203. A Novel Synthesis of 2,2-Disubstituted 3-Amino-2*H*-azirines Based on the Reaction between Amide Enolates and Diphenyl Phosphorochloridate

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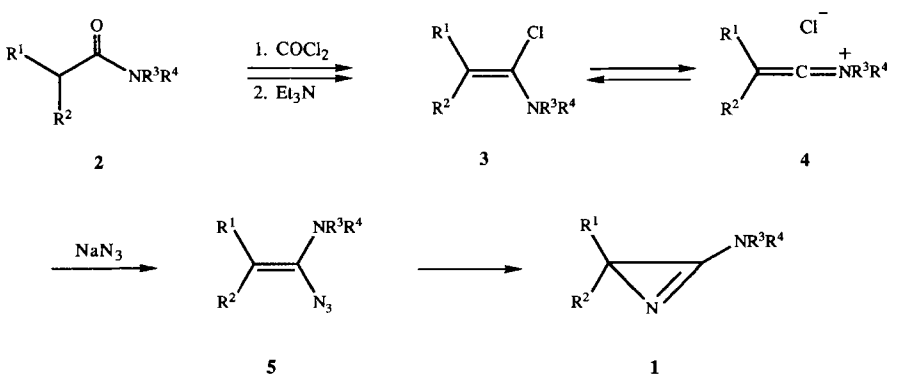
A novel synthesis of 2,2-disubstituted 3-amino-2*H*-azirines based on the reaction between amide enolates and diphenyl phosphorochloridate (DPPCl), followed by treatment with NaN_3 is presented. The yields obtained in general are excellent, and the method is suitable for laboratory-scale preparations as well as for larger amounts.

Introduction. – 3-Amino-2*H*-azirines **1** are known to be valuable synthetic intermediates for a wide variety of applications [1]. *E.g.*, the use of 2,2-disubstituted 3-amino-2*H*-azirines **1** as synthons for α,α-disubstituted amino-acid residues in peptide chemistry [1] [2] as well as in the construction of new heterocyclic systems is of remarkable importance [1] [3–6].

On the other hand, the most general synthesis of 3-amino-2*H*-azirines **1** is based on the method developed by *Rens* and *Ghosez* in 1970 [7]. In this procedure, *N,N*-disubstituted amides of type **2** (R^1–$R^4 \neq H$) are treated with phosgene, followed by base-catalyzed HCl elimination to yield α-chloro-enamines **3**, which are purified by distillation. Reaction with NaN_3 *via* keteniminium salts **4** gives α-azido-enamines **5**, which *in situ* eliminate N_2 to afford **1** [8] [9] (*Scheme 1*).

Scheme 1



2 **3** **4** **5** **1**

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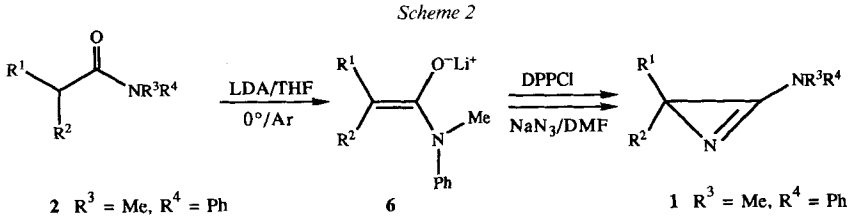
In the case of 2,2-dialkyl-3-(dimethylamino)-2*H*-azirines (**1**, R^1, R^2 = alkyl; R^3, R^4 = Me), reaction with phosgene in CH_2Cl_2 and with NaN_3 in Et_2O or DMF leads to azirines in *ca.* 70% yield. However, for slower-reacting amides **2** (R^1 and/or R^3 = aryl), modified reaction conditions are needed. *E.g.*, in the reaction with phosgene, the corresponding chloro-enamine **3** is formed spontaneously, if *ca.* 5% DMF is added to the CH_2Cl_2 [10] [11]. A second possibility is offered by a route *via* the corresponding thioamides, where HCl elimination to the chloro-enamine occurs without the addition of a base [12]. A slightly modified route has also been used to synthesize C(2)-monosubstituted 3-amino-2*H*-azirines, by saturating the initial amide solution with HCl in order to avoid a second and spontaneous HCl elimination to the corresponding ynamines [13].

Other approaches leading to 3-amino-2*H*-azirines **1**, though they are less general, include, for instance, the thermal decomposition of 4*H*-1,2,3-triazoles [14] [15], photolysis, and thermolysis of isoxazoles [16], and a modified *Neber* reaction [17].

In the '*Ghosez* synthesis', the availability of the starting materials, the relatively low costs of the reagents, together with the high yields generally obtained, and the absence of by-products, render this procedure very attractive, especially suitable for large-scale preparations. However, the need of isolation of sensitive chloro-enamine intermediates **3** and the requirement of special equipment to handle highly toxic phosgene, are serious draw-backs in this synthesis. Therefore, the development of an alternative methodology for the preparation of **1**, that could match the following features, would be of interest: *a*) Easy availability of the starting material. As in the '*Ghosez* synthesis', *N,N*-disubstituted amides of type **2**, would constitute attractive compounds. *b*) Simplification of the required equipment. *c*) Avoiding the use of toxic phosgene and the need of the isolation of the very sensitive chloro-enamine intermediates **3**. *d*) Good overall chemical yields, providing access to new 3-amino-2*H*-azirines. *e*) Suitable procedure for use in laboratory-scale as well as in large-scale preparations.

