N-Thio- and *N*-selenophenacylamidines: electrophilic activation as a route to some 1-hetero-3-aza-4-dimethylaminobuta-1,3-dienes

Gabriel T. Manh,[a] Franck Purseigle,[a] Didier Dubreuil,[a] Jean Paul Pradère,*[a] André Guingant,[a] Renée Danion-Bougot,[b] Daniel Danion[b] and Loic Toupet[c]

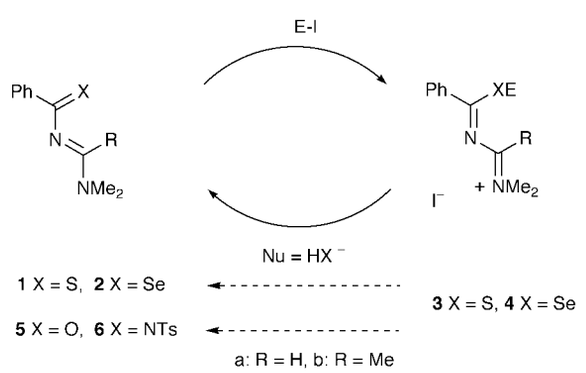
[a] *Laboratoire de Synthèse Organique, UMR au CNRS 6513, 2 rue de la Houssinière, BP 92208, 44322 Nantes Cedex 3, France*
[b] *Laboratoire de Synthèse et Electrosynthèse Organiques, UMR au CNRS 6510, Université de Rennes I-Beaulieu, 35042 Rennes Cedex, France*
[c] *Groupe Matière Condensée et Matériaux, UMR au CNRS 6626, Université de Rennes I-Beaulieu, 35042 Rennes Cedex, France*

Received (in Cambridge, UK) 20th April 1999, Accepted 30th July 1999

The preparation of 2-phenyl-4-dimethylamino-1-aza-, 1-oxa-, 1-thia-, 1-selena-3-azabuta-1,3-dienes as well as their 4-methyl derivatives is described following a new heteroatom interchange reaction process. Heteronucleophilic attack at one particular reactive site of bis-electrophilic amidinium salts is the key feature of the process. In addition, we also disclose that the substituted 1-oxa-3-aza- and 1,3-diazabuta-1,3-dienes can be obtained by a reactional transformation cascade initiated by either silver acetate addition or tosyl azide [3+2] cycloaddition onto the CS or CSe double bonds of the 1-thia- and 1-selena-3-azabuta-1,3-diene analogues.

Introduction

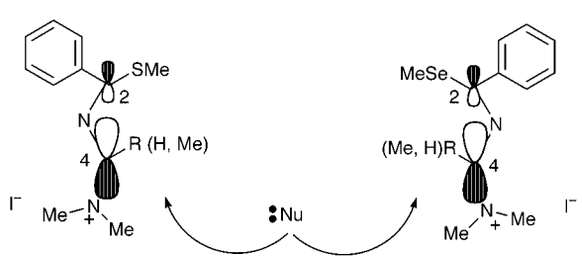
Heterobutadienes are useful building blocks in heterocyclic chemistry and during the last few years they have increasingly been used in [4 + 2] cycloadditions to prepare a large variety of natural products.[1] Some reports from this laboratory disclosed that efficient hetero Diels–Alder reactions could be effected by treatment of substituted 1-thia-3-azabuta-1,3-dienes **1** (*N*-thiophenacylamidines) and 1-selena-3-azabuta-1,3-dienes **2** (*N*-selenophenacylamidines) with several electron-poor dienophiles[2] and such a methodology was also applied to the first asymmetric synthesis of the *4H*-dihydro-1,3-thiazine skeleton.[3] The reactivity of phenacylamidines such as **1** and **2** has mainly been exploited for their ability to successfully participate in [4 + 2] cycloadditions. However, in the literature there are few examples of the transformation of *N*-thioacylamidines into five-membered heterocycles *via* their corresponding amidinium and 1,2,4-dithiadiazolium salts.[4] In this paper, we wish to report a hitherto unexplored facet of amidinium salt chemistry in showing that **3** and **4**, derived from dienes **1** and **2**, respectively, are key intermediates for the facile transformation of dienes **1**(**2**) into dienes **2**(**1**) as well as dienes **1**,**2** into dienes **5**,**6** following an overall heteroatom interchange reaction process[5] as portrayed in general terms in Scheme 1. Additionally, we also report results which establish that strategies based on either 1) silver acetate nucleophilic attack or 2) tosyl azide [3 + 2] dipolar cycloaddition on **1**,**2**, are also effective for the preparation of 1-oxa-3-aza- and 1,3-diazabuta-1,3-dienes **5** and **6**, respectively.



Scheme 1

Results and discussion

As previously reported for the *N*-thiophenacylformamidine **1a**,[6] its methyl-substituted analogue **1b** and the related *N*-selenophenacylformamidine **2b** react with methyl iodide at room temperature to give, almost quantitatively, the hetero substituted amidinium salts **3b** and **4b**, respectively (Scheme 1, E = Me). These salts are bis-electrophiles and, as such, are prone to nucleophilic attack at both the C-2 and C-4 positions. Semi-empirical calculations effected at the PM3 level on amidinium salts **3a** and **4a** clearly indicated that the electron deficiency is seen to be concentrated on C-4 and that the LUMO has the greatest coefficient located on C-4 (Scheme 2).

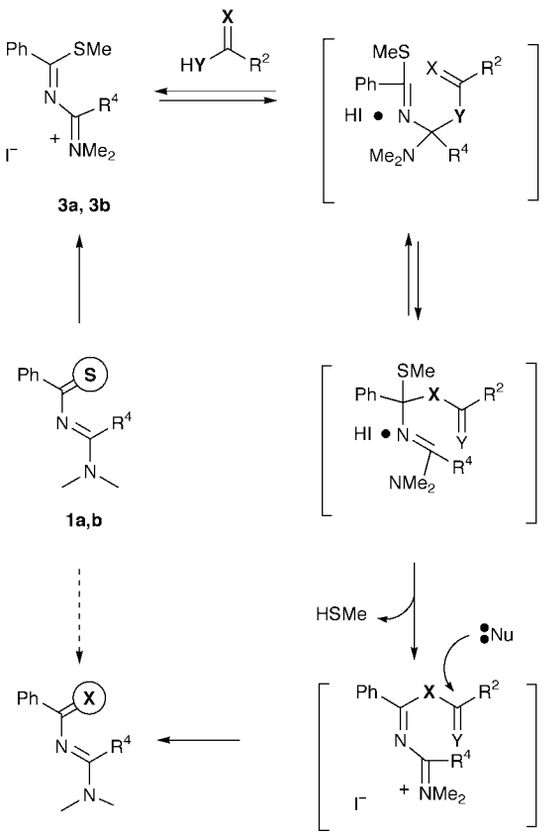


Scheme 2

The same conclusions are also valid for both **3b** and **4b** although calculations indicated less marked differences between the C-2 and C-4 reactive sites.[7] Consequently, it appears that, under either charge or orbital control, nucleophilic species should be preferentially directed to carbon C-4.

Although this situation seems, *a priori*, unfavourable to meet our purpose, this may in fact not be the overall controlling factor in determining the product structure since the heteroatom interchange at C-2 does not necessarily imply that the incoming nucleophile would be kinetically directed to this site. Indeed, in the case where the incoming nucleophile is

an ambident species of general formula HY–C(R)=X (X,Y= heteroatoms), reversibility or possible rearrangement of the primary addition product followed by an irreversible transformation toward the targeted diene induced by a nucleophilic entity (*e.g.* HY–C(R)=X itself) may well overcome the above problem (Scheme 3; the overall process corresponds to an addition of the nucleophile by its X terminus at C-2 of **3**).

