# Variation in site of lithiation with ring substituent of *N′*-aryl-*N*,*N*-dimethylureas: application in synthesis

**Keith Smith,* Gamal A. El-Hiti† and Amba P. Shukla**

*Department of Chemistry, University of Wales Swansea,‡ Swansea, UK SA2 8PP*

***Received (in Cambridge) 30th April 1999, Accepted 17th June 1999***

Lithiation of various *N′*-aryl-*N*,*N*-dimethylureas takes different courses depending on the substituent in the aryl ring. *N′*-(4-Chlorophenyl)-, *N′*-(4-fluorophenyl)- and *N′*-(4-trifluoromethylphenyl)-*N*,*N*-dimethylureas are doubly lithiated, on nitrogen and on the carbon at position 2, with *n*-butyllithium or *tert*-butyllithium at 0 °C. The lithium reagents thus obtained react with a variety of electrophiles (iodomethane, $D_2O$, benzophenone, benzaldehyde, phenyl isocyanate and phenyl isothiocyanate) to give the corresponding 2-substituted derivatives, in very good yields for the chloro and fluoro derivatives. Reaction of the dilithio reagent of *N′*-(4-chlorophenyl)-*N*,*N*-dimethylurea with 2-chlorocyclohexanone gives an 82% isolated yield of 4a-hydroxy-*N*-(dimethylaminocarbonyl)-1,2,3,4,4a,9a-hexahydrocarbazole, which on treatment with trifluoroacetic acid affords *N*-(dimethylaminocarbonyl)-1,2,3,4-tetrahydrocarbazole in 97% yield. Double lithiation of *N′*-phenyl- and *N′*-(4-methylphenyl)-*N*,*N*-dimethylureas is achieved using *tert*-butyllithium at −20 °C, and takes place on nitrogen and predominantly on one of the two methyl groups of the urea. The lithium reagents so produced also react with a range of electrophiles to give the corresponding *N*-methyl-substituted compounds in very good yields. Lithiation of the *N′*-(4-methoxyphenyl)-analogue with *tert*-butyllithium at 0 °C or at −20 °C takes place on nitrogen, and then partially on carbon at position 3 but primarily on a methyl group of the urea, leading to a mixture of ring substitution, methyl substitution and disubstitution (in the ring and on the methyl group) on reaction with representative electrophiles. However, disubstituted derivatives are obtained in very good yields when 3 molar equivalents of *tert*-butyllithium are used to form a trianion. Attempted lithiation of the *N′*-(4-nitrophenyl) analogue was not successful under various reaction conditions.

## Introduction

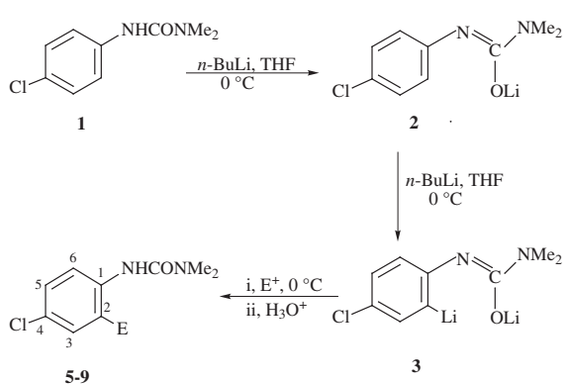
Organolithium reagents continue to play an important role in synthetic chemistry[1–18] since they facilitate a large number of synthetic transformations. In particular, lithiation of aromatic compounds often occurs proximate to substituents that possess oxygen or nitrogen atoms,[1,2] while aza-substituted carbanions have become useful intermediates for the synthesis of amines and their derivatives.[19]

In a separate piece of work we have reported the preparation of lithio derivatives from *N′*-(2-bromophenyl)-*N*,*N*-dimethylurea *via* bromine–lithium exchange and on their use in a novel approach to the synthesis of isatins.[20] We used the bromine–lithium exchange approach because direct *ortho*-lithiation of *N′*-phenyl-*N*,*N*-dimethylurea did not provide the desired compounds. Our continuing interests in the use of directed lithiation for organic synthesis,[21] and the success of the isatin synthesis, however, prompted us to carry out further studies on direct lithiation of *N′*-aryl-*N*,*N*-dimethylureas, which are more readily accessible than their bromo-substituted counterparts. We now report that the lithiation reaction is highly dependent on the nature of substituents on the aryl ring. In favourable cases, the lithio compounds can indeed be generated in high yield *via* direct lithiation. In other cases, lithiation may occur on the *N*-methyl groups of the urea moiety or elsewhere on the aromatic ring.

## Results and discussion

*N′*-Aryl-*N*,*N*-dimethylureas were prepared by the action of triphosgene on substituted anilines, followed by reaction with dimethylamine at 0 °C in the presence of triethylamine.[22] Some were prepared from reactions of aryl isocyanates with dimethylamine and some from the reactions of substituted anilines with dimethylcarbamoyl chloride in the presence of triethylamine as a base.[23]

It was hoped that lithiation of *N′*-aryl-*N*,*N*-dimethylureas would take place as for pivaloylaminobenzene,[24] so that substitution at position 2 could be achieved. Fortunately, lithiation of *N′*-(4-chlorophenyl)-*N*,*N*-dimethylurea (**1**) occurred smoothly and rapidly with butyllithium (2.5 equiv.) at 0 °C in THF. Two equivalents of butyllithium were required, the first one to deprotonate the urea to form the monolithio reagent **2** and the second to deprotonate at position 2 to give the dilithio intermediate **3** (Scheme 1). The dilithio intermediate **3** was confirmed by alkylation with excess methyl iodide, which gave *N′*-(4-chloro-2-methylphenyl)-*N*,*N*,*N′*-trimethylurea (**4**) in 80% isolated yield.




**Scheme 1**

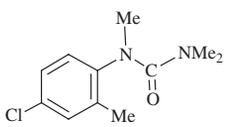
The same result was obtained when *tert*-butyllithium was

† Permanent address: Department of Chemistry, Faculty of Science, Tanta University, Tanta, Egypt.
‡ Formerly known as the University College of Swansea.

**Table 1** Products from reaction of dilithio compound **3** with electrophiles according to Scheme 1

| Product | Electrophile | E | Yield (%)[a] | Mp/°C |
|---|---|---|---|---|
| **5** | $D_2O$ | D | 83 | 172[b] |
| **6** | $(Ph)_2CO$ | $(Ph)_2C(OH)$ | 82 | 179–181[b] |
| **7** | PhCHO | PhCH(OH) | 78 | 142[b] |
| **8** | PhNCO | PhNHCO | 80 | 307[c] |
| **9** | PhNCS | PhNHCS | 72 | 286[c] |

[a] Yields reported for isolated, purified materials. [b] Crystallisation from ethyl acetate. [c] Crystallisation from ethyl acetate–hexane.

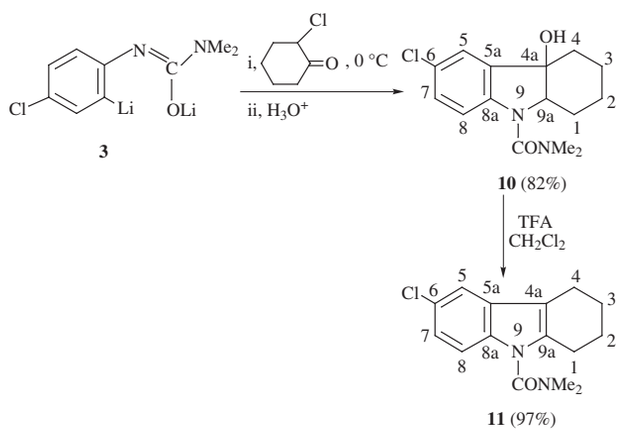


**4**

used as the lithiating reagent. Moreover, even when excess butyllithium (3 equiv.) was used, no side chain lithiation took place on the methyl groups of the urea.

The general utility of the dianion **3** was demonstrated by its further reactions with a range of electrophiles ($D_2O$, benzophenone, benzaldehyde, phenyl isocyanate, phenyl isothiocyanate) to give the corresponding *N′*-(2-substituted-4-chlorophenyl)-*N*,*N*-dimethylurea derivatives **5**–**9** (Scheme 1) in very good yields (Table 1).

We also found that under similar conditions the biselectrophile, 2-chlorocyclohexanone, reacted with the dilithio reagent **3** at both electrophilic centres to produce 6-chloro-4a-hydroxy-9-(dimethylaminocarbonyl)-1,2,3,4,4a,9a-hexahydrocarbazole (**10**) in 82% isolated yield. Generation of 6-chloro-9-(dimethylaminocarbonyl)-1,2,3,4-tetrahydrocarbazole (**11**) was then efficiently accomplished in 97% yield by treatment of **10** with a trace of trifluoroacetic acid in dichloromethane (Scheme 2).



**Scheme 2**

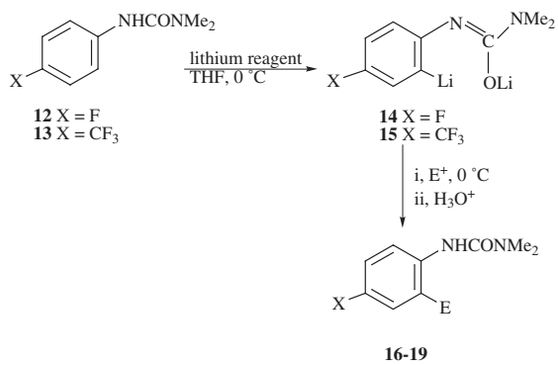
Our success in lithiating compound **1** prompted us to attempt lithiation of *N′*-(4-fluorophenyl)-*N*,*N*-dimethylurea (**12**). Unfortunately, attempted lithiation with *n*-BuLi was not successful. However, good lithiation was achieved using *t*-BuLi at 0 °C (Scheme 3). Initial addition of *t*-BuLi provided a yellow solution until approximately 1 equiv. had been added and then gave a reddish brown solution as the remaining *t*-BuLi was added. Reaction of the dianion **14** with electrophiles ($D_2O$, benzophenone, benzaldehyde) at 0 °C gave rise to substituted ureas **16**–**18** (Scheme 3) in very good yields (Table 2).

Lithiation of *N′*-(4-trifluoromethylphenyl)-*N*,*N*-dimethylurea (**13**) was achieved using 2.2 mol equivalents of *n*-BuLi to form the dilithio reagent **15**. However, reaction of **15** with benzophenone at 0 °C afforded the corresponding substituted urea **19**

**Table 2** Products from reaction of dilithio reagents **14** and **15** with electrophiles according to Scheme 3

| Product | X | Electrophile | E | Yield (%)[a] | Mp/°C |
|---|---|---|---|---|---|
| **16** | F | $D_2O$ | D | 88 | 128–129 |
| **17** | F | $(Ph)_2CO$ | $(Ph)_2C(OH)$ | 78 | 225–226 |
| **18** | F | PhCHO | PhCH(OH) | 77 | 166 |
| **19** | $CF_3$ | $(Ph)_2CO$ | $(Ph)_2C(OH)$ | 31 | 223–224 |

[a] Yields reported for isolated purified materials.