2. Results and Discussion. – In this context, we wish to present our results concerning the synthesis of 3-amino-2*H*-azirines **1**, based on the reaction of the corresponding amide enolates with diphenyl phosphorochloridate (DPPCl). Thus, when a solution of the corresponding amide **2** (R^3 = Me, R^4 = Ph) in dry THF is treated at 0° under Ar with a base like lithium diisopropylamide (LDA), and, after 1 h, the formed amide enolate **6** is treated at 0° with DPPCl, as smooth reaction takes place leading to the corresponding

Scheme 2

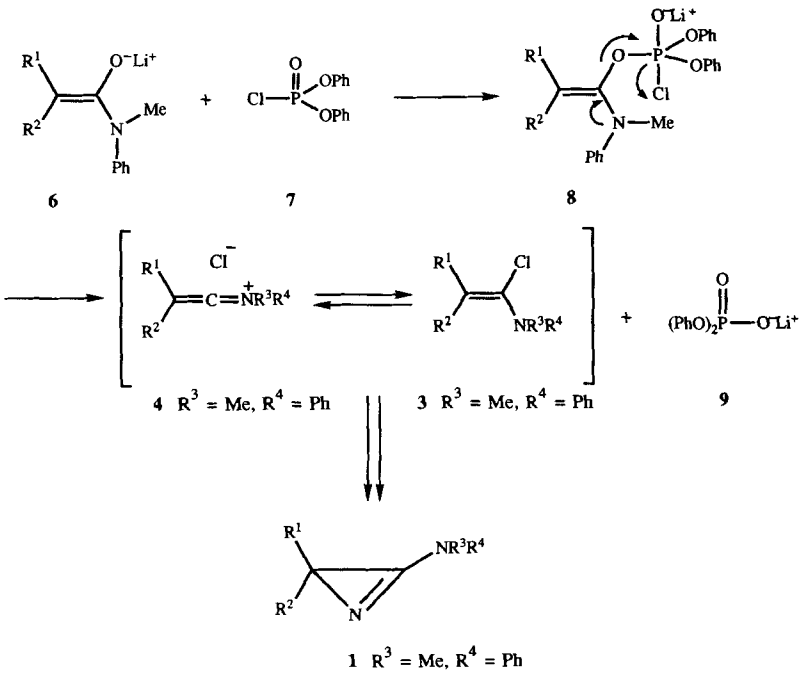


2 R^3 = Me, R^4 = Ph **6** **1** R^3 = Me, R^4 = Ph

chloro-enamines **3** (R^3 = Me, R^4 = Ph). Filtration of the solution containing **3**, under Ar, into a suspension of NaN_3 in dry DMF furnishes after 3–4 days at room temperature 2,2-disubstituted 3-amino-2*H*-azirines **1** (R^3 = Me, R^4 = Ph; *Scheme 2*).

A reaction mechanism is proposed in *Scheme 3*. Formation of the amide enolate **6** by means of LDA[3]) and nucleophilic attack onto the phosphorous reagent **7**, gives the first intermediate **8**, which immediately leads to the keteniminium salt **4** (R^3 = Me, R^4 = Ph) and lithium diphenyl phosphate **9**, a colourless solid, that precipitates from the reaction medium. Treatment of **4** with NaN_3 in DMF then yields the 3-amino-2*H*-azirine **1**[4]).

Scheme 3



In general, 2,2-disubstituted 3-(*N*-methyl-*N*-phenylamino)-2*H*-azirines **1** (R^3 = Me, R^4 = Ph) were obtained in good-to-excellent yields (*Table 1*). Only in the case of **9i**, the yield is lower, probably due to the instability of the amide-enolate intermediate **6i** under these conditions, though in the classical method the yield is similar [10].

The azirines **1a–i**, some of which had previously been synthesized by the phosgene method, were characterized by their spectroscopical data (see *Exper. Part*) and,

[3]) Other bases such as NaHMDS or LiHMDS (sodium or lithium hexamethyldisilazane) have been employed with similar results.

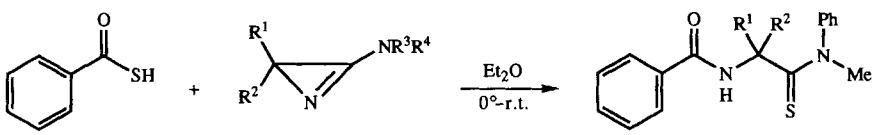
[4]) Since the whole operation is performed under Ar with magnetic stirring, and because there is no need to isolate chloro-enamines **3**, two three-necked reaction vessels, which have their central necks joined by a glass tube fitted with a frit, are used for the reaction. Reaction vessel A contains the corresponding amide **2** and is provided with a septum, through which the solvent and the base are added, and a two-way Y neck for admitting inert Ar. Reaction vessel B contains NaN_3 and is also provided with a septum for adding dry DMF, and is connected by a valve to the vacuum line for the filtration [18]. After the first part of the transformation has been performed, and most of the phosphonate salt **9** has precipitated, the position of the vessels are inverted, and the reaction mixture in vessel A is filtered into the NaN_3/DMF suspension in vessel B which is being vigorously stirred.

Table 1. *Synthesized 2,2-Disubstituted 3-(N-Methyl-N-phenylamino)-2H-azirines* **1** (R^3=Me, R^4=Ph)

1	R^1	R^2	Yield [%]
a	Me	Me	94
b	Me	$PhCH_2$	78
c	Ph	Et	78
d	Ph	Me	90
e	$PhCH_2$	Et	79
f	CH_2=$CHCH_2$	Me	85
g	$-(CH_2)_3-$		86
h	$-(CH_2)_4-$		87
i	$-(CH_2)_5-$		45

chemically, by making use of the smooth reaction of benzothiocarboxylic acid **10** with 2,2-disubstituted 3-amino-2*H*-azirines [10] [11] (*Scheme 4*). The resulting crystalline thioamides **11** can be isolated easily by filtration in analytically and spectroscopically pure form (*Table 2*).

