Convenient syntheses of 2,3,4,5-tetrahydro-1,4-benzothiazepines, -1,4-benzoxazepines and -1,4-benzodiazepines

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4-Benzotriazolylmethyl-2,3,4,5-tetrahydro-1,4-benzothiazepines **5a**,**b**, -1,4-benzoxazepine (**12**) and -1,4-benzodiazepine (**20**) are obtained *via* aluminium chloride mediated intramolecular cyclizations of *N*,*N*-bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2-(arylthio)ethan-1-amines **4a**,**b**, -2-(phenoxy)ethan-1-amine (**11**) and -*N*-[2-(*N′*-methylanilino)ethyl]amine (**19**), respectively. Subsequent nucleophilic substitutions of the benzotriazolyl group in **5a**,**b**, **12** and **20** succeeded with Grignard reagents, triethyl phosphite, sodium borohydride, and a silyl enol ether to give novel 2,3,4,5-tetrahydro-1,4-benzothiazepines **6**–**9**, -1,4-benzoxazepines **13** and **14**, and -1,4-benzodiazepines **21**–**23** in good yields.

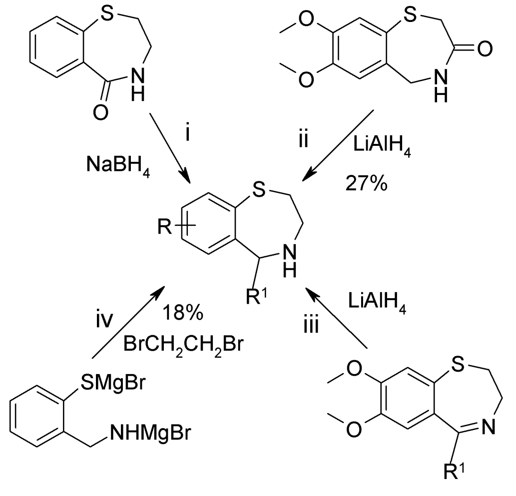
Introduction

1,4-Benzothiazepine derivatives are of considerable interest because of their biological activity as inhibitors of HIV-1 integrase, antitumor antibiotics, enzyme inhibitors, muscle relaxants and anticonvulsants, sedatives and hypnotics.[1] 1,4-Benzoxazepines are also of pharmacological interest due to their activity on the central nervous system, as enzyme inhibitors, or as analgesics and antitussives.[1c,2] 1,4-Benzodiazepines are important building blocks in various biologically active compounds, which show hypolipidermic, central nervous system, anti-cancer, and anxiolytic activity.[3] They are also effective against Meniere's disease.[4] One recent paper has shown imidazole-containing tetrahydrobenzodiazepines to be effective as inhibitors of farnesyltransferase.[5]

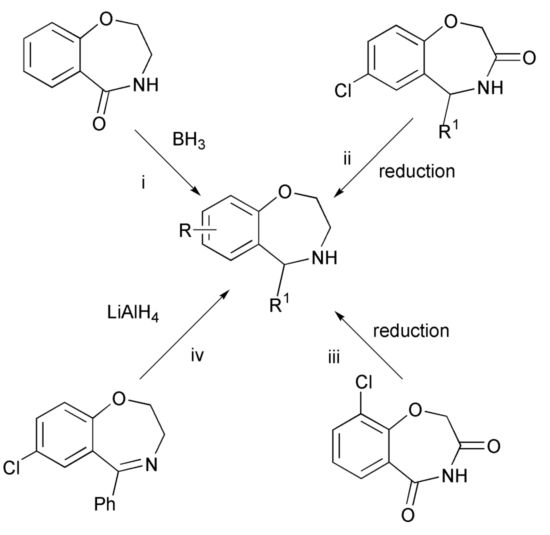
Many synthetic procedures exist for the preparation of 2-oxo-, 3-oxo-, 5-oxo- and 3,5-dioxo-1,4-benzothiazepines[6] and for dihydro-1,4-benzothiazepines.[7] However, relatively few publications relate to the preparation of 2,3,4,5-tetrahydro-1,4-benzothiazepines containing no carbonyl groups, and most of these involve reduction of a carbonyl group containing precursor such as (i) 5-oxo-1,4-benzothiazepine;[1c,8a] (ii) 3-oxo-1,4-benzothiazepine;[6b] and (iii) 2,3-dihydro-7,8-dimethoxy-1,4-benzothiazepines[1d,7d] (Scheme 1). We know of only one article describing a direct ring synthesis of a tetrahydro-1,4-benzothiazepine in 18% yield by condensing 2-$BrMgSC_6H_4CH_2$-NHMgBr with $BrCH_2CH_2Br$ (Scheme 1, iv).[8b]

Similarly, most syntheses of 2,3,4,5-tetrahydro-1,4-benzoxazepines involve reduction of the carbonyl group(s) as in (i) 5-oxo-2,3,4,5-tetrahydro-1,4-benzoxazepine;[1c] (ii) 3-oxo-2,3,4,5-tetrahydro-1,4-benzoxazepines;[9a,b] and (iii) 3,5-dioxo-2,3,4,5-tetrahydro-1,4-benzoxazepine;[9c,d] or a double bond as in (iv) 2,3-dihydro-1,4-benzothiazepine.[2a] (Scheme 2).

Syntheses of 1,4-benzodiazepines have been much studied.[10] Most previous preparations of *N*-substituted-2,3,4,5-tetrahydro-1,4-benzodiazepines involved *N*-substitution of a preexisting 2,3,4,5-tetrahydro-1,4-benzodiazepine. For example, 4-acyl-2,3,4,5-tetrahydro-1,4-benzodiazepines were readily prepared by the selective acylation of 2,3,4,5-tetrahydro-1,4-benzodiazepines with esters, acid chlorides, carboxylic acids or sulfonyl chlorides. Reactions of 4-acyl-2,3,4,5-tetrahydro-1,4-benzodiazepines with 5-formylimidazole and $NaBH(OAc)_3$ gave 1-alkyl-4-acyl-2,3,4,5-tetrahydro-1,4-benzodiazepines. 1-Acyl-4-alkyl-2,3,4,5-tetrahydro-1,4-benzodiazepines were also produced *via* selective Boc protection at the 4-position, followed by acylation, deprotection and alkylation.[5] 1-Benzyl-4-methyl-2,3,4,5-tetrahydro-1,4-benzodiazepine was previously



Scheme 1



Scheme 2

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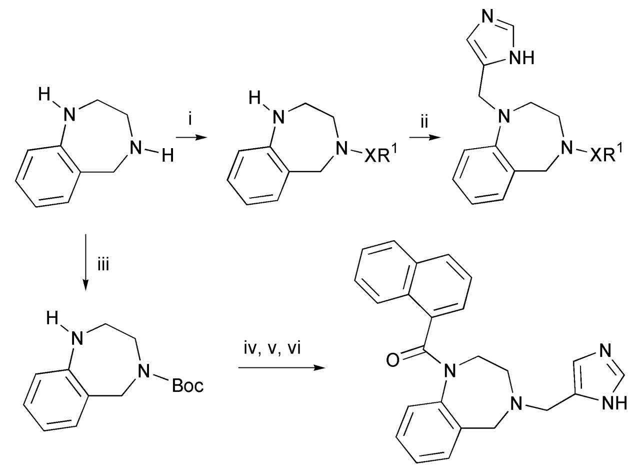


Scheme 3 i) R^1CO_2Et, R^1COCl, R^1CO_2H or R^1SO_2Cl (X = CO or SO_2); ii) 5-formylimidazole, $NaBH(OAc)_3$; iii) (t-$BuOCO)_2O$; iv) 1-naphthoyl chloride; v) TFA; vi) same as ii).

obtained by the reduction of the corresponding benzoyl-derivative with $LiAlH_4$[11] (see Scheme 3).