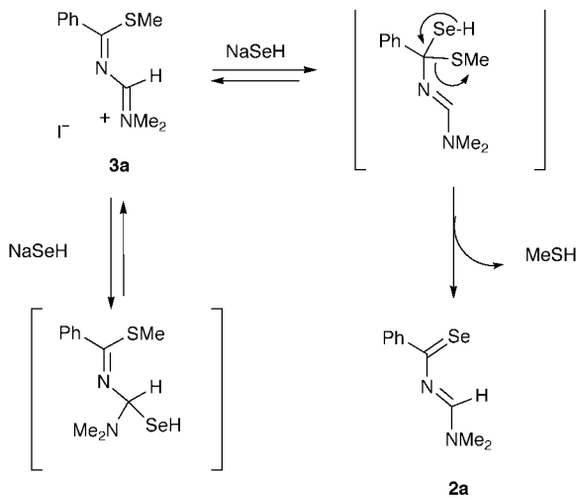


Scheme 3

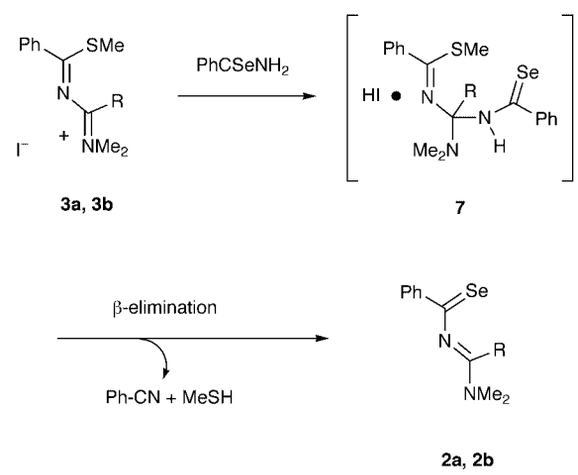
S→Se Heteroatom interconversion reaction process

With the above considerations in mind, we first elected to study the possibility of transforming dienes **1a**,**1b** to dienes **2a**,**2b** (S→Se heteroatom interconversion). Indeed, the action of hydroselenide on the thiomethylamidinium **3a** led to the expected formation of **2a** isolated in 50% yield. A related approach described by Liebscher, led to the formation of **2a** in 37% yield from the chloroamidinium salt precursor.[8] However, the action of selenobenzamide on the thiomethylamidinium salt **3b** proved far more efficient, leading to selenophenacylamidine **2b** in up to 80% isolated yield. This interconversion process may be interpreted in different ways depending on the nature of the incoming nucleophile. In the case where the nucleophile is NaSeH, the formation of diene **2a** is easily explained by the establishment of a rapid C-4→C-2 equilibration process followed by the loss of MeSH as shown in Scheme 4.

The situation appears more complex when selenobenzamide is the approaching nucleophile. Although an overall process as depicted in Scheme 4 represents a plausible mechanistic interpretation, provided the selenium atom is the nucleophilic center, it was ruled out, however, on the basis of previous investigations.[4b] As a result, the mechanism as shown in Scheme 3 (X = Se, Y = NH) could well explain the formation of diene **2b**. β-Elimination of the thioimidate moiety in intermediate **7** rather than its [3,3] rearrangement could also help to account for the product formation (Scheme 5). Experimental discrimination between the two processes seems difficult since, in



Scheme 4



Scheme 5

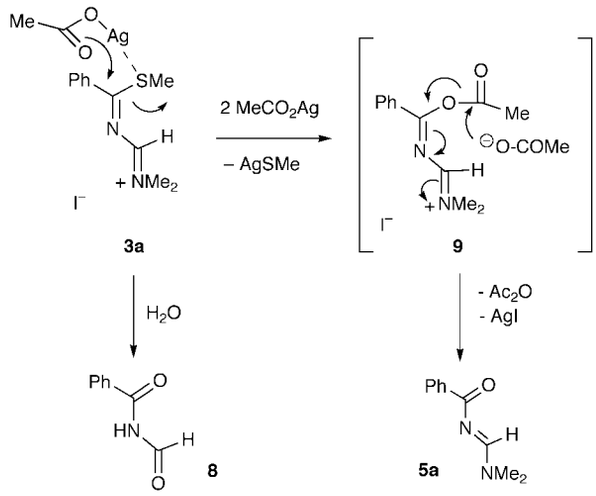
both cases, the accompanying by-products (benzonitrile and methanethiol) are the same.

The action of thiobenzamide on the selenoamidinium salt **4b** with the same reaction conditions proved to be less efficient leading to *N*-thiophenacylamidine **1b** in only 17% yield. Not surprisingly, switching selenobenzamide for the less nucleophilic benzamide left **3b** and **4b** unchanged.

S,Se→O and Se→S Heteroatom interconversion reaction processes

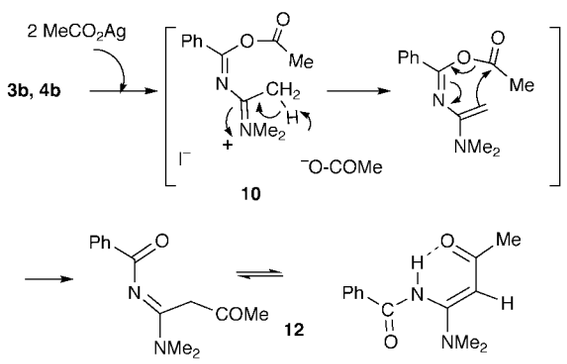
In order to perform the S→O interconversion,[9] amidinium salt **3a** was first treated with a boiling aqueous ethanolic solution for 30 min. A rather complex mixture formed from which imide **8**, resulting from water addition at both electrophilic sites of **3a**, could be isolated in 42% yield. By contrast, when amidinium salt **3a** was subjected to the action of 2 equivalents of silver acetate in dry acetonitrile, a regioselective reaction leading to the formation of phenacylamidine **5a**, as the sole isolated product (40% yield), was observed. The formation of diene **5a** could be explained by the mechanism depicted in Scheme 3 (X = Y = O) or by a mechanism featuring a direct silver acetate attack at C-2 to give the key intermediate **9** (Scheme 6). Though plausible, the latter mechanism seems less probable in view of results to be reported later in this paper which suggest that sulfur complexation by a metal should preferentially direct the nucleophile towards C-4.

Surprisingly, under the same reaction conditions, amidinium salts **3b**,**4b** were both transformed into compound **12** (mixture of tautomer forms) in 60 and 85% yield, respectively. Distinction between each of the two forms of **12** was facilitated by



Scheme 6

direct comparison of their ^{13}C NMR spectra with that of compound **5b** prepared by reaction of benzamide with dimethylformamide dimethyl acetal (see Experimental section). Additionally, an X-ray analysis of compound **12** revealed that, in the solid state, it exists in the enamino ketone form (Fig. 1). The formation of **12**, resulting from both a heteroatom interchange (S,Se→O) and an acylation reaction at the methyl substituent of the starting amidinium salts, can be accounted for by a reaction mechanism featuring a) formation of the *O*-acylamidinium salt intermediate **10**; b) acetate-induced deprotonation of the amidinium moiety leading to intermediate **11** and c) intramolecular capture of the acetyl residue by the enamine moiety previously generated (Scheme 7).



