Aggregative activation in heterocyclic chemistry. Part 6.† A surprising NH₃ effect during metallation of 2-methoxypyridine with a multimetal complex base: C-3 *versus* C-6 metallation

Philippe Gros, Yves Fort and Paul Caubère *

Laboratoire de Chimie Organique I, ERS-CNRS 634, Faculté des Sciences, Université Henri Poincaré Nancy-I, BP 239, F-54506 Vandoeuvre-les-Nancy Cédex, France

The new bimetallic complex base prepared from $Me_2N(CH_2)_2OH$ (DMAE), $NaNH_2$ and BuLi has been found to exhibit a particular behaviour. Thus, the presence of ammonia in these basic aggregates induces the C-3 metallation of 2-methoxypyridine while the base obtained from DMAE, NaH and BuLi promoted, like BuLi–DMAELi, metallation at the C-6 position. A reaction profile showed that both metallated species can be obtained by removing and adding ammonia respectively.

Introduction

Using 2-methoxypyridine **1** as a substrate, we previously showed[1] that the basicity/nucleophilicity ratio [B/N]R of BuLi was considerably increased when the lithium reagent was involved in the complex base (CB) BuLi–$Me_2N(CH_2)_2OLi$ (BuLi–DMAELi) which, according to our previous definition,[2] must be considered as a unimetal super base (USB). Thus while BuLi reacted with **1** to give the lithium derivative **2**, the CB apparently led mainly to **4** (Scheme 1). We actually showed that
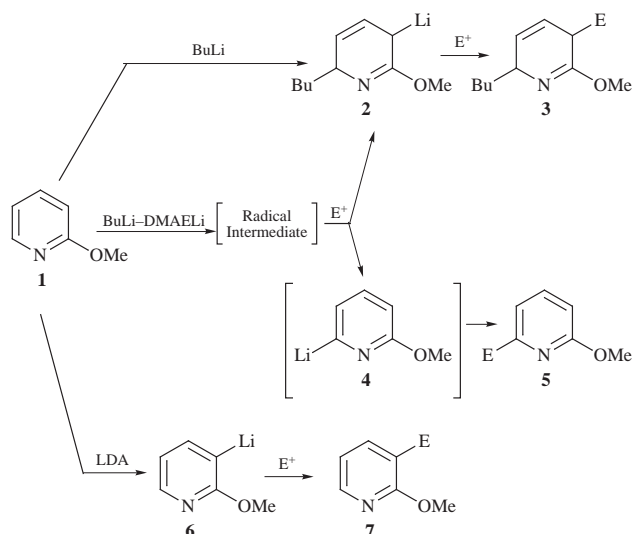
Scheme 1

4 was not formed during the so-called metallation step but from a radical intermediate[1] during electrophilic trapping.

On the other hand it is known that, according to the complex-induced proximity effect (CIPE),[3] a classical base such as LDA reacts with **1** to give **6**. The unusual apparent metallation observed with the CB has been attributed to the complexation of **1** with the aggregates of the super base. In such a complexation the lithium cation must play an important role and direct the association of **1** with the CB aggregates thanks to a strong interaction with the nitrogen of the pyridine ring. Finally we also previously showed[4] that the insertion of an alkali cation other than Na^+ into the aggregates of a CB $NaNH_2$–RONa led to a modulation of the properties of the starting CB. Taking the above data into account we concluded

† For Part 5 in this series, see *J. Chem. Soc., Perkin Trans. 1*, 1997, 3597.

that the incorporation of a sodium containing base into BuLi–DMAELi ought to have as a consequence a modulation of the basicity as well as a change in the regioselectivity of the metallation.