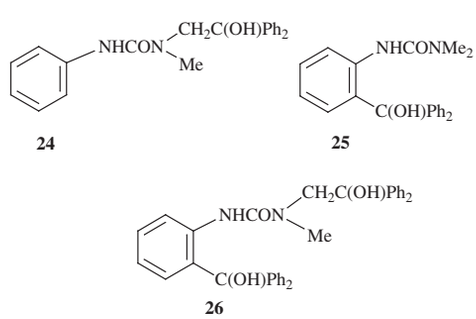
**16-19**

**Scheme 3**

(Scheme 3) in only 31% isolated yield (Table 2) and 61% unreacted starting material was recovered. We conducted a series of experiments under different reaction conditions using various proportions of lithiating reagents in attempts to improve the yield of compound **19**. However, none of the conditions tried were more successful. It is not clear what factors limit the yield in this case.

From the results obtained it appeared that *ortho*-lithiation was successful for cases in which there was an electron-withdrawing group at position 4 of the phenyl ring. Lithiation of *N′*-(4-nitrophenyl)-*N*,*N*-dimethylurea was therefore attempted with *n*- or *tert*-butyllithium under various reaction conditions. However, this resulted in production of a tarry residue in all cases. No further attempts were made to find conditions under which this lithiation could be effected.

Attention was next turned to lithiation of *N′*-phenyl-*N*,*N*-dimethylurea (**20**) and *N′*-(4-methylphenyl)-*N*,*N*-dimethylurea (**21**). Attempted lithiation of either substrate with *n*-BuLi was unsuccessful, the starting material being recovered intact. However, lithiation could be achieved by use of *t*-BuLi (2.2 equiv.) at 0 °C. For example, trapping of the lithiated reagent of compound **20** with benzophenone (1.2 equiv.) at 0 °C resulted in isolation of a mixture of three products, **24** (17%), **25** (10%) and **26** (8%) together with a highly polar material which adsorbed at the top of the column.



**24** **25**



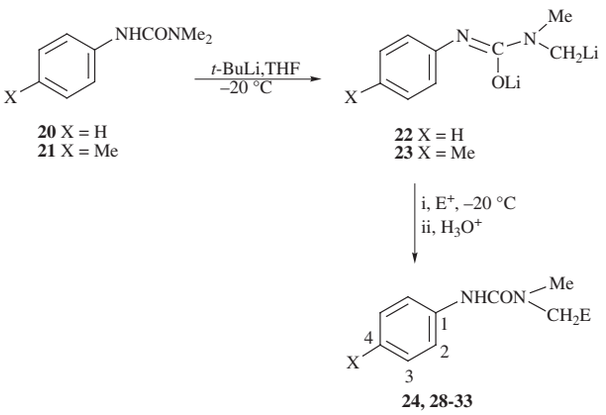
**26**

A series of experiments was conducted to try to find conditions under which only one product would be obtained. It was found that double lithiation of **20** using *t*-BuLi (2.4 equiv.) at −20 °C for 2 h is more selective, occurring predominately on the nitrogen and one of the two methyl groups of the urea to form

**Table 3** Products from reaction of dilithio reagents **22** and **23** with electrophiles according to Scheme 4

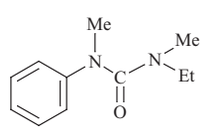
| Product | X | Electrophile | E | Yield (%)[a] | Mp/°C |
|---|---|---|---|---|---|
| **24** | H | $(Ph)_2CO$ | $(Ph)_2C(OH)$ | 82 | 147 |
| **28** | H | $D_2O$ | D | 92 | 134–135 |
| **29** | H | PhCHO | PhCH(OH) | 78 | 138–139 |
| **30** | H |  |  | 75 | 136–137 |
| **31** | Me | $(Ph)_2CO$ | $(Ph)_2C(OH)$ | 79 | 162–163 |
| **32** | Me | $D_2O$ | D | 90 | 156–157 |
| **33** | Me | PhCHO | PhCH(OH) | 75 | 146–147 |

[a] Yields reported for isolated, purified materials.




**Scheme 4**

the dilithio reagent **22** (Scheme 4). Reaction of the dilithio reagent **22** with excess methyl iodide at −20 °C for 2 h gave compound **27** in 80% isolated yield.



**27**

Lithiation of compound **21** using *t*-BuLi (2.4 equiv.) at −20 °C was similarly successful, giving the dilithio reagent **23**. Moreover, lithiation of **20** using 3 equiv. of *t*-BuLi led to formation of a trilithio reagent, which on reaction with benzophenone (2.0 equiv.) afforded the disubstituted product **26** in 81% isolated yield.

In order to test the versatility of the intermediate dilithio reagents **22** and **23**, they were reacted with several electrophiles (benzophenone, $D_2O$, benzaldehyde, 2-chlorocyclohexanone) to give the corresponding *N′*-aryl-*N*-methyl-*N*-(substituted methyl)ureas **24** and **28**–**33** (Scheme 4) in very good yields (Table 3).

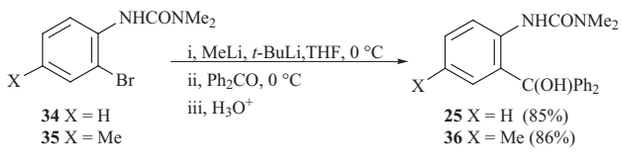
As can be seen from Table 3, there is little difference between the yields in the phenylurea series and those in the 4-methylphenylurea series and the yields are generally very good.

Clearly, direct lithiation on the ring without concomitant lithiation on a methyl residue of the urea group was not a realistic hope with **20** and **21** as substrates. However, ring substitution could be achieved *via* bromine–lithium exchange of *N′*-(2-bromophenyl)-*N*,*N*-dimethylurea (**34**) or *N′*-(2-bromo-4-methylphenyl)-*N*,*N*-dimethylurea (**35**). One mol equivalent of MeLi was used to deprotonate the nitrogen, followed by 2 mol equivalents of *t*-BuLi at 0 °C to achieve the bromine–lithium exchange.[19] Reaction of the dilithio reagents thus obtained with benzophenone afforded the corresponding substituted derivatives **25** and **36** (Scheme 5) in 85% and 86% isolated yields, respectively.

**Table 4** Products from the reaction of the lithio reagents derived from compound **37** with benzophenone (2.2 equiv.) according to Scheme 6 under different reaction conditions

| *t*-BuLi/ mmol | Reaction temperature/°C | Yield of products (%)[a] **38** | **39** | **40** |
|---|---|---|---|---|
| 2.2 | 0 | 6 | 62 | 4 |
| 2.2 | −20 | 2 | 50 | 16 |
| 2.2 | −78 | — | — | — |
| 3.3 | 0 | 2 | 2 | 77 |
| 3.3 | −20 | — | — | 87 |

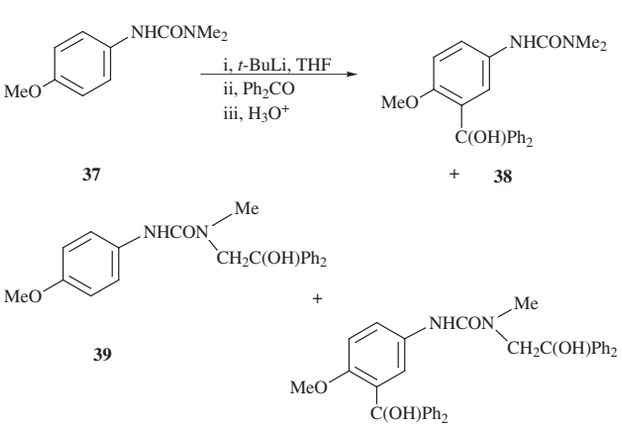
[a] Yields reported for isolated, purified materials.




**Scheme 5**

In order to see if the dilithio reagents obtained by direct lithiation of **20** (*i.e.* **22**) and by bromine–lithium exchange from **34** could be interconverted under conditions that were more forcing than those used in their preparation, each reagent was allowed to stand for 48 h at room temperature and was then trapped with benzophenone. The dilithio reagent **22** gave **24** in 61% isolated yield. The dilithio reagent derived from compound **34** gave compound **25** in 63% isolated yield. There was no evidence for formation of the alternative product, **25** or **24**, respectively, in either case, despite the lower yields obtained. Thus, it is clear that decomposition of the dilithio reagent occurs more rapidly than thermodynamic equilibration under these conditions.

It appeared from the results with **20** and **21** that neutral or electron-donating substituents discouraged *ortho*-lithiation, thereby leading to preferential lithiation on one of the *N*-methyl groups. With this idea in mind, attention was finally turned to lithiation of *N′*-(4-methoxyphenyl)-*N*,*N*-dimethylurea (**37**). It was found that lithiation of **37** was not efficient under conditions similar to those found to be optimal for compounds **1**, **12**, **13**, **20** or **21**. Thus, lithiation with *t*-BuLi (2.2 equiv.) at −20 °C followed by reaction with benzophenone (2.2 equiv.) led to a mixture of ring substitution, methyl substitution and disubstitution (in the ring and on the methyl group) to afford compounds **38** (2%), **39** (50%) and **40** (16%) (Scheme 6). The




**Scheme 6**

lithiation reaction was therefore studied under a variety of conditions (Table 4). From this study it was found that the disubstituted derivative **40** could be obtained in 87% isolated yield

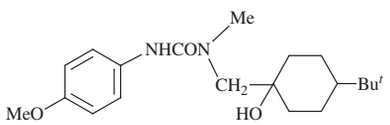
**Table 5** Products from the reaction of the lithio reagents derived from compound **37** with 4-*tert*-butylcyclohexanone (2.2 equiv.)

| *t*-BuLi (mmol) | Reaction temperature/°C | Yield of product (%)[a] **41** | **42** |
|---|---|---|---|
| 2.2 | 0 | 68 | 14 |
| 2.2 | −20 | 70 | 10 |
| 2.2 | −78 | — | — |
| 3.3 | 0 | 15 | 60 |
| 3.3 | −20 | 20 | 65 |

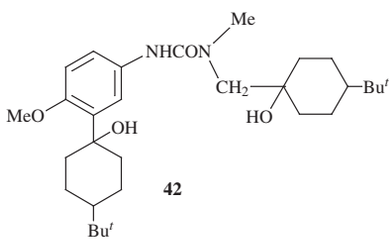
[a] Yields reported for isolated, purified materials.

when 3 equiv. of *tert*-butyllithium were used to form a trilithio reagent at −20 °C. No lithiation takes place at −78 °C using *n*-BuLi, *t*-BuLi or LDA. However, a reasonable yield (62%) of methyl-substituted product **39** could be obtained by use of 2.2 equiv. of *tert*-butyllithium at 0 °C.

Similar results were obtained when 4-*tert*-butylcyclohexanone was used as an electrophile. The products, **41** and **42**, were isolated in amounts similar to those formed in the corresponding reactions with benzophenone (Table 5).

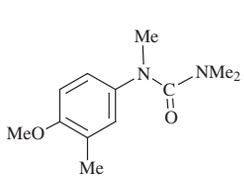



**41**

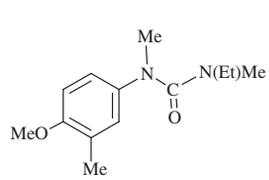



**42**

Lithiation of compound **37** using *t*-BuLi (2.2 equiv.) at 0 °C followed by reaction with excess methyl iodide resulted in the formation of *N*′-[(4-methoxy-3-methyl)phenyl]-*N*′,*N*,*N*-trimethylurea (**43**) and *N*′-methyl-*N*′-[(4-methoxy-3-methyl)-phenyl]-*N*-ethyl-*N*-methylurea (**44**) in 2% and 21% isolated yields, respectively. However, using *t*-BuLi (3.3 equiv.) at −20 °C, followed by reaction with excess methyl iodide, afforded compounds **43** and **44** in 14% and 70% isolated yields, respectively.




