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ACYLATED 2,2-DIMETHYLAZIRIDINES:[1] REGIOSELECTIVITY OF RING OPENING BY SODIUM THIOPHENOLATE; BORDERLINE S_N2 DUE TO PLANARIZATION OF NITROGEN PYRAMID

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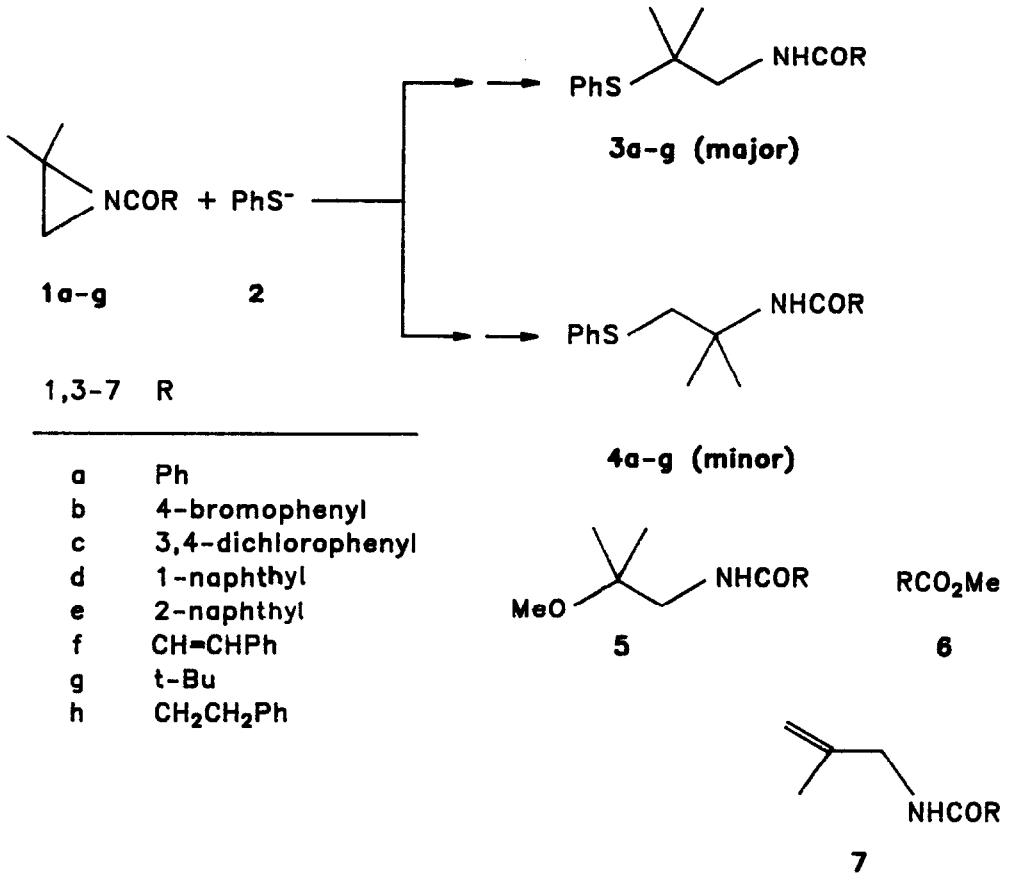
Key Words: aziridines; nucleophilic attack; preferred abnormal opening; leaving group quality of N-acylaziridines; planation of N pyramid.

Abstract - 2,2-Dimethylaziridines **1** carrying a COR group on nitrogen are opened by $PhS^{\ominus}$ with a regioselectivity RS = abnormal:normal $\geq$ 20 in MeOH and 5-16 in THF. Practically no influence of COR on RS was found except for the poorest oxidant **1g** (R = tBu) that gave the highest RS (95, MeOH). This rules out an SET mechanism for the abnormal opening. Absence of homolytic ring opening is directly shown by the failure to detect products resulting from cyclization of a homolytically formed radical when COR is cinnamoyl (**1f**). Direct nucleophilic attack is indicated by suppression of any reaction with $PhS^{\ominus}$ when the steric hindrance is increased (N-benzoylaziridine **13**). The observed S_N2 borderline behaviour with **1** is explained by reaction in a flattened nitrogen conformation of the otherwise poorly reactive **1**. Carboxamide resonance in this (nearly) planar conformation generates a substantial positive charge on N which will shift the mechanism closer to S_N1 by partial heterolysis of the N-CMe_2 bond prior to attack by $PhS^{\ominus}$.

Ring opening of N-acylated 2,2-dimethylaziridine **1** by nucleophiles **Nu** in absence of acids proceeds[2-4] with apparent attack on the tertiary carbon of the aziridine ring ("abnormal opening"). No "normal" attack on the unsubstituted carbon has been observed so far. A sterically non-demanding single electron transfer (SET) mechanism has been proposed[2] to account for this behaviour and was recently[5] verified in reactions with the trityl anion. In the proposed mechanism an electron is transferred from **Nu** to **1** generating the ketyl of **1**. This step will depend both on the reduction potential of **1** and on the oxidation potential of **Nu**. Representative values for the former have recently[6] been published which make the SET step for many **Nus** thermodynamically very unfavourable as e. g. for amines whose reaction with **1** moreover was found to be rather sensitive to steric hindrance[3]. Thus, an alternative mechanism may exist in addition to SET.