In the present publication we report the results supporting this hypothesis as well as an unexpected observation dealing with the influence of the reaction medium on the nature of the metallated species formed.
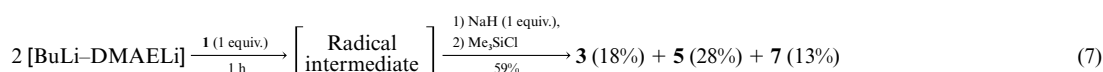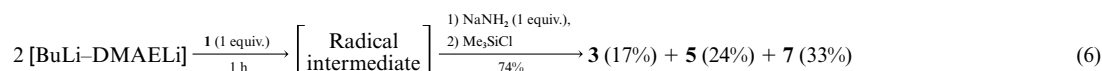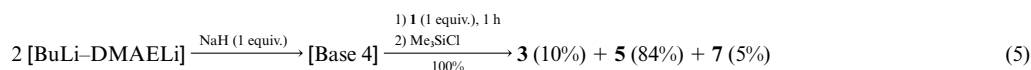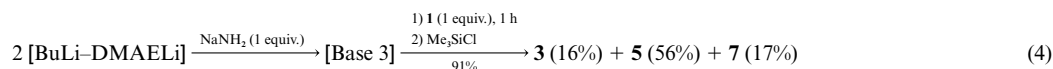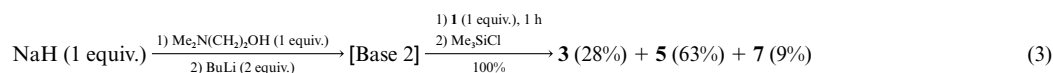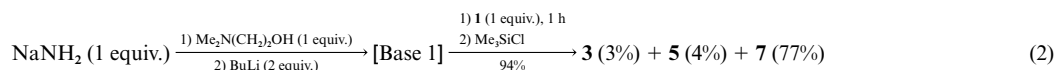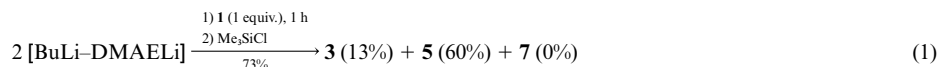
Results and discussion

The results obtained during our investigations on the activation of $NaNH_2$ and NaH[5] led us to choose these reagents as a source of sodium cation to modulate the properties of BuLi–DMAELi. Using hexane as solvent and Me_3SiCl as trapping electrophile the results reported in reactions (1)–(7) (Scheme 2) were obtained.

[Base 1] and [Base 2] [reactions (2) and (3)] are actually multimetal super bases (MSB)[2] at first glance resembling reagents studied by others.[6] From this point of view the differences observed between reactions (1)–(3) led us to conclude that at least a part of **7** corresponding to metallation at the C-3 position should be due to the presence of Na^+ in the MSB. This conclusion was supported by reactions (4) and (5) in which sodium containing bases, insoluble in hexane, were associated with BuLi–DMAELi. Confirmation of the role played by Na^+ was finally obtained with reactions (6) and (7) in which the sodium containing bases were added once the radical intermediate previously postulated[1] was formed. However the formation of **7** could not be due only to the presence of Na^+ since under identical conditions the yield of this compound unexpectedly varied with the nature of the counter-anion of the added sodium containing base. Curiously the ratio **7**:**5** was always larger with $NaNH_2$ than with NaH, and the selectivity for **7** was particularly marked in reaction (2). This surprising result could be due to some NH_2^- and/or NH_3 inserted in the aggregates. Since a higher yield of metallation at the C-3 position was observed during reaction (2), the first step of which led to the formation of NH_3, we attributed to NH_3 the main part of the regioselectivity. To check this hypothesis we performed the reactions reported in reactions (8)–(13) (Scheme 3). For the sake of comparison we have also reported reactions (2) and (3).

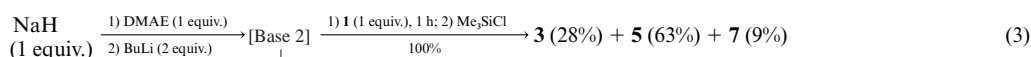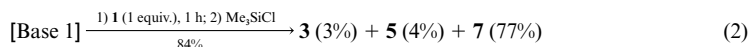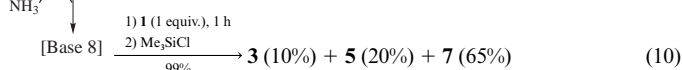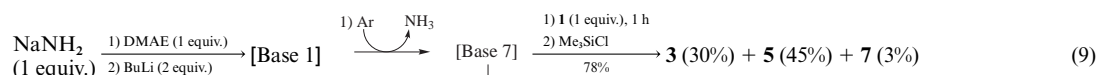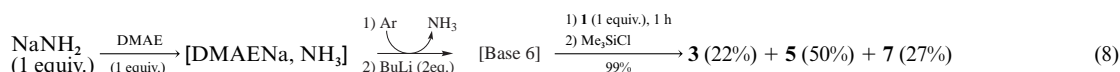From these results it is clear that NH_3 played an important role in the formation of **7**. Indeed the amount of C-3 metallated species was considerably decreased when NH_3 was removed from the reaction medium by bubbling argon (Ar) [compare reactions (8) and (9) with (10) and (2)]. The difference observed