**43**




**44**

## Conclusion

We have demonstrated lithiation procedures that allow electrophilic substitution of *N*′-aryl-*N*,*N*-dimethylureas to provide efficient syntheses of substituted ureas. Electron-withdrawing groups on the phenyl ring of the urea induce ring substitution; hydrogen and electron-donating groups induce methyl substitution. A methoxy substituent gives some ring substitution, but next to the methoxy group rather than next to the urea, with the major product being derived from methyl substitution, as for other electron-donating groups.

## Experimental

Melting points were determined on an electrothermal digital melting point apparatus and are reported uncorrected. IR spectra were recorded on a Perkin-Elmer 1725X spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker spectrometer operating at 400 MHz for $^1$H and 100 MHz for $^{13}$C measurements. Chemical shifts are reported in parts per million relative to tetramethylsilane; *J* values are given in Hz. Assignments of signals are based on coupling patterns and expected chemical shift values and have not been rigorously confirmed. Signals with similar characteristics might be interchanged. Low-resolution mass spectra were recorded on a VG 12-253 spectrometer, electron impact (EI) at 70 eV and chemical ionization (CI) by use of ammonia as ionizing gas. Accurate mass data were obtained on a VG ZAB-E instrument. Elemental analyses were obtained from the laboratories of the University of Wales Cardiff. Column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). Organolithiums were obtained from Aldrich Chemical Company and their concentration estimated prior to use by the method of Watson and Eastham.[25] THF was distilled from sodium benzophenone ketyl. Other chemicals were obtained from Aldrich Chemical Company and used without further purification. Solvents were purified by standard procedures.[26,27] IR spectra were in agreement with the assigned structures.

### General procedure for the lithiation of *N*′-(4-chlorophenyl)-*N*,*N*-dimethylurea 1 and subsequent reactions with electrophiles

To a cooled (0 °C), stirred solution of compound **1** (0.20 g, 1.0 mmol) in THF (10 cm$^3$) under nitrogen, a solution of *n*-BuLi (2.5 mol dm$^{-3}$; 1.0 cm$^3$, 2.50 mmol) in heptane was added. Formation of the dilithio reagent was observed as a yellowish solution. The mixture was stirred at 0 °C for 2 h, after which an electrophile (1.2 mmol; as solution in THF if solid) was added. The mixture was stirred for 2 h at 0 °C then the cooling bath was removed and the mixture allowed to warm to room temperature. The mixture was diluted with diethyl ether (5 cm$^3$) and quenched with aqueous saturated ammonium chloride solution (5 cm$^3$). The organic layer was separated, washed with water (2 × 10 cm$^3$), dried ($MgSO_4$) and evaporated under reduced pressure. The product obtained was recrystallised from the appropriate solvent (see Table 1).

***N*′-(4-Chloro-2-methylphenyl)-*N*,*N*,*N*′-trimethylurea 4.** Viscous oil; $\delta_H$($CDCl_3$) 7.28 (d, *J* 8.9, 1 H, 6-H), 7.22 (d, *J* 2.2, 1 H, 3-H), 6.97 (d, *J* 8.9, 1 H, 5-H), 3.03 (s, 3 H, $NCH_3$), 2.61 [s, 6 H, $N(CH_3)_2$] and 2.25 (s, 3 H, $CH_3$); $\delta_C$($CDCl_3$) 162.26 (s, C=O), 136.01 (s, C-2), 131.33 (s, C-1), 131.19 (d, C-3), 129.41 (d, C-5), 125.45 (s, C-4), 124.42 (d, C-6), 38.91 (q, $NCH_3$), 37.78 [q, $N(CH_3)_2$] and 17.58 (q, $CH_3$); *m*/*z* (EI) 226 ($M^+$, 32%), 212 (20), 181 (17), 154 (19), 125 (10), 85 (30) and 72 (100); *m*/*z* (CI) 244 ($M^+$+$NH_4$, 5%), 227 ($MH^+$, 100), 213 (20) and 72 (5) (Found: $MH^+$, 227.0951. Calc. for $C_{11}H_{16}ClN_2O$: 227.0951) (Found: C, 58.3; H, 6.7; N, 12.4. Calc. for $C_{11}H_{15}{}^{35}ClN_2O$: C, 58.38; H, 6.66; N, 12.39%).

***N*′-(4-Chloro-2-[$^2H_1$]phenyl)-*N*,*N*-dimethylurea 5.** $\delta_H$([$^2H_6$]-DMSO) 8.33 (s, exch., 1 H, NH), 8.48 (d, *J* 8.7, 1 H, 6-H), 7.20 (m, 2 H, 3-H and 5-H) and 2.92 [s, 6 H, $N(CH_3)_2$]; $\delta_C$([$^2H_6$]-DMSO) 155.45 (s, C=O), 139.61 (s, C-1), 127.91 (d, C-3), 127.82 (d, C-5), 125.13 (s, C-4), 120.97 (d, C-6), 120.46 (s, C-2) and 36.15 [q, $N(CH_3)_2$]; *m*/*z* (EI) 199 ($M^+$, 12%), 184 (5), 154 (7), 126 (6), 72 (100) and 44 (15) (Found: $M^+$, 199.0623. Calc. for $C_9H_{10}{}^2H^{35}ClN_2O$: 199.0623).

***N*′-[2-(Diphenylhydroxymethyl)-4-chlorophenyl]-*N*,*N*-dimethylurea 6.** $\delta_H$([$^2H_6$]DMSO) 8.86 (s, exch., 1H, NH), 8.14 (d, *J* 8.8, 1 H, 6-H), 7.47 (s, exch., 1 H, OH), 7.32–7.18 (m, 11 H, 5-H and 2 Ph), 6.40 (d, *J* 2.5, 1 H, 3-H) and 2.66 [s, 6 H,

$N(CH_3)_2$]; $\delta_C$([$^2H_6$]DMSO) 154.58 (s, C=O), 144.98 (s, C-1 of Ph's), 138.18 (s, C-2), 136.03 (s, C-1), 128.70 (d, C-3), 127.59 (d, C-3 of Ph's), 127.40 (d, C-2 of Ph's), 127.34 (d, C-4 of Ph's), 127.12 (d, C-5), 124.80 (s, C-4), 122.45 (d, C-6), 81.77 (s, C-OH) and 35.48 [q, $N(CH_3)_2$]; *m/z* (EI) 380 ($M^+$, 10%), 364 (30), 362 (100), 335 (18) and 318 (31); *m/z* (CI) 381 ($MH^+$, 10%), 365 (20), 363 (34), 296 (17), 294 (61), 260 (13), 199 (9), 183 (8), 89 (9), 52 (12) and 46 (100) (Found: $MH^+$, 381.1370. Calc. for $C_{22}H_{22}{}^{35}ClN_2O_2$: 381.1370) (Found: C, 69.33; H, 5.68; N, 7.36. Calc. for $C_{22}H_{21}ClN_2O_2$: C, 69.38; H, 5.56; N, 7.36%).

***N′*-[4-Chloro-2-(phenylhydroxymethyl)phenyl]-*N*,*N*-dimethylurea 7.** $\delta_H$($CDCl_3$) 8.11 (d, *J* 8.8, 1 H, 6-H), 7.76 (s, exch., 1 H, NH), 7.31–7.22 (m, 6 H, 5-H and Ph), 7.04 (d, *J* 2.5, 1 H, 3-H), 5.71 (d, *J* 3.5, exch., 1 H, OH), 4.87 (d, *J* 3.5, 1 H, CH) and 2.64 [s, 6 H, $N(CH_3)_2$]; $\delta_C$($CDCl_3$) 155.71 (s, C=O), 140.47 (s, C-1 of Ph), 136.94 (s, C-2), 133.33 (s, C-1), 128.53 (d, C-3), 128.45 (d, C-3 of Ph), 128.36 (d, C-2 of Ph), 127.83 (d, C-4 of Ph), 126.80 (d, C-5), 126.43 (s, C-4), 121.68 (d, C-6), 74.84 (d, CH) and 35.93 [q, $N(CH_3)_2$]; *m/z* (EI) 304 ($M^+$, 2%), 286 (11), 259 (9), 242 (7), 214 (100), 179 (20), 165 (12), 152 (16), 105 (8), 90 (9), 72 (60) and 45 (28); *m/z* (CI) 305 ($MH^+$, 5%), 287 (52), 277 (8), 260 (25), 218 (52), 209 (2), 72 (5) and 46 (100) (Found: $MH^+$, 305.1057. Calc. for $C_{16}H_{18}{}^{35}ClN_2O_2$: 305.1057) (Found: C, 63.1; H, 5.6; N, 9.2. Calc. for $C_{16}H_{17}ClN_2O_2$: C, 63.14; H, 5.63; N, 9.21%).

***N′*-[2-(Anilinocarbonyl)-4-chlorophenyl]-*N*,*N*-dimethylurea 8.** $\delta_H$([$^2H_6$]DMSO) 10.50 (s, exch., 1 H, PhNH), 10.47 (s, exch., 1 H, NHCO), 8.35 (d, *J* 9.0, 1 H, 6-H), 7.90 (d, *J* 2.4, 1 H, 3-H), 7.71 (d, *J* 7.5, 2 H, 2-H of Ph), 7.50 (dd, *J* 2.4, 9.0, 1 H, 5-H), 7.37 (t, *J* 7.5, 2 H, 3-H of Ph), 7.15 (t, *J* 7.5, 1 H, 4-H of Ph) and 2.94 [s, 6 H, $N(CH_3)_2$]; $\delta_C$([$^2H_6$]DMSO) 166.49 (s, PhNHC=O), 154.49 (s, C=O), 139.96 (s, C-1 of Ph), 138.20 (s, C-2), 138.18 (s, C-1), 131.63 (d, C-3), 128.49 (d, C-3 of Ph), 128.02 (d, C-5), 124.31 (s, C-4), 124.26 (d, C-6), 121.35 (d, C-4 of Ph), 121.14 (d, C-2 of Ph) and 35.72 [q, $N(CH_3)_2$]; *m/z* (EI) 317 ($M^+$, 25%), 300 (27), 272 (52), 225 (89), 180 (92), 153 (53), 126 (17), 93 (100), 72 (43) and 46 (45); *m/z* (CI) 318 ($MH^+$, 95%), 290 (17), 273 (15), 225 (44) and 46 (100) (Found: $MH^+$, 318.1009. Calc. for $C_{16}H_{17}{}^{35}ClN_3O_2$: 318.1009) (Found: C, 60.5; H, 5.1; N, 13.2. Calc. for $C_{16}H_{16}ClN_3O_2$: C, 60.55; H, 5.08; N, 13.25%).