Scheme 1

To investigate this possibility we studied reactions between thiophenolate ion **2** and various aziridines **1**. We hoped to find out whether ring opening of **1** by this moderately reducing[7] **Nu** is regiospecific or only highly regioselective. The latter finding would allow a search for factors which influence the quantitative ratio of isomeric products. **2** as strong and sterically undemanding **Nu** might be a good candidate for a non-SET attack. With **2** a search for the hitherto missing normal product in a large excess of the main product would neither suffer from secondary reactions nor from complicated ^{1}H NMR spectra, crucial signals arising from opened **1** only. Finally, the possibility to independently synthesize the "normal" product **4** would allow to detect and to identify even traces of **4** by comparison with authentic material.

Table 1. Reactions of **1** with thiophenolate **2**.

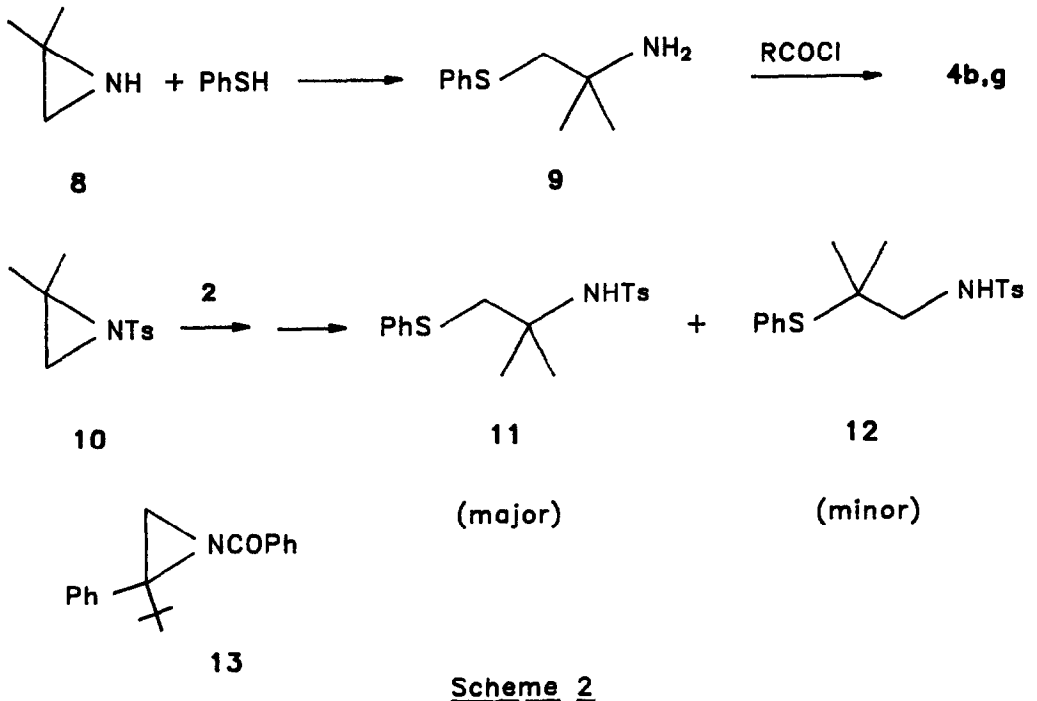
run	mmol of Na	Naph[c]	PhSH	**1**		ml MeOH	ml THF	time days	% of products[a,b] **3**	**4**	**5**	**6**	**7**
1	5		10	5	**1a**	50		8	58	1.4	15		7
2	5		7	5	**1a**	20		8	39	1.3	3	18	2
3	5		10	5	**1b**	40		8	59	3	16		6
4	3.4		5	3.4	**1b**	40		8	47	1.4	4	11	4
5	3		2.9	1.4	**1c**	30		0.8	48	1.6			(tr)
6	5		10	3.9	**1g**	20		8	38	0.4	29		12
7	10		15	5	**1g**	20		4	(40)	(tr)	(25)		(21)
8	20	20	20	5	**1a**		100	18	74	10			0
9	20	20	25	5	**1a**		110	8	69	10			0
10	3	2.9	2.9	1.43	**1c**		30	0.8	48	3			(3)
11	4.4	4.4	4.4	2.22	**1d**		40	7	68	6			(tr)
12	4.4	4.4	4.4	2.22	**1e**		40	7	72	6			
13	20	20	20	5	**1f**		100	18	63	11			8
14	20	20	25	5	**1f**		115	8	57	12			3

[a] Yields in parentheses are from ^{1}H NMR analysis.
[b] tr = trace.
[c] Naph = naphthalene, required to generate naphthalenide which was employed for the deprotonation of PhSH in THF.