We now report a direct, high-yielding, convenient approach to 2,3,4,5-tetrahydro-1,4-benzothiazepines, -1,4-benzoxazepines and -1,4-benzodiazepines not involving reduction of a corresponding carbonyl or unsaturated derivative. 2,3,4,5-Tetrahydro-1,4-benzothiazepines **6**–**9**, -1,4-benzoxazepines **13** and **14** and -1,4-benzodiazepines **21**–**23** were obtained in good yields *via* the nucleophilic substitutions of 4-benzotriazolylmethyl-2,3,4,5-tetrahydro-1,4-benzothiazepines **5a**,**b**, -1,4-benzoxazepine **12** and -1,4-benzodiazepine **20**. Intermediates **5a**,**b**, **12** and **20** are produced from the intramolecular cyclizations of *N*,*N*-bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2-(arylthio)ethan-1-amines **4a**,**b**, -2-(phenoxy)ethan-1-amine **11** and -*N*-[2-(*N′*-methylanilino)ethyl]amine **19**, respectively.

Results and discussion

The Mannich condensation of 2-(arylsulfanyl)ethylamine **1a**,**b**,[12] benzotriazole (**2**) and formaldehyde (**3**) gave *N*,*N*-bis-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2-(arylthio)ethan-1-amines **4a**,**b** in 85% and 81% yields, respectively. When a mixture of methanol–water was used as the solvent, compounds **4a**,**b** were separated out, essentially pure (determined by NMR and microanalysis) after washing, and were used directly for the subsequent reactions.

When compounds **4a**,**b** were treated with 3 equiv. of $AlCl_3$ in CH_2Cl_2, one of the benzotriazole moieties was removed to form the cyclization products 4-benzotriazolylmethyl-2,3,4,5-tetrahydro-1,4-benzothiazepines **5a**,**b** in 86% and 91% yields, respectively (Scheme 1). Although starting materials **4a**,**b** were Bt^1 (benzotriazol-1-yl) isomers only, compounds **5a**,**b** were each obtained as a mixture of Bt^1 and Bt^2 (benzotriazol-2-yl) isomers in which the Bt^1 isomer predominated. This indicated that there was an equilibrium between the cyclization products **5a**,**b** and **X** (Scheme 4). We report the ^1H and ^{13}C NMR data of the major Bt^1 isomers and the ratio of Bt^1 and Bt^2 isomers determined by ^1H NMR spectroscopy (see Experimental section). According to our previous work,[13] Bt^1 and Bt^2 are both good leaving groups, and removal of benzotriazolyl groups from Bt^1 and Bt^2 isomers in the presence of a Lewis acid results in the same iminium cation **X**. Therefore, compounds **5a**,**b** were each used as mixtures of two isomers for the subsequent reactions. Compounds **4a**,**b** and **5a**,**b** were characterized by their ^1H and ^{13}C NMR spectra and microanalysis. The aliphatic region of the ^1H NMR spectra of **4a**,**b** showed one singlet ascribed to two $BtCH_2N$ (at 5.65 ppm). In the spectra of **5a**,**b**, two singlets were observed (at *ca.* 5.40 ppm and 4.20 ppm) which were ascribed to $BtCH_2N$ and $ArCH_2N$ fragments, respectively. The correct numbers of quaternary carbons for **5a**,**b**, determined by Attached Proton Test (APT) spectra, further support their structures.

The benzotriazole moieties in 4-benzotriazolylmethyl-2,3,4,5-tetrahydro-1,4-benzothiazepines **5a**,**b** were easily substituted by nucleophiles because of the equilibrium between **X** and **5a**,**b**. Indeed, Grignard reagents replaced the Bt moiety smoothly at room temperature. Treatment of **5a**,**b** with various Grignard reagents in THF gave 2,3,4,5-tetrahydro-1,4-benzothiazepines **6a**–**f** in 84–97% yields. With the help of 2 equiv. of $ZnBr_2$ to coordinate the benzotriazole anion in **X**, the iminium cations were trapped by $P(OEt)_3$ to give the derivatives **7a** and **7b** in 78% and 77% yield, respectively. Using $BF_3{\cdot}Et_2O$ instead of $ZnBr_2$ as the Lewis acid, an analogous reaction of **5a** with 1-phenyl-1-(trimethylsilyloxy)ethylene resulted in 3-[2,3,4,5-tetrahydro-1,4-benzothiazepin-4-yl]-1-phenylpropan-1-one **8** in 48% yield.

We also successfully reduced the Bt moiety with $NaBH_4$. Treatment of **5a** with sodium borohydride in dry THF furnished the 4-methyl-2,3,4,5-tetrahydro-1,4-benzothiazepine–borane complex (**9**) (Scheme 4). The NMR of **9** showed restricted rotation as compared to other compounds such as **6** and **8**. All peaks in the aliphatic region of the ^1H NMR spectrum were low and broad. All of them became sharper when the ^1H NMR spectrum was recorded at 60 °C rather than at 25 °C. The singlet (at 2.45 ppm) ascribed to the NCH_3 group became sharp and distinct. The signal of NCH_2Ar, which was a broad singlet at 25 °C, appeared as a distinct doublet (at 4.56 ppm). In the aliphatic region of the ^{13}C NMR spectrum, the peaks which were low and broad at 25 °C, were well shaped at 60 °C except for the peak at 46.3 ppm.