***N′*-[2-(Anilinothiocarbonyl)-4-chlorophenyl]-*N*,*N*-dimethylurea 9.** $\delta_H$([$^2H_6$]DMSO) 12.06 (s, exch., 1 H, PhNH), 9.20 (s, exch., 1 H, NHCO), 7.94 (d, *J* 8.9, 1 H, 6-H), 7.65 (d, *J* 7.5, 2 H, 2-H of Ph), 7.57 (d, *J* 2.5, 1 H, 3-H), 7.43 (m, 3 H, 5-H and 3-H of Ph), 7.27 (t, *J* 7.5, 1 H, 4-H of Ph) and 2.88 [s, 6 H, $N(CH_3)_2$]; $\delta_C$([$^2H_6$]DMSO) 193.21 (s, PhNHC=S), 154.84 (s, C=O), 139.85 (s, C-1 of Ph), 135.31 (s, C-2), 134.22 (s, C-1), 129.08 (d, C-3), 128.40 (d, C-3 of Ph), 127.19 (d, C-5), 126.34 (d, C-6), 125.62 (s, C-4), 124.05 (d, C-2 of Ph), 123.49 (d, C-4 of Ph) and 35.95 [q, $N(CH_3)_2$]; *m/z* (EI) 287 (100%), 255 (10), 224 (7), 196 (5), 142 (12), 109 (15), 77 (30) and 45 (24); *m/z* (CI) 334 ($MH^+$, 5%), 300 (10), 289 (96), 272 (6), 259 (10), 94 (9) and 46 (100) (Found: $M^+$, 334.0781. Calc. for $C_{16}H_{17}{}^{35}ClN_3OS$: 334.0781) (Found: C, 57.5; H, 4.9; N, 12.7. Calc. for $C_{16}H_{16}ClN_3OS$: C, 57.64; H, 4.84; N, 12.61%).

**6-Chloro-4a-hydroxy-*N*-(dimethylaminocarbonyl)-1,2,3,4,4a, 9a-hexahydrocarbazole 10.** Mp 168 °C; $\delta_H$([$^2H_6$]DMSO) 7.22–7.15 (m, 2 H, 5-H and 7-H), 6.77 (d, *J* 8.5, 1 H, 8-H), 5.41 (s, exch., 1 H, OH), 3.84 (t, *J* 4.9, 1 H, 9a-H), 2.90 [s, 6 H, $N(CH_3)_2$] and 1.79–1.23 (m, 8 H, 1-H, 2-H, 3-H and 4-H); $\delta_C$([$^2H_6$]-DMSO) 159.23 (s, C=O), 142.00 (s, C-5a), 137.30 (s, C-8a), 128.92 (d, C-5), 128.70 (d, C-7), 122.54 (d, C-8), 122.18 (s, C-6), 77.10 (s, C-4a), 69.35 (d, C-9a), 37.79 [q, $N(CH_3)_2$], 33.78 (t, C-4), 22.94 (t, C-1), 21.33 (t, C-2) and 20.69 (t, C-3); *m/z* (EI) 294 ($M^+$, 10%), 276 (15), 204 (5), 93 (7), 72 (100) and 57 (12); *m/z* (CI) 295 ($MH^+$, 5%), 277 (100), 206 (15), 72 (20) and 46 (8) (Found: $M^+$, 294.1135. Calc. for $C_{15}H_{19}{}^{35}ClN_2O_2$: 294.1135) (Found: C, 61.1; H, 6.5; N, 9.5. Calc. for $C_{15}H_{19}ClN_2O_2$: C, 61.10; H, 6.50; N, 9.51%).

**Synthesis of 6-chloro-*N*-(dimethylaminocarbonyl)-1,2,3,4-tetrahydrocarbazole 11**

To a stirred solution of hydroxyamide **10** (0.073 g, 0.25 mmol) in dichloromethane (10 $cm^3$), trifluoroacetic acid (0.010 g, 0.010 mmol) was added. After 1 h saturated $Na_2CO_3$ solution (10 $cm^3$) was added and the mixture was then extracted with dichloromethane (2 × 10 $cm^3$). The solvent was removed under reduced pressure to give **11** (0.067 g, 97%) as a colourless oil. $\delta_H$($CDCl_3$) 7.41 (s, 1 H, 5-H), 7.25 (d, *J* 8.7, 1 H, 8-H), 7.11 (dd, *J* 1.9, 8.7, 1 H, 7-H), 2.95 [s, 6 H, $N(CH_3)_2$], 2.70 (m, 2 H, 1-H), 2.59 (m, 2 H, 4-H) and 1.82 (m, 4 H, 2-H and 3-H); $\delta_C$($CDCl_3$) 152.76 (s, C=O), 136.75 (s, C-5a), 133.00 (s, C-8a), 129.07 (s, C-9a), 123.40 (s, C-6), 121.78 (d, C-5), 117.26 (d, C-7), 112.53 (d, C-8), 112.25 (s, C-4a), 37.26 [q, $N(CH_3)_2$], 22.47 (t, C-3), 22.37 (t, C-2), 22.33 (t, C-4) and 20.27 (t, C-1); *m/z* (EI) 276 ($M^+$, 15%), 204 (5) and 72 (100); *m/z* (CI) 277 ($MH^+$, 100%), 243 (3), 206 (12) and 72 (19) (Found: $M^+$, 276.1029. Calc. for $C_{15}H_{17}{}^{35}ClN_2O$: 276.1029) (Found: C, 65.2; H, 6.2; N, 10.1. Calc. for $C_{15}H_{17}ClN_2O$: C, 65.08; H, 6.20; N, 10.13%).

**General procedure for the lithiation of *N′*-(4-fluorophenyl)-*N*,*N*-dimethylurea 12 and subsequent reactions with electrophiles**

To a cooled (0 °C), stirred solution of compound **12** (0.182 g, 1.0 mmol) in THF (10 $cm^3$) under nitrogen, a solution of *t*-BuLi (1.7 mol $dm^{-3}$; 1.47 $cm^3$, 2.5 mmol) in heptane was added in a dropwise manner. Formation of the dilithio reagent was observed as a brownish solution. The mixture was stirred at 0 °C for 1.5 h, after which an electrophile (1.2 mmol; as a solution in THF if solid) was added. The mixture was stirred at 0 °C for 1 h, then removed from the cooling bath and allowed to warm to room temperature; it was then diluted with diethyl ether (5 $cm^3$) and quenched with aqueous saturated ammonium chloride solution (5 $cm^3$). The organic layer was separated, washed with water (2 × 10 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure. The crude material obtained was crystallised from diethyl ether–ethyl acetate (1:1) to give white crystals.

***N′*-(4-Fluoro-2-[$^2H_1$]phenyl)-*N*,*N*-dimethylurea 16.** $\delta_H$([$^2H_6$]-DMSO) 8.20 (s, exch., 1 H, NH), 7.45, 7.43 (2 d, *J* 5.0, 1H, 6-H), 7.01 (m, 2 H, 3-H and 5-H) and 2.91 [s, 6 H, $N(CH_3)_2$]; $\delta_C$([$^2H_6$]DMSO) 158.51 (s, C=O), 156.15, 155.78 (2 s, C-4), 136.93 (s, C-1), 121.45, 121.37 (2 d, C-6), 119.72 (s, C-2), 114.69, 114.60 (2 d, C-5), 114.47, 114.38 (2 d, C-3) and 36.23 [q, $N(CH_3)_2$]; *m/z* (EI) 184 ($M^+$ + 1, 12%), 183 ($M^+$, 27), 166 (5), 138 (10), 111 (13), 84 (23), 72 (100) and 42 (24); *m/z* (CI) 201 ($M^+ + NH_4$, 11%), 184 ($MH^+$, 100), 167 (8) and 72 (11) (Found: $M^+$, 183.0919. Calc. for $C_9H_{10}{}^2HFN_2O$: 183.0918).

***N′*-[2-(Diphenylhydroxymethyl)-4-fluorophenyl]-*N*,*N*-dimethylurea 17.** $\delta_H$([$^2H_6$]DMSO) 8.77 (s, exch., 1 H, NH), 8.07 (2 d, *J* 6.0, 1 H, 6-H), 7.75 (s, exch., 1 H, OH), 7.33 (m, 6 H, 3-H and 4-H of 2 Ph), 7.19 (d, *J* 8.0, 4 H, 2-H of 2 Ph), 7.11 (dt, *J* 3.0, 8.8, 1 H, 3-H), 6.10 (dd, *J* 3.0, 10.4, 1 H, 5-H) and 2.59 [s, 6 H, $N(CH_3)_2$]; $\delta_C$([$^2H_6$]DMSO) 157.24 (s, C=O), 154.92, 154.61 (2 s, C-4), 145.19 (s, C-1 of Ph's), 136.46 (s, C-2), 135.83 (s, C-1), 127.98 (d, C-3 of Ph's), 127.37 (d, C-2 of Ph's), 126.45 (d, C-4 of Ph's), 122.89, 122.82 (2 d, C-6), 115.74, 115.50 (2 d, C-3), 114.35, 114.14 (2 d, C-5), 81.68 (s, C-OH) and 35.45 [q, $N(CH_3)_2$]; *m/z* (EI) 364 ($M^+$, 8%), 347 (20), 346 (100), 345 (16), 319 (13), 203 (45) and 202 (35); *m/z* (CI) 365 ($MH^+$, 6%), 349 (12), 347 (20), 279 (100), 278 (20), 260 (16), 202 (22), 200 (31) and 183 (90) (Found: $M^+$, 364.1585. Calc. for $C_{22}H_{21}FN_2O_2$: 364.1587) (Found: C, 72.4; H, 5.8; N, 7.5. Calc. for $C_{22}H_{21}FN_2O_2$: C, 72.49; H, 5.81; N, 7.69%).

***N′*-[4-Fluoro-2-(hydroxyphenylmethyl)phenyl]-*N*,*N*-dimethylurea 18.** $\delta_H$([$^2H_6$]DMSO) 8.40 (s, exch., 1 H, NH), 7.70, 7.67 (2 d, *J* 5.5, 1 H, 6-H), 7.32–7.01 (m, 7 H, 3-H, 5-H and Ph), 6.64 (d, *J* 5.1, 1 H, CH), 5.86 (d, *J* 5.1, exch., 1 H, OH) and 2.83 [s, 6 H, $N(CH_3)_2$]; $\delta_C$([$^2H_6$]DMSO) 158.98 (s, C=O), 156.61, 155.40 (2 s, C-4), 142.90 (s, C-1 of Ph), 137.01, 136.95 (2 s, C-2), 134.31 (s, C-1), 128.10 (d, C-3 of Ph), 127.10 (d, C-4 of Ph), 126.24 (d, C-2 of Ph), 124.51, 124.43 (2 d, C-6), 114.50, 114.27 (2 d, C-3), 113.85, 113.64 (2 d, C-5), 72.46 (d, CH) and 35.87 [q, $N(CH_3)_2$]; *m*/*z* (EI) 288 ($M^+$, 4%), 270 (9), 226 (7), 216 (8), 198 (20), 183 (6), 105 (10), 88 (18), 77 (17), 72 (100) and 44 (34); *m*/*z* (CI) 289 ($MH^+$, 42%), 273 (47), 271 (51), 202 (100), 183 (70), 106 (21), 91 (20), 89 (43), 72 (27) and 63 (67) (Found: $MH^+$, 289.1339. Calc. for $C_{16}H_{18}FN_2O_2$: 289.1352) (Found: C, 66.5; H, 6.2; N, 9.6. Calc. for $C_{16}H_{17}FN_2O_2$: C, 66.63; H, 5.95; N, 9.72%).