REGIOSELECTIVITY (RS) OF RING OPENING BY 2: RESULTS AND DISCUSSION

Absence or presence of $NHCH_2$ coupling was a simple and reliable means of distinction between structures **3** and **4** in reactions of **2** with **1a-g** (Table 1). A further means were the chemical shifts of CMe_2: 1.23-1.36 ppm for **3** and 1.42-1.62 ppm for **4**. In all runs **3** was the main product but was always accompanied by **4**. Both products could at least partially be separated from one another by column chromatography. **4b** and **4g** were independently synthesized (Scheme 2) starting from thiophenol and the aziridine base **8** (comp. ref.[8]). Ring opening of in situ protonated **8** by in situ generated **2** (pK_a ca. 9 for both reactants) yielded exclusively the "normal" product **9**. Reaction of **9** with p-bromobenzoyl chloride or pivaloyl chloride provided **4b** or **4g**, respectively.

In methanol (runs 1-7) yields of **4** were ≤3% as compared to around 50% of **3**. Except for the pivaloylaziridine **1g**, a significant influence of the acyl group in **1** on the yields or on the regioselectivity of opening (RS =



Scheme 2

"abnormal":"normal" = 3:4) was not detectable. RS was 20-41 for the aroyl aziridines and 95 (run 6) for **1g**. The SET mechanism as well as an electron withdrawing influence of COR should give a high RS for **1c** (not found in run 5) and a particular low RS for **1g**. No **3** can have been lost by conversion into **5** or **7** since **3a** proved to be stable toward **2** (9 days) as well as toward methoxide (7 days) without formation of any **5a** or **7a**.

The general switch[2] in RS from $\gg 1$ to $\ll 1$ on going from acyl activation to sulfonyl activation was verified by reaction of **2** with the tosylaziridine **10** in methanol (Scheme 2). The product (96%) was mainly **11** excluding an exceptional behaviour of **2**. The ^{1}H-NMR spectrum (300 MHz) revealed 6% admixture of the "abnormal" product **12** by comparison (signals of CMe_2, Me of Ts, NCH_2) with an authentic sample that had been isolated from a complex product mixture which formed in a very slow reaction (3 months) when **10** was dissolved in an excess of thiophenol. In contrast to **1**, the formation of both isomeric products from **10** is not novel.[4d,4e,9]

What is the reason for the observed RS with **1**? Formation of the minor product **4** is compatible with common S_N2. Exclusively abnormal opening of

1 has been found in fast reactions catalyzed by a strong acid.[9] The introduced double activation[9] (positive charge on N) is strong enough to generate a carbenium ion which is intramolecularly trapped by the oxygen of **1**. This S_N1 path requires that only extremely poor nucleophiles are present.[10] In a primary or secondary alcohol as solvent, double activation had rapidly formed ethers of type **5** (main products) by nucleophilic attack of a solvent molecule on the loosened (borderline S_N2) tertiary carbon of protonated **1** (pK_a estimated <-3).[9] However, double activation cannot play an important role in runs 1-7 of Table 1. Buffering of thiophenol by its conjugate base **2** decreases the effective acidity of the medium. The concentrations of free thiophenol are low and decrease with the progress of the reaction since each N-anion of **3** or **4**, that is formed from **1** and **2**, deprotonates one molecule of thiophenol. Moreover, in run 5 there was no free thiophenol from the very beginning. A substantial influence of thiophenol and/or the solvent methanol was definitely excluded in runs 8-14 by using the solvent THF without free thiophenol. Here, the yields of **4** generally increased only slightly (up to a maximum of 12% in run 14) without a corresponding increase in **3**: RS was between 5 (run 14) and 16 (run 10) as compared to 20-41 (95 for **1g**) in methanol. A direct comparison with the methanol results is possible with **1a,c**. For **1a** RS was 41 (run 1) or 30 (run 2) in methanol and 7 (run 8 and 9) in THF, for **1c** it was 30 and 16, respectively. This change is not dramatic and its significance may appear questionable with respect to the experimental precision. Twice, a THF run was repeated with an excess of free thiophenol: runs 9 and 14. Run 9 had practically the same result as run 8 without free thiophenol. The result of run 14 differed only slightly from run 13 without free thiophenol. Both pairs of runs (8/9, 13/14) show that free thiophenol can only slightly increase the yield of **3** at best.

A correlation with the activating power of RCO or leaving group (LG) quality of RCON as measured by the pK_a of RCO_2H[11] is not detectable: **1d** 3.60; **1c** 3.64; **1b** 3.96; **1e** 4.14; **1a** 4.20; **1f** 4.42; **1g** 5.04. Since RCO of **1d-f** can be reduced to the ketyl more easily than COR of **1a,b** (for **1a,f** comp. ref.[6]) and even much more easily[6] than COR of **1g**, an SET pathway to **3** is very unlikely. An even stronger argument against SET is the failure to detect any cyclized product in runs 13 and 14. SET to **1f** must lead to the radical $RCON^{\ominus}CH_2CMe_2^{\cdot}$ which is intramolecularly trapped by the double bond ending up in pyrrolidone structures (comp. ref.[12]). Finally, **2** did not at all react with **13** (methanol, 30 days). Aziridines **1a** and **13** differ significantly only in the shielding of the aziridine ring against nucleophilic attack but not in the reducibility (comp. ref.[5]).