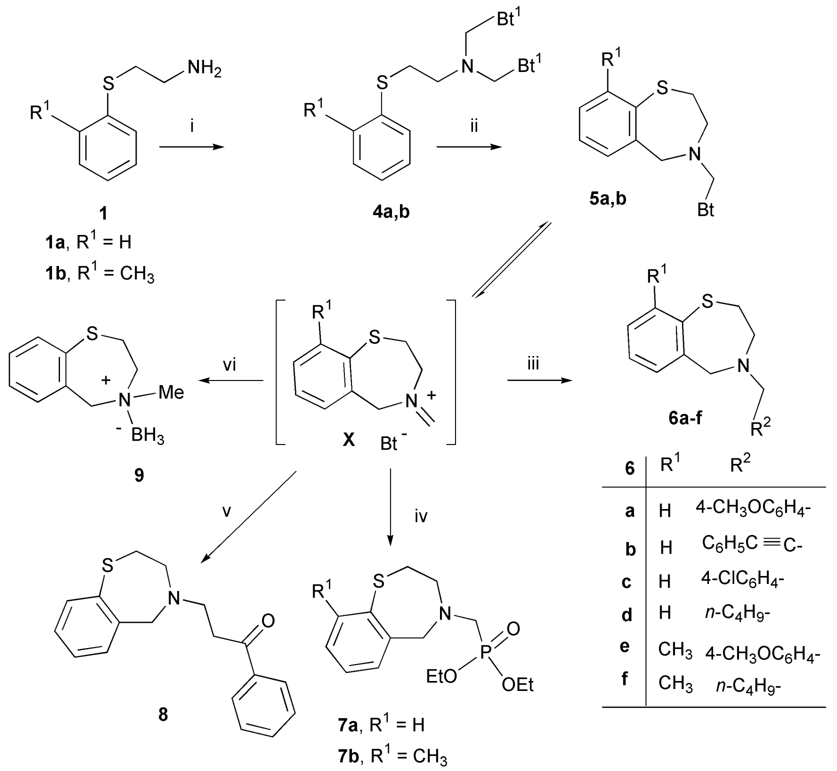
We successfully extended this methodology to synthesize 2,3,4,5-tetrahydro-1,4-benzoxazepines. *N*,*N*-Bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2-(phenoxy)ethan-1-amine **11** and 4-benzotriazolylmethyl-2,3,4,5-tetrahydro-1,4-benzoxazepine **12** were obtained in 78% and 86% yields, respectively, from 2-phenoxyethylamine **10** using a procedure similar to that discussed for the syntheses of **4** and **5** (Scheme 5). Pure **11** was also obtained after a similar work-up procedure. Compound **12** was a mixture of Bt^1 and Bt^2 isomers in which the Bt^1 isomer predominated. We provide the ^1H and ^{13}C NMR data of the Bt^1 isomer and the ratio of the two isomers. The cyclized product **12** is well supported by NMR spectra and microanalysis.

When 4-benzotriazolylmethyl-2,3,4,5-tetrahydro-1,4-benzoxazepine (**12**) was used as the starting material, 2,3,4,5-tetrahydro-1,4-benzoxazepine derivatives **13a**,**b** and diethyl 2,3,4,5-tetrahydro-1,4-benzoxazepin-4-ylmethylphosphonate (**14**) were obtained *via* procedures similar to those described for the syntheses of compounds **6** and **7**, respectively.

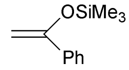
This methodology also works very well in the preparation of 2,3,4,5-tetrahydro-1,4-benzodiazepine. *N*-Methyl-*N*-phenyl-1,2-ethanediamine **18** was prepared in 90% yield from *N*-methylaniline **15** as reported *via* reaction of *N*-methylbenzenaminium chloride (**16**) with oxazolidin-2-one (**17**).[14]

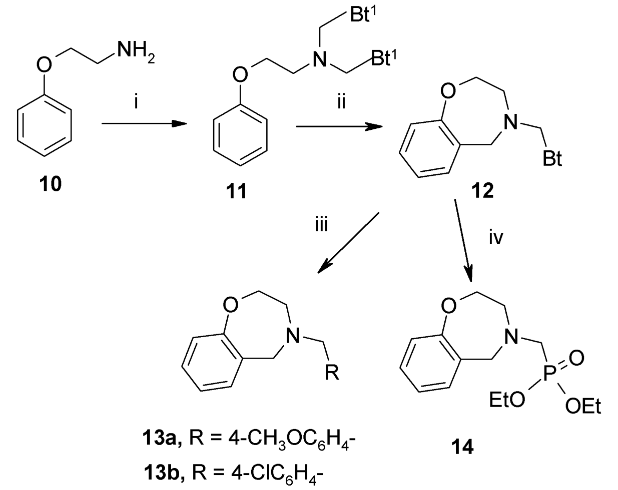
Reaction of diamine **18** with 2 equiv. of benzotriazole and 2 equiv. of formaldehyde produced *N*,*N*-bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-*N*-[2-(*N′*-methylanilino)ethyl]amine **19** in 92% yield as a sole Bt^1 isomer. Treatment of **19** with 3 equiv. of $AlCl_3$ removed only one benzotriazolyl moiety to form 4-benzotriazolylmethyl-1-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine **20** *via* the intramolecular Friedel–Crafts reaction similar to its oxygen and sulfur analogs. Compound **20** was obtained as a mixture of Bt^1 and Bt^2 isomers in a 4.4 : 1 ratio and was used directly for the subsequent reactions.

Nucleophilic substitutions of **20** with 1.5 equiv. of a Grignard reagent (p-ClC_6H_4MgBr, $CH_2{=}CHMgBr$, or $PhCH_2MgCl$) in THF gave 1-methyl-4-substituted-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepines **21a**–**c** in 68–76% yields. Compounds **21a**–**c** were fully characterized by ^1H and ^{13}C NMR spectra and

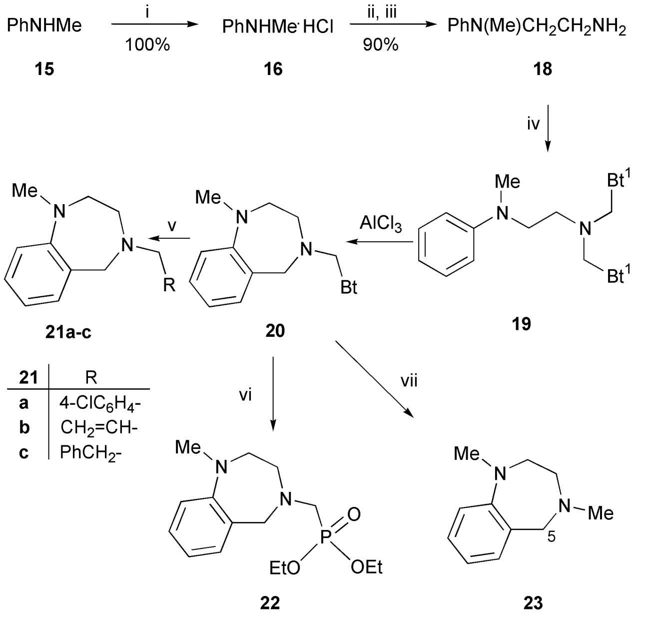


6	R^1	R^2
a	H	4-$CH_3OC_6H_4$-
b	H	$C_6H_5C{\equiv}C$-
c	H	4-ClC_6H_4-
d	H	n-C_4H_9-
e	CH_3	4-$CH_3OC_6H_4$-
f	CH_3	n-C_4H_9-

Scheme 4 i) Benzotriazole (BtH), HCHO; ii) $AlCl_3$; iii) Grignard reagents; iv) $P(OEt)_3$, $ZnBr_2$; v) $BF_3{\cdot}Et_2O$,  ; vi) $NaBH_4$.