$$2\,[\text{BuLi–DMAELi}] \xrightarrow[73\%]{\substack{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h} \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (13\%) + \mathbf{5}\ (60\%) + \mathbf{7}\ (0\%) \tag{1}$$

$$\text{NaNH}_2\ (1\ \text{equiv.}) \xrightarrow[2)\ \text{BuLi}\ (2\ \text{equiv.})]{1)\ \text{Me}_2\text{N(CH}_2)_2\text{OH}\ (1\ \text{equiv.})} [\text{Base 1}] \xrightarrow[94\%]{\substack{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h} \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (3\%) + \mathbf{5}\ (4\%) + \mathbf{7}\ (77\%) \tag{2}$$

$$\text{NaH}\ (1\ \text{equiv.}) \xrightarrow[2)\ \text{BuLi}\ (2\ \text{equiv.})]{1)\ \text{Me}_2\text{N(CH}_2)_2\text{OH}\ (1\ \text{equiv.})} [\text{Base 2}] \xrightarrow[100\%]{\substack{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h} \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (28\%) + \mathbf{5}\ (63\%) + \mathbf{7}\ (9\%) \tag{3}$$

$$2\,[\text{BuLi–DMAELi}] \xrightarrow{\text{NaNH}_2\ (1\ \text{equiv.})} [\text{Base 3}] \xrightarrow[91\%]{\substack{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h} \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (16\%) + \mathbf{5}\ (56\%) + \mathbf{7}\ (17\%) \tag{4}$$

$$2\,[\text{BuLi–DMAELi}] \xrightarrow{\text{NaH}\ (1\ \text{equiv.})} [\text{Base 4}] \xrightarrow[100\%]{\substack{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h} \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (10\%) + \mathbf{5}\ (84\%) + \mathbf{7}\ (5\%) \tag{5}$$

$$2\,[\text{BuLi–DMAELi}] \xrightarrow[1\ \text{h}]{\mathbf{1}\ (1\ \text{equiv.})} \left[\begin{array}{c}\text{Radical} \\ \text{intermediate}\end{array}\right] \xrightarrow[74\%]{\substack{1)\ \text{NaNH}_2\ (1\ \text{equiv.}), \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (17\%) + \mathbf{5}\ (24\%) + \mathbf{7}\ (33\%) \tag{6}$$

$$2\,[\text{BuLi–DMAELi}] \xrightarrow[1\ \text{h}]{\mathbf{1}\ (1\ \text{equiv.})} \left[\begin{array}{c}\text{Radical} \\ \text{intermediate}\end{array}\right] \xrightarrow[59\%]{\substack{1)\ \text{NaH}\ (1\ \text{equiv.}), \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (18\%) + \mathbf{5}\ (28\%) + \mathbf{7}\ (13\%) \tag{7}$$

3, **5**, **7** are the products of Scheme 1 with E = Me$_3$Si; the radical intermediate is the one proposed in ref. 1

Scheme 2

$$\text{NaNH}_2\ (1\ \text{equiv.}) \xrightarrow[(1\ \text{equiv.})]{\text{DMAE}} [\text{DMAENa, NH}_3] \xrightarrow[2)\ \text{BuLi}\ (2\text{eq.})]{1)\ \text{Ar}\quad\text{NH}_3} [\text{Base 6}] \xrightarrow[99\%]{\substack{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h} \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (22\%) + \mathbf{5}\ (50\%) + \mathbf{7}\ (27\%) \tag{8}$$

$$\text{NaNH}_2\ (1\ \text{equiv.}) \xrightarrow[2)\ \text{BuLi}\ (2\ \text{equiv.})]{1)\ \text{DMAE}\ (1\ \text{equiv.})} [\text{Base 1}] \xrightarrow{1)\ \text{Ar}\quad\text{NH}_3} [\text{Base 7}] \xrightarrow[78\%]{\substack{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h} \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (30\%) + \mathbf{5}\ (45\%) + \mathbf{7}\ (3\%) \tag{9}$$

$$\xrightarrow{\text{NH}_3} [\text{Base 8}] \xrightarrow[99\%]{\substack{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h} \\ 2)\ \text{Me}_3\text{SiCl}}} \mathbf{3}\ (10\%) + \mathbf{5}\ (20\%) + \mathbf{7}\ (65\%) \tag{10}$$

$$[\text{Base 1}] \xrightarrow[84\%]{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h};\ 2)\ \text{Me}_3\text{SiCl}} \mathbf{3}\ (3\%) + \mathbf{5}\ (4\%) + \mathbf{7}\ (77\%) \tag{2}$$

$$\text{NaH}\ (1\ \text{equiv.}) \xrightarrow[2)\ \text{BuLi}\ (2\ \text{equiv.})]{1)\ \text{DMAE}\ (1\ \text{equiv.})} [\text{Base 2}] \xrightarrow[100\%]{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h};\ 2)\ \text{Me}_3\text{SiCl}} \mathbf{3}\ (28\%) + \mathbf{5}\ (63\%) + \mathbf{7}\ (9\%) \tag{3}$$

$$\xrightarrow{\text{NH}_3} [\text{Base 9}] \xrightarrow[85\%]{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h};\ 2)\ \text{Me}_3\text{SiCl}} \mathbf{3}\ (8\%) + \mathbf{5}\ (2\%) + \mathbf{7}\ (75\%) \tag{11}$$

$$\text{LiNH}_2\ (1\ \text{equiv.}) \xrightarrow[2)\ \text{BuLi}\ (2\ \text{equiv.})]{1)\ \text{DMAE}\ (1\ \text{equiv.})} [\text{Base 5}] \xrightarrow[97\%]{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h};\ 2)\ \text{Me}_3\text{SiCl}} \mathbf{3}\ (53\%) + \mathbf{5}\ (39\%) + \mathbf{7}\ (5\%) \tag{12}$$

$$2\,[\text{BuLi–DMAELi}] \xrightarrow[41\%]{1)\ \mathbf{1}\ (1\ \text{equiv.}),\ 1\ \text{h};\ 2)\ \text{NH}_3;\ 3)\ \text{Me}_3\text{SiCl}} \mathbf{3}\ (16\%) + \mathbf{5}\ (35\%) + \mathbf{7}\ (0\%) \tag{13}$$

Scheme 3

between reactions (8) and (9) could be due to the fact that NH$_3$ was more strongly complexed with DMAE–Na than with [Base 1]. The reintroduction of NH$_3$ into [Base 7] [see reaction (10)] led to [Base 8] whose properties were very close to those of the original [Base 1] [compare reactions (10) and (2)]. The important role of NH$_3$ was confirmed with [Base 2] prepared with NaH [reaction (3)]. Introduction of NH$_3$ into this base led to [Base 9] [reaction (11)] behaving like [Base 1], directly prepared from NaNH$_2$. Finally the reactions reported in reactions (12) and (13) in which the only cation included in [Base 5] was Li$^+$ confirmed that the NH$_3$ effect was strongly related to the presence of Na$^+$ in the bases.

In the above experiments the introduction or removal of NH$_3$ was performed before the addition of the substrate **1** and it was of course of interest to know if the conjugated effects of Na$^+$ and NH$_3$ played a role during the metallation step. So, we studied reaction (2) in which NaNH$_2$ was used as the added

sodium containing base. The evolution of the reaction performed under a slow stream of Ar or N$_2$ was monitored by GC analysis of the metallated species trapped with Me$_3$SiCl. The results obtained have been summarized in Fig. 1.

Interestingly the maximum yield of metallation at the C-3 position was obtained after 1 h during which the C-6 position was metallated very slowly. After 1 h the yields of C-6 metallated species increased to the prejudice of those of C-3. This observation was attributed to the slow removal of NH$_3$ from the aggregates. This hypothesis was confirmed by bubbling Ar through the reaction medium after one hour of metallation. Under such conditions the disappearance of the C-3 metallated species was accelerated as well as the formation of the C-6 species. After the evolution due to the argon bubbling stopped, NH$_3$ was introduced with, as a consequence, a decrease in the C-6 metallated species and an increase in the C-3 one.

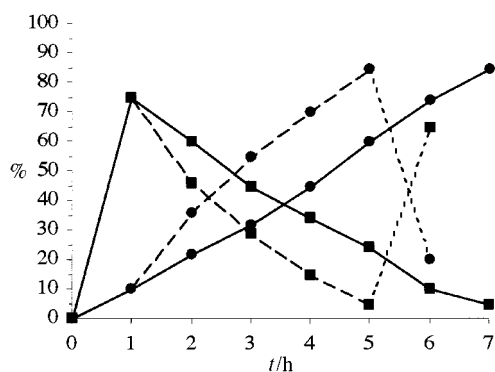Although we were unable to obtain any variation by further