SET and acid catalysis is ruled out in the present case. The strong dependence on activation by acyl or sulfonyl attributes the mechanistic problem to the RCON structure and an inherent peculiarity of it since the RSO_2N structure leads to S_N2 compatible behaviour. In general, regioselectivity and rate of ring opening of aziridines can depend on the LG quality of its nitrogen as consequence of the substituent[9], on the flatness or inversion of the nitrogen pyramid[9,13], on steric[9,14] and benzylic[9,14,15] effects. Estimating the LG capacity from the pK_a values of RSO_2NH_2 (10-12) and $RCONH_2$ (estimated 15-18 in an alcoholic solution[16], probably higher in THF) ignores the non-planar structure[9] of N-acylaziridines. Anions of sulfonamides can be expected to prefer conformations similar to sulfonamides which form a rather flat and variable pyramid.[17] There will be no great conformational and energetic difference between a common sulfonamide anion and the LG displaced from an N-sulfonylaziridine in the inversional ground state (IGS) of the latter. The respective difference between a common carboxamide anion, being strictly planar, and the LG displaced from an N-acylaziridine in its IGS will be large, making

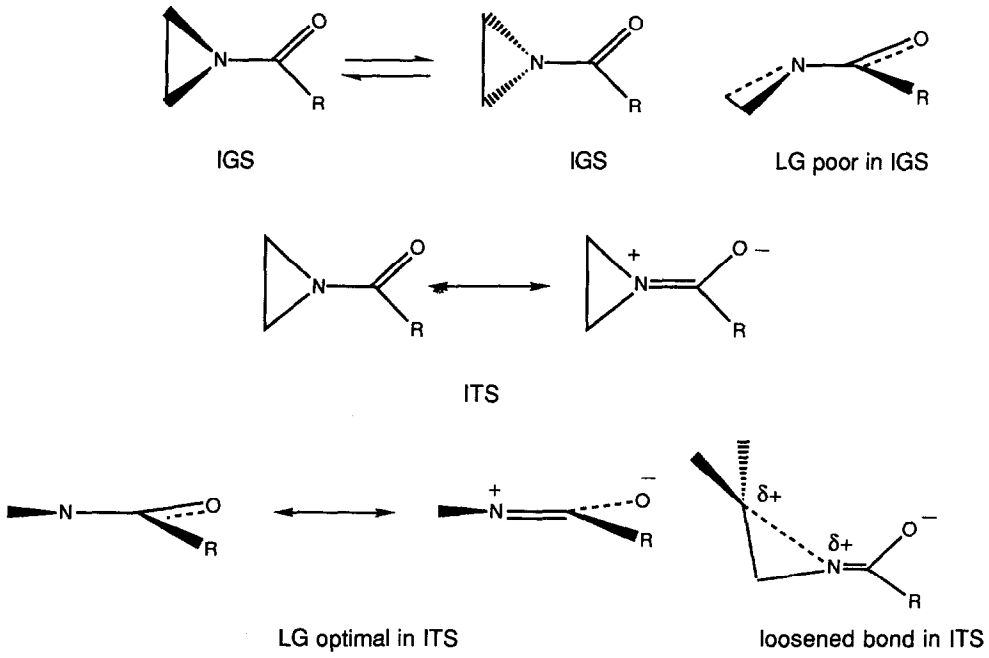


Figure 1. Effect of nitrogen planation

the LG much poorer than estimated from a pK_a of $RCONH_2$. The IGS reactivity of an N-acylaziridine must be very poor. However, its reactivity will enormously increase in or near the planar transition state of inversion (ITS, Figure 1). This follows from the higher ring strain and more so from a probably dramatic increase in LG quality. This enhanced reactivity should influence the regioselectivity of ring opening. In the ITS the RCON group, which is ketone like in the IGS, will become a real carboxamide with a pronounced partial charge on the nitrogen thus approaching double activation (Figure 1). The positive charge should preferrably loosen the $N-CMe_2$ bond resulting in abnormal opening by nucleophilic attack on the loosened tertiary carbon. This hypothesis would also apply to activation by dinitrophenyl.[2,3] The proposed "planarization effect" must profit from hydrogen bonding that lowers the energy of the dipolar ITS. This can explain the decrease of RS on going from the solvent methanol to THF. The normal opening to **4** may be the result of a displacement in or near the IGS. This is compatible with the high RS for **1g** since the nitrogen inversion of **1g** should be accelerated by a sterically flattened IGS and more so by an increased resonance stabilization of the ITS. In contrast to **1a-f** the carbonyl of **1g** is not conjugated with R.

THE BY-PRODUCTS

The methyl ethers **5** are formed in a slow reaction (long term runs 1-4 and 6) of **1** with the solvent (comp. ref.[9]). In a control experiment **1a** gave quantitatively **5a** after 8 days in methanol. An acidic catalysis by methanol was indicated by ^{1}H-NMR experiments in which the stronger base **1g** reacted faster with tetradeuteriomethanol than **1a**: after 21 hours at 28°C (and further two days at room temperature) the conversion of **1** to deuterated **5** was 90% (complete) for **1g** but only 50% (64%) for **1a**. An experiment with **1c** in methanol (2 days, room temperature: 17% **1c**, 31% **5c**, 52% **6c**) confirmed the expected inverse dependence of basicity and carbonyl reactivity on the electron withdrawing power of the acyl group in **1**.