Scheme 5 i) BtH, HCHO; ii) $AlCl_3$; iii) RMgBr; iv) $P(OEt)_3$, $ZnBr_2$.



21	R
a	4-ClC_6H_4-
b	CH_2=CH-
c	$PhCH_2$-

Scheme 6 i) HCl–EtOAc (1 M); ii) oxazolidin-2-one (**17**), neat; iii) 1 M NaOH; iv) BtH, HCHO; v) Grignard reagents; vi) $P(OEt)_3$, $ZnBr_2$; vii) $NaBH_4$.

microanalysis or HRMS results. Treatment of **20** with 1.2 equiv. of triethyl phosphite in the presence of $ZnBr_2$ furnished diethyl (1-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepin-4-ylmethyl)phosphonate (**22**) in 69% yield (Scheme 6).

Reaction of **20** with 2 equiv. of $NaBH_4$ at room temperature replaced the benzotriazolyl group with hydrogen to afford 1,4-dimethyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (**23**) in 73% yield. The methylene protons, the 5-position, in **23** appear at 4.31 and 3.79 ppm in ^{1}NMR spectra as an AB system with 13.6 Hz coupling constants.

Conclusion

In summary, we have developed efficient and convenient methods for the syntheses of diverse 4-substituted 2,3,4,5-tetrahydro-1,4-benzothiazepines, -1,4-benzoxazepines and -1,4-benzodiazepines. Intramolecular cyclizations of *N*,*N*-bis-(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2-(arylthio)ethan-1-amines, -2-(phenoxy)ethan-1-amine and -*N*-[2-(*N′*-methylanilino)-ethyl]amine are followed by nucleophilic substitutions of the remaining benzotriazolyl groups in the cyclized products with Grignard reagents, triethyl phosphite, sodium borohydride, and a silyl enol ether.

The methodology discussed in this paper allows the substituents at the 4-position of 1,4-benzothiazepines, 1,4-benzoxazepines and 1,4-benzodiazepines to be varied easily. The nature and orientation of substitutents at the other positions are derived from the starting materials.

Experimental

THF was distilled from sodium–benzophenone prior to use. All mps were determined using a Bristoline hot-stage microscope and are uncorrected. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a 300 NMR spectrometer in $CDCl_3$ (with TMS for ^{1}H and $CDCl_3$ for ^{13}C as the internal reference); J values are given in Hz. All of the reactions were carried out under N_2. Column chromatography was performed on silica gel (230–400 mesh).

N,*N*-Bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2-(phenylthio)ethan-1-amine 4a

2-(Phenylsulfanyl)ethylamine (**1**, 1.53 g, 10 mmol) and benzotriazole (**2**, 2.39 g, 20 mmol) were dissolved in methanol–water (40 : 10 mL). Formaldehyde (**3**, 1.62 g, 20 mmol, 37% aqueous solution) was then slowly added to the solution. The reaction mixture was stirred for 12 h at room temperature. The precipitate was filtered off, washed with cold Et_2O, and dried to give the product as a white powder (3.74 g, 90%); mp 89–90 °C (colorless plates from CH_2Cl_2–Et_2O) (Found: C, 63.56; H, 5.08; N, 23.79. $C_{22}H_{21}N_7S$ requires C, 63.59; H, 5.09; N, 23.60%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.09 (2H, d, J 8.2), 7.64 (2H, d, J 8.5), 7.52 (2H, t, J 8.0), 7.41 (2H, t, J 8.0), 7.27–7.21 (5H, m), 5.64 (4H, s, 2 BtCH_2N), 3.19 (2H, t, J 6.7), 3.08 (2H, t, J 6.7); δ_C (75 MHz, $CDCl_3$) 146.0, 134.9, 133.0, 129.4, 129.1, 128.0, 126.4, 124.3, 120.0, 109.8, 64.4, 50.1, 32.1.

N,*N*-Bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2-[(2-methylphenyl)thio]ethan-1-amine 4b

Following the same procedure as **4a** using 2-[(2-methylphenyl)thio]ethylamine as starting material, the title compound (3.78 g, 88%) was obtained as colorless plates; mp 124–125 °C (from CH_2Cl_2–Et_2O) (Found: C, 64.32; H, 5.65; N, 23.16. $C_{23}H_{23}N_7S$ requires C, 64.31; H, 5.40; N, 22.83%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.09 (2H, d, J 8.2), 7.66 (2H, d, J 8.2), 7.51 (2H, t, J 7.3), 7.41 (2H, t, J 7.6), 7.14–7.07 (4H, m), 5.65 (4H, s, 2 BtCH_2N), 3.21 (2H, t, J 6.7), 3.06 (2H, t, J 7.0), 2.26 (3H, s); δ_C (75 MHz, $CDCl_3$) 146.1, 137.8, 134.3, 133.1, 130.3, 128.2, 128.0, 126.5, 126.1, 124.2, 120.0, 109.8, 64.4, 50.1, 31.3, 20.3.

4-Benzotriazolylmethyl-2,3,4,5-tetrahydro-1,4-benzothiazepine 5a

A mixture of **4a** (3.35 g, 8 mmol) and $AlCl_3$ (3.2 g, 24 mmol) in dry CH_2Cl_2 (60 mL) was stirred at 25 °C for 12 h. Then 2 M NaOH solution (40 mL) was added to quench the reaction. The aqueous phase was extracted with CH_2Cl_2. The combined organic layer was washed with 1 M NaOH, brine, and dried over anhydrous Na_2SO_4. Removal of the solvent *in vacuo* gave the crude product, which was purified by column chromatography (eluent: EtOAc : hexanes = 1 : 4–1 : 2) to give a mixture of Bt^1 and Bt^2 isomers in a 5.2 : 1 ratio (1.92 g, 81%); mp 117–118 °C (from EtOAc–hexanes) (Found: C, 64.72; H, 5.50; N, 19.07. $C_{16}H_{16}N_4S$ requires C, 64.84; H, 5.44; N, 18.90%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.08 (1H, d, J 8.2), 7.64 (1H, d, J 8.2), 7.56 (1H, d, J 6.7), 7.50 (1H, t, J 7.0), 7.40 (1H, d, J 7.9), 7.26–7.15 (3H, m), 5.40 (2H, s, BtCH_2N), 4.20 (2H, s, PhCH_2N), 3.42–3.39 (2H, m), 2.86–2.84 (2H, m); δ_C (75 MHz, $CDCl_3$) 146.2, 142.2, 136.7, 132.9, 132.7, 132.5, 130.7, 127.8, 127.4, 124.0, 120.0, 110.2, 66.9, 57.9, 56.5, 32.1.