### Synthesis of *N′*-[2-(diphenylhydroxymethyl)-4-trifluoromethylphenyl]-*N*,*N*-dimethylurea 19

To a cooled (0 °C), stirred solution of **13** (0.232 g, 1.0 mmol) in THF (10 $cm^3$) under nitrogen, a solution of *n*-BuLi (1.7 mol $dm^{-3}$; 1.30 $cm^3$, 2.2 mmol) in heptane was added in a dropwise manner. The mixture was stirred at 0 °C for 1 h, after which a solution of benzophenone (0.22 g, 1.2 mmol) in THF (5 $cm^3$) was added. The mixture was stirred at 0 °C for 1 h, then removed from the cooling bath and allowed to warm to room temperature; it was then diluted with diethyl ether (5 $cm^3$) and quenched with aqueous saturated ammonium chloride solution (5 $cm^3$). The organic layer was separated, washed with water (2 × 10 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure. The residue obtained was purified by column chromatography using diethyl ether–light petroleum (bp 30–40 °C) to give compound **19** (0.128 g, 0.31 mmol; 31%) and unreacted starting material (0.197 g, 0.61 mmol; 61%). $\delta_H$([$^2H_6$]DMSO) 9.19 (s, exch., 1 H, NH), 8.42 (d, *J* 8.7, 1 H, 6-H), 7.89 (s, exch., 1 H, OH), 7.63 (d, *J* 8.7, 1 H, 5-H), 7.40–7.31 (m, 6 H, 3-H and 4-H of 2 Ph), 7.17 (d, *J* 8.8, 4 H, 2-H of 2 Ph), 6.64 (d, *J* 1.7, 1 H, 3-H) and 2.66 [s, 6 H, $N(CH_3)_2$]; $\delta_C$([$^2H_6$]DMSO) 154.11 (s, C=O), 144.86 (s, C-1 of Ph's), 143.18 (s, C-2), 134.02 (s, C-1), 128.12 (d, C-3 of Ph's), 127.68 (d, C-4 of Ph's), 127.66 (d, C-5), 127.36 (d, C-2 of Ph's), 125.77 (s, C-4), 125.43 (d, C-3), 120.30 (centre of $CF_3$ quartet), 120.28 (d, C-6), 81.88 (s, C-OH) and 35.53 [q, $N(CH_3)_2$]; *m*/*z* (EI) 414 ($M^+$, 10%), 396 (100), 377 (25), 352 (50), 340 (28) and 335 (65); *m*/*z* (CI) 415 ($MH^+$, 9%), 397 (20), 328 (6), 200 (32), 183 (39), 136 (14), 106 (50), 94 (100), 78 (49) and 74 (70) (Found: $MH^+$, 415.1633. Calc. for $C_{23}H_{22}F_3N_2O_2$: 415.1633) (Found: C, 66.4; H, 5.2; N, 6.5. Calc. for $C_{23}H_{21}F_3N_2O_2$: C, 66.64; H, 5.11; N, 6.76%).

### General procedure for the lithiation of *N′*-phenyl-*N*,*N*-dimethylurea 20, and *N′*-(4-methylphenyl)-*N*,*N*-dimethylurea 21

To a cooled (−20 °C) stirred solution of compound **20** or **21** (1.0 mmol) in THF (10 $cm^3$) under nitrogen, was added a solution of *t*-BuLi (1.7 mol $dm^{-3}$; 1.41 $cm^3$, 2.40 mmol) in pentane. The mixture was stirred at −20 °C for 2 h, after which an electrophile (1.2 mmol; as a solution in THF if solid) was added. The solution thus obtained was stirred for 2 h at −20 °C, then the cooling bath was removed and the mixture was allowed to warm to room temperature; it was then diluted with ether (5 $cm^3$) and quenched with aqueous saturated ammonium chloride solution (5 $cm^3$). The organic layer was separated, washed with water (2 × 10 $cm^3$), dried ($MgSO_4$), filtered and evaporated under reduced pressure. The residue obtained was purified by column chromatography using light petroleum (bp 30–40 °C)–diethyl ether mixtures.

***N′*-Phenyl-*N*-[(2,2-diphenyl)-2-(hydroxy)ethyl]-*N*-methylurea 24.** $\delta_H$([$^2H_6$]DMSO) 8.53 (s, exch., 1 H, NH), 7.50 (d, *J* 8.6, 4 H, 2-H of 2 Ph), 7.40–7.18 (m, 8 H, 3-H, 4-H of 2 Ph, 2-H and 3-H), 6.94 (t, *J* 7.3, 1 H, 4-H), 6.60 (s, exch., 1 H, OH), 4.18 (s, 2 H, $CH_2$) and 2.56 (s, 3 H, $CH_3$); $\delta_C$([$^2H_6$]DMSO) 157.28 (s, C=O), 145.85 (s, C-1 of Ph's), 140.25 (s, C-1), 128.30 (d, C-2), 127.78 (d, C-3 of Ph's), 126.72 (d, C-4 of Ph's), 126.42 (d, C-2 of Ph's), 121.83 (d, C-3), 119.70 (d, C-4), 78.38 (s, C-OH), 58.98 (t, $CH_2$) and 36.94 (q, $CH_3$); *m*/*z* (EI) 346 ($M^+$, 3%), 328 (12), 285 (9), 256 (95), 180 (22), 165 (15), 105 (23), 77 (42), 72 (100) and 44 (38); *m*/*z* (CI) 347 ($MH^+$, 8%), 329 (27), 260 (100), 200 (19), 183 (40), 165 (31), 94 (42) and 63 (28) (Found: $M^+$, 346.1681. Calc. for $C_{22}H_{22}N_2O_2$: 346.1681) (Found: C, 76.2; H, 6.6; N, 8.1. Calc. for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09%).

***N′*-[2-(Diphenylhydroxymethyl)phenyl]-*N*,*N*-dimethylurea 25.** Mp 222–223 °C; $\delta_H$([$^2H_6$]DMSO) 8.92 (s, exch., 1 H, NH), 8.11 (d, *J* 8.2, 1 H, 6-H), 7.62 (s, exch., 1H, OH), 7.35–7.22 (m, 7 H, 3-H, 4-H of 2 Ph and 3-H), 7.17 (d, *J* 7.5, 4 H, 2-H of 2 Ph), 6.80 (d, *J* 8.2, 1 H, 4-H), 6.38 (d, *J* 8.2, 1 H, 5-H) and 2.61 [s, 6 H, $N(CH_3)_2$]; $\delta_C$([$^2H_6$]DMSO) 154.60 (s, C=O), 145.87 (s, C-1 of Ph's), 139.51 (s, C-1), 134.02 (s, C-2), 129.04 (d, C-3), 127.98 (d, C-5), 127.81 (d, C-3 of Ph's), 127.48 (d, C-2 of Ph's), 127.19 (d, C-4 of Ph's), 120.94 (d, C-4), 120.46 (d, C-6), 82.07 (s, C-OH) and 35.50 [q, $N(CH_3)_2$]; *m*/*z* (EI) 346 ($M^+$, 15%), 328 (22), 256 (88), 183 (23), 105 (25), 77 (90) and 72 (100); *m*/*z* (CI) 347 ($MH^+$, 2%), 329 (10), 260 (25), 200 (5), 183 (10), 165 (8), 94 (56), 52 (48) and 46 (100) (Found: $M^+$, 346.1681. Calc. for $C_{22}H_{22}N_2O_2$: 346.1681) (Found: C, 76.4; H, 6.5; N, 8.0. Calc. for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09%).

***N′*-[2-(Diphenylhydroxymethyl)phenyl]-*N*-[(2,2-diphenyl-2-hydroxy)ethyl]-*N*-methylurea 26.** Mp 227 °C; $\delta_H$([$^2H_6$]DMSO) 8.97 (s, exch., 1 H, NH), 8.07 (dd, *J* 1.2, 7.8, 1 H, 6-H), 7.40–7.16 (m, 22 H, 4 Ph, 5-H and one OH), 6.85 (dt, *J* 1.2, 7.8, 1 H, 4-H), 6.49 (dd, *J* 1.2, 7.8, 1 H, 3-H), 6.21 (s, exch., 1 H, the other OH), 3.94 (s, 2 H, $CH_2$) and 2.21 (s, 3 H, $CH_3$); $\delta_C$([$^2H_6$]DMSO) 157.42 (s, C=O), 145.72, 145.48 (2 s, C-1 of Ph's), 138.54 (s, C-1), 134.67 (s, C-2), 129.17 (d, C-3), 127.77 (d, C-5), 127.47, 127.36 (2 d, C-3 of Ph's), 127.41, 127.21 (2 d, C-2 of Ph's), 126.30, 126.03 (2 d, C-4 of Ph's), 121.69 (d, C-4), 121.03 (d, C-6), 82.01, 78.26 (2 s, 2 × C-OH), 59.57 (t, $CH_2$) and 36.24 (q, $CH_3$); *m*/*z* (CI) 529 ($MH^+$, 3%), 511 (6), 260 (70), 210 (28), 200 (37), 183 (100) and 94 (56) (Found: $MH^+$, 529.2491. Calc. for $C_{35}H_{33}N_2O_3$: 529.2491) (Found: C, 79.4; H, 6.0; N, 5.3. Calc. for $C_{35}H_{32}N_2O_3$: C, 79.50; H, 6.11; N, 5.30%).

***N′*-Phenyl-*N*-ethyl-*N*,*N′*-dimethylurea 27.** Viscous oil; $\delta_H$($CDCl_3$) 7.31 (t, *J* 7.8, 2 H, 3-H), 7.10 (d, *J* 7.8, 2 H, 2-H), 7.07 (t, *J* 7.8, 1 H, 4-H), 3.21 (q, *J* 7.1, 2 H, $CH_2$), 3.19 (s, 3 H, $NCH_3$), 2.56 (s, 3 H, $CH_3NCH_2$) and 0.98 (t, *J* 7.1, 3 H, $CH_3CH_2$); $\delta_C$($CDCl_3$) 161.70 (s, C=O), 147.12 (s, C-1), 129.39 (d, C-3), 124.24 (d, C-4), 123.80 (d, C-2), 44.52 (t, $CH_2$), 35.70 (q, $NCH_3$), 35.25 (q, $CH_3NCH_2$) and 12.17 (q, $CH_3CH_2$); *m*/*z* (EI) 192 ($M^+$, 20%), 177 (35), 162 (21), 108 (15), 77 (100), 72 (56) and 44 (41); *m*/*z* (CI) 193 ($MH^+$, 100%), 179 (2), 165 (20), 108 (8), 86 (6), 60 (7) and 45 (8) (Found: $M^+$, 192.1263. Calc. for $C_{11}H_{16}N_2O$: 192.1263) (Found: C, 68.6; H, 8.4; N, 14.6. Calc. for $C_{11}H_{16}FN_2O$: C, 68.70; H, 8.39; N, 14.58%).

***N′*-Phenyl-*N*-[$^2H_1$]methyl-*N*-methylurea 28.** $\delta_H$($CDCl_3$) 7.36 (d, *J* 7.8, 2 H, 2-H), 7.23 (t, *J* 7.8, 2 H, 3-H), 6.98 (t, *J* 7.8, 1 H, 4-H), 6.69 (s, exch., 1 H, NH), 2.93 (s, 3 H, $CH_3$) and 2.91 (1 : 1 : 1 t, *J* 2.0, 2 H, $CH_2$); $\delta_C$($CDCl_3$) 155.99 (s, C=O), 139.38 (s, C-1), 128.65 (d, C-3), 122.77 (d, C-2), 120.12 (d, C-4), 36.34 (q, $CH_3$) and 36.45, 36.12, 35.78 (1 : 1 : 1 t, $CH_2$); *m*/*z* (EI) 165 ($M^+$, 3%), 150 (12), 119 (9), 77 (100), 72 (55) and 44 (32); *m*/*z* (CI) 166 ($MH^+$, 100%), 151 (2), 119 (2), 73 (11) and 47 (16) (Found: $M^+$, 165.1012. Calc. for $C_9H_{11}{}^2HN_2O$: 165.1012).

***N′*-Phenyl-*N*-[(2-hydroxy-2-phenyl))ethyl]-*N*-methylurea 29.** $\delta_H$($CDCl_3$) 8.25 (s, exch., 1 H, NH), 7.36–6.96 (m, 10 H, 2-H, 3-H, 4-H and Ph), 5.08 (d, *J* 3.5, exch., 1 H, OH), 4.71 (d, *J* 8.3, 1 H, CH), 3.60, 3.53 (2 d, *J* 8.3, 1 H, 1-H of $CH_2$), 3.56 (dd,

*J* 1.8, 15.3, 1 H, 1-H of $CH_2$) and 2.72 (s, 3 H, $CH_3$); $\delta_C$($CDCl_3$) 157.83 (s, C=O), 141.62 (s, C-1 of Ph), 139.50 (s, C-1), 128.80 (d, C-3), 128.47 (d, C-3 of Ph), 127.71 (d, C-4 of Ph), 125.71 (d, C-2 of Ph), 122.45 (d, C-4), 119.31 (d, C-2), 73.25 (d, CH), 58.18 (t, $CH_2$) and 35.73 (q, $CH_3$); *m*/*z* (EI) 250 (3%), 177 (5), 164 (6), 152 (9), 132 (20), 119 (100), 105 (12), 91 (72), 77 (55), 64 (46) and 51 (38); *m*/*z* (CI) 271 ($MH^+$, 5%), 251 (10), 178 (50), 152 (100), 134 (22), 119 (20) and 94 (56) (Found: $MH^+$, 271.1447. Calc. for $C_{16}H_{19}N_2O_2$: 271.1447) (Found: C, 71.0; H, 6.8; N, 10.3. Calc. for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.70; N, 10.35%).

***N*′-Phenyl-*N*-[(1-hydroxy-2-chlorocyclohexyl)methyl]-*N*-methylurea 30.** $\delta_H$([$^2H_6$]DMSO) 8.47 (s, exch., 1 H, NH), 7.40 (d, *J* 7.5, 2 H, 2-H), 7.22 (t, *J* 7.5, 2 H, 3-H), 6.92 (t, *J* 7.5, 1 H, 4-H), 5.23 (s, exch., 1 H, OH), 4.10, 4.07 (2 d, *J* 4.5, 1 H, 2-H of cyclohexyl), 3.72, 3.28 (2 d, *J* 14.8, 2 H, $CH_2$), 3.03 (s, 3 H, $CH_3$) and 1.96–1.28 (m, 8 H, 3-H, 4-H, 5-H and 6-H of cyclohexyl); $\delta_C$([$^2H_6$]DMSO) 158.69 (s, C=O), 140.28 (s, C-1), 128.16 (d, C-3), 121.60 (d, C-4), 119.46 (d, C-2), 73.68 (s, C-1 of cyclohexyl), 67.08 (d, C-2 of cyclohexyl), 57.29 (t, $CH_2$), 37.36 (q, $CH_3$), 33.56 (t, C-6 of cyclohexyl), 32.12 (t, C-3 of cyclohexyl), 25.04 (t, C-4 of cyclohexyl) and 19.81 (t, C-5 of cyclohexyl); *m*/*z* (CI) 297 ($MH^+$, 100%), 261 (90), 243 (49), 178 (86), 164 (11), 151 (12), 142 (38), 119 (22) and 94 (18) (Found: $MH^+$, 297.1370. Calc. for $C_{15}H_{22}{}^{35}ClN_2O_2$: 297.1370) (Found: C, 60.9; H, 7.0; N, 9.5. Calc. for $C_{15}H_{21}ClN_2O_2$: C, 60.71; H, 7.13; N, 9.43%).

***N*′-(4-Methylphenyl)-*N*-[(2,2-diphenyl-2-hydroxy)ethyl]-*N*-methylurea 31.** $\delta_H$([$^2H_6$]DMSO) 8.40 (s, exch., 1 H, NH), 7.50 (d, *J* 7.3, 4 H, 2-H of 2 Ph), 7.31 (d, *J* 7.3, 4 H, 3-H of 2 Ph), 7.23 (m, 4 H, 4-H of 2 Ph and 2-H), 7.02 (d, *J* 8.2, 2 H, 3-H), 6.63 (s, exch., 1 H, OH), 4.18 (s, 2 H, $CH_2$), 2.58 (s, 3 H, $NCH_3$) and 2.22 (s, 3 H, $CH_3$); $\delta_C$([$^2H_6$]DMSO) 157.40 (s, C=O), 145.98 (s, C-1 of Ph's), 137.72 (s, C-1), 130.66 (s, C-4), 128.74 (d, C-3), 127.79 (d, C-3 of Ph's), 126.70 (d, C-4 of Ph's), 126.42 (d, C-2 of Ph's), 119.91 (d, C-2), 78.39 (s, C-OH), 58.94 (t, $CH_2$), 36.97 (q, $NCH_3$) and 20.38 (q, $CH_3$); *m*/*z* (EI) 360 ($M^+$, 10%), 342 (62), 299 (22), 285 (18), 270 (75), 265 (35), 253 (100) and 239 (12); *m*/*z* (CI) 361 ($MH^+$, 9%), 271 (35), 254 (40), 212 (33), 210 (70), 200 (71), 183 (100), 182 (98) and 165 (15) (Found: $M^+$, 360.1834. Calc. for $C_{23}H_{24}N_2O_2$: 360.1838) (Found: C, 76.8; H, 6.7; N, 7.6. Calc. for $C_{23}H_{24}N_2O_2$: C, 76.62; H, 6.72; N, 7.78%).

***N*′-(4-Methylphenyl)-*N*-[$^2H_1$]methyl-*N*-methylurea 32.** $\delta_H$([$^2H_6$]DMSO) 8.12 (s, exch., 1 H, NH), 7.30 (d, *J* 8.4, 2 H, 2-H), 7.00 (d, *J* 8.4, 2 H, 3-H), 2.90 (s, 3 H, $NCH_3$), 2.88 (1 : 1 : 1 t, *J* 2.0, 2 H, $CH_2$) and 2.22 (s, 3 H, $CH_3$); $\delta_C$([$^2H_6$]DMSO) 155.85 (s, C=O), 138.13 (s, C-1), 130.30 (s, C-4), 128.56 (d, C-3), 119.93 (d, C-2), 34.24 (q, $NCH_3$), 36.21, 35.99, 35.79 (1 : 1 : 1 t, $CH_2$) and 20.40 (q, $CH_3$); *m*/*z* (EI) 179 ($M^+$, 55%), 133 (14), 106 (16), 91 (11), 77 (31), 73 (100) and 72 (42); *m*/*z* (CI) 197 ($M^+ + NH_4$, 9%), 180 ($MH^+$, 100) and 73 (16) (Found: $M^+$, 179.1170. Calc. for $C_{10}H_{13}{}^2HN_2O$: 179.1169).

***N*′-(4-Methylphenyl)-*N*-[(2-hydroxy-2-phenyl)ethyl]-*N*-methylurea 33.** $\delta_H$([$^2H_6$]DMSO) 8.32 (s, exch., 1 H, NH), 7.40–7.23 (m, 7 H, 2-H and Ph), 7.01 (d, *J* 8.2, 2 H, 3-H), 5.79 (d, *J* 2.9, exch., 1 H, OH), 4.81 (q, *J* 5.8, 1 H, CH), 3.41 (d, *J* 5.8, 2 H, $CH_2$), 2.86 (s, 3 H, $NCH_3$) and 2.23 (s, 3 H, $CH_3$); $\delta_C$([$^2H_6$]DMSO) 156.00 (s, C=O), 143.55 (s, C-1 of Ph), 138.05 (s, C-1), 130.29 (s, C-4), 128.69 (d, C-3), 128.04 (d, C-3 of Ph), 127.08 (d, C-4 of Ph), 126.01 (d, C-2 of Ph), 119.63 (d, C-2), 71.68 (d, CH), 57.03 (t, $CH_2$), 36.01 (q, $NCH_3$) and 20.42 (q, $CH_3$); *m*/*z* (EI) 284 ($M^+$, 6%), 266 (40), 194 (17), 189 (13), 178 (100), 177 (65) and 161 (12); *m*/*z* (CI) 285 ($MH^+$, 26%), 195 (27), 178 (13), 136 (18), 134 (22), 125 (18), 108 (100) and 78 (9) (Found: $MH^+$, 285.1593. Calc. for $C_{17}H_{21}N_2O_2$: 285.1603) (Found: C, 71.8; H, 7.1; N, 9.9. Calc. for $C_{17}H_{20}N_2O_2$: C, 71.79; H, 7.09; N, 9.86%).

**General procedure for the synthesis of *N*′-[2-(diphenylhydroxymethyl)phenyl]-*N*,*N*-dimethylurea 25 and *N*′-[2-(diphenylhydroxymethyl)-4-methylphenyl]-*N*,*N*-dimethylurea 36**

To a cooled solution (0 °C) of compound **34** or **35** (1.0 mmol) in THF (10 $cm^3$) under nitrogen was added a solution of methyllithium (1.0 mol $dm^{-3}$; 1.1 $cm^3$, 1.1 mmol) in tetrahydrofuran in order to deprotonate the nitrogen. Bromine–lithium exchange was then effected by the addition of *tert*-butyllithum (1.7 mol $dm^{-3}$; 2.47 $cm^3$, 2.1 mmol) in heptane. The mixture was stirred at 0 °C for 1 h, after which a solution of benzophenone (0.22 g, 1.2 mmol) in THF (5 $cm^3$) was added. The mixture was stirred for an additional 1 h at 0 °C, then removed from the cooling bath and allowed to warm to room temperature. It was then diluted with diethyl ether (5 $cm^3$) and quenched with aqueous saturated ammonium chloride solution (5 $cm^3$). The organic layer was separated, washed with water (2 × 10 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure. The solid obtained was crystallised from ethyl acetate to give compound **25** or **36**.

***N*′-[2-(Diphenylhydroxymethyl)-4-methylphenyl]-*N*,*N*-dimethylurea 36.** Mp 206–207 °C; $\delta_H$([$^2H_6$]DMSO) 8.78 (s, exch.,1 H, NH), 7.96 (d, *J* 8.3, 1 H, 6-H), 7.50 (s, exch., 1 H, OH), 7.33–7.24 (m, 6 H, 3-H, 4-H of 2 Ph), 7.16 (d, *J* 8.1, 4 H, 2-H of 2 Ph), 7.02 (d, *J* 8.3, 1 H, 5-H), 6.18 (d, *J* 1.4, 1 H, 3-H), 2.59 [s, 6 H, $N(CH_3)_2$] and 2.06 (3 H, $CH_3$); $\delta_C$([$^2H_6$]DMSO) 154.96 (s, C-1 of Ph's), 154.66 (s, C=O), 137.05 (s, C-2), 134.14 (s, C-1), 129.58 (d, C-3), 128.92 (s, C-4), 128.28 (d, C-5), 127.69 (d, C-3 of Ph's), 127.50 (d, C-2 of Ph's), 127.09 (d, C-4 of Ph's), 121.19 (d, C-6), 82.00 (s, C-OH), 35.49 [q, $N(CH_3)_2$] and 20.70 (q, $CH_3$); *m*/*z* (EI) 360 ($M^+$, 6%), 342 (100), 327 (10), 299 (26), 298 (24) and 281 (15); *m*/*z* (CI) 361 ($MH^+$, 10%), 343 (56), 274 (58), 200 (60), 183 (64), 108 (29), 91 (62), 78 (55), 74 (65) and 63 (100) (Found: $M^+$, 360.1848. Calc. for $C_{23}H_{24}N_2O_2$: 360.1838) (Found: C, 76.8; H, 6.7; N, 7.7. Calc. for $C_{23}H_{24}N_2O_2$: C, 76.62; H, 6.72; N, 7.78%).

**General procedure for the lithiation of *N*′-(4-methoxyphenyl)-*N*,*N*-dimethylurea 37 and reactions with electrophiles**

To a cooled (0 °C or −20 °C), stirred solution of compound **37** (0.20 g, 1.02 mmol) in THF (10 $cm^3$) under nitrogen, was added a solution of *t*-BuLi (1.7 mol $dm^{-3}$; 2.2 or 3.3 mmol) in heptane. Formation of the lithio reagent was observed as a yellow solution. The mixture was stirred at 0 or −20 °C for 2 h, after which an electrophile (1.2 or 2.2 mmol) (as a solution in THF if solid) was added. The solution thus obtained was stirred for 2 h at 0 or −20 °C, then the cooling bath was removed and the mixture allowed to warm to room temperature. It was then diluted with diethyl ether (5 $cm^3$) and quenched with aqueous saturated ammonium chloride solution (5 $cm^3$). The organic layer was separated, washed with water (2 × 10 $cm^3$), dried ($MgSO_4$), filtered and evaporated under reduced pressure. The residue obtained was purified by column chromatography using light petroleum (30–40 °C)–diethyl ether mixtures. The electrophiles used were benzophenone (Table 4), 4-*tert*-butylcyclohexanone (Table 5) and methyl iodide.

***N*′-[3-(Diphenylhydroxymethyl)-4-methoxyphenyl]-*N*,*N*-dimethylurea 38.** Mp 141 °C; $\delta_H$($CDCl_3$) 8.55 (s, exch., 1 H, NH), 7.92 (d, *J* 9.0, 1 H, 5-H), 7.55 (s, exch., 1 H, OH), 7.45–7.10 (m, 10 H, 2 Ph), 6.86 (dd, *J* 3.0, 9.0, 1 H, 6-H), 5.94 (d, *J* 3.0, 1 H, 2-H), 3.85 (s, 3 H, $OCH_3$) and 2.60 [s, 6 H, $N(CH_3)_2$]; $\delta_C$($CDCl_3$) 154.71 (s, C=O), 152.88 (s, C-4), 145.61 (s, C-1 of Ph's), 135.99 (s, C-3), 132.49 (s, C-1), 127.56 (d, C-3 of Ph's), 127.30 (d, C-4 of Ph's), 126.98 (d, C-2 of Ph's), 122.66 (d, C-2), 116.27 (d, C-6), 111.28 (d, C-5), 81.71 (s, C-OH), 54.80 (q, $OCH_3$) and 35.32 [q, $N(CH_3)_2$]; *m*/*z* (EI) 376 ($M^+$, 2%), 358 (12), 286 (71), 270 (12), 242 (15), 165 (18), 105 (21), 77 (22), 72 (100) and 42 (19) (Found: $M^+$, 376.1787. Calc. for $C_{23}H_{24}N_2O_3$:

376.1787) (Found: C, 73.2; H, 6.5; N, 7.3. Calc. for $C_{23}H_{24}N_2O_3$: C, 73.38; H, 6.43; N, 7.44%).

***N′*-(4-Methoxyphenyl)-*N*-[(2,2-diphenyl-2-hydroxy)ethyl]-*N*-methylurea 39.** Mp 79–80 °C; $\delta_H(CDCl_3)$ 7.46 (d, *J* 9.0, 2 H, 3-H), 7.34–7.21 (m, 11 H, NH and 2 Ph), 6.80 (d, *J* 9.0, 2 H, 2-H), 5.35 (s, exch., 1 H, OH), 4.16 (s, 3 H, $OCH_3$), 3.76 (s, 2 H, $CH_2$) and 2.41 (s, 3 H, $NCH_3$); $\delta_C(CDCl_3)$ 158.66 (s, C=O), 155.90 (s, C-4), 145.20 (s, C-1 of Ph's), 131.81 (s, C-1), 128.18 (d, C-3 of Ph's), 127.82 (d, C-4 of Ph's), 126.57 (d, C-2 of Ph's), 122.33 (d, C-3), 114.09 (d, C-2), 78.85 (s, C-OH), 60.94 (t, $CH_2$), 55.51 (q, $OCH_3$) and 37.10 (q, $NCH_3$); *m*/*z* (EI) 376 ($M^+$, 5), 358 (10), 331 (15), 286 (51), 254 (60), 209 (89) and 208 (100); *m*/*z* (CI) 377 ($MH^+$, 25), 359 (8), 271 (8), 254 (10), 212 (17), 210 (18), 183 (62), 181 (49), 124 (100), 105 (10), 52 (44) and 44 (62) (Found: $MH^+$, 377.1865. Calc. for $C_{23}H_{25}N_2O_3$: 377.1865) (Found: C, 73.3; H, 6.3; N, 7.5. Calc. for $C_{23}H_{24}N_2O_3$: C, 73.38; H, 6.43; N, 7.44%).

***N′*-[3-(Diphenylhydroxymethyl)-4-methoxyphenyl]-*N*-(2,2-diphenyl-2-hydroxyethyl)-*N*-methylurea 40.** Mp 186 °C; $\delta_H$-([$^2H_6$]DMSO) 8.62 (s, exch., 1 H, NH), 7.86 (d, *J* 9.0, 1 H, 5-H), 7.47 (s, exch., 1 H, OH), 7.40–7.11 (m, 20 H, 4 Ph), 6.85 (dd, *J* 3.0, 9.0, 1 H, 6-H), 6.22 (s, exch., 1 H, $CH_2C$-OH), 5.90 (d, *J* 3.0, 1 H, 2-H), 3.91 (s, 3 H, $OCH_3$), 3.30 (s, 2 H, $CH_2$) and 2.26 (s, 3 H, $NCH_3$); $\delta_C$([$^2H_6$]DMSO) 156.89 (s, C=O), 153.35 (s, C-4), 146.24, 145.60 (2 s, C-1 of Ph's), 136.46 (s, C-3), 131.95 (s, C-1), 127.71, 127.65 (2 d, C-3 of Ph's), 127.41, 127.21 (2 d, C-4 of Ph's), 126.42, 126.21 (2 d, C-2 of Ph's), 123.07 (d, C-5), 116.46 (d, C-2), 111.44 (d, C-6), 81.86 (s, ArC-OH), 78.04 (s, $CH_2C$-OH), 58.43 (t, $CH_2$), 54.96 (q, $OCH_3$) and 38.97 (q, $NCH_3$); *m*/*z* (EI) 358 (5), 314 (12), 286 (43), 242 (10), 210 (9), 183 (8), 165 (9), 105 (40), 77 (52) and 44 (100); *m*/*z* (CI) 559 ($MH^+$, 5%), 542 (16), 332 (20), 286 (8), 254 (12), 228 (40), 200 (30), 183 (100) and 105 (21) (Found: $MH^+$, 559.2597. Calc. for $C_{36}H_{35}N_2O_4$: 559.2597) (Found: C, 77.3; H, 6.0; N, 5.0. Calc. for $C_{36}H_{34}N_2O_4$: C, 77.40; H, 6.13; N, 5.01%).

***N′*-(4-Methoxyphenyl)-*N*-[(1-hydroxy-4-*tert*-butylcyclohexyl)-methyl]-*N*-methylurea 41.** Mp 164–165 °C; NMR spectra show a mixture of two geometrical isomers, a and b, in a ratio 1 : 6; $\delta_H(CDCl_3)$ of **41a**, 8.64 (s, exch., 1 H, NH), 7.92 (d, *J* 8.9, 2 H, 3-H), 7.40 (m, 2 H, 2-H), 3.78 (s, 3 H, $OCH_3$), 3.23 (s, 2 H, $CH_2$), 3.15 (s, exch., 1 H, OH), 2.98 (s, 3 H, $NCH_3$), 1.80–0.96 (m, 9 H, cyclohexyl) and 0.80 [s, 9 H, $C(CH_3)_3$]; $\delta_H(CDCl_3)$ of **41b**, 8.90 (s, exch., 1 H, NH), 7.25 (d, *J* 8.9 Hz, 2 H, 3-H), 6.88 (d, *J* 8.9, 2 H, 2-H), 3.77 (s, 3 H, $OCH_3$), 3.23 (s, 2 H, $CH_2$), 3.15 (s, exch., 1 H, OH), 2.99 (s, 3 H, $NCH_3$), 1.80–0.96 (m, 9 H, cyclohexyl) and 0.88 [s, 9 H, $C(CH_3)_3$]; $\delta_C(CDCl_3)$ of **41a**, 156.50 (s, C=O), 154.29 (s, C-4), 132.09 (s, C-1), 124.31 (d, C-3), 114.22 (d, C-2), 75.22 (s, C-1 of cyclohexyl), 61.90 (t, $CH_2$), 55.51 (q, $OCH_3$), 47.62 (d, C-4 of cyclohexyl), 38.32 (t, C-2 of cyclohexyl), 38.29 (q, $NCH_3$), 32.27 [s, $C(CH_3)_3$], 27.94 [q, $C(CH_3)_3$] and 25.54 (t, C-3 of cyclohexyl); $\delta_C(CDCl_3)$ of **41b**, 158.23 (s, C=O), 155.16 (s, C-4), 132.92 (s, C-1), 121.17 (d, C-3), 113.97 (d, C-2), 73.17 (s, C-1 of cyclohexyl), 61.98 (t, $CH_2$), 55.61 (q, $OCH_3$), 47.89 (d, C-4 of cyclohexyl), 38.29 (q, $NCH_3$), 35.45 (C-2 of cyclohexyl), 32.42 [s, $C(CH_3)_3$], 27.55 [q, $C(CH_3)_3$] and 22.01 (t, C-3 of cyclohexyl); *m*/*z* (EI) 348 ($M^+$, 11%), 259 (5), 194 (30), 177 (18), 149 (93), 134 (19), 121 (20), 108 (21), 72 (28), 57 (90) and 44 (100) (Found: $M^+$, 348.2413. Calc. for $C_{20}H_{32}N_2O_3$: 348.2413) (Found: C, 69.1; H, 9.0; N, 8.0. Calc. for $C_{20}H_{32}N_2O_3$: C, 68.93; H, 9.26; N, 8.04%).

***N′*-[3-(1-Hydroxy-4-*tert*-butylcyclohexyl)-4-methoxyphenyl]-*N*-[(1-hydroxy-4-*tert*-butylcyclohexyl)methyl]-*N*-methylurea 42.** Mp 179 °C; NMR spectra show the presence of a single isomer only. $\delta_H(CDCl_3)$ 9.11 (s, exch., 1 H, NH), 7.90 (d, *J* 8.6, 1 H, 5-H), 6.77 (m, 3 H, OH, 2-H and 6-H), 4.06 (s, exch., 1 H, the other OH), 3.75 (s, 3 H, $OCH_3$), 3.30 (s, 2 H, $CH_2$), 3.06 (s, 3 H, $NCH_3$), 2.59–0.95 (m, 18 H, 2 cyclohexyl) and 0.90, 0.86 [2 s, 18 H, 2 × $C(CH_3)_3$]; $\delta_C(CDCl_3)$ 157.87 (s, C=O), 154.81 (s, C-4), 137.13 (s, C-3), 131.77 (s, C-1), 124.09 (d, C-5), 111.85 (d, C-6), 111.48 (d, C-2), 74.27, 72.11 (2 s, 2 × C-1 of cyclohexyl), 61.77 (t, $CH_2$), 55.51 (q, $OCH_3$), 48.15, 47.41 (2 d, 2 × C-4 of cyclohexyl), 38.07 (q, $NCH_3$), 36.58, 36.30 (2 t, 2 × C-2 of cyclohexyl), 32.44, 32.40 [2 s, 2 × $C(CH_3)_3$], 27.61, 27.58 [2 q, 2 × $C(CH_3)_3$] and 22.41, 20.20 (2 t, 2 × C-3 of cyclohexyl); *m*/*z* (EI) 502 ($M^+$, 4%), 330 (10), 303 (28), 259 (88), 244 (10), 204 (12), 174 (27), 160 (30), 136 (22), 100 (31), 81 (25), 57 (97), 55 (40), 45 (92) and 44 (100) (Found: $M^+$, 502.3771. Calc. for $C_{30}H_{50}N_2O_4$: 502.3771) (Found: C, 71.7; H, 10.1; N, 5.4. Calc. for $C_{30}H_{50}N_2O_4$: C, 71.67; H, 10.02; N, 5.57%).

***N′*-(4-Methoxy-3-methylphenyl)-*N′*,*N*,*N*-trimethylurea 43.** Viscous oil, $\delta_H(CDCl_3)$ 6.94 (d, *J* 8.9, 1 H, 5-H), 6.74 (d, *J* 2.8, 1 H, 2-H), 6.70 (dd, *J* 2.8, 8.9, 1 H, 6-H), 3.79 (s, 3 H, $OCH_3$), 3.02 (s, 3 H, $NCH_3$), 2.59 [s, 6 H, $N(CH_3)_2$] and 2.17 (s, 3 H, $CH_3$); $\delta_C(CDCl_3)$ 162.80 (s, C=O), 157.52 (s, C-4), 138.44 (s, C-1), 135.58 (s, C-3), 127.62 (d, C-5), 116.24 (d, C-6), 112.30 (d, C-2), 55.40 (q, $OCH_3$), 39.28 (q, $NCH_3$), 37.87 [q, $N(CH_3)_2$] and 17.91 (q, $CH_3$); *m*/*z* (EI) 222 ($M^+$, 22%), 178 (8), 163 (12), 150 (47), 136 (19), 122 (15), 85 (33), 72 (100) and 43 (48); *m*/*z* (CI) 223 ($MH^+$, 89%), 209 (12), 152 (40), 138 (43), 130 (35), 108 (25), 88 (20), 60 (55), 52 (77) and 44 (100) (Found: $M^+$, 222.1368. Calc. for $C_{12}H_{18}N_2O_2$: 222.1368) (Found: C, 64.7; H, 8.2; N, 12.7. Calc. for $C_{12}H_{18}N_2O_2$: C, 64.82; H, 8.17; N, 12.61%).

***N′*-(4-Methoxy-3-methylphenyl)-*N*-ethyl-*N′*,*N*-dimethylurea 44.** Viscous oil, $\delta_H(CDCl_3)$ 7.01 (d, *J* 9.0, 1 H, 5-H), 6.86 (d, *J* 3.0, 1 H, 2-H), 6.75 (dd, *J* 3.0, 9.0, 1 H, 6-H), 3.81 (s, 3 H, $OCH_3$), 3.19 (q, *J* 7.1, 2 H, $CH_2$), 3.00 (s, 3 H, $NCH_3$), 2.48 (s, 3 H, $ArNCH_3$), 2.25 (s, 3 H, $ArCH_3$) and 0.85 (t, 3 H, *J* 7.1, $CH_3CH_2$); $\delta_C(CDCl_3)$ 162.71 (s, C=O), 157.59 (s, C-4), 138.63 (s, C-3), 135.70 (s, C-1), 125.83 (d, C-5), 116.22 (d, C-6), 112.30 (d, C-2), 55.41 (q, $OCH_3$), 40.88 (t, $CH_2$), 39.29 (q, $NCH_3$), 35.29 (q, $ArCH_3$), 17.89 (q, $ArNCH_3$) and 12.24 (q, $CH_3CH_2$); *m*/*z* (EI) 236 ($M^+$, 10%), 222 (5), 150 (22), 99 (29), 86 (95), 72 (25), 58 (100) and 42 (18) (Found: $M^+$, 236.1525. Calc. for $C_{13}H_{20}N_2O_2$: 236.1525) (Found: C, 66.0; H, 8.5.1; N, 11.9. Calc. for $C_{13}H_{20}N_2O_2$: C, 66.05; H, 8.54; N, 11.86%).

## Acknowledgements

G. A. El-Hiti thanks the University of Wales Swansea for financial support and the Royal Society of Chemistry for an international author grant. We thank the EPSRC Mass Spectrometry Service, University of Wales Swansea, for recording mass spectra for us. We also thank the EPSRC and the University of Wales for grants that enabled the purchase of NMR equipment used in the course of this work.

## References

1 P. Beak, W. J. Zajdel and D. B. Reitz, *Chem. Rev.*, 1984, **84**, 471; V. Snieckus, *Chem. Rev.*, 1990, **90**, 879; V. Snieckus and P. Beak, *Acc. Chem. Res.*, 1982, **15**, 305; N. S. Narasimhan and R. S. Mali, *Synthesis*, 1983, 957; K. Smith, *Chem. Br.*, 1982, 29; V. Snieckus, *Bull. Soc. Chim. Fr.*, 1988, 67.
2 H. W. Gschwend and H. R. Rodriguez, *Org. React.* (*N.Y.*), 1979, **26**, 1.
3 O. Sugimoto, M. Sudo and K. Tanji, *Tetrahedron Lett.*, 1999, **40**, 2139.
4 S. Ebdrup, M. S. Jensen and P. Veds, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 351.
5 P. Gros, Y. Fort and P. Caubére, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 1685.
6 S. S. Mandal, S. S. Samanta, C. Deb and A. De, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 2559.
7 D. A. Taylor and J. A. Joule, *J. Chem. Soc.*, *Chem. Commun.*, 1979, 642; M. Watanabe and V. Snieckus, *J. Am. Chem. Soc.*, 1980, **102**, 1457; R. Radinov, M. Haimova and E. Simova, *Synthesis*, 1986, 886.

8 A. Godard, Y. Robin and G. Quéguiner, *J. Organomet. Chem.*, 1987, **336**, 1.
9 J. M. Jacquelin, Y. Robin, A. Godard and G. Quéguiner *Can. J. Chem.*, 1988, **66**, 1135.
10 F. Marsais and G. Quéguiner, *Tetrahedron*, 1983, **39**, 2009.
11 J. M. Jacquelin, F. Marsais, A. Godard and G. Quéguiner *Synth. Commun.*, 1986, 670.
12 F. Marsais, E. Bouley and G. Quéguiner, *J. Organomet. Chem.*, 1979, **171**, 273.
13 Y. Robin, A. Godard and G. Quéguiner *J. Heterocycl. Chem.*, 1987, **24**, 1487.
14 A. Turck, N. Plé and G. Quéguiner *Heterocycles*, 1994, **37**, 2149; N. Plé, A. Turck, A. Heynderickx and G. Quéguiner *J. Heterocycl. Chem.*, 1994, **31**, 1311.
15 H. Gilman and J. W. Morton, *Org. React.*, 1954, **8**, 285.
16 D. W. Slocum and C. A. Jennings, *J. Org. Chem.*, 1976, **41**, 3553.
17 I. Forbes, R. A. Pratt and R. A. Raphael, *Tetrahedron Lett.*, 1978, 3965.
18 P. Beak and R. A. Brown, *J. Org. Chem.*, 1979, **44**, 4464.
19 P. Beak and D. B. Reitz, *J. Org. Chem.*, 1981, **48**, 4316.
20 K. Smith, G. A. El-Hiti and A. C. Hawes, *Synlett*, 1999, 945.
21 See for example; K. Smith, G. A. El-Hiti and A. Hamilton, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 4041; K. Smith, D. Anderson and I. Matthews, *J. Org. Chem.*, 1996, **61**, 662; K. Smith, G. A. El-Hiti, M. F. Abdel-Megeed and M. A. Abdo, *J. Org. Chem.*, 1996, **61**, 647; K. Smith, G. A. El-Hiti, M. F. Abdel-Megeed and M. A. Abdo, *J. Org. Chem.*, 1996, **61**, 656; K. Smith, G. A. El-Hiti, M. A. Abdo and M. F. Abdel-Megeed, *J. Chem. Soc.*, *Perkin Trans. 1*, 1995, 1029; K. Smith, A. P. Shukla and I. Matthews, *Sulfur Lett.*, 1996, **20**, 121; K. Smith, D. Anderson and I. Matthews, *Sulfur Lett.*, 1995, **18**, 79; K. Smith, C. M. Lindsay, I. K. Morris, I. Matthews and G. J. Pritchard, *Sulfur Lett.*, 1994, **17**, 197; K. Smith and G. J. Pritchard, *Angew. Chem.*, 1990, **102**, 298; *Angew. Chem.*, *Int. Ed. Engl.*, 1990, **29**, 282; K. Smith, C. M. Lindsay and G. J. Pritchard, *J. Am. Chem. Soc.*, 1989, **111**, 665; K. Smith, G. A. El-Hiti, M. F. Abdel-Megeed and M. A. Abdo, *Collect. Czech. Chem. Commun.*, 1999, **64**, 515.
22 K. Smith, G. A. El-Hiti and A. C. Hawes, unpublished results.
23 R. A. Franz, *J. Org. Chem.*, 1962, **27**, 4341; W. L. Nelson, *J. Org. Chem.*, 1975, **40**, 3658; D. G. Crosby and C. Niemann, *J. Am. Chem. Soc*., 1954, **76**, 4458; *Aust. J. Chem.*, 1975, **28**, 413; *J. Org. Chem.*, 1968, **33**, 3928, 3931.
24 W. Führer and H. W. Gschwend, *J. Org. Chem.*, 1979, **44**, 1133.
25 S. C. Watson and J. F. Eastham, *J. Organomet. Chem.*, 1967, **9**, 165.
26 *Vogel's Textbook of Practical Organic Chemistry*: 5th edn., Longman, Harlow, 1989.
27 D. D. Perrin and W. L. F. Armarego, *Purification of Laboratory Chemicals*, Pergamon, 3rd edn., Butterworth Heinemann, Oxford, 1988.

*Paper 9/03464A*