Scheme 4



10 **1** R^3 = Me, R^4 = Ph **11**

Table 2. *Synthesized N-[1-(N-Methyl-N-phenylthiocarbamoyl)alkyl]benzamides* **11**

11	R^1	R^2	Yield [%]	M.p. [°]
a	Me	Me	94	166.6–167
b	Me	$PhCH_2$	94	150–151
c	Ph	Et	75	205–206
d	Ph	Me	82	163–163.8
e	$PhCH_2$	Et	95	128–129
f	CH_2=$CHCH_2$	Me	91	115.6–116
g	$-(CH_2)_3-$		91	155.5–156
h	$-(CH_2)_4-$		93	164–164.7
i	$-(CH_2)_5-$		90	141–142

This last reaction was generally carried out in dry Et_2O by adding **10** to a solution of azirine **1** at 0°. The reaction mixture was then stirred for 5–6 h, whilst raising the temperature from 0° to room temperature.

In summary, a new and convenient method for the synthesis of 2,2-disubstituted 3-(*N*-methyl-*N*-phenylamino)-2*H*-azirines **1** (R^3 = Me, R^4 = Ph) has been developed, which is specially suited for laboratory-scale preparations, although some of the azirines have also been prepared in amounts up to 20 g. Furthermore, this new methodology allows to prepare new types of azirines [19] [20] whose access was limited with the phosgene method. The preparation of 2,2-disubstituted 3-amino-2*H*-azirines in enan-

tiomerically pure form is a major goal in this field, and the use of this procedure has provided promising results [20].

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Experimental Part

General. See [21]. Unless otherwise stated, IR spectra in $CHCl_3$ and ^1H- (300 MHz) and ^{13}C-NMR (50.4 MHz) spectra were recorded in $CDCl_3$. MS: at 70 eV, CI-MS: with 2-methylpropane or NH_3 as carrier gas.

1. *Synthesis of 2,2-Disubstituted 3-(*N*-methyl-*N*-phenylamino)-2*H*-azirines* **1**. *General Procedure.* To a soln. of 10–50 mmol of the corresponding amide **2** in 50–250 ml of dry THF (*ca.* 5 ml/mmol) at 0° and under Ar, 1.1 equiv. of LDA (8–37 ml, 1.5M in cyclohexane, *Aldrich* or *Fluka*) were added. The soln. was stirred at 0° for 60–75 min, then, 1.03 equiv. of DPPCl were added *via* a syringe at 0°. After 20–30 min, the ice bath was removed and the mixture stirred for 20–24 h. The solid which precipitate from the mixture was filtered off under Ar, the THF soln. containing the chloro-enamine **3** was dropped into 5–25 ml of a dry DMF suspension containing 3 equiv. of NaN_3, and the mixture was then stirred for 3–4 days at r.t. Then, Et_2O was added, the mixture filtered through *Celite* pad, and the solvent removed under reduced pressure. The resulting residue was dissolved in Et_2O, washed twice with 5% $NaHCO_3$, and the aq. layer washed with Et_2O. The combined org. layers were dried ($MgSO_4$). Removal of the solvent under reduced pressure and distillation through a *Vigreux* column or in the *Kugelrohr* led to the corresponding 3-amino-2*H*-azirines **1**.

1.1. *2,2-Dimethyl-3-(*N*-methyl-*N*-phenylamino)-2*H*-azirine* (**1a**). From 20.0 g (113 mmol) of *2,*N*-dimethyl-*N*-phenylpropanamide* (**2a**); distillation at 110°/2·10^{-2} Torr: 18.48 g (94%) **1a**. Colorless oil. IR: 3020*w*, 2980*s*, 2950*w*, 2920*w*, 1750*s*, 1600*s*, 1500*s*, 1435*m*, 1425*w*, 1410*w*, 1370*m*, 1330*m*, 1295*w*, 1285*m*, 1235*m*, 1140*w*, 1125*s*, 1100*w*, 1080*w*, 1030*w*, 1000*w*, 950*m*, 890*w*, 690*s*, 665*w*, 635*w*. ^1H-NMR: 7.25–7.15 (*m*, 3 arom. H); 6.9–6.85 (*m*, 2 arom. H); 3.22 (*s*, MeN); 1.23 (*s*, 2 Me). ^{13}C-NMR: 142.4 (*s*, 1 arom. C); 129.3, 122.9, 115.9 (3*d*, 5 arom. CH); 25.4 (*q*, $(CH_3)_2C$). At r.t., C(2), C(3), and MeN could not be detected. CI-MS: 175 (100, $[M + 1]^+$).

1.2. *2-Benzyl-2-methyl-3-(*N*-methyl-*N*-phenylamino)-2*H*-azirine* (**1b**). From 5.0 g (19.7 mmol) of *2-benzyl-*N*-methyl-*N*-phenylpropanamide* (**2b**); distillation at 130°/2·10^{-2} Torr: 3.85 g (78%) **1b**. Slightly yellow oil. IR: 3060*w*, 2980*s*, 2920*m*, 1750*s*, 1600*s*, 1500*s*, 1455*m*, 1420*w*, 1380*m*, 1325*m*, 1275*m*, 1240*m*, 1180*w*, 1160*w*, 1110*s*, 1080*w*, 1055*w*, 1035*m*, 1000*w*, 950*m*, 820*w*, 700*s*, 695*s*, 660*m*, 640*w*. ^1H-NMR ((D$_6$)DMSO/343 K): 7.4–7.05 (*m*, 10 arom. H); 3.24 (*s*, MeN); 2.95 (br. *s*, PhCH_2); 1.34 (*s*, Me). ^{13}C-NMR ((D$_6$)DMSO/343 K): 165.1 (*s*, C=N); 143.2, 137.7 (2*s*, 2 arom. C); 129.2, 128.9, 127.5, 125.7, 122.5, 116.4 (6*d*, 10 arom. CH); 43.9 (*t*, PhCH_2); 35.1 (*q*, MeN); 23.1 (*q*, Me). C(2) could not be detected. CI-MS: 251 (100, $[M + 1]^+$).