The methyl esters **6** are produced by the reaction of **1** with methoxide (comp. ref.[9]) which arises from the N-anions of **3** and **4** in runs 2 and 4 as soon as the excess of thiophenol has been converted to **2**. The combined experimental yields (40% and 48%) of **3** and **4** in both runs agree well with the yields (40% and 47% thioethers) expected from the excess of thiophenol. This generation of methoxide in the absence of free thiophenol must depend on the acidities of **3** and **4**. Relative acidities for **3a**, **4a**, **3b**, **4b** and methanol can be estimated from values[16] for $RCONH_2$ in isopropanolic

solution when one considers the statistical effect (2:1) and the acidity lowering effect of an alkyl group: **3a**, **4a** < **3b**, **4b** ≈ MeOH < **3c**, **4c**. This sequence is in accord with the results of runs 1-7. A further discussion of the by-products is given in ref.[18].

EXPERIMENTAL

^{1}H-NMR spectra (90 MHz, 250 MHz, 300 MHz, 200 MHz, 60 MHz, $CDCl_3$, internal TMS): Bruker HX 90E, WM 250, AC 300, AC 200 or Varian A 60A. Chemical shifts are given in ppm, coupling constants in Hz, multiplicities as: s, d, t, m, m_c (m centred at). Mass spectra: Varian MAT 311A at 80 eV. m/e and (r. i.)$_c$= relative intensity are given.

All runs were conducted at room temperature in dry solvents under nitrogen which was free from air and moisture. Column chromatography (column dimensions given in cm): silica gel Merck 0.063-0.2 mm.

Starting Materials

Aziridines **1a**[9], **1g**[19], **1f**[12] and **13**[12] are known. **1b-e** were prepared from **8** and the respective acyl chloride according to a proven method.[20]

N-(4-Bromobenzoyl)-2,2-dimethylaziridine (**1b**). Yield 95%. M.p. 37°C; IR ν 1667/cm; H-NMR (90 MHz) δ 1.28 (s, 6H, 2 Me), 2.34 (s, 2H, CH_2), 7.54-7.89 (m, 4 aromatic H). Anal. Calcd. for $C_{11}H_{12}BrNO$: C, 51.99; H, 4.76; N, 5.51. Found: C, 52.16; H, 4.77; N, 5.43.

N-(3,4-Dichlorobenzoyl)-2,2-dimethylaziridine (**1c**). Yield 84%. M.p. 44-45°C; IR ν 1670, 1665/cm; H-NMR (300 MHz) δ 1.30 (s, 6H, 2 Me), 2.36 (s, 2H, CH_2), 7.54 (d, 8.3 Hz, 1H, 5-H of Ar), 7.79 (dd, 8.4 Hz, 2.0 Hz, 1H, 6-H of Ar), 8.05 (d, 1.9 Hz, 1H, 2-H of Ar). Anal. Calcd. f. $C_{11}H_{11}Cl_2NO$: C, 54.12; H, 4.54; N, 5.74. Found: C, 53.86; H, 4.74; N, 5.67.

2,2-Dimethyl-N-(1-naphthoyl)aziridine (**1d**). Yield 73%. Oil; IR (film) ν 1670/cm; H-NMR (200 MHz) δ 1.19 (s, 6H, 2 Me), 2.37 (s, 2H, CH_2), 7.49-7.69 (m, 3H, 3-H + 6-H + 7-H of Ar), 7.87 (m_c, 1H, 5-H of Ar), 7.99 (d, 8.3 Hz, 1H, 4-H of Ar), 8.08 (d, 7.1 Hz, 1H, 2-H of Ar), 8.75 (m_c, 1H, 8-H of Ar). Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.79; H, 6.71; N, 6.22. Found: C, 79.71; H, 6.84; N, 6.11.

2,2-Dimethyl-N-(2-naphthoyl)aziridine (**1e**). Yield 56%. Oil; IR (film) ν 1668/cm; H-NMR (300 MHz) δ 1.32 (s, 6H, 2 Me), 2.40 (s, 2H, CH_2), 7.53-7.62 (m, 2H, 6-H + 7-H of Ar), 7.88-7.92 (m, 2H, 5-H + 8-H of Ar), 7.96-8.04 (m, 2H, 3-H + 4-H of Ar), 8.53 (s, 1H, 1-H of Ar). Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.64; H, 6.86; N, 6.27.