Scheme 7

The nature of both the metal counter ion and the heteroatom in the incoming nucleophile greatly influenced the course and efficiency of this transformation. Thus, switching silver acetate for potassium acetate resulted in the formation of **12** in low yield (17%) whereas the action of potassium thioacetate led to the phenacylthioformamidine **1b** in 57% isolated yield (Se→S heteroatom interchange, Scheme 8).

Parenthetically, it is worth noting that the S,Se→O heteroatom interchange may also be effected by treating the *N*-thio- and *N*-selenophenacylamidines **1b**,**2b** with silver acetate in dry acetonitrile. In that case, the ability of the silver ion to coordinate with the thioamide [10] or selenoamide function is sufficient to promote and drive the reaction selectively toward the formation of **12** in 50 and 80% yield, respectively (Scheme 9).

S,Se→N Heteroatom interconversion reaction process

In the last few years, effort has been devoted toward the synthesis of 1,3-diazabuta-1,3-dienes which are suitable precursors for nitrogen-containing heterocycles.[1,11] We have thought to use

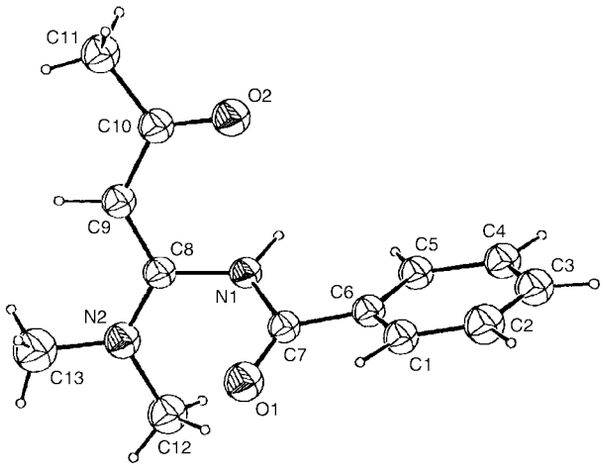
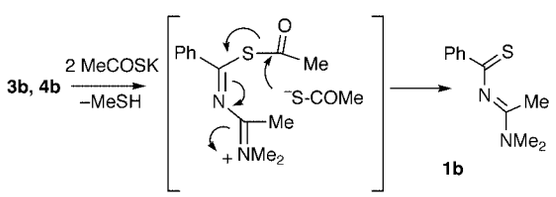
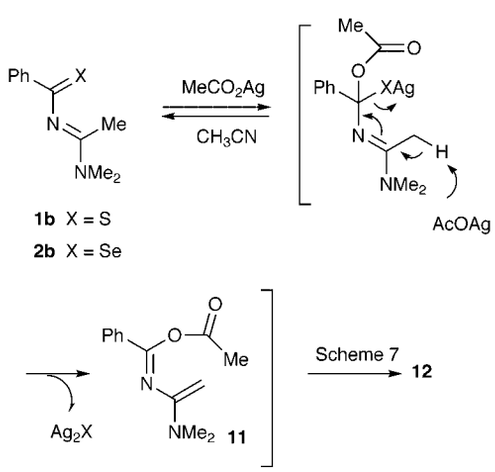


Fig. 1 ORTEP [14] diagram of **12**.

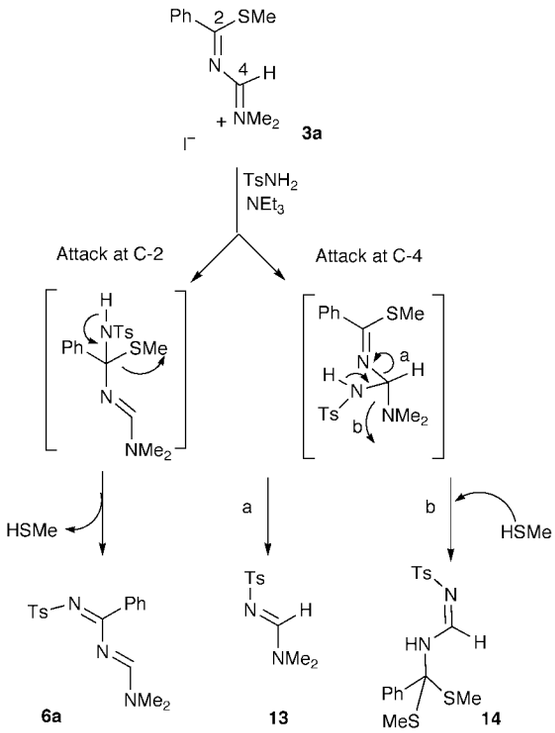


Scheme 8



Scheme 9

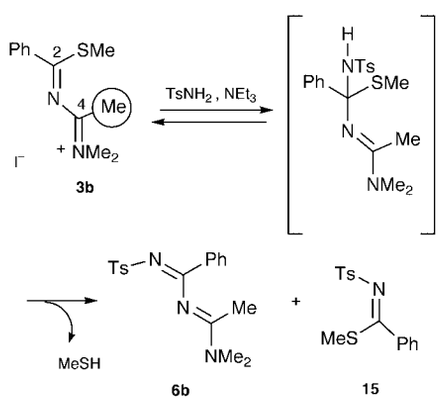
the electrophilic properties of amidinium salts as reported above to design a new and efficient preparation of these synthetically useful dienes and, toward this end, we first explored the behaviour of toluene-*p*-sulfonamide as the incoming nucleophile. Its reaction with amidinium salt **3a** in acetonitrile containing triethylamine (2 equivalents) led to a mixture of three compounds identified as being the *N*-tosylamidine **13** (38%), the dithioacetal derivative **14** (40%), and the 1,3-diazabuta-1,3-diene **6a** (18%). Although the marginal formation of diene **6a** was rather disappointing, this reaction is not without interest from a mechanistic point of view. Thus, if it were not possible to choose between the two reaction paths that can operate in the reaction between an ambident nucleophile and an amidinium salt such as **3**, the formation of **14** clearly shows that a non-ambident nucleophile, *i.e.* toluene-*p*-sulfonamide, was selectively directed toward the electrophilic C-4 site of **3a** (Scheme 10). Conversely, the small amount of diene **6a** probably results from attack at the electrophilic C-2 site of **3a**. Quite interestingly, enhancement in the site selectivity of the attack at C-4 could be achieved when a metal with strong sulfur affinity was added to the reaction medium. Thus, by the simple action of adding mercury(II) chloride to the reaction mixture,



Scheme 10

the formation of diene **6a** could be entirely suppressed, the reaction leading to the thioacetal derivative **14** (32%).

The same reaction with amidinium salt **3b** and toluene-*p*-sulfonamide followed a different course leading, by preferential attack at C-2, to 1,3-diazabuta-1,3-diene **6b** isolated in low yield (20%) along with thioimidate **15** (15%). The presence of a cumbersome methyl substituent at C-4 may discourage the toluene-*p*-sulfonamide from approaching this centre or, if not, it favours the equilibration process (Scheme 11).



Scheme 11

Given the previous results that favoured the formation of the thioacetal derivative **13** at the expense of **6a**, a different strategy had to be devised to obtain the latter compound. From heterodienes **1a** and **1b** we anticipated that a cascade reaction pathway featuring a tosyl azide [3 + 2] cycloaddition, preferentially at the CS (CSe) double bond,[12] followed by ring contraction and sulfur (selenium) extrusion processes could finally lead to 1,3-diazadienes **6a**,**6b** as shown in Scheme 12. Indeed, mixing heterodiene **1a** with tosyl azide (5 equivalents) in boiling toluene for 4 hours, led to the expected formation of **6a** in a satisfactory yield of 75%. Heterodienes **1b**,**2b** behaved the same way leading to 1,3-diazadiene **6b** in 87 and 94% yields, respectively.