1.3. *2-Ethyl-3-(*N*-methyl-*N*-phenylamino)-2-phenyl-2*H*-azirine* (**1c**). From 5.0 g (19.7 mmol) of *N-methyl-2,*N*-diphenylbutanamide* (**2c**); distillation at 120°/2·10^{-2} Torr: 3.85 g (78%) **1c**. Slightly yellow oil. IR: 3020*w*, 2990*s*, 1760*s*, 1600*s*, 1500*s*, 1460*w*, 1395*w*, 1315*w*, 1295*w*, 1260*w*, 1240*w*, 1190*m*, 1165*w*, 1115*m*, 1070*w*, 1050*w*, 1030*w*, 1010*w*, 965*m*, 825*w*, 700*s*, 665*w*, 620*w*. ^1H-NMR ((D$_6$)DMSO/353 K): 7.45–7.0 (*m*, 10 arom. H); 3.42 (*s*, MeN); 2.35–2.1 (2*qd*, J = 7.4, 7.5, CH_2); 0.82 (*t*, J = 7.4, Me). ^{13}C-NMR (235 K): Two conformers: 159.3, 158.3 (*s*, C=N); 142.6, 142.4, 141.7, 141.5 (4*s*, 2 arom. C); 129.3, 129.2, 128.1, 127.8, 126.7, 126.4, 126.1, 126.0, 123.1, 122.7, 116.5, 115.0 (12*d*, 10 arom. CH); 51.5, 50.0 (*s*, C(2)); 37.3, 33.5 (*q*, MeN); 25.5, 25.2 (*t*, CH_2); 12.3, 10.2 (*q*, Me). CI-MS: 251 (100, $[M + 1]^+$).

1.4. *2-Methyl-3-(*N*-methyl-*N*-phenylamino)-2-phenyl-2*H*-azirine* (**1d**). From 5.0 g (20.9 mmol) of *N-methyl-2,*N*-diphenylpropanamide* (**2d**); distillation at 120°/2·10^{-2} Torr: 4.44 g (90%) **1d**. Slightly yellow oil. IR: 3060*w*, 2995*m*, 2920*w*, 1755*s*, 1600*s*, 1505*s*, 1450*m*, 1425*w*, 1390*m*, 1375*m*, 1320*w*, 1290*w*, 1280*w*, 1260*w*, 1190*m*, 1160*w*, 1110*s*, 1080*w*, 1070*w*, 1030*m*, 1010*w*, 965*m*, 915*w*, 895*w*, 700*s*, 660*w*, 645*w*, 635*w*, 625*w*. ^1H-NMR ((D$_6$)DMSO): 7.65–7.05 (*m*, 10 arom. H); 3.35 (*s*, MeN); 1.77 (*s*, Me). ^{13}C-NMR ((D$_6$)DMSO): 162.0 (*s*, C=N); 147.8, 146.1 (2*s*, 2 arom. C); 133.5, 132.3, 130.6, 130.0, 127.1, 119.9 (6*d*, 10 arom. CH); 25.8 (*q*, Me). At r.t., C(2) could not be detected. CI-MS: 237 (100, $[M + 1]^+$).

1.5. *2-Benzyl-2-ethyl-3-(*N*-methyl-*N*-phenylamino)-2*H*-azirine* (**1e**). From 3.0 g (11.2 mmol) of *2-benzyl-*N*-methyl-*N*-phenylbutanamide* (**2e**); distillation at 140°/2·10^{-2} Torr: 2.34 g (79%) **1e**. Slightly yellow oil. IR: 3060*w*, 2970*m*, 2930*w*, 1750*s*, 1600*s*, 1500*s*, 1450*m*, 1420*w*, 1375*w*, 1340*w*, 1320*w*, 1280*w*, 1185*w*, 1160*w*, 1110*s*, 1085*w*,

1030*w*, 1010*w*, 1000*w*, 965*m*, 890*w*, 700*s*, 690*m*, 660*w*. ^{1}H-NMR ((D$_6$)DMSO): 7.5–7.05 (*m*, 10 arom. H); 3.21 (*s*, MeN); 3.0–2.9 (*m*, CH$_2$); 1.78 (br. *d*, *J* = 7, CH$_2$); 0.75–0.65 (br. *t*, Me). ^{13}C-NMR ((D$_6$)DMSO): 163.9 (*s*, C=N); 142.1, 137.9 (2*s*, 2 arom. C); 129.4, 129.0, 127.7, 125.8, 122.5, 116.4 (6*d*, 10 arom. CH); 42.6 (*t*, PhCH$_2$); 27.2 (*t*, CH$_2$); 9.6 (*q*, Me). At r.t., C(2) could not be detected. CI-MS: 265 (100, $[M + 1]^+$).

1.6. *2-Allyl-2-methyl-3-(*N*-methyl-*N*-phenylamino)-2*H*-azirine* (**1f**). From 3.0 g (14.8 mmol) of *2,*N*-dimethyl-*N*-phenylpent-4-enamide* (**2f**); distillation at 135°/2·10^{-2} Torr: 2.51 g (85%) **1f**. Slightly yellow oil. IR: 3070*w*, 2980*s*, 2920*m*, 1755*s*, 1600*s*, 1505*s*, 1450*w*, 1420*w*, 1410*w*, 1375*m*, 1330*m*, 1320*m*, 1290*w*, 1280*w*, 1245*m*, 1175*w*, 1160*w*, 1125*m*, 1110*s*, 1050*w*, 1035*w*, 1000*m*, 960*w*, 920*s*, 690*s*, 665*m*, 620*w*, 610*w*. ^{1}H-NMR: 7.4–7.35 (*m*, 3 arom. H); 7.15–7.05 (*m*, 2 arom. H); 5.71 (br. *s*, CH=); 5.05–5.0 (*m*, CH$_2$=); 3.44 (*s*, MeN); 2.49 (br. *s*, CH$_2$); 1.45 (*s*, Me). ^{13}C-NMR ((D$_6$)DMSO): 165.4 (*s*, C=N); 142.1 (*s*, 1 arom. C); 134.4 (*d*, CH=); 129.1, 122.5 (2*d*, 3 arom. CH); 116.9 (*t*, CH$_2$=); 116.0 (*d*, arom. CH); 42.0 (*q*, MeN); 23.2 (*t*, CH$_2$); 23.2 (*q*, Me). At r.t., C(2) could not be detected. CI-MS: 201 (100, $[M + 1]^+$).