Synthesis of 1,1-dimethyl-2-phenylthioethylamine (**9**) and of authentic samples of **4b,g**

500 mg (7 mmol) of **8** were added to a stirred solution of 2.32 g (21 mmol) of PhSH in 50 ml of MeOH. The next day MeOH was removed in a rotat. evaporator. The residue was chromatographed (40x2.7, CH_2Cl_2/MeOH 9:1). After elution of excess PhSH there were obtained 896 mg (71%) of **9**. Oil; IR (film) ν 3260-3460/cm; H-NMR (60 MHz) δ 1.22 (s, 6H, 2 Me), 2.30 (s br, 2H, NH_2, removeable by D_2O), 3.02 (s, 2H, CH_2), 7.05-7.40 (m, 5H, Ph). **9** was further characterized by its benzoic acid salt which was prepared as follows. **9** (1.4 mmol) was added to an ethereal solution of benzoic acid (1.4 mmol). The next day the crystalline precipitate was collected and washed with ether to give 335 mg (86%) of **9**x$PhCO_2H$. M.p. 141°C; IR ν 2500-3100, 1620, 1530, 1390/cm; H-NMR (200 MHz) δ 1.32 (s, 6H, 2 Me), 3.20 (s, 2H, CH_2), 4.80 (s br, 3H, NH_3^+), 7.12-7.2 (m, 3H, m-H + p-H of PhS), 7.2-7.30 (m, 2H, o-H of PhS), 7.41 (m_c, 2H, m-H of PhCO),

7.48 (m_c, 1H, p-H of PhCO), 8.01-8.06 (m, 2H, o-H of PhCO). Anal. Calcd. for $C_{17}H_{20}NO_2S$: C, 67.28; H, 6.98; N, 4.62. Found: C, 67.36; H, 6.93; N, 4.48. - Authentic samples of **4b,g** were prepared as follows. Solutions of 400 mg (2.2 mmol) of **9** in 30 ml of CH_2Cl_2 and of 97 mg (2.4 mmol) of sodium hydroxide in 1 ml of water were mixed and rapidly stirred. A solution of 435 mg (2 mmol) of 4-bromobenzoyl chloride in 10 ml of CH_2Cl_2 was added dropwise. After 1 day stirring the organic layer was washed with water and evaporated to give 577 mg (72%) of **4b**. In the same manner 64% of **4g** were obtained.

N-(1,1-Dimethyl-2-phenylthioethyl)-4-bromobenzamide (**4b**). M.p. 103-104°C; IR ν 3260, 1655, 1550/cm; H-NMR (90MHz) δ 1.55 (s, 6H, 2 Me), 3.46 (s, 2H, CH_2), 6.06 (s br, 1H, NH), 7.05-7.35 (m, 5H, PhS), 7.43 (m_c, 4H, ArCO); MS (110°C), m/e (r. i.) 365 (1, M), 363 (1, M), 242 (10, M - $PhSCH_2$), 240 (10, M - $PhSCH_2$), 185 (41, ArCO), 183 (42, ArCO), 164 (100, M - $ArCONH_2$). Anal. Calcd. for $C_{17}H_{18}BrNOS$: C, 56.09; H, 4.98; N, 3.88. Found: C, 56.01; H, 5.05; N, 3.86.

N-(1,1-Dimethyl-2-phenylthioethyl)trimethylacetamide (**4g**). M.p. 52-53°C; IR ν 3300, 1639, 1535/cm; H-NMR (90 MHz) δ 1.11 (s, 9H, tBu), 1.42 (s, 6H, 2 Me), 3.41 (s, 2H, CH_2), 5.61 (s br, 1H, NH), 7.15 (m_c, 1H, p-H of Ph), 7.26 (m_c, 2H, m-H of Ph), 7.37 (m_c, 2H, o-H of Ph); MS (60°C), m/e (r. i.) 265 (5, M), 164 (100, M - $tBuCONH_2$), 142 (21, M - $PhSCH_2$), 123 (4, $PhSCH_2$), 109 (3, PhS), 85 (15, tBuCO), 57 (40, tBu). Anal. Calcd. for $C_{15}H_{23}NOS$: C, 67.88; H, 8.73; N, 5.28. Found: C, 67.64; H, 8.72; N, 5.00.

Runs of Table 1

General procedure. Amounts of reagents and solvents are given in Table 1. Runs 1-7 (a) differed from runs 8-14 (b) in the preparation of the basic solution required for the conversion of PhSH into **2**. (a) Sodium was dissolved in MeOH (amounts of Table 1 minus 5 ml) or (b) sodium was stirred over night in the solution of naphthalene in THF (amounts of Table 1 minus 5 ml). PhSH was added. 1-2 Hours later aziridine **1** (dissolved in 5 ml of MeOH or THF, respectively) was rapidly added to the stirred solution of **2**. After the time given in Table 1, the solvent was removed in a rotat. evaporator. The residue was taken up in CH_2Cl_2 and twice washed with water. The water was extracted several times with CH_2Cl_2. The combined organic layers were dried and evaporated to dryness. The residue was subjected to chromatography unless otherwise stated.

Run 1. Chromatography (30x3, CH_2Cl_2/$MeCO_2Et$ 9:1) provided 402 mg of a non-polar fore-run (mainly PhSSPh and $PhSCH_2SPh$, arisen from **2** by reaction with air or CH_2Cl_2, respectively), then 840 mg of a mixture consisting (H-NMR, 250 MHz) of 20 mg (1.4%) of **4a**, 820 mg (58%) of **3a** and 62 mg (7%) of **7a** which was recognized by the very characteristic signals of its non-aromatic moiety[9]. H-NMR (250 MHz) of **7a** δ 1.75 (s, 3H, Me), 3.96 (d, 5.4 Hz, 2H, NCH_2), 4.82 (m_c, 2H, $C=CH_2$), 6.23 (s br, 1H, NH), 7.32-7.47 (m, 3H, m-H + p-H of Ph), 7.70-7.75 (m, 2H, o-H of Ph). **3a** and **4a** are characterized in run 8.