The structures of dienes **6a** and **6b** were obtained by single crystal X-ray analysis as depicted in Figs. 2 and 3. It can be

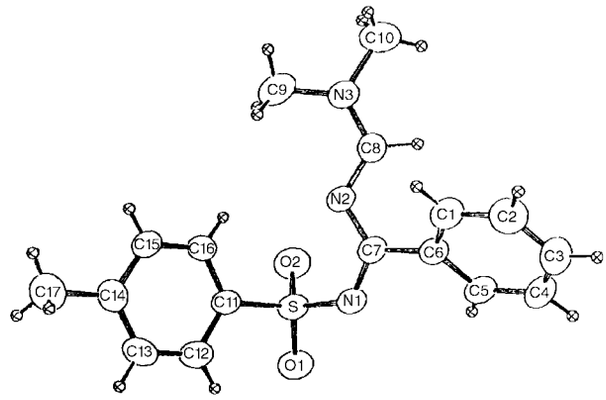


Fig. 2 ORTEP[14] diagram of **6a**.

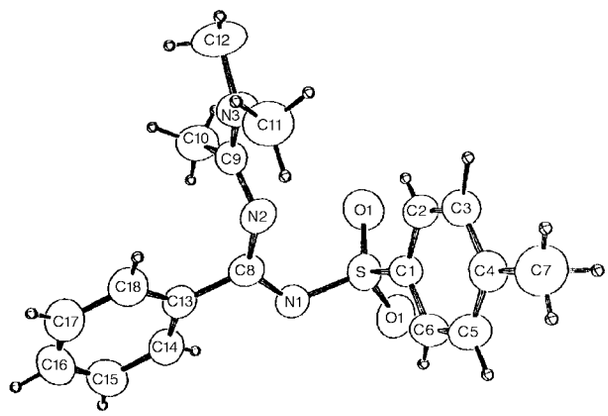
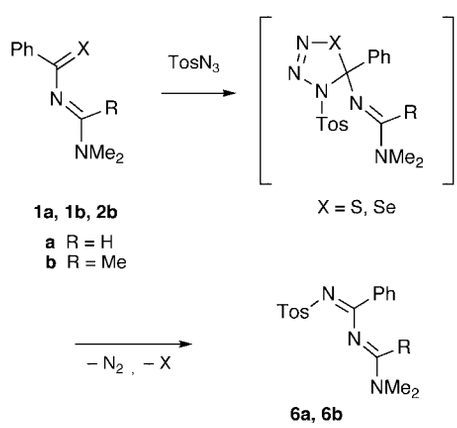


Fig. 3 ORTEP[14] diagram of **6b**.



Scheme 12

recognised that, similarly to the results of a computational study conducted at the PM3 level, both dienes possess 1*Z*,3*E* configurations and adopt an s-*trans* conformation with significant deviations from planarity.[13]

Dienes **1** and **2** have already been reported to engage in [4 + 2] cycloaddition reactions,[2,3] but the synthetic potentialities of dienes **5** and **6** have not yet been delineated. Preliminary studies have revealed that, under experimental conditions that permitted the easy condensation of the parent heterodienes **1a** and **1b** with methyl vinyl ketone, dienes **5**,**6** were reluctant to undergo cycloadditions. This is not really surprising in view of the fact that 1) the s-*trans* conformation[15] would inhibit the [4 + 2] cycloaddition process, 2) the known examples of cyclocondensation reactions involving 4-amino-1,3-diazabutadienes worked satisfactorily with ketene-derivatives[16] and a stepwise mechanism was put forward to explain the results[17] and 3) dienes **5** and **6** are predicted to be far less amenable to cyclo-

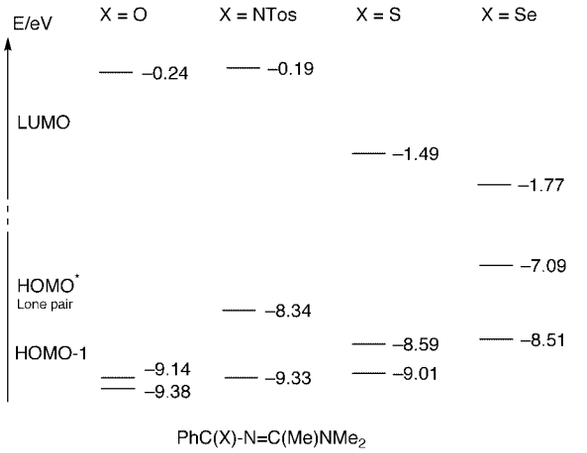


Fig. 4 Energy levels of FMO for **1b**, **2b**, **5b**, **6b**.

addition than their S and Se congeners **1**,**2** by consideration of frontier orbital levels (Fig. 4).

Conclusion

We have shown that heteroatom interchange between 1-thia- and 1-selena-3-azabutadienes on the one hand (**1**→**2**) and between 1-thia (selena) and 1-oxa-3-aza- or 1,3-diaza-butadienes on the other hand (**1**,**2**→**5** and **1**,**2**→**6**) could be easily executed *via* the transitory formation of amidinium salts **3** and **4**. Although the latter examples embody two electrophilic sites, conditions that allow the regioselective direction of nucleophilic species were found. Additionally, we have also shown that, in cases where the precedented strategy could not be satisfactorily applied, the potential properties of the CS or CSe double bonds as dipolarophiles[18] in dienes **1**,**2** could be advantageously employed to reach the targeted dienes. In particular, we have found that tosyl azide [3 + 2] cycloaddition at the CS (CSe) double bond of dienes **1**,**2** initiates a sequential reaction process that finally provides 1,3-diazadienes **6a**,**6b** in practically useful yields. Further studies aimed at identifying the chemical reactivity of dienes **5** and **6** are currently under way.

Experimental

X-Ray analysis †

Compound 6a. $C_{17}H_{19}N_3O_2S$, $M_r = 329.4$, monoclinic, $P2_1/n$, $a = 13.330(2)$, $b = 8.404(2)$, $c = 15.100(2)$ Å, $\beta = 100.20(1)°$, $V = 1664.8(5)$ Å^{-3}, $Z = 4$, $D_x = 1.314$ Mg m^{-3}, λ(Mo-Kα) = 0.71073Å, $\mu = 2.07$ cm^{-1}, $F(000) = 696$, $T = 293$ K. The sample (0.50 × 0.35 × 0.20 mm) is studied on an automatic diffractometer CAD4 NONIUS with graphite monochromatized Mo-Kα radiation.[19] The cell parameters are obtained by fitting a set of 25 high-theta reflections. The data collection ($2\theta_{max}$ = 50°, scan $\omega/2\theta = 1$, $t_{max} = 60$ s, range *hkl*: *h* 0.15 *k* 0.9 *l* −17.17, intensity controls without appreciable decay (0.2%) gives 3041 reflections of which 2909 were independent (2031 with $I > 2.0\sigma(I)$). After Lorentz and polarization corrections,[20] the structure was solved with SIR-97[21] which reveals the non-hydrogen atoms of the structure. After anisotropic refinement, all the hydrogen atoms are found with a Fourier Difference. The whole structure was refined with SHELXL97[22] by the full-matrix least-square techniques (use of *F* magnitude; *x*, *y*, *z*, β_{ij} for S, C, O and N atoms, *x*, *y*, *z* in riding mode for methyl H atoms, *x*, *y*, *z* for the other H atoms; 239 variables and 2909 observations; calc $w = 1/[\sigma^2(F_o^2) + (0.0599P)^2 + 0.6055P]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting $R = 0.037$, $R_w = 0.077$ and $S_w = 1.029$ (residual $\Delta\rho \leq 0.35$ e Å^{-3}).

† CCDC reference number 207/354. See http://www.rsc.org/suppdata/p1/1999/2821 for crystallographic files in .cif format.

Atomic scattering factors were issued from International Tables for X-Ray Crystallography.[23] ORTEP views were realized with PLATON98.[24] All the calculations were performed on a Silicon Graphics Indy computer.

Compound 6b. $C_{18}H_{21}N_3O_2S$, $M_r = 343.44$, orthorhombic, $P2_12_12_1$, $a = 8.032(3)$, $b = 13.044(2)$, $c = 17.604(4)$ Å, $V = 1844.4(9)$ Å^{-3}, $Z = 4$, $D_x = 1.237$ Mg m^{-3}, λ(Mo-Kα) = 0.71073 Å, $\mu = 1.90$ cm^{-1}, $F(000) = 728$, $T = 293$ K. The sample (0.30 × 0.30 × 0.45 mm) is studied on an automatic diffractometer CAD4 NONIUS with graphite monochromatized Mo-Kα radiation.[19] The cell parameters are obtained by fitting a set of 25 high-theta reflections. The data collection ($2\theta_{max}$ = 50°, scan $\omega/2\theta = 1$, $t_{max} = 60$ s, range *hkl*: *h* 0.8 *k* 0.14 *l* 0.18, intensity controls without appreciable decay (0.3%) gives 1840 reflections from which 1324 were independent with $I > 2.0\sigma(I)$. After Lorentz and polarization corrections,[20] the structure was solved with SIR-97[21] which reveals the non-hydrogen atoms of the structure. After anisotropic refinement, all the hydrogen atoms are found with a Fourier Difference. The whole structure was refined with SHELXL97[22] by the full-matrix least-square techniques (use of *F* magnitude; *x* *y*, *z*, β_{ij} for S, C, O and N atoms, H atoms in riding mode; 218 variables and 1324 observations; calc $w = 1/[\sigma^2(F_o^2) + (0.0668P)^2 + 0.5051P]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting $R = 0.033$, $R_w = 0.1070$ and $S_w = 1.18$ (residual $\Delta\rho \leq 0.18$ e Å^{-3}).

Atomic scattering factors were issued from International Tables for X-Ray Crystallography.[23] ORTEP views were realized with PLATON98.[24] All the calculations were performed on a Silicon Graphics Indy computer.

Compound 12. $C_{13}H_{16}N_2O_2{\cdot}H_2O$, $M_r = 250.29$, monoclinic, $P2_1/n$, $a = 12.638(7)$, $b = 7.998(2)$, $c = 12.968(1)$ Å, $\beta = 93.15(1)°$, $V = 1308.8(8)$ Å^{-3}, $Z = 4$, $D_x = 1.270$ Mg m^{-3}, λ(Mo-Kα) = 0.71073 Å, $\mu = 0.91$ cm^{-1}, $F(000) = 536$, $T = 293$ K. The sample (0.42 × 0.35 × 0.33 mm) is studied on automatic diffractometer CAD4 NONIUS with graphite monochromatized Mo-Kα radiation.[19] The cell parameters are obtained by fitting a set of 25 high-theta reflections. The data collection ($2\theta_{max}$ = 54°, scan $\omega/2\theta = 1$, $t_{max} = 60$ s, range *hkl*: *h* 0.16 *k* 0.8 *l* −16.16, intensity controls without appreciable decay (1.1%) gives 2770 reflections from which 2651 were independent (2143 with $I > 1.5\sigma(I)$). After Lorentz and polarization corrections,[20] the structure was solved with SIR-97[21] which reveals the non-hydrogen atoms of the structure. After anisotropic refinement, all the hydrogen atoms are found with a Fourier Difference. The whole structure was refined with SHELXL 97[22] by the full-matrix least-square techniques (use of F magnitude; *x*, *y*, *z*, β_{ij} for C, O and N atoms, *x*, *y*, *z* for H atoms; 213 variables and 2651 observations; $\omega = 1/[\sigma^2(F_o)^2 + (0.0889P)^2 + 1.2514P]$ where $P = (F_o^2 + 2F_c^2)/3$ with the resulting $R = 0.061$, $R_\omega = 0.166$ and $S_\omega = 1.043$ (residual $\Delta\rho \leq 0.76$ e Å^{-3}).

Atomic scattering factors were issued from International Tables for X-Ray Crystallography.[23] ORTEP views were realized with PLATON98.[24] All the calculations were performed on a Silicon Graphics Indy computer.

General procedures

NMR spectra (^{1}H at 200 MHz and ^{13}C at 50.3 MHz) were recorded with a Bruker AC 200 spectrometer. Chemical shifts (δ) are expressed in parts per million (ppm) referenced to residual chloroform (7.27 ppm). Coupling constants, *J*, are given in hertz (Hz). Multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Mass spectra *m*/*z* (% base peak) were recorded on an HP 5889A spectrometer EI (70 eV). Infra-red spectra were carried out on a Bruker IFS 45WHR Fourier transform IR spectrophotometer. Melting points were determined on a C. REICHERT microscope apparatus and are uncorrected. Elemental analyses were

carried out on a Perkin-Elmer 2400, C, H, N elemental analyser at the Microanalyse Service of CNRS (Vernaison, France). Tetrahydrofuran (THF) was prepared by pre-drying on KOH pellets followed by distillation from Na–benzophenone. Diethyl ether was distilled from Na–benzophenone. Acetonitrile, ethyl acetate and methylene chloride were dried by distillation over P_2O_5 and toluene was distilled from sodium. All solvents were freshly distilled by standard methods prior to use. Flash chromatography was performed on silica gel Merck 60 230–400 mesh. Thin layer chromatography was performed on precoated plates of silica gel $60F_{254}$ (Merck, Art 7735).

4-Dimethylamino-4-methyl-2-phenyl-1-thia-3-azabuta-1,3-diene 1b

Method A. The heterodiene **1b** (90% yield) was obtained by condensation of *N*,*N*-dimethylacetamide dimethyl acetal in excess thiobenzamide using a procedure described in the literature.[2a]

Method B. Methylselenoamidinium salt **4b** (600 mg, 1.5 mmol) was dissolved in dry CH_3CN (20 ml). Potassium thioacetate (420 mg, 2.95 mmol) was added under nitrogen and the mixture was stirred at room temperature for 2 h. The mixture was filtered on a pad of Celite to remove insoluble non-organic material and the solvent was removed *in vacuo*. Column chromatography afforded the title diene (4:1 petroleum ether–ethyl acetate) in 57% yield. From **3b**, an identical procedure led to **1b** in 58% yield.