4-Benzotriazolylmethyl-9-methyl-2,3,4,5-tetrahydro-1,4-benzothiazepine 5b

Following the same procedure as for **5a** using **4b** as the starting material, compound **5b** (2.03 g, 82%) was obtained as a mixture of Bt^1 and Bt^2 isomers in a 6.1 : 1 ratio; mp 86–87 °C (colorless prisms from EtOAc–hexanes) (Found: C, 65.70; H, 5.99. $C_{17}H_{18}N_4S$ requires C, 65.78; H, 5.84%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.09 (1H, d, J 8.2), 7.65 (1H, d, J 8.2), 7.50 (1H, t, J 7.0), 7.39 (1H, t, J 7.3), 7.13 (3H, br s), 5.42 (2H, s, BtCH_2N), 4.23 (2H, s, ArCH_2N), 3.36–3.34 (2H, m), 2.84–2.81 (2H, m), 2.47 (3H, s); δ_C (75 MHz, $CDCl_3$) 146.2, 142.5, 140.2, 136.7, 133.0, 129.5, 128.5, 127.4, 127.1, 124.0, 119.1, 110.3, 67.3, 58.4, 55.9, 32.1, 21.9.

4-(4-Methoxybenzyl)-2,3,4,5-tetrahydro-1,4-benzothiazepine 6a

To a solution of **5a** (0.30 g, 1 mmol) in anhydrous THF (15 mL) at 0 °C, 4-methoxyphenylmagnesium bromide (3 ml, 1.5 mmol, 0.5 M in THF) was added dropwise. The solution was stirred for 2 h at 0 °C, and for 10 h at room temperature. Then the solvent was evaporated. The residue was dissolved in Et_2O, washed with 20% NH_4Cl, 2 M NaOH and brine. The organic solution was dried over anhydrous Na_2SO_4. After removal of the solvent *in vacuo*, the residue was purified by column chromatography (eluent: EtOAc : hexanes : Et_3N = 1 : 7 : 0.05) and recrystallized from Et_2O to give the product as colorless prisms (0.25 g, 88%); mp 85–86 °C (Found: C, 71.59; H, 6.98; N, 4.89. $C_{17}H_{19}NOS$ requires C, 71.54; H, 6.71; N, 4.91%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.55 (1H, t, J 4.7), 7.22–7.15 (4H, m), 7.02 (1H, t, J 5.0), 6.86 (2H, d, J 8.2), 4.11 (2H, s, PhCH_2N), 3.81 (3H, s, CH_3O), 3.49 (2H, s, 4-CH$_3$OPhCH_2N), 3.33–3.30 (2H, m), 2.81–2.78 (2H, m); δ_C (75 MHz, $CDCl_3$) 158.6, 143.2, 137.1, 132.2, 130.9, 130.7, 129.9, 127.2(2), 113.6, 59.2, 57.7, 56.0, 55.2, 30.3.

4-(3-Phenylprop-2-yn-1-yl)-2,3,4,5-tetrahydro-1,4-benzothiazepine 6b

Following the same procedure as **6a** using (phenylethynyl)magnesium bromide (1.5 ml, 1.0 M in THF) as Grignard reagent, compound **6b** (0.25 g, 90%) was obtained as a yellow oil; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.54 (1H, dd, J 7.3, 1.5), 7.46–7.43 (2H, m), 7.35–7.30 (4H, m), 7.25–7.17 (2H, m), 4.24 (2H, s, PhCH_2N), 3.53 (2H, s, CCH_2N), 3.44–3.41 (2H, m), 2.87–2.83 (2H, m); δ_C (75 MHz, $CDCl_3$) 142.4, 137.0, 132.3, 131.6(2), 130.8, 128.2(2), 128.1, 127.5, 127.4, 122.9, 85.2, 84.9, 59.5, 57.9, 44.5, 31.2. HRMS calcd for $C_{18}H_{18}NS$ (M + 1): 280.1160. Found: 280.1148.

4-(4-Chlorobenzyl)-2,3,4,5-tetrahydro-1,4-benzothiazepine 6c

Following the same procedure as **6a** using 4-chlorophenylmagnesium bromide (1.5 ml, 1.0 M in ether) as Grignard reagent, compound **6c** (0.27 g, 93%) was purified by recrystallization; mp 83–84 °C (colorless prisms from CH_2Cl_2) (Found: C, 66.28; H, 5.64; N, 4.61. $C_{16}H_{16}ClNS$ requires C, 66.31; H, 5.56; N, 4.83%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.57–7.54 (1H, m), 7.30–7.21 (4H, m), 7.17–7.14 (2H, m), 6.97–6.94 (1H, m), 4.09 (2H, s, PhCH_2N), 3.50 (2H, s, 4-ClPhCH_2N), 3.33–3.30 (2H, m), 2.79–2.76 (2H, m); δ_C (75 MHz, $CDCl_3$) 142.9, 137.3, 137.1, 132.6, 132.3, 130.8, 130.0, 128.4, 127.3, 127.2, 59.0, 58.0, 55.8, 30.3.

4-Pentyl-2,3,4,5-tetrahydro-1,4-benzothiazepine 6d

Following the same procedure as **6a** using butylmagnesium bromide (0.75 ml, 2.0 M in ether) as Grignard reagent, compound **6d** (0.21 g, 89%) was obtained as a yellowish oil (Found: C, 71.34; H, 8.71; N, 6.32. $C_{14}H_{21}NS$ requires C, 71.44; H, 8.99; N, 5.95%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.53 (1H, d, J 7.0), 7.23–7.11 (3H, m), 4.13 (2H, s, PhCH_2N), 3.33–3.30 (2H, m), 2.76–2.73 (2H, m), 2.35 (2H, t, J 7.4), 1.54–1.45 (2H, m), 1.34–1.22 (4H, m), 0.88 (3H, t, J 6.7); δ_C (75 MHz, $CDCl_3$) 143.1, 136.9, 132.2, 130.6, 127.2, 127.1, 59.4, 58.1, 52.2, 30.0, 29.5, 27.0, 22.5, 14.0.

4-(4-Methoxybenzyl)-9-methyl-2,3,4,5-tetrahydro-1,4-benzothiazepine 6e

Following a similar procedure as for **6a** using **5b** instead of **5a**, compound **6e** (0.26 g, 87%) was purified by recrystallization; mp 71–72 °C (colorless prisms from Et_2O) (Found: C, 71.99; H, 7.41; N, 4.66. $C_{18}H_{21}NOS$ requires C, 72.20; H, 7.07; N, 4.68%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.21 (2H, d, J 8.5), 7.10–7.02 (2H, m), 6.87–6.83 (3H, m), 4.11 (2H, s, $\mathrm{PhC}H_2\mathrm{N}$), 3.81 (3H, s), 3.51 (2H, s, 4-$\mathrm{CH_3OPhC}H_2\mathrm{N}$), 3.27–3.24 (2H, m), 2.79–2.76 (2H, m), 2.47 (3H, s); δ_C (75 MHz, $CDCl_3$) 158.5, 143.2, 139.4, 137.1, 130.8, 129.8, 128.8, 128.7, 126.4, 113.5, 59.5, 57.1, 56.4, 55.1, 30.4, 21.9.