Fig. 1 Effect of ammonia on regioselectivity: (– – – –) argon bubbling; (- - - - - -) addition of NH$_3$; (■) metallation at C-3 (**7**); (●) metallation at C-6 (**5**)

Table 1 Effect of LiNH$_2$ on metallation with BuLi–DMAELi–NaH base^a

NaH (1 equiv.) $\xrightarrow[\substack{\text{2) LiNH}_2\ (x\ \text{equiv.})\\ \text{3) BuLi (2 equiv.)}}]{\text{1) Me}_2\text{N(CH}_2)_2\text{OH (1 equiv.)}}$ [Base] $\xrightarrow[\text{2) Me}_3\text{SiCl}]{\text{1) 1 (1 equiv.), 1 h}}$ **3 + 5 + 7**

LiNH$_2$ (equiv.)	Conv. (%)	**3** (%)^b	**5** (%)^b	**7** (%)^b
None	100	28	63	9
0.01	98	27	35	36
0.05	100	23	37	40
0.11	99	15	70	14
0.27	99	10	76	13
0.5	100	10	75	15
1	100	2	84	14

^{a} Base prepared from NaH (8 mmol); DMAE (8 mmol); LiNH$_2$ (y mmol); BuLi (16 mmol); metallation performed on 8 mmol of 2-methoxypyridine at 0 °C in hexane. ^{b} GC yields.

Ar bubbling, these experiments clearly showed that NH$_3$ intervenes during the metallation step as well as in the stabilization of the metallated species formed. Of course no accurate explanation may be given for this phenomenon but it is clear that some kind of complexation of NH$_3$ with the aggregates of the bases as well as with those containing the metallated species took place. Thus we wondered if during our previous[1] reactions with BuLi–DMAELi the apparent lithiation at the C-6 position might not be due to the initial formation of the C-3 metallated species evolving instantaneously towards the C-6 one in the absence of NH$_3$. This alternative was discarded for the reasons given hereafter. The reaction represented in reaction (12) led only to a very small amount of **7** while NH$_3$ was formed during the preparation of the corresponding lithium containing base [Base 5]. Moreover, in the reaction reported in reaction (13), **1** reacted with BuLi–DMAELi for 1 hour as previously described,[1] then NH$_3$ was bubbled through the reaction flask. The result was a decrease in the global yield but no formation of **7** was observed. These data confirmed that without Na$^+$, the effect of NH$_3$ on the properties of the Li$^+$ containing CB was unimportant.

Last but not least remained a question dealing with the possible formation of a radical intermediate during the reactions performed in the presence of Na$^+$ and NH$_3$. In our previous publication we showed that addition of HMPA to the species resulting from the reaction of **1** with BuLi–DMAELi led to 90% of 6,6′-dimethoxy-2,2′-bipyridine.[1] Presently, under the metallation conditions given in reaction (2), addition of HMPA led to 84% of **3**, resulting from nucleophilic addition, and 14% of **1** was recovered; no coupling product was detected. So, it may be concluded that this cation impeded the formation of the radicaloid intermediate previously postulated or favoured its evolution towards the formation of metallated pyridines. We tentatively propose that 3- and/or 6-sodium 2-methoxypyridine are the main organometallic reagents formed during these reactions and that these species are in equilibrium, the proportion of each depending on the environment. Thus, NH$_3$ would favour the C-3 metallated species while the C-6 isomer would be the more stable without NH$_3$. However, we have no idea of how the equilibrium takes place.

A number of complementary experiments (see Experimental section) showed that the reaction medium was much more complex than it appeared at first glance. Control experiments showed that none of the reactions observed took place without BuLi and that under our conditions 2-dimethylaminoethanol (DMAE) quantitatively reacted with BuLi as well as with NaH or NaNH$_2$. However, with NaNH$_2$, only 6% of the expected amount of NH$_3$ evolved, the rest remaining complexed in the reaction medium. Moreover, while solutions of NH$_3$ in hexane did not react with BuLi even in the presence of DMAELi, 10% of butane evolved in the presence of DMAENa. This behaviour may be attributed to an increase in the ionic character of the