1.7. *2-(*N*-Methyl-*N*-phenylamino)-1-azaspiro[2.3]hex-1-ene* (**1g**). From 2.0 g (10.6 mmol) of *N*-*methyl*-*N*-*phenylcyclobutanamide* (**2g**); distillation at 140°/2·10^{-2} Torr: 1.69 g (86%) **1g**. Slightly yellow oil. IR: 3040*w*, 2990*s*, 1755*s*, 1600*s*, 1500*s*, 1455*w*, 1420*w*, 1390*w*, 1330*m*, 1295*w*, 1285*m*, 1250*s*, 1185*w*, 1110*s*, 1070*m*, 1035*m*, 1010*w*, 930*w*, 890*w*, 835*w*, 690*s*, 675*m*, 665*m*. ^{1}H-NMR: 7.65–7.05 (*m*, 5 arom. H); 3.44 (*s*, MeN); 2.6–2.45, 2.45–2.35, 2.1–1.9 (3*m*, 2 H each). ^{13}C-NMR ((D$_6$)DMSO/353 K): 164.3 (*s*, C=N); 142.0 (*s*, 1 arom. C); 128.7, 122.4, 116.0 (3*d*, 5 arom. CH); 34.3 (*q*, MeN); 33.3 (*t*, 2 CH$_2$); 13.0 (*t*, CH$_2$). C(2) could not be detected. CI-MS: 187 (100, $[M + 1]^+$).

1.8. *2-(*N*-Methyl-*N*-phenylamino)-1-azaspiro[2.4]hept-1-ene* (**1h**). From 5.0 g (24.6 mmol) of *N*-*methyl*-*N*-*phenylcyclopentanamide* (**2h**); distillation at 140°/2·10^{-2} Torr: 4.28 g (87%) **1h**. Colorless oil, that solidifies at 0°. IR: 3040*w*, 2970*s*, 2870*w*, 1750*s*, 1600*s*, 1500*s*, 1450*w*, 1440*w*, 1420*w*, 1330*w*, 1320*w*, 1270*w*, 1270*w*, 1240*w*, 1190*m*, 1160*w*, 1120*w*, 1110*w*, 1095*s*, 1030*m*, 1010*w*, 1000*w*, 970*s*, 815*w*, 690*s*, 660*m*. ^{1}H-NMR ((D$_6$)DMSO): 7.4–7.25 (*m*, 3 arom. H); 7.15–7.05 (*m*, 2 arom. H); 3.34 (*s*, MeN); 1.8–1.4 (*m*, 8 H). ^{13}C-NMR ((D$_6$)DMSO): 160.9 (*s*, C=N); 142.3 (*s*, 1 arom. C); 129.2, 122.4, 115.7 (3*d*, 5 arom. CH); 34.6 (*t*, 2 CH$_2$); 25.4 (*t*, 2 CH$_2$). At r.t., C(2) could not be detected. CI-MS: 201 (100, $[M + 1]^+$).

1.9. *2-(*N*-Methyl-*N*-phenylamino)-1-azaspiro[2.5]oct-1-ene* (**1i**). From 3.0 g (14.0 mmol) of *N*-*methyl*-*N*-*phenylcyclohexanamide* (**2i**); distillation at 135°/2·10^{-2} Torr: 1.34 g (45%) **1i**. Slightly yellow oil. IR: 3000*m*, 2970*m*, 2940*s*, 2860*m*, 1750*s*, 1600*s*, 1500*s*, 1450*m*, 1425*w*, 1390*w*, 1360*w*, 1320*w*, 1300*w*, 1285*m*, 1260*m*, 1240*w*, 1190*s*, 1160*m*, 1115*w*, 1095*w*, 1070*w*, 1025*m*, 1010*w*, 940*s*, 900*w*, 690*s*, 660*w*. ^{1}H-NMR: 7.45–7.05 (*m*, 5 arom. H); 3.45 (*s*, MeN); 2.0–1.2 (*m*, 10 H). ^{13}C-NMR ((D$_6$)DMSO): 166.9 (*s*, C=N); 142.2 (*s*, 1 arom. C); 128.5, 122.3, 116.5 (3*d*, 5 arom. CH); 34.9, 24.9, 24.2 (3*t*, 5 CH$_2$). At r.t., C(2) could not be detected. CI-MS: 215 (100, $[M + 1]^+$).

2. *Synthesis of* N-*[1-(*N*-Methyl-*N*-phenylthiocarbamoyl)alkyl]benzamides* **11**. *General Procedure.* To a well stirred soln. of 1.0–2.5 mmol of the corresponding **1** in 4–6 ml of dry Et$_2$O, 1 equiv. of *thiobenzoic acid* (**10**) was added at 0°. The mixture was allowed to react for 8–10 h raising the temp. from 0° to r.t. Then, the formed solid was filtered off, washed with hexane/Et$_2$O and dried in high vacuum.