N-(2-Methoxy-2-methylpropyl)benzamide (**5a**). Oil; IR (film) ν 3460, 3315, 1650, 1540, 1076/cm; H-NMR (300 MHz) δ 1.22 (s, 6H, 2 Me), 3.23 (s, 3H, MeO), 3.49 (d, 5.6 Hz, 2H, CH_2), 6.51 (s br, 1H, NH), 7.40-7.52 (m, 3H, m-H + p-H of Ph), 7.80 (m_c, 2H, o-H of Ph). Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.25; H, 8.19; N, 6.44.

Run 2. No chromatography. The residue (740 mg) consisted (H-NMR, 300 MHz) of 551 mg (39%) of **3a**, 18 mg (1.3%) of **4a**, 27 mg (2.7%) of **5a**, 123 mg (18%) of **6a** (comparison with authentic **6a**) and 17 mg (2%) of **7a**.

Run 3. Chromatography (30x3, CH_2Cl_2/$MeCO_2Et$ 9:1) provided 333 mg of a non-polar fore-run (mainly PhSSPh and $PhSCH_2SPh$) followed by 810 mg of a mixture consisting (H-NMR, 250 MHz) of 59 mg (3%) of **4b** and 751 mg of **3b**. Further elution yielded 322 mg (total 1073 mg equal to 59%) of **3b**, 78 mg (6%) of **7b** and 204 mg (16%) of **5b**.

N-(2-Methyl-2-phenylthiopropyl)-4-bromobenzamide (**3b**). M.p. 95-97°C; IR ν 3300, 1655, 1555/cm; H-NMR (250 MHz) δ 1.30 (s, 6H, 2 Me), 3.39 (d, 5.6 Hz, 2H, CH_2), 6.73 (t br, Ca. 6 Hz, 1H, NH), 7.24-7.55 (m, 5H, PhS), 7.63 (m_c, 4H, ArCO). Anal. Calcd. for $C_{17}H_{18}BrNOS$: C, 56.09; H, 4.98; N, 3.88. Found: C, 56.26; H, 5.17; N, 3.80.[17]

N-(2-Methoxy-2-methylpropyl)-4-bromobenzamide (**5b**). M.p. 67-68°C; IR ν 3260, 1640, 1520, 1082/cm; H-NMR (300 MHz) δ 1.22 (s, 6H, 2 Me), 3.24 (s, 3H, MeO), 3.47 (d, 5.5 Hz, 2H, CH_2), 6.45 (s br, 1H, NH), 7.55-7.60 (m, 2H, m-H of Ar), 7.64-7.68 (m, 2H, o-H of Ar). MS (63°C), e/m (r. i.) 287 (0.04, M), 285 (0.04, M), 272 (0.1, M - Me), 270 (0.1, M - Me), 256 (0.6, M - MeO), 254 (0.6, M - MeO), 185 (5, ArCO), 183 (5, ArCO), 157 (3, Ar), 155 (3, Ar), 73 (100, $MeOCMe_2$). Anal. Calcd. for $C_{12}H_{16}BrNO_2$: C, 50.37; H, 5.64; N, 4.89. Found: 50.65; H, 5.58; N, 4.89.

N-Methallyl-4-bromobenzamide (**7b**). M.p. 110-111°C; IR ν 3340, 1640, 1555/cm; H-NMR (90 MHz) δ 1.77 (s, 3H, Me), 3.98 (d, 5.9 Hz, 2H, NCH_2), 4.88 (m_c, 2H, $C=CH_2$), 6.55 (s br, 1H, NH), 7.48-7.73 (m, 4H, Ar); MS (70°C), m/e (r. i.) 255 (20, M), 253 (22, M), 185 (99, ArCO), 183 (100, ArCO), 157 (22, Ar), 155 (22, Ar). Anal. Calcd. for $C_{11}H_{12}BrNO$: C, 51.99; H, 4.76; N, 5.51. Found: C, 51.70; H, 4.66; N, 5.32.

Run 4. Chromatography (30x3) with CH_2Cl_2 provided 87 mg of a non-polar fore-run (mainly PhSSPh) and 79 mg (11%) of **6b** (comparison with authentic **6b**). Elution with $CH_2Cl_2/MeCO_2Et$ (9:1) yielded 7 mg of **4b**, 147 mg of a mixture and 455 mg of **3b**. The mixture consisted (H-NMR, 90 MHz) of 10 mg (total 17 mg equal to 1.4%) of **4b** and 137 mg (total 592 mg equal to 47%) of **3b**.

Run 5. Chromatography (30x3) with CH_2Cl_2 removed a non-polar fore-run (mainly PhSH and PhSSPh). Elution with $CH_2Cl_2/MeCO_2Et$ (9:1) gave 252 mg of a mixture consisting (H-NMR, 250 MHz) 244 mg (48%) of **3c** and 8 mg (1.6%) of **4c**. **3c** and **4c** are characterized in run 10.