sodium alkoxide allowing the formation of RO$^-\cdots$H$_3$N species, increasing the acidity of NH$_3$ protons. However, these results meant that some LiNH$_2$ could be formed and which took place in the reactions observed in the medium containing sodium alkoxides and NH$_3$. This hypothesis was verified and as reported in Table 1 it appeared that the ratio **3**:**5**:**7** depended on the amount of LiNH$_2$. In addition we must mention that no gas evolution was observed during reaction (2) (Scheme 1) and that butane was evolved only during the hydrolysis after trapping with Me$_3$SiCl! We have no explanation for this surprising observation but we cannot discard the possibility that the C-3 substituted compound was formed during the hydrolysis of the trapped intermediate (see Scheme 4).
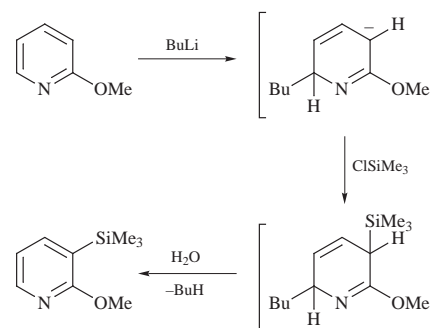
Scheme 4

Finally, various electrophiles were used to trap the species formed during the reaction of **1** with the base prepared from NaNH$_2$ [Base 1] (see Table 2). A systematic study showed that good yields could be obtained by using 2 equivs. of base and THF as a trapping co-solvent. As expected, the directing effect of Na$^+$ and NH$_3$ did not depend on the nature of the electrophile.
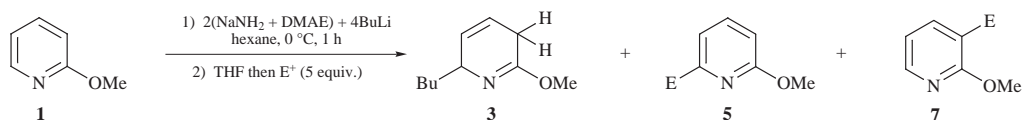
Conclusions

This work confirms how complicated the apparent proton abstractions are with MSB. Moreover it highlights the important influence that the conjugated acids generated *in situ* during the proton abstraction may have on the results observed. More generally, it appears that the possible intervention of such a phenomenon must be considered in the interpretation of acid–base organic reactions.

Experimental

General methods

^{1}H and ^{13}C NMR spectra were recorded on a Bruker spectrometer at 400 and 100 MHz respectively with TMS as internal

Table 2 Metallation of 2-methoxypyridine with the BuLi–DMAELi–NaNH$_2$ base and condensation with electrophiles[a]

E$^+$	E	Conv. (%)	3 (%)[b]	5 (%)[b]	7 (%)[b]	Product	Isolated yield (%)[c]
ClSiMe$_3$	SiMe$_3$	93	7	12	73	7a	62
MeSSMe	SMe	85	4	10	70	7b	60
CH$_3$OD	D	75	5	—	65[d]	7c	—
MeI	Me	88	15	—	70	7d	55
HexI	Hex	98	20	2	75	7e	63
HexBr	Hex	95	44	9	42	7e	35
Me$_2$CO	Me$_2$COH	70	26	—	42	7f	38
EtMeCO	EtMeCOH	83	9	2	65	7g	57
C$_5$H$_{11}$COH	C$_5$H$_{11}$CHOH	91	60	—	30	7h	25
(c-C$_3$H$_5$)$_2$CO	(c-C$_3$H$_5$)$_2$COH	85	21	—	63	7i	57
Bu^{t}COH	Bu^{t}CHOH	93	20	—	65	7j	60

[a] Base prepared from NaNH$_2$ (8 mmol), DMAE (8 mmol), BuLi (16 mmol); metallation performed on 4 mmol of 2-methoxypyridine at 0 °C in 25 ml of hexane; condensation performed by adding THF (25 ml) 5 min before electrophile (20 mmol). [b] GC yields. [c] After purification on a Chromatotron. [d] Determined by GC–MS and ^{1}H NMR.

Table 3

| Compound | δ | | | |
	CH$_3$N	CH$_2$N	CH$_2$O	O–H
Me$_2$N(CH$_2$)$_2$OH	2.20 (s, 6H)	2.40 (t, J 5, 2H)	3.60 (t, J 8, 2H)	4.20 (s, 1H)
Me$_2$N(CH$_2$)$_2$ONa	2.20–2.30 (m, 8H)		4.10 (t, J 5, 2H)	—

standard and CDCl$_3$ as solvent. GC analysis was performed with the internal standard method on a Shimadzu GC-14A apparatus using a HP1 25 m column and temperature programming. GC–MS measurements (EI and CI) were performed on HP5971A spectrometers. Elemental analysis were performed by the Service Central d'Analyse du CNRS (Vernaison, France).

Preparation of bases from NaNH$_2$ or NaH (Base 1 or Base 2)
To a suspension of sodamide or sodium hydride (8 mmol) in hexane (5 ml) at 0 °C was added dropwise a solution of 2-dimethylaminoethanol (DMAE) (8 mmol, 720 mg) in hexane (5 ml). After 15 min at 0 °C, BuLi (16 mmol, 10 ml) was added dropwise. After 30 min at 0 °C the Complex Base (8 mmol based on sodium alcoholate) was obtained as a yellow or white suspension.

Procedure for ammonia introduction into Base 2
After addition of 2-dimethylaminoethanol to sodium hydride as described above, the flask containing the mixture was connected to a generator of ammonia. Excess ammonia was introduced for 1 h, the flask was then disconnected from the generator and BuLi was added dropwise to the reaction mixture. After 30 min at 0 °C a yellow suspension was obtained.

Procedure for production of ammonia
A Schlenk tube equipped with a dropping funnel was connected to the flask used for the base preparation. The Schlenk tube was charged with a suspension of sodamide (51 mmol, 2 g) in THF (10 ml). A solution of *tert*-butyl alcohol (60 mmol, 4.4 g) in THF (10 ml) was placed in the dropping funnel and added dropwise thus producing ammonia.

Determination of the amount of ammonia
The reactor was connected to a series of two traps filled with an aqueous solution of phenolphthalein. The evolved gas was bubbled into the traps giving a rose-pink solution. A 0.2 M

H$_2$SO$_4$ solution was then added until disappearance of the pink color. The added volume allowed direct determination of the amount of ammonia.

Formation of amino-alcoholates
After addition of *N,N*-dimethylaminoethanol to sodamide in hexane as described above, a sample of the solution was taken and subjected to ^{1}H NMR analysis (see Table 3).

Metallation of 2-methoxypyridine at C-3 and condensation with ClSiMe$_3$
A solution of 2-methoxypyridine (8 mmol, 872 mg) in hexane (5 ml) was added to the base prepared from NaNH$_2$ as described above at 0 °C. After 1 h at 0 °C, freshly distilled chlorotrimethylsilane (10 mmol, 1.1 g) was added neat to the reaction mixture, the temperature was maintained at 0–5 °C for 1 h and allowed to warm to room temperature. The hydrolysis was then performed with 10 ml of water.

General procedure for preparation of C-3 substituted 2-methoxypyridine
A solution of 2-methoxypyridine (4 mmol, 436 mg) in hexane (5 ml) was added to the base prepared from NaNH$_2$ as described above in hexane (20 ml) at 0 °C. After 1 h at 0 °C, THF (25 ml) was added and the reaction mixture was stirred for 5 min at 0 °C. An appropriate electrophile (20 mmol) was then added neat, the temperature was maintained at 0–5 °C for 1 h and allowed to warm to room temperature. The hydrolysis was then performed with 10 ml of water. After aqueous work-up and drying (MgSO$_4$), the products were purified on a Chromatotron using AcOEt–hexane mixtures as eluent.

Products
2-Butyl-2,5-dihydro-6-methoxypyridine (2),[7] 2-methoxy-6-(trimethylsilyl)pyridine (5a),[1] 2-methoxy-3-(trimethylsilyl)pyridine (7a),[8] 3-deuterio-2-methoxypyridine (7c),[8] 3-methyl-2-methoxypyridine (7d),[8]

6-hexyl-2-methoxypyridine **(5e)**,[1] 2-(2-methoxy-3-pyridyl)-propan-2-ol **(7f)**,[8] 2-(2-methoxy-3-pyridyl)butan-2-ol **(7g)**,[8] 2-(2-methoxy-3-pyridyl)hexanol **(7h)**[8] were found to be identical (spectroscopic data) to authentic samples.

3-(Methylthio)-2-methoxypyridine (7b). Oil, δ_H 2.45 (s, 3H, CH$_3$S), 4.00 (s, 3H, CH$_3$O), 6.85 (dd, 1H, J 7 and 5, H5), 7.35 (dd, 1H, J 7 and 2, H4), 7.95 (dd, 1H, J 8 and 2, H6); δ_C 14.5 (CH$_3$S), 54.2 (CH$_3$O), 117.6 (C3), 122.85 (C2), 133.8 (C4), 142.7 (C6), 160.5 (C2); m/z 156 (M + H$^+$) (Found: C, 54.48; H, 5.92; N, 8.85; S, 20.72. C$_7$H$_9$NOS requires C, 54.19; H, 5.81; N, 9.03; S, 20.65%).

3-Hexyl-2-methoxypyridine (7e). Oil, δ_H 0.95 (t, 3H, J 8, CH$_3$), 1.35–1.70 (m, 8H, CH$_2$), 2.90 (t, 2H, J 7.8, CH$_2$C=N), 3.90 (s, 3H, CH$_3$), 6.60 (dd, 1H, J 7 and 5, H5), 7.35 (d, 1H, J 7 and 5, H5), 7.97 (dd, 1H, J 5 and 2, H6); δ_C 14.5 (CH$_3$), 23.3 (CH$_2$), 29.3–32.2 (CH$_2$), 53.6 (CH$_3$O), 117 (C5), 125.9 (C3), 137.9 (C4), 144.3 (C6), 162.5 (C2); m/z 193 (M$^+$) (Found: C, 74.65; H, 10.02; N, 7.33. C$_{12}$H$_{19}$NO requires C, 74.57; H, 9.91; N, 7.25%).

(2-Methoxy-3-pyridyl)dicyclopropylmethanol (7i). Oil, δ_H 0.20–0.55 (m, 8H, CH$_2$C), 1.25 (m, 2H, CHCH$_2$), 3.90 (s, 3H, CH$_3$O), 4.60 (s, 1H, OH), 6.90 (dd, 1H, J 8 and 2, H5), 7.85 (dd, 1H, J 8 and 2, H4), 8.05 (dd, 1H, J 5 and 2, H6); δ_C 0.7 (CH), 19.7 (CH$_2$), 53.5 (CH$_3$O), 73.2 (C−OH), 117.4 (C3), 129.7 (C5), 136.4 (C4), 145.1 (C6), 161.3 (C2); m/z 220 (M + H$^+$) (Found: C, 71.33; H, 8.01; N, 6.22. C$_{13}$H$_{17}$NO$_2$ requires C, 71.23; H, 7.76; N, 6.39%).

1-(2-Methoxy-3-pyridyl)-2,2-dimethylpropanol (7j). Oil, δ_H 0.95 (s, 9H, CH$_3$C), 3.90 (s, 3H, CH$_3$O), 4.05 (s, 1H, CHO), 4.30 (s, 1H, OH), 6.80 (dd, 1H, J 7 and 5, H5), 7.60 (dd, 1H, J 7 and 2, H4), 8.05 (dd, 1H, J 5 and 2, H6); δ_C 26.2 (CH$_3$C), 37.2 (−C−), 53.5 (CH$_3$O), 77.1 (CH−OH), 116.9 (C5), 124.9 (C3), 138.2 (C4), 145.7 (C6), 161.5 (C2); m/z 196 (M + H$^+$) (Found: C, 67.93; H, 9.01; N, 6.94. C$_{11}$H$_{17}$NO$_2$ requires C, 67.66; H, 8.78; N, 7.17%).

References

1 Ph. Gros, Y. Fort and P. Caubère, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, 3071.

2 P. Caubère, *Chem. Rev.*, 1993, **93**, 2317 and references cited therein.

3 (*a*) P. Beak and A. I. Meyers, *Acc. Chem. Res.*, 1986, **19**, 356; (*b*) V. Snieckus, *Chem. Rev.*, 1990, **90**, 879.

4 B. Jamart-Grégoire, Y. Fort, M. J. Quirin and P. Caubère, *J. Chem. Soc.*, *Chem. Commun.*, 1992, **19**, 1459.

5 (*a*) P. Caubère, *Acc. Chem. Res.*, 1974, **7**, 301; (*b*) P. Caubère, *Top. Curr. Chem.*, 1978, **73**, 50 and references cited therein.

6 (*a*) L. Lochmann, J. Pospisil, J. Vodnansky, J. Trekoval and D. Lim, *Collect. Czech. Chem. Commun.*, 1965, **30**, 2187; (*b*) L. Lochmann and D. Lim, *J. Organomet. Chem.*, 1973, **50**, 9; (*c*) M. Schlosser, *Mod. Synth. Methods*, 1992, **6**, 227.

7 E. W. Thomas, *J. Org. Chem.*, 1986, **51**, 2184.

8 F. Trécourt, M. Mallet, F. Marsais and G. Quéguiner, *J. Org. Chem.*, 1988, **53**, 1367.