2.1. N-*[1-Methyl-1-(*N*-methyl-*N*-phenylthiocarbamoyl)ethyl]benzamide* (**11a**). From 348 mg (2.0 mmol) of **1a**: 574 mg (92%) **11a**. Colorless powder. M.p. 166.6–167.5°. IR (KBr): 3290*m*, 3030*w*, 3005*m*, 2985*w*, 2935*w*, 1640*s*, 1605*w*, 1580*m*, 1540*s*, 1490*s*, 1460*m*, 1435*s*, 1380*m*, 1360*s*, 1310*s*, 1260*m*, 1215*w*, 1175*w*, 1160*w*, 1100*s*, 1075*m*, 1025*w*, 1020*w*, 1005*w*, 995*w*, 890*w*, 875*w*, 800*w*, 770*m*, 705*s*, 690*m*, 650*m*, 630*w*, 615*w*. ^{1}H-NMR: 7.65–7.15 (*m*, 10 arom. H, NH); 3.74 (*s*, MeN); 1.76 (*s*, 2 Me). ^{13}C-NMR: 208.8 (*s*, C=S); 165.2 (*s*, C=O); 147.3, 134.9 (2*s*, 2 arom. C); 131.2, 129.4, 128.2, 128.1, 126.8, 126.1 (6*d*, 10 arom. CH); 62.8 (*s*, C(1')); 51.3 (*q*, MeN); 29.4 (*q*, 2 Me). CI-MS: 313 (100, $[M + 1]^+$). Anal. calc. for $C_{18}H_{20}N_2OS$ (312.42): C 69.19, H 6.45, N 8.96, S 10.26; found: C 69.35, H 6.30, N 9.20, S 10.41.

2.2. N-*[1-Methyl-1-(*N*-methyl-*N*-phenylthiocarbamoyl)-2-phenylethyl]benzamide* (**11b**). From 375 mg (1.5 mmol) of **1b**: 547 mg (94%) **11b**. Colorless powder. M.p. 150–151°. IR (KBr): 3430*m*, 3325*m*, 3050*w*, 3020*w*, 2920*w*, 1650*s*, 1600*m*, 1590*m*, 1580*m*, 1535*m*, 1510*s*, 1490*s*, 1450*m*, 1430*m*, 1355*s*, 1310*m*, 1250*w*, 1230*w*, 1200*w*, 1180*w*, 1140*w*, 1105*s*, 1085*m*, 1070*m*, 1050*w*, 1030*w*, 1000*w*, 985*w*, 950*w*, 930*w*, 9000*w*, 800*w*, 770*m*, 760*m*, 755*s*, 700*s*, 690*s*, 640*m*, 625*m*. ^{1}H-NMR ((D$_6$)DMSO): 7.6–7.05 (*m*, 15 arom. H, NH); 3.69 (*s*, PhC*H*$_2$); 3.53 (*s*, MeN); 1.54 (*s*, Me). ^{13}C-NMR: > 200 (*s*, C=S); 165.9 (*s*, C=O); 147.5, 136.7, 134.8 (3*s*, 3 arom. C); 131.2, 130.6, 129.2, 128.2, 128.1, 127.9, 126.8, 125.9, 125.9 (9*d*, 15 arom. CH); 65.8 (*s*, C(1')); 51.4 (*q*, MeN); 45.8 (*t*, PhC*H*$_2$); 26.9 (*q*, Me). CI-MS: 389 (100, $[M + 1]^+$). Anal. calc. for $C_{24}H_{24}N_2OS$ (388.52): C 74.19, H 6.22, N 7.21, S 8.25; found: C 74.15, H 6.23, N 7.30, S 8.19.

2.3. N*[1-(*N*-Methyl-*N*-phenylthiocarbamoyl)-1-phenylpropyl]benzamide* (**11c**). From 500 mg (2.0 mmol) of **1c**: 585 mg (75%) **11c**. Colorless powder. M.p. 206°. IR (KBr): 3210*s*, 3060*w*, 3000*m*, 2960*m*, 2930*w*, 1660*s*, 1600*m*,

1575*m*, 1510*s*, 1480*s*, 1460*s*, 1430*s*, 1370*s*, 1340*m*, 1320*m*, 1300*m*, 1280*m*, 1245*m*, 1200*m*, 1170*m*, 1150*m*, 1130*m*, 1120*m*, 1105*m*, 1090*m*, 1075*m*, 1060*m*, 1030*m*, 1005*m*, 990*m*, 965*w*, 925*m*, 900*m*, 8490*w*, 805*w*, 775*s*, 705*s*, 690*s*, 645*w*, 610*m*. ^{1}H-NMR: 7.9–7.85 (*m*, 2 arom. H); 7.5–7.1 (*m*, 12 arom. H); 6.75 (br. *s*, 1 arom. H); 5.68 (*s*, NH); 3.73 (*s*, MeN); 3.16, 2.22 (2 br. *s*, CH_3CH_2); 1.00 (br. *s*, CH_3CH_2). ^{13}C-NMR: > 200 (*s*, C=S); 163.0 (*s*, C=O); 142.51, 142.50, 135.4 (3*s*, 3 arom. C); 131.0, 128.7, 128.6, 128.5, 128.3, 127.8, 127.2, 127.0, 125.5 (9*d*, 15 arom. CH); 68.4 (*s*, C(1′)); 52.2 (*q*, MeN); 24.4 (*t*, CH_3CH_2); 8.4 (*q*, CH_3CH_2). CI-MS: 389 (100, $[M + 1]^+$), 371 (84), 279 (41), 268 (22), 238 (25). Anal. calc. for $C_{24}H_{24}N_2OS$ (388.52): C 74.19, H 6.22, N 7.21, S 8.25; found: C 74.38, H 6.33, N 7.07, S 8.15.

2.4. N-*[1-(*N-*Methyl*-N-*phenylthiocarbamoyl)-1-phenylethyl]benzamide* (**11d**). From 354 mg (1.5 mmol) of **1d**: 460 mg (82%) **11d**. Slightly yellow powder. M.p. 163.1–163.8°. IR (KBr): 3220*w*, 3060*w*, 3020*w*, 2930*w*, 1650*s*, 1600*w*, 1580*m*, 1495*s*, 1480*s*, 1460*s*, 1440*s*, 1375*s*, 1365*s*, 1285*m*, 1240*m*, 1220*w*, 1180*m*, 1150*m*, 1105*m*, 1090*m*, 1070*m*, 1055*m*, 1025*w*, 1000*w*, 975*m*, 920*m*, 850*w*, 800*w*, 770*m*, 700*s*, 665*w*, 650*w*, 610*m*. ^{1}H-NMR: 7.9–7.85 (*m*, 2 arom. H); 7.45–7.1 (*m*, 12 arom. H); 6.75 (br. *s*, 1 arom. H); 5.85 (br. *s*, NH); 3.75 (*s*, MeN); 2.20 (br. *s*, Me). ^{13}C-NMR: > 200 (*s*, C=S); 162.8 (*s*, C=O); 141.9, 135.2 (2*s*, 2 arom. C); 130.8, 128.0, 127.6, 127.4, 126.8, 126.7, 126.6, 126.2, 126.1 (9*d*, 15 arom. CH); 64.8 (*s*, C(1′)); 52.5 (*q*, MeN); 22.4 (*q*, Me). CI-MS: 375 (100, $[M + 1]^+$). Anal. calc. for $C_{23}H_{22}N_2OS$ (374.49): C 73.76, H 5.92, N 7.48, S 8.56; found: C 73.53, H 5.79, N 7.43, S 8.31.

2.5. N-*[1-Benzyl-1-(*N-*methyl*-N-*phenylthiocarbamoyl)propyl]benzamide* (**11e**). From 300 mg (1.4 mmol) of **1e**: 433 mg (95%) **11e**. Colorless powder. M.p. 128–129°. IR (KBr): 3240*m*, 3040*w*, 3020*w*, 2970*w*, 2930*w*, 2880*w*, 1640*s*, 1600*m*, 1590*m*, 1580*m*, 1550*s*, 1510*m*, 1490*s*, 1460*s*, 1445*s*, 1430*m*, 1365*s*, 1325*m*, 1290*m*, 1250*w*, 1220*w*, 1170*w*, 1150*w*, 1100*m*, 1080*m*, 1070*m*, 1030*w*, 1000*w*, 990*w*, 970*w*, 945*w*, 925*w*, 885*w*, 830*w*, 810*w*, 800*w*, 780*w*, 750*w*, 705*s*, 695*s*, 645*w*, 620*w*. ^{1}H-NMR: 7.67 (br. *s*, 2 arom. H); 7.5–7.15 (*m*, 13 arom. H, NH); 3.96, 3.81 (br. 2*s*, CH_2); 3.80 (*s*, MeN); 3.39 (*d*, J = 14, 1 H); 2.65 (br. *s*, 1 H); 0.94 (*t*, J = 7.1, CH_3CH_2). ^{13}C-NMR: 205.9 (*s*, C=S); 165.2 (*s*, C=O); 143.5, 136.8, 135.8 (3*s*, 3 arom. C); 131.0, 129.9, 129.6, 128.7, 128.3, 127.9, 126.9, 126.5, 126.0 (9*d*, 15 arom. CH); 70.0 (*s*, C(1′)); 57.5 (*q*, MeN); 41.2 (*t*, $PhCH_2$); 27.9 (*t*, CH_3CH_2); 8.0 (*q*, CH_3CH_2). CI-MS: 403 (100, $[M + 1]^+$). Anal. calc. for $C_{25}H_{26}N_2OS$ (402.55): C 74.59, H 6.51, N 6.95, S 7.96; found: C 74.40, H 6.48, N 7.20, S 8.21.

2.6. N-*[1-Methyl-1-(*N-*methyl*-N-*phenylthiocarbamoyl)but-3-enyl]benzamide* (**11f**). From 200 mg (1.0 mmol) of **1f**: 307 mg (91%) **11f**. Colorless powder. M.p. 115.6–116°. IR (KBr): 3390*m*, 3065*w*, 3000*w*, 2980*w*, 1660*s*, 1580*m*, 1560*w*, 1515*s*, 1485*s*, 1465*m*, 1430*m*, 1365*s*, 1310*m*, 1295*m*, 1260*w*, 1240*m*, 1190*w*, 1070*w*, 1160*w*, 1140*w*, 1100*s*, 1075*w*, 1045*w*, 1030*w*, 1000*m*, 945*w*, 920*m*, 895*w*, 855*w*, 845*w*, 805*w*, 770*m*, 730*m*, 700*s*, 650*w*, 625*w*. ^{1}H-NMR: 7.65–7.6 (*m*, 2 arom. H); 7.5–7.2 (*m*, 8 arom. H, NH); 5.8–5.65 (*m*, CH(3′)); 5.1–5.05 (*m*, CH_2(4′)); 3.75 (*s*, MeN); 3.34, 2.79 (2*dd*, J = 7.2, 7.5, CH_2(2′)); 1.73 (*s*, Me). ^{13}C-NMR: 207.6 (*s*, C=S); 165.0 (*s*, C=O); 145.0, 135.1 (2*s*, 2 arom. C); 133.2, 131.2, 129.4, 128.5, 126.8 (5*d*, 10 arom. CH); 126.2 (*d*, C(3′)); 118.9 (*t*, C(4′)); 65.0 (*s*, C(1′)); 51.6 (*q*, MeN); 42.8 (*t*, C(2′)); 26.6 (*q*, Me). CI-MS: 339 (100, $[M + 1]^+$). Anal. calc. for $C_{20}H_{22}N_2OS$ (338.46): C 70.97, H 6.55, N 8.27, S 9.47; found: C 70.48, H 6.34, N 8.22, S 9.68.

2.7. N-*[1-(*N-*Methyl*-N-*phenylthiocarbamoyl)cyclobutyl]benzamide* (**11g**). From 400 mg (2.2 mmol) of **1g**: 637 mg (91%) **11g**. Colorless powder. M.p. 155.5–156.2°. IR (KBr): 3270*s*, 3050*w*, 3000*w*, 2940*m*, 1635*s*, 1600*w*, 1580*m*, 1530*s*, 1490*s*, 1460*m*, 1430*m*, 1370*s*, 1310*m*, 1290*m*, 1235*w*, 1175*w*, 1155*w*, 1120*m*, 1090*m*, 1070*m*, 1020*w*, 1005*w*, 930*w*, 860*w*, 800*m*, 870*m*, 715*s*, 705*s*, 645*w*, 630*m*, 615*w*. ^{1}H-NMR: 7.5–7.45 (*m*, 3 arom. H); 7.45–7.35 (*m*, 2 arom. H); 7.3–7.25 (*m*, 3 arom. H); 7.05–7.0 (*m*, 2 arom. H); 5.77 (*s*, NH); 3.70 (*s*, MeN); 3.25–3.2 (*m*, 2 H); 2.05–1.85 (*m*, 4 H). ^{13}C-NMR: > 200 (*s*, C=S); 165.7 (*s*, C=O); 146.5, 139.8 (2*s*, 2 arom. C); 131.5, 129.4, 128.3, 127.9, 126.8, 125.8 (6*d*, 10 arom. CH); 65.5 (*s*, C(1′)); 49.0 (*q*, MeN); 36.6, 15.4 (2*t*, 3 CH_2). CI-MS: 325 (100, $[M + 1]^+$). Anal. calc. for $C_{19}H_{20}N_2OS$ (324.44): C 70.33, H 6.21, N 8.63, S 9.88; found: C 70.52, H 6.39, N 8.76, S 9.76.

2.8. N-*[1-(*N-*Methyl*-N-*phenylthiocarbamoyl)cylopentyl]benzamide* (**11h**). From 500 mg (2.5 mmol) of **1h**: 790 mg (93%) of **11h** as slightly yellow solid. M.p. 164–164.7°. IR (KBr): 3400*s*, 3060*w*, 2960*m*, 2870*w*, 1655*s*, 1580*m*, 1510*s*, 1485*s*, 1450*s*, 1430*s*, 1365*s*, 1305*m*, 1280*s*, 1245*m*, 1200*m*, 1170*m*, 1160*w*, 1125*s*, 1100*s*, 1070*m*, 1025*m*, 1000*m*, 950*w*, 920*w*, 845*w*, 800*w*, 780*m*, 720*s*, 710*s*, 640*w*, 625*m*. ^{1}H-NMR: 7.5–7.3 (*m*, 5 arom. H); 7.15–7.05 (*m*, 5 arom. H); 5.36 (br. *s*, NH); 3.72 (*s*, MeN); 2.95–2.85, 2.1–2.05, 1.95–1.85, 1.65–1.6 (4*m*, each 2 H). ^{13}C-NMR: > 200 (*s*, C=S); 165.3 (*s*, C=O); 147.5, 134.0 (2*s*, 2 arom. C); 131.4, 129.2, 128.2, 127.6, 126.7, 125.5 (6*d*, 10 arom. CH); 72.6 (*s*, C(1′)); 50.4 (*q*, MeN); 43.5, 24.7 (2*t*, 4 CH_2). CI-MS: 339 (100, $[M + 1]^+$). Anal. calc. for $C_{20}H_{22}N_2OS$ (338.46): C 70.97, H 6.55, N 8.27, S 9.47; found: C 70.97, H 6.41, N 8.35, S 9.55.

2.9 N-*[1-(*N-*Methyl*-N-*phenylthiocarbamoyl)cyclohexyl]benzamide* (**11i**). From 500 mg (2.3 mmol) of **1i**: 820 mg (90%) **11i**. Slightly yellow solid. M.p. 141–142°. IR: 3450*w*, 3060*w*, 2930*s*, 2860*m*, 1670*s*, 1600*w*, 1580*w*, 1510*s*, 1485*s*, 1465*s*, 1435*m*, 1370*s*, 1290*m*, 1270*w*, 1240*w*, 1110*s*, 1075*w*, 1060*w*, 1030*w*, 1005*w*, 970*w*, 920*w*, 860*w*, 705*s*, 660*w*, 640*w*, 620*w*. ^{1}H-NMR: 7.5–7.4 (*m*, 3 arom. H); 7.35–7.3 (*m*, 2 arom. H); 7.15–7.0 (*m*, 5 arom. H); 5.36 (br. *s*,

NH); 3.70 (*s*, MeN); 2.55–2.4 (*m*, 2 CH_2); 1.7–1.6 (*m*, CH_2); 1.3–1.2 (*m*, 2 CH_2). ^{13}C-NMR: 208.9 (*s*, C=S); 165.04 (*s*, C=O); 147.6, 134.2 (2*s*, 2 arom. C); 131.3, 129.2, 128.1, 127.3, 126.5, 125.0 (6*d*, 10 arom. CH); 65.7 (*s*, C(1')); 51.0 (*q*, MeN); 36.8, 24.6, 21.9 (3*t*, 5 CH_2). CI-MS: 353 (100, $[M + 1]^+$). Anal. calc. for $C_{21}H_{24}N_2OS$ (352.50): C 70.97, H 6.55, N 8.27, S 9.47; found: C 70.97, H 6.41, N 8.35, S 9.55.

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