Run 6. Chromatography (30x3) with toluene/$MeCO_2Et$ (9:1) provided 307 mg of a non-polar fore-run (mainly PhSSPh). Elution with toluene/$MeCO_2Et$ (7:1) yielded 3 mg (0.4%) of **4g** and 381 mg of **3g**. Elution with toluene/$MeCO_2Et$ (1:1) gave 11 mg (total 392 mg equal to 38%) of **3g**, 210 mg (29%) of **5g** and 70 mg (12%) of **7g** (authentic **7g** and its characterization were kindly provided by Dr. Werry[21,5]).

N-(2-Methyl-2-phenylthiopropyl)trimethylacetamide (**3g**). M.p. 94-95°C; IR ν 3230, 1645, 1548/cm; H-NMR (300 MHz) δ 1.23 (s, 6H, 2Me), 1.27 (s, 9H, tBu), 3.18 (d, 5.6 Hz, 2H, CH_2), 6.30 (s br, 1H, NH), 7.31-7.40 (m, 3H, m-H + p-H of Ph), 7.46-7.49 (m, 2H, o-H of Ph); MS (60°C), m/e (r. i.) 265 (17, M), 156 (56, M - PhS), 152 (11), 151 (100, $PhSCMe_2$), 109 (10, PhS), 72 (20), 57 (80, tBu). Anal. Calcd. for $C_{15}H_{23}NOS$: C, 67.88; H, 8.73; N, 5.28. Found: C, 67.57; H, 8.77; N, 5.10.

N-(2-Methoxy-2-methylpropyl)trimethylacetamide (**5g**). Oil; IR (film) ν 3470, 3380, 1655, 1535, 1082/cm; H-NMR (200 MHz) δ 1.15 (s, 6H, 2 Me), 1.21 (s, 9H, tBu), 3.20 (s, 3H, MeO), 3.27 (d, 5.5 Hz, 2H, CH_2), 6.00 (s br, 1H, NH). Anal. Calcd. for $C_{10}H_{21}NO_2$: C, 64.13; H, 11.30; N, 7.48. Found: C, 64.19; H, 11.33; N, 7.52.

N-(Methallyl)trimethylacetamide (**7g**).[21,5] M.p. 72-73°C; IR ν 3340, 1642, 1532/cm; H-NMR (300 MHz) δ 1.23 (s, 9H, tBu), 1.73 (s, 3H, C=CMe), 5.75 (s br, 1H, NH). Anal. Calcd. for $C_9H_{17}NO$: C, 69.63; H, 11.03; N, 9.02. Found: C, 69.91; H, 11.10; N, 9.19.

Run 7. No Chromatography. The residue (1.387 g) contained (H-NMR, 300 MHz, internal standard) 532 mg (40%) of **3g**, 20 mg (1.5%) of **4g**, 233 mg (25%) of **5g** and 163 mg (21%) of **7g**.

Run 8. Chromatography (40x4) with toluene removed the hydrocarbons and PhSH (and perhaps non-polar artifacts). Elution with toluene/$MeCO_2Et$ (10:1) provided a small fore-run, 119 mg of **4a**, 433 mg of a mixture and 646 mg of **3a**. The mixture consisted (H-NMR, 250 MHz) of 19 mg (total 138 mg equal to 10%) of **4a** and 414 mg (total 1060 mg equal to 74%) of **3a**.

N-(2-Methyl-2-phenylthiopropyl)benzamide (**3a**). M.p. 124-126°C; IR ν 3290, 1640, 1535/cm; H-NMR (90 MHz) δ 1.31 (s, 6H, 2 Me), 3.41 (d, 5.7 Hz, 2H, CH_2), 6.81 (t br, ca. 6 Hz, 1H, NH), 7.31-7.56 (m, 8H, PhS, m-H + p-H of PhCO), 7.80-7.85 (m, 2H, o-H of PhCO); MS (80°C), m/e (r. i.) 285 (11, M), 176 (42, M - PhS), 151 (68, $PhSCMe_2$), 105 (100, PhCO), 77 (36, Ph). Anal. Calcd. for $C_{17}H_{19}NOS$: C, 71.54; H, 6.71; N, 4.91. Found: C, 71.56; H, 6.70; N, 4.72.

N-(1,1-Dimethyl-2-phenylthioethyl)benzamide (**4a**). M.p. 77-79°C; IR ν 3260, 1655, 1550/cm; H-NMR (90 MHz) δ 1.55 (s, 6H, 2 Me), 3.49 (s, 2H, CH_2), 6.16 (s br, 1H, NH), 7.10-7.27 (m, 5H, PhS), 7.31-7.47 (m, 3H, m-H + p-H of PhCO), 7.56-7.60 (m, 2H, o-H of PhCO); MS (80°C), m/e (r. i.) 285 (4, M), 164 (81, M - $PhCONH_2$), 105 (100, PhCO), 77 (39, Ph). Anal. Calcd. for $C_{17}H_{19}NOS$: C, 71.54; H, 6.71; N, 4.91. Found: C, