ammonia at 25°C.

H ₂ O volume fraction	0% H ₂ O	10% H ₂ O	20% H ₂ O	30% H ₂ O
rate/s ⁻¹	6.71×10^{-6}	1.93×10^{-5}	5.2×10^{-5}	1.40×10^{-4}
molar ratio (amine/alcohol)	—	110 :1	42:1	12:1
k _{rel.}	1	2.9	7.7	21

3.2 Nucleophilic substitution of benzyl chlorides

Table S23 The rate for the benzyl chloride with different concentration of phenoxide in liquid ammonia at 25°C ($I = 0.3$ M, KClO_4)

[phenoxide]/M	[KClO4]/M	$10^3 k_{\text{obs}}/\text{s}^{-1}$
0	0.3	1.18
0.05	0.25	2.41
0.1	0.2	3.23
0.2	0.1	4.38
0.3	0	5.30

Table S24 Second order rate constant for 4-substituted benzyl chloride with phenoxide anion in liquid ammonia at 25°C

substituent	σ_p	$10^2 k_2 (\text{M}^{-1} \text{s}^{-1})$
4-MeO	-0.27	4.02
4-Me	-0.17	1.48
4-H	0	2.01
4-Cl	0.23	4.93
4-COOMe	0.45	5.28
4-CN	0.66	13.4

Table S25 The rate for the benzyl chloride with different concentration of morpholine in liquid ammonia at 25°C

[morpholine]/M	$10^3 k_{\text{obs}}/\text{s}^{-1}$
0	8.89
0.1	1.30
0.2	1.60
0.4	2.38
0.75	3.62
1.0	4.18

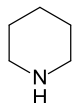
Table S26 Second order rate constant for 4-substituted benzyl chloride with sodium triazolate in liquid ammonia at 25°C

substituent	σ_p	$10^2 k_2 (M^{-1} s^{-1})$
4-MeO	-0.27	0.917
4-Me	-0.17	0.863
4-H	0	0.942
4-Cl	0.23	1.58
4-COOMe	0.45	1.70
4-NO ₂	0.78	6.59

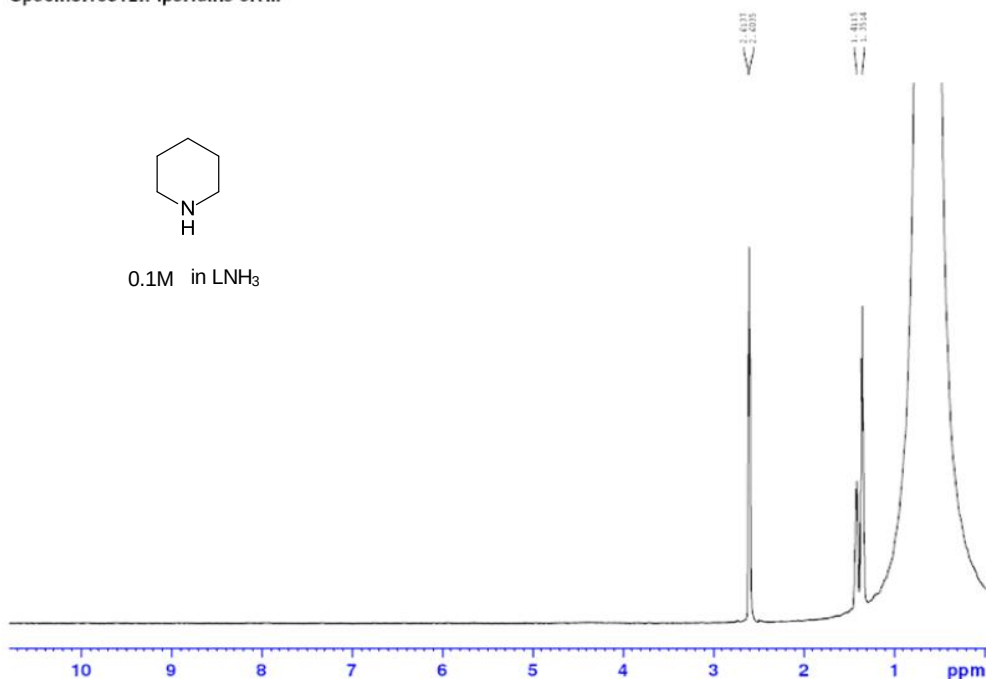
Table S27 Second order rate constant for 4-substituted benzyl chloride with piperidine in liquid ammonia at 25°C

substituent	σ_p	$10^2 k_2 (M^{-1} s^{-1})$
4-Me	-0.17	1.79
4-H	0	1.70
4-Cl	0.23	1.34
4-COOMe	0.45	1.27
4-CN	0.66	1.96
4-NO ₂	0.78	2.06

Spec.no.16512:Piperidine 0.1M



0.1M in LNH_3



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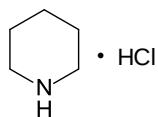
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UL: 1.0000000 sec
TDO: 1

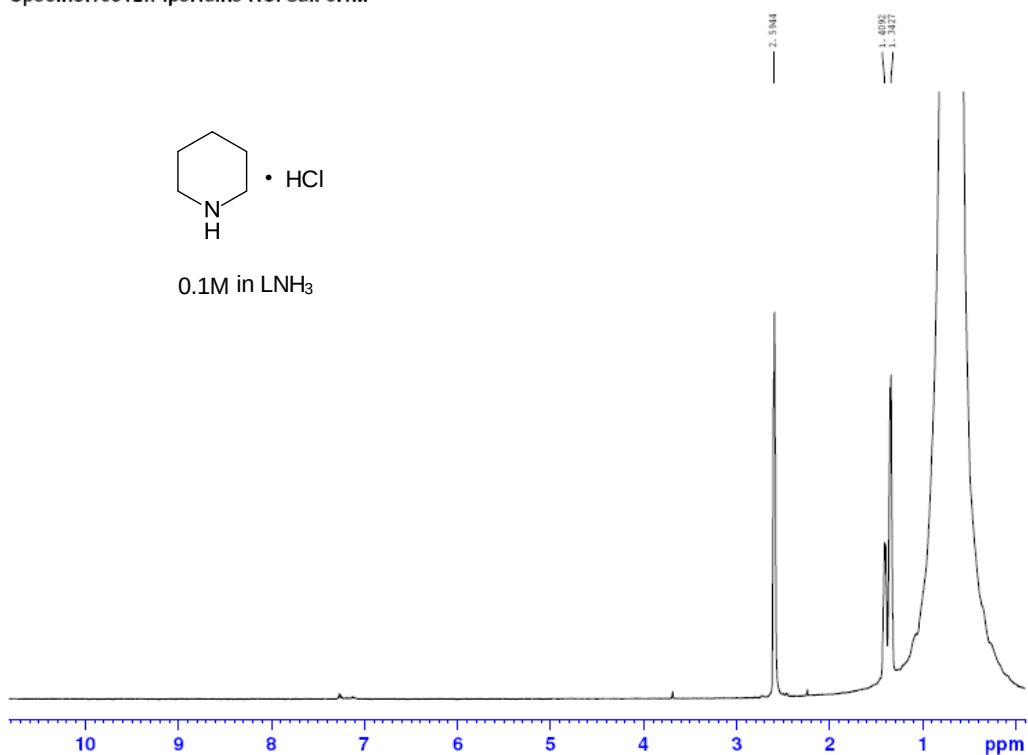
----- CHANNEL f1 -----
NUC1: 1H
P1: 9.70 usec
PL1: 0.10 dB
SFO1: 500.1330995 MHz

F2 - Processing parameters
SI: 32768
SF: 500.1330971 MHz
WDW: EM
SSB: 0
LB: 0.30 Hz
GB: 0
PC: 1.00

Spec.no.16512:Piperidine HCl salt 0.1M



0.1M in LNH_3



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HUDDERSFIELD

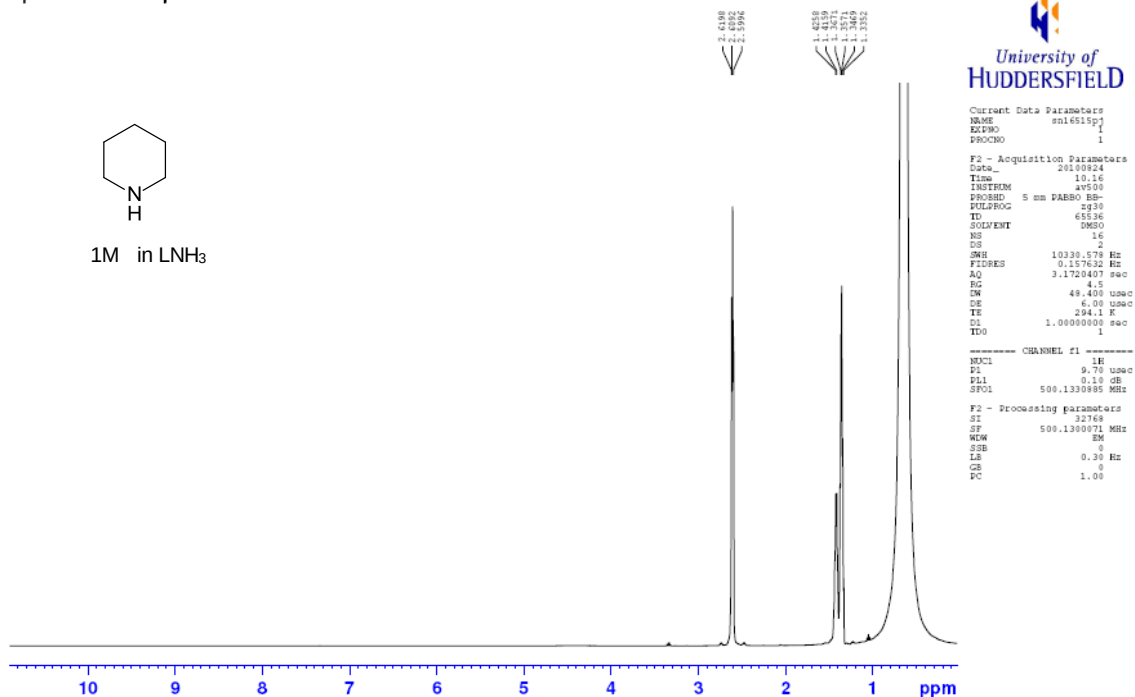
Current Data Parameters
NAME: sol16512p
EXPNO: 1
PROCNO: 1

F2 - Acquisition Parameters
Date_: 20100820
Time: 10.33
INSTRUM: av500
PROBHD: 5 mm PABBO BB-
PULPROG: zg30
TD: 65536
SOLVENT: DMSO
NS: 16
DS: 2
SWH: 10330.578 Hz
FIDRES: 0.157632 Hz
AQ: 3.1720407 sec
RG: 4.5
DM: 48.400 usec
DE: 6.00 usec
TE: 296.2 K
UL: 1.0000000 sec
TDO: 1

----- CHANNEL f1 -----
NUC1: 1H
P1: 9.70 usec
PL1: 0.10 dB
SFO1: 500.1330995 MHz

F2 - Processing parameters
SI: 32768
SF: 500.1330971 MHz
WDW: EM
SSB: 0
LB: 0.30 Hz
GB: 0
PC: 1.00

Spec.no.16515: Piperidine 1M



Spec.no.16514: Piperidine HCl salt 1M