9-Methyl-4-pentyl-2,3,4,5-tetrahydro-1,4-benzothiazepine 6f

Following a similar procedure as for **6e** using butylmagnesium bromide (0.75 ml, 2.0 M in ether) as Grignard reagent, compound **6f** (0.22 g, 88%) was obtained as a yellowish oil (Found: C, 72.44; H, 9.67; N, 5.86. $C_{15}H_{23}NS$ requires C, 72.23; H, 9.29; N, 5.62%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.26 (3H, br s), 4.12 (2H, s, $\mathrm{ArC}H_2\mathrm{N}$), 3.29–3.26 (2H, m), 2.75–2.73 (2H, m), 2.46 (3H, s), 2.37 (2H, t, *J* 7.4), 1.56–1.46 (2H, m), 1.36–1.22 (4H, m), 0.89 (3H, t, *J* 7.1); δ_C (75 MHz, $CDCl_3$) 143.3, 139.6, 137.0, 128.9, 128.6, 126.6, 59.8, 57.7, 52.9, 30.3, 29.6, 27.2, 22.6, 22.0, 14.1.

Diethyl 2,3,4,5-tetrahydro-1,4-benzothiazepin-4-ylmethylphosphonate 7a

To a solution of **5a** (0.30 g, 1.0 mmol) in dry THF (15 mL) at 0 °C, $ZnBr_2$ (0.45 g, 2 mmol) was added. The solution was stirred for 20 min before triethyl phosphite (0.2 g, 1.2 mmol) was added dropwise. After stirring at room temperature for 10 h, the solvent was evaporated. The residue was dissolved in EtOAc, and the solution was washed with 2 M NaOH and water. The organic layer was dried over Na_2SO_4. After removal of the solvent *in vacuo*, the residue was purified by column chromatography (eluent: EtOAc : hexanes = 1 : 3–2 : 1) to give **7a** (0.25 g, 79%) as a yellowish oil (Found: C, 53.01; H, 7.02; N, 4.82. $C_{14}H_{22}NO_3PS$ requires C, 53.32; H, 7.03; N, 4.44%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.56 (1H, dd, *J* 7.0, 1.5), 7.32 (1H, dd, *J* 7.0, 1.5), 7.24–7.15 (2H, m), 4.28 (2H, s, $\mathrm{PhC}H_2\mathrm{N}$), 4.15 (4H, q, *J* 7.4, 2$\mathrm{OC}H_2\mathrm{CH_3}$), 3.50–3.47 (2H, m), 2.75–2.72 (2H, m), 2.72 (2H, s, $\mathrm{PC}H_2\mathrm{N}$), 1.33 (6H, t, *J* 7.0); δ_C (75 MHz, $CDCl_3$) 142.3, 137.0, 132.5, 131.3, 127.4, 127.3, 62.0 (d, *J* 6.9), 60.5 (d, *J* 7.4), 59.4 (d, *J* 8.6), 46.9 (d, *J* 168.9), 29.8, 16.4 (d, *J* 5.7).

Diethyl [9-methyl-2,3,4,5-dihydro-1,4-benzothiazepin-4-ylmethyl]phosphonate 7b

Following a similar procedure as for **7a** using **5b** instead of **5a**, compound **7b** (0.25 g, 76%) was obtained as a yellowish oil; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.20–7.17 (1H, m), 7.15–7.10 (2H, m), 4.34 (2H, s, $\mathrm{ArC}H_2\mathrm{N}$), 4.16 (4H, q, *J* 7.3), 3.50–3.48 (2H, m), 2.83 (2H, d, *J* 10.8), 2.76–2.73 (2H, m), 2.46 (3H, s), 1.33 (6H, t, *J* 7.0); δ_C (75 MHz, $CDCl_3$) 141.4, 139.9, 136.9, 129.4 (2), 126.7, 62.0 (d, *J* 6.3), 60.6 (d, *J* 8.5), 58.5 (d, *J* 8.4), 47.0 (d, *J* 167.4), 29.6, 21.8, 16.4 (d, *J* 5.3). HRMS calcd for $C_{15}H_{25}NO_3SP$ (M + 1): 330.1293. Found: 330.1263.

3-[2,3-Dihydro-1,4-benzothiazepin-4-yl]-1-phenylpropan-1-one 8

$BF_3 \cdot Et_2O$ (0.43 g, 3 mmol) was added dropwise to a stirred solution of the compound **5a** (0.30 g, 1.0 mmol) in CH_2Cl_2 (15 mL) at 0 °C. The yellow mixture was stirred for 10 min before the addition of 1-phenyl-1-(trimethylsilyloxy)ethylene (0.29 g, 1.5 mmol). The mixture was stirred at 0 °C for 2 h and overnight at 25 °C. The reaction was quenched with water, and washed with 2 M NaOH and water. The organic layer was dried over $MgSO_4$. After removal of CH_2Cl_2 *in vacuo*, the residue was purified by column chromatography (eluent: EtOAc : hexanes = 1 : 8–1 : 5) to give the product **8** (0.13 g, 44%) as a yellowish oil; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.96 (2H, d, *J* 7.3), 7.57–7.53 (2H, m), 7.47 (2H, dd, *J* 7.8, 7.3), 7.27–7.25 (1H, m), 7.23–7.14 (2H, m), 4.19 (2H, s, $\mathrm{PhC}H_2\mathrm{N}$), 3.38–3.35 (2H, m), 3.18 (2H, t, *J* 7.1), 2.86 (2H, t, *J* 7.1), 2.81–2.76 (2H, m); δ_C (75 MHz, $CDCl_3$) 199.1, 142.9, 136.9, 136.8, 133.1, 132.4, 130.6, 128.6, 128.0, 127.5, 127.4, 59.5, 58.2, 47.0, 37.0, 30.1. HRMS calcd for $C_{18}H_{20}NOS$ (M + 1): 298.1266. Found: 298.1264.

4-Methyl-2,3,4,5-tetrahydro-1,4-benzothiazepine–borane complex 9

A mixture of **5a** (0.60 g, 2 mmol) and $NaBH_4$ (0.15 g, 4 mmol) was stirred at 25 °C for 12 h in dry THF (20 mL). After evaporation of the solvent *in vacuo*, the residue was dissolved in EtOAc. The organic phase was washed with 1 M NaOH, brine, and dried over anhydrous Na_2SO_4. After removal of the EtOAc *in vacuo*, the residue was purified by column chromatography (eluent: EtOAc : hexanes : Et_3N = 1 : 9 : 0.05) to afford **9** (0.13 g, 67%); mp 111–112 °C (colorless prisms from EtOAc–hexanes) (Found: C, 62.23; H, 8.68; N, 7.26. $C_{10}H_{16}NSB$ requires C, 62.19; H, 8.35; N, 7.25%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.52–7.48 (1H, m), 7.27–7.26 (3H, m), 4.56 (1H, d, *J* 13.8), 4.16 (1H, d, *J* 13.8), 3.42 (1H, dd, *J* 11.7, 11.4), 3.24–3.18 (1H, m), 3.14–3.09 (1H, m), 2.94 (1H, dd, *J* 13.2, 10.3), 2.45 (3H, s, $\mathrm{NC}H_3$), 2.40–1.21 (3H, br s, $\mathrm{B}H_3$); δ_C (75 MHz, $CDCl_3$) 137.5, 136.1 (br), 133.2, 132.7, 129.7, 128.3, 66.0, 63.7 (br), 48.0 (br), 28.4.