Method C. Methylselenoamidinium salt **4b** (800 mg, 2 mmol) was dissolved in dry CH_2Cl_2 (20 ml). Thiobenzamide (275 mg, 3.2 mmol) and triethylamine (4 mmol) were added successively under a nitrogen atmosphere. The mixture was stirred at room temperature for 4 h then concentrated under reduced pressure. The crude product was purified by flash chromatography (4:1 petroleum ether–ethyl acetate) to give **1b** in 17% yield. Mp 112 °C (from ethanol) (Found: C, 64.29; H, 6.69; S, 15.68. $C_{11}H_{14}N_2S$ requires C, 64.04; H, 6.84; N, 13.58; S, 15.54%); δ_C 18.0 (Me), 39.2 (NMe_2), 127.6, 128.8, 131.8 and 142.6 (Ph), 167.8 (C-4) and 202.7 (C-2); *m*/*z* 206 (M^+, 70%), 173 (100), 129 (26), 121 (61), 77 (45), 56 (30); ν_{max}(KBr)/cm^{-1} 1624 and 1590.

4-Dimethylamino-4-methyl-2-phenyl-1-selena-3-azabuta-1,3-diene 2b

Method A. Using a procedure similar to that described above for the synthesis of **1b**, compound **2b** was obtained from selenobenzamide in 92% yield.[2h]

Method B. Methylthioamidinium salt **3b** (350 mg, 1 mmol) was dissolved in dry CH_2Cl_2 (20 ml). Selenobenzamide (184 mg, 1 mmol) and triethylamine (2 mmol) were added successively under nitrogen. The mixture was stirred at room temperature for 2 h then concentrated under reduced pressure. The crude product was purified by flash chromatography (7:3 petroleum ether–ethyl acetate; R_f 0.16) to give **2b** in 80% yield. (Physical properties of **2b** can be found in reference 2*h*.)

General procedure for methylheteroamidinium salts 3a, 3b and 4b

The heterodiene precursors **1a**, **1b** or **2b** (1 mmol) were dissolved in methyl iodide used as solvent. The colourless solutions were stirred at rt for 30 min under nitrogen. In all cases the addition of diethyl ether to the mixture induced the precipitation of the amidinium salts. After filtration, the solids were washed with diethyl ether.

3a.[6] Mp 173 °C (from diethyl ether) (Found: C, 39.03; H, 4.54; N, 7.92. $C_{11}H_{15}N_2SI$ requires C, 39.53; H, 4.52; N, 8.38; S, 9.59%); δ_H 2.75 (3H, s, SMe), 3.64 and 3.73 (6H, 2s, NMe_2), 7.58–7.78 (5H, m, C_6H_5), 8.57 (1H, s, H-4); δ_C 17.1 (SMe, $^1J_{CH}$ = 144 Hz), 39.6 and 45.8 (NMe_2, $^1J_{CH}$ = 143 Hz), 129.5, 129.9, 134.3, 134.7 (Ph), 160.3 (C-4, $^1J_{CH}$ = 192 Hz), 196.9 (C-2); ν_{max}(KBr)/cm^{-1} 1649, 1578, 1556 (for IR spectra values of amidines and imidates see ref. 25).

3b. Mp 163–164 °C (from diethyl ether) (Found: C, 41.35; H, 4.95; N, 8.10. $C_{12}H_{17}N_2SI$ requires C, 41.39; H, 4.92; N, 8.04; S, 9.21%); δ_H 2.35 and 2.66 (6H, s, $2CH_3$), 3.60 and 3.78 (6H, 2s, NMe_2), 7.65 (s, 5H, Ph); δ_C 16.1 and 22.3 (2Me), 42.2 and 43.5 (NMe_2), 127.3, 130.0, 133.8 and 137.5 (Ph), 171.3 and 181.3 (C-2 and C-4); ν_{max}(KBr)/cm^{-1} 1624 and 1590.

4b. Mp 111–113 °C (from diethyl ether) (Found: C, 35.95; H, 4.54; N, 7.74. $C_{12}H_{17}N_2SeI$ requires C, 36.48; H, 4.34; N, 7.09%); δ_H 2.47 and 2.57 (6H, 2s, 2Me), 3.55 and 3.79 (6H, 2s, NMe_2), 7.65 (5H, s, Ph); δ_C 10.4 and 21.8 (2Me), 42.1 and 43.5 (NMe_2), 127.0, 129.8, 133.7 and 135.3 (Ph), 170.6 and 181.4 (C-2 and C-4); ν_{max}(KBr)/cm^{-1} 1626, 1575.

4-Dimethylamino-2-phenyl-1-oxa-3-azabuta-1,3-diene 5a

Methylthioamidinium salt **3a** (534 mg, 1.6 mmol) was dissolved in dry CH_3CN (20 ml). Silver acetate (534 mg, 3.2 mmol) was added under nitrogen and the mixture was stirred at room temperature for 30 min. The mixture was then filtered on a pad of Celite to remove insoluble non-organic material and the solvent was removed *in vacuo*. Column chromatography of the crude material afforded the title diene (3:2 petroleum ether–ethyl acetate) in 40% yield. Colourless needles, mp 76 °C (from diethyl ether) (Found: C, 68.48; H, 6.82; N, 15.36. $C_{10}H_{12}N_2O$ requires C, 68.16; H, 6.86; N, 15.90; O, 9.08%). The physical and spectral properties of isolated **5a** were in accordance with literature values.[26]

General procedures for *N*-(*p*-tolylsulfonyl)-1,3-diazabuta-1,3-dienes 6 (and adducts 13, 14, 15)

Method A. To a stirred solution of amidinium salt **3a** (668 mg, 2 mmol) dissolved in dry CH_3CN (20 mL) were subsequently added, under a dry nitrogen atmosphere, toluene-*p*-sulfonamide (340 mg, 2 mmol), Et_3N (0.56 mL, 4 mmol) and mercury(II) chloride (944 mg, 2 mmol). The mixture was stirred at room temperature for 1.5 h and then concentrated under reduced pressure. The crude product was purified by flash chromatography (3:2 petroleum ether–ethyl acetate) to give **14** in 32% yield. In the absence of mercury salt, the isolated reaction products were identified as diazabutadiene **6a**, *N*-tosyl amidine **13** and formamidine **14** (18, 38 and 40% yields, respectively). Starting from the amidinium salt **3b**, the same experimental procedure led to the formation of diazabutadiene **6b** isolated in 20% yield along with *N*-tosyl methylthiobenzimidate **15** (15% yield).

Method B. To a solution of *N*-thiophenacylformamidine **1a** in dry toluene (30 mL) was added toluene-*p*-sulfonyl azide[27] (1 g, 5 mmol) under a nitrogen atmosphere. The mixture was stirred at reflux for 4 h and then concentrated under reduced pressure. The crude product was purified by flash chromatography (3:2 petroleum ether–ethyl acetate) to give **6a** in 75% yield. Starting from *N*-thio- or *N*-selenophenacylformamidine **1b**, **2b**, 1,3-diazabuta-1,3-diene **6b** could be obtained in 87 and 94% yields respectively, following the same experimental procedure as above.

4-Dimethylamino-2-phenyl-1-(*p*-tolylsulfonyl)-1,3-diazabuta-1,3-diene 6a. Mp 170–171 °C (from light petroleum) (Found: C, 61.69; H, 5.78; N, 12.56. $C_{17}H_{19}N_3O_2S$ requires C, 62.01; H, 5.78; N, 12.77%); δ_H 2.37 (3H, s, Me), 2.97 and 3.38 (6H, 2s, NMe_2), 7.14–7.70 (9H, m, Ph, C_6H_4), 8.37 (1H, s, CH=N); δ_C 21.5 (Me), 38.8 and 41.1 (NMe_2), 127.0, 127.8, 129.2, 129.5,

130.9, 131.0, 138.3, 142.6 (Ph, C_6H_4), 169.5 and 174.1 (C-2, C-4); *m/z* 329 (M^+, 9%), 238 (33), 174 (95), 173 (25), 172 (22), 119 (43), 118 (51), 116 (41), 104 (100), 91 (92), 77 (31), 71 (76), 65 (27), 44 (23); ν_{max}(KBr)/cm^{-1} 1597, 1520.