N,*N*-Bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-2-phenoxyethan-1-amine 11

Following the same procedure as for **4a** using 2-phenoxyethylamine **10** instead of **1**, the title compound (3.11 g, 78%) was obtained as a white solid; mp 94–95 °C (colorless prisms from MeOH) (Found: C, 66.27; H, 5.29; N, 24.77. $C_{22}H_{21}N_7O$ requires C, 66.15; H, 5.30; N, 24.54%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.09 (2H, d, *J* 8.2), 7.73 (2H, d, *J* 8.2), 7.48 (2H, t, *J* 7.1), 7.40 (2H, d, *J* 7.5), 7.27 (2H, t, *J* 8.2), 6.97 (1H, t, *J* 7.3), 6.82 (2H, d, *J* 7.9), 5.77 (4H, s, 2 $\mathrm{BtC}H_2\mathrm{N}$), 4.10 (2H, t, *J* 4.8), 3.83 (2H, t, *J* 4.8); δ_C (75 MHz, $CDCl_3$) 158.0, 146.1, 133.2, 129.6, 127.9, 124.2, 121.3, 119.9, 114.3, 110.1, 66.9, 64.8, 49.7.

4-Benzotriazolylmethyl-2,3,4,5-tetrahydro-1,4-benzoxazepine 12

Following the same procedure as **5a** using **11** instead of **4a**, compound **12** was obtained as a mixture of Bt^1 and Bt^2 isomers in a 5.6 : 1 ratio (1.48 g, 66%); mp 67–69 °C (colorless prisms from EtOAc–hexanes) (Found: C, 68.52; H, 5.80; N, 20.20. $C_{16}H_{16}N_4O$ requires C, 68.55; H, 5.75; N, 19.99%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.07 (1H, d, *J* 7.9), 7.65 (1H, d, *J* 7.9), 7.50 (1H, t, *J* 7.6), 7.39 (1H, t, *J* 7.6), 7.18 (2H, dd, *J* 7.6, 7.3), 7.09 (2H, dd, *J* 7.3, 6.4), 5.51 (2H, s, $\mathrm{BtC}H_2\mathrm{N}$), 4.10 (2H, t, *J* 4.1), 3.97 (2H, s, $\mathrm{PhC}H_2\mathrm{N}$), 3.20–3.18 (2H, m); δ_C (75 MHz, $CDCl_3$) 159.6, 145.9, 133.2, 130.6, 130.3, 128.9, 127.5, 124.0, 123.5, 120.8, 119.9, 110.1, 70.8, 68.1, 56.7, 55.9.

4-(4-Methoxybenzyl)-2,3,4,5-tetrahydro-1,4-benzoxazepine 13a

Following a similar procedure as **6a** using **12** instead of **5a** as starting material, compound **13a** (0.20 g, 74%) was purified by recrystallization; mp 80–82 °C (colorless needles from Et_2O) (Found: C, 75.63; H, 7.39; N, 5.16. $C_{17}H_{19}NO_2$ requires C, 75.81; H, 7.11; N, 5.20%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.24–7.16 (3H, m), 7.03–6.98 (3H, m), 6.87 (2H, d, *J* 8.5), 4.09–4.06 (2H, m), 3.81 (3H, s), 3.80 (2H, s, $\mathrm{PhC}H_2\mathrm{N}$), 3.58 (2H, s, 4-$\mathrm{CH_3OPhC}H_2\mathrm{N}$), 3.09–3.06 (2H, m); δ_C (75 MHz, $CDCl_3$) 160.0, 158.7, 131.9, 130.8, 130.6, 130.1, 128.5, 123.3, 120.7, 113.6, 70.2, 58.1, 58.0, 57.9, 55.2.

4-(4-Chlorobenzyl)-2,3,4,5-tetrahydro-1,4-benzoxazepine 13b

Following the same procedure as **13a** using 4-chlorophenylmagnesium bromide (1.5 ml, 1.0 M in ether) as Grignard reagent, compound **13b** (0.23 g, 84%) was obtained as a yellowish oil (Found: C, 70.19; H, 6.21; N, 5.45. $C_{16}H_{16}ClNO$ requires C, 70.20; H, 5.89; N, 5.12%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.31–7.23 (4H, m), 7.20 (1H, dd, *J* 8.1, 4.1), 7.03 (1H, d, *J* 7.9), 6.99 (2H, d, *J* 4.1), 4.07 (2H, dd, *J* 4.3, 4.1), 3.78 (2H, s), 3.60

(2H, s), 3.08 (2H, dd, *J* 4.3, 4.0); δ_C (75 MHz, $CDCl_3$) 160.0, 137.2, 132.8, 131.6, 130.6, 130.2, 128.6, 128.5, 123.4, 120.8, 70.1, 58.1, 58.0, 57.9.

Diethyl 2,3,4,5-tetrahydro-1,4-benzoxazepin-4-ylmethylphosphonate 14

Following a similar procedure as for **7a** using **12** instead of **5a** as starting material, compound **14** (0.21 g, 70%) was obtained as a yellowish sticky oil (Found: C, 55.77; H, 7.76; N, 4.83. $C_{14}H_{22}NO_4P$ requires C, 56.18; H, 7.41; N, 4.68%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.27–7.17 (2H, m), 7.04–7.00 (2H, m), 4.18 (4H, q, *J* 7.0), 4.04 (2H, s), 4.04 (2H, t, *J* 4.3), 3.29 (2H, t, *J* 4.3), 2.84 (2H, d, *J* 11.3), 1.33 (6H, t, *J* 7.0); δ_C (75 MHz, $CDCl_3$) 159.9, 131.1, 131.0, 128.8, 123.5, 120.9, 69.2, 62.1 (d, *J* 6.9), 59.5 (d, *J* 9.2), 59.2 (d, *J* 9.2), 48.6 (d, *J* 166.6), 16.5 (d, *J* 5.7).

N,*N*-Bis(1*H*-1,2,3-benzotriazol-1-ylmethyl)-*N*-[2-(*N*′-methylanilino)ethyl]amine 19

Following the same procedure as **4a** using **18** instead of **1**, the title compound (3.80 g, 92%) was purified by recrystallization; mp 132–133 °C (colorless prisms from EtOAC) (Found: C, 66.70; H, 6.05; N, 27.27. $C_{23}H_{24}N_8$ requires C, 66.97; H, 5.86; N, 27.16%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 8.09 (2H, d, *J* 8.0), 7.57–7.38 (6H, m), 7.16 (2H, t, *J* 6.8), 6.70 (1H, t, *J* 6.8), 6.54 (2H, d, *J* 6.7), 5.66 (4H, s, 2 $BtCH_2N$), 3.40–3.32 (2H, m), 3.16–3.08 (2H, m), 2.74 (3H, s); δ_C (75 MHz, $CDCl_3$) 148.5, 146.0, 133.0, 129.3, 127.9, 124.2, 120.0, 116.7, 112.2, 109.7, 65.0, 51.4, 47.7, 38.8.

4-Benzotriazolylmethyl-1-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine 20

Following the same procedure as for **5a** using **19** instead of **4a**, compound **20** (2.02 g, 86%) was obtained as a mixture of Bt^1 and Bt^2 isomers in a 4.4 : 1 ratio; mp 130–131 °C (colorless crystals from $CHCl_3$–Et_2O) (Found: C, 69.48; H, 6.62; N, 23.65. $C_{17}H_{19}N_5$ requires C, 69.60; H, 6.53; N, 23.87%); δ_H (300 MHz, $CDCl_3$, Me_4Si) Bt^1: 8.08 (1H, d, *J* 7.7), 7.67 (1H, d, *J* 7.8), 7.50 (1H, t, *J* 7.3), 7.38 (1H, t, *J* 7.3), 7.24–7.15 (2H, m), 6.91 (2H, d, *J* 7.7), 5.50 (2H, s), 3.93 (2H, s), 3.03 (4H, s), 2.88 (3H, s); Bt^2: 7.96–7.85 (2H, m), 7.43–7.33 (2H, m), 7.24–7.15 (2H, m), 6.91 (2H, d, *J* 7.7), 5.67 (2H, s), 3.98 (2H, s), 3.03 (4H, s), 2.88 (3H, s); δ_C (75 MHz, $CDCl_3$) Bt^1: 152.3, 146.0, 133.3, 130.6, 129.6, 128.2, 127.3, 123.8, 120.8, 119.8, 115.7, 110.3, 68.0, 57.8, 55.0, 54.2, 42.7.

4-(4-Chlorobenzyl)-1-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine 21a

Following a similar procedure as for **6a** using **20** instead of **5a** as starting material, and 4-chlorophenylmagnesium bromide (1.5 mL, 1.0 M in ether) as Grignard reagent, compound **21a** (0.21 g, 72%) was obtained as a colorless oil (Found: C, 70.80; H, 6.77; N, 9.87. $C_{17}H_{19}ClN_2$ requires C, 71.19; H, 6.68; N, 9.77%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.26 (4H, s), 7.26–7.18 (1H, m), 6.96–6.82 (3H, m), 3.74 (2H, s), 3.52 (2H, s), 2.98–2.90 (4H, m), 2.88 (3H, s); δ_C (75 MHz, $CDCl_3$) 152.5, 137.5, 132.5, 130.8, 130.3, 130.2, 128.3, 127.9, 120.6, 115.5, 58.8, 57.7, 56.3, 54.1, 42.9.

4-Allyl-1-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (21b)

Following a similar procedure as for **21a** using vinylmagnesium bromide (1.5 mL, 1.0 M in THF) as Grignard reagent, compound **21b** (0.14 g, 68%) was obtained as a colorless oil (Found: C, 76.87; H, 9.29; N, 14.03. $C_{13}H_{18}N_2$ requires C, 77.18; H, 8.97; N, 13.85%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.22–7.17 (1H, m), 7.10 (1H, d, *J* 7.1), 6.88–6.83 (2H, m), 5.97–5.83 (1H, m), 5.20–5.14 (2H, m), 3.76 (2H, s), 3.08 (2H, d, *J* 6.1), 2.98–2.89 (4H, m), 2.88 (3H, s); δ_C (75 MHz, $CDCl_3$) 152.4, 135.9, 130.8, 130.2, 127.8, 120.5, 117.6, 115.4, 58.9, 58.0, 56.3, 54.4, 42.8.

1-Methyl-4-phenylethyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (21c)

Following a similar procedure as for **21a** using benzylmagnesium chloride (1.5 mL, 1.0 M in ether) as Grignard reagent, compound **21c** (0.20 g, 76%) was obtained as a colorless oil (Found: N, 10.85. $C_{18}H_{22}N_2$ requires N, 10.52%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.25–7.14 (7H, m), 6.89 (2H, d, *J* 7.0), 3.88 (2H, s), 3.00–2.96 (4H, m), 2.88 (3H, s), 2.96–2.82 (2H, m), 2.69–2.62 (2H, m); δ_C (75 MHz, $CDCl_3$) 152.3, 140.3, 130.7, 130.1, 128.6, 128.3, 127.9, 125.9, 120.6, 115.5, 59.0, 56.5, 56.0, 53.9, 42.9, 34.2. HRMS calcd for $C_{18}H_{23}N_2$ (M + 1): 267.1861. Found: 267.1850.

Diethyl (1-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepin-4-ylmethyl)phosphonate 22

Following a similar procedure as for **7a** using **20** instead of **5a** as starting material, compound **22** (0.22 g, 69%) was obtained as a colorless oil (Found: C, 57.64; H, 8.28; N, 9.26. $C_{15}H_{25}N_2O_3P$ requires C, 57.68; H, 8.07; N, 8.97%); δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.23–7.15 (2H, m), 6.90 (2H, d, *J* 7.7), 4.20–4.10 (4H, m), 3.98 (2H, s), 3.14–3.11 (2H, m), 2.94–2.91 (2H, m), 2.88 (3H, s), 2.78 (2H, d, *J* 11.0), 1.33 (6H, t, *J* 7.0); δ_C (75 MHz, $CDCl_3$) 152.3, 131.1, 129.4, 127.9, 120.4, 115.5, 61.8 (d, *J* 6.9), 60.2 (d, *J* 9.2), 57.3 (d, *J* 8.6), 52.9, 48.1 (d, *J* 167.8), 42.8, 16.3 (d, *J* 5.7).

1,4-Dimethyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine 23

Following a similar procedure as for **9** using **20** instead of **5a** as starting material, compound **23** (0.26 g, 73%) was obtained as a colorless oil; δ_H (300 MHz, $CDCl_3$, Me_4Si) 7.31 (1H, td, *J* 7.8, 1.1), 7.12 (1H, d, *J* 6.7), 6.91 (2H, t, *J* 7.3), 4.31, 3.79 (2H, AB, *J* 13.6), 3.46 (1H, dd, *J* 13.7, 5.9), 3.30–3.22 (1H, m), 3.07–2.99 (1H, m), 2.91–2.85 (1H, m), 2.89 (3H, s), 2.48 (3H, s); δ_C (75 MHz, $CDCl_3$) 151.1, 132.1, 129.9, 123.8, 120.6, 115.7, 64.6, 61.2, 50.9, 47.3, 41.5. HRMS calcd for $C_{11}H_{16}N_2$: 176.1313. Found: 176.1305.

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