4-Dimethylamino-2-phenyl-1-(*p*-tolylsulfonyl)-1,3-diazapenta-1,3-diene 6b. Mp 125–126 °C (from light petroleum) (Found: C, 63.16; H, 6.24; N, 11.93. $C_{18}H_{21}N_3O_2S$ requires C, 62.95; H, 6.16; N, 12.23%); δ_H 2.05 and 2.39 (6H, 2s, 2Me), 3.04 and 3.11 (6H, 2s, NMe_2), 7.22–7.93 (9H, m, Ph, C_6H_4); δ_C 19.6 (Me), 21.0 (Me), 38.1 (NMe_2), 126.5, 127.8, 128.5, 128.8, 131.8, 135.7, 139.9, 141.6 (Ph, C_6H_4), 158.6 and 166.9 (C-4, C-2); *m/z* 344 (M^+ + 1, 3%), 188 (96), 176 (30), 173 (34), 155 (21), 104 (57), 91 (100), 65 (25), 56 (22), 44 (43); ν_{max}(KBr)/cm^{-1} 1614, 1583.

N-Acylbenzamide 8

To a solution of methylthioamidinium salt **3a** (534 mg, 1.6 mmol) in dry acetonitrile were added silver nitrate (533 mg, 3.2 mmol) and water (1 mL). The mixture was stirred at room temperature for 30 min and then concentrated under reduced pressure. The crude product was flash-chromatographed (3:2 petroleum ether–ethyl acetate) to give **8** (42% yield) as white crystals. Mp 110–111 °C (from diethyl ether) (Found: C, 64.56; H, 4.86; N, 9.40. $C_8H_7NO_2$ requires C, 64.42; H, 4.73; N, 9.39%); δ_C 128.1, 129.0, 131.0, 133.9 (Ph), 164.6 (HCO, $^1J_{CH}$ = 208 Hz), 166.8 (CO); the other spectral properties of **8** (^{1}H NMR and IR) were in full accordance with literature values.[28]

Compounds 12

Using a procedure similar to that described above for the synthesis of **5a**, compound **12** (two tautomer forms in solution, *vide infra*) was obtained either from *N*-heterophenacylamidines **1b** and **2b** (50 and 80% yields, respectively) or from amidinium salts **3b** and **4b** (60 and 85% yields, respectively) (Found: C, 67.60; H, 7.21; N, 12.35; O, 13.78. $C_{13}H_{16}N_2O_2$ requires C, 67.22; H, 6.94; N, 12.06; O, 13.78%); *m/z* 232 (M^+, 25%), 189 (25), 105 (100), 77 (57), 44 (41); ν_{max}(film)/cm^{-1} 1721, 1695 and 1623.

***N*-(1-Dimethylamino-3-oxobutylidene)benzamide.** δ_H 2.17 (3H, s, Me), 2.9 and 3.1 (6H, 2s, NMe_2), 3.8 (2H, s, CH-2), 7.2–8.1 (5H, 2m, Ph); δ_C 31.8 (Me, $^1J_{CH}$ = 126.2 Hz), 39.3 (NMe_2 $^1J_{CH}$ = 142.2 Hz), 45.8 (CH_2, $^1J_{CH}$ = 128.2 Hz), 128.9, 129.3 130.3, 138.5 (Ph), 164.0, 176.3, 201.7 (C=N, 2 C=O).

***N*-(1-Dimethylamino-3-oxobut-1-enyl)benzamide (enamino ketone form).** δ_H 1.9 (3H, s, Me), 2.8 (6H, s, NMe_2), 4.7 (1H, s, CH), 13.4 (1H, s, NH), 7.3 and 7.4 (5H, 2m, Ph); δ_C 30.6 (Me, $^1J_{CH}$ = 126.2 Hz), 40.9 (NMe_2, $^1J_{CH}$ = 142.2 Hz), 85.8 (C=CH, $^1J_{CH}$ = 159.4 Hz), 129.0, 129.5, 133.4, 137.1 (Ph), 158.5, 166.8, 195.3 (2 C=O, C=CH).

N-(*p*-Tolylsulfonyl)-*N*′,*N*′-dimethylformamidine 13

Mp 113–114 °C (from light petroleum) (Found: C, 53.39; H, 6.29; N, 12.51; S, 14.47. $C_{10}H_{14}N_2O_2S$ requires C, 53.08; H, 6.24; N, 12.38; O, 14.14; S, 14.17%); δ_H 2.39 (3H, s, Me), 3.00 and 3.11 (6H, 2s, NMe_2), 7.23–7.78 (4H, 2d, C_6H_4), 8.12 (1H, s, CH=N); δ_C 21.4 (Me, $^1J_{CH}$ = 127 Hz), 35.4 and 41.4 (NMe_2, $^1J_{CH}$ = 138.5 Hz), 126.4, 129.3, 139.6, 142.4 (C_6H_4), 159.1 (CH=N, $^1J_{CH}$ = 184 Hz); *m/z* 226 (M^+, 27%), 91 (73), 71 (100), 65 (42), 44 (83); ν_{max}(KBr)/cm^{-1} 1626.

N-(*p*-Tolylsulfonyl)-*N*′-[bis(methylthio)phenylmethyl]formamidine 14

Mp 60–61 °C (from diethyl ether) (Found: C, 53.67; H, 5.10; N, 7.35; S, 24.98. $C_{17}H_{20}N_2O_2S_3$ requires C, 53.66; H, 5.30; N, 7.36; O, 8.41; S, 25.27%); δ_H 1.98 (6H, s, SMe), 2.42 (3H, s, Me), 6.91 (1H, br s, NH), 7.27–7.79 (9H, m, Ph and C_6H_4), 8.78 (1H, br s, CH=N); δ_C 14.0 (SMe), 21.7 (Me), 77.4 (PhC), 126.6, 127.0, 127.7, 128.5, 129.2, 129.4, 129.8, 138.3, 139.1, 143.4 (Ph, C_6H_4), 160.1 (CH=N, $^1J_{CH}$ = 183 Hz); *m/z* 317 (M^+ + 1, 30%), 155 (64), 104 (24), 91 (100), 65 (26); ν_{max}(KBr)/cm^{-1} 1615 (C=N), 3285 (NH).

N-(*p*-Tolylsulfonyl)methylthiobenzimidate 15

Mp 111 °C (from light petroleum) (Found: C, 58.72; H, 4.89; S, 20.52. $C_{15}H_{15}NO_2S_2$ requires C, 58.99; H, 4.95; N, 4.59; O, 10.48; S, 20.99%); δ_H 2.39 (6H, s, MeC_6H_4, SMe), 7.21–7.78 (9H, m, Ph and C_6H_4); δ_C 15.9 and 21.5 (2Me), 126.9, 127.5, 128.1, 129.2, 131.4, 136.1, 138.7, 143.2 (Ph, C_6H_4), 185.7 (C=N); *m/z* 306 (CI, M^+, 100%), 258 (35), 155 (91), 105 (30), 91 (100), 77 (20), 65 (35); ν_{max}(KBr)/cm^{-1} 1596, 1546.

References

1 (*a*) D. L. Boger and S. M. Weinreb, in *Hetero Diels–Alder Methodology in Organic Synthesis*, ed. H. H. Wasserman, Academic Press, San Diego, 1987; (*b*) W. Carruthers, in *Cycloaddition Reactions in Organic Synthesis*, ed. J. E. Baldwin and P. D. Magnus, Pergamon Press, Oxford, 1990, vol. 8; (*c*) D. L. Boger, in *Comprehensive Organic Synthesis*, ed. L. A. Paquette, Pergamon Press, Oxford, 1991, vol. 5, p. 451; (*d*) H. Waldmann, *Synthesis*, 1994, 535; (*e*) L. Tietze and G. Kettschau, *Top. Curr. Chem.*, 1997, **189**, 1.

2 (*a*) J. C. Meslin and H. Quiniou, *Bull. Soc. Chim. Fr.*, 1979, **116**, 347; (*b*) J. C. Rozé, J. P. Pradère, G. Duguay, A. Guevel, C. G. Tea and H. Quiniou, *Sulfur Lett.*, 1983, **1**, 115; (*c*) C. G. Tea, J. P. Pradère and H. Quiniou, *J. Org. Chem.*, 1985, **50**, 1545; (*d*) J. P. Pradère, J. C. Rozé, H. Quiniou, R. Danion-Bougot, D. Danion and L. Toupet, *Can. J. Chem.*, 1986, **64**, 597; (*e*) C. Cellerin, C. G. Tea, J. P. Pradère, A. Guingant and P. Guenot, *Sulfur Lett.*, 1988, **8**, 205; (*f*) J. P. Pradère, F. Tonnard, A. Abouelfida, C. Cellerin, M. Andriamanamihaja, B. Jousseaume, L. Toupet and P. Guénot, *Bull. Soc. Chim. Fr.*, 1993, **130**, 610; (*g*) D. Dubreuil, J. P. Pradère, N. Giraudeau, M. Goli and F. Tonnard, *Tetrahedron Lett.*, 1995, **36**, 237; (*h*) F. Purseigle, D. Dubreuil, A. Marchand, J. P. Pradère, M. Goli and L. Toupet, *Tetrahedron*, 1998, **54**, 2545.

3 A. Marchand, D. Mauger, A. Guingant and J. P. Pradère, *Tetrahedron: Asymmetry*, 1995, **6**, 853.

4 (*a*) J. Liebscher, M. Pätzel and Y. F. Kelboro, *Synthesis*, 1989, 672; (*b*) C. Cellerin, J. P. Pradère, D. Danion and F. Tonnard, *C. R. Acad. Sci. Paris*, 1991, **313**, Série II, 517; (*c*) A. Rolfs and J. Liebscher, *J. Org. Chem.*, 1997, **62**, 3480.

5 For a preliminary study about the heteroatom interconversion reaction concept as shown in Scheme 1, see reference 4*a*. See also for related work: (*a*) H. G. Gold, *Angew. Chem.*, 1960, **72**, 956; (*b*) J. Liebscher and H. Hartmann, *Synthesis*, 1976, 403.

6 J. C. Meslin, A. Reliquet, F. Reliquet and C. G. Tea, *C. R. Acad. Sci. Paris*, 1978, **286**, Série C, 397.

7 (*a*) Semi empirical PM3 calculations were carried out with SPARTAN software (4.0 version) on a Silicon Graphics Indy. For PM3 calculations see: J. J. P. Stewart, *Comput. Chem.*, 1989, **42**, 12; (*b*) F. Purseigle, PhD Thesis (30/01/97), University of Nantes.

8 J. Liebscher, *Synthesis*, 1988, 655.

9 For a recent review on conversion of the thiocarbonyl group into the carbonyl group, see: A. Corsaro and V. Pistarà, *Tetrahedron*, 1998, **54**, 15027.

10 M. Avalos, R. Babiano, C. J. Duran, J. L. Jiménez and J. C. Palacios, *Tetrahedron Lett.*, 1994, **35**, 477.

11 J. Barluenga and M. Thomas, in *Advances in Heterocyclic Chemistry*, ed. A. R. Katritzky, Academic Press, San Diego, 1993, vol. 57, p. 61.

12 H. Schaumann, in *The chemistry of double-bonded functional groups*, ed. S. Patai, Interscience Publication, John Wiley and Sons, New York, 1989, vol. 2, ch. 17, p. 1338.

13 Selected torsion angles: N1–C2–N3–C4 equal to −153.76° in **6a** and 123.47° in **6b**; C2–N3–C4–N2 equal to −170.83° in **6a** and 166.54° in **6b**.

14 C. K. Johnson, ORTEP Report ORNL-3794, Oak Ridge National Laboratory, Tenessee, USA, 1965.

15 S. N. Mazumdar and M. P. Mahajan, *Synthesis*, 1990, 417.

16 (*a*) P. Luthardt and E. U. Würthwein, *Tetrahedron Lett.*, 1988, **29**, 921; (*b*) S. N. Mazumdar and M. P. Mahajan, *Tetrahedron*, 1991, **47**, 1473; (*c*) S. N. Mazumdar, S. Mukherjee, A. Z. Sharma, D. Sengupta and M. P. Mahajan, *Tetrahedron*, 1994, **50**, 7579; (*d*) P. D. Dey, A. K. Sharma, P. V. Bharatam and M. P. Mahajan,

Tetrahedron, 1997, **53**, 13829; (*e*) A. K. Sharma and M. P. Mahajan, *Tetrahedron*, 1997, **53**, 13841.
17 (*a*) K. Burger, E. Huber, N. Sewald and H. Partscht, *Chem. Ztg.*, 1986, **110**, 83; (*b*) W. M. F. Fabian and G. Kollenz, *J. Phys. Org. Chem.*, 1994, **7**, 1; (*c*) E. Rossi, G. Abbiati and E. Pini, *Tetrahedron*, 1997, **53**, 14107.
18 For dipolarophilic properties of **1** see: R. Danion-Bougot, R. Tuloup, D. Danion, J. P. Pradère and F. Tonnard, *Sulfur Lett.*, 1989, **9**, 245.
19 C. K. Fair, MolEN. An Interactive Intelligent System for Crystal Structure Analysis, Enraf-Nonius, Delft, The Netherlands, 1990.
20 A. L. Spek, HELENA. Program for the handling of CAD4-Diffractomer output SHELX(S/L), 1997, Utrecht University, Utrecht, The Netherlands.
21 A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori and R. Spagna, *J. Appl. Crystallogr.*, 1998, **31**, 74.
22 G. M. Sheldrick, SHELX93. Program for the refinement of crystal structures, 1993, University of Göttingen, Germany.
23 *International tables for X-ray crystallography*, Kynoch Press (present distributor D. Reidel, Dordrecht), Birmingham, 1974, vol. IV.
24 A. L Spek, PLATON. A multipose crystallographic tool, 1998, Utrecht University, Utrecht, The Netherlands.
25 G. Häfelinger, in *The chemistry of amidines and imidates*, ed. S. Patai, Interscience Publication, John Wiley and Sons, New York, 1975, ch. 1, p. 53.
26 A. J. Blake, H. McNab and M. E. Ann Murray, *J. Chem. Soc., Perkin Trans. 1*, 1989, 589.
27 M. Regitz, J. Hocker and A. Liedhegener, *Organic Syntheses*, ed. J. Wiley and Sons, New York, 1988, Coll. Vol. V, p. 179.
28 B. Seiller, D. Heins, C. Bruneau and P. H. Dixneuf, *Tetrahedron*, 1995, **51**, 10901.

Paper 9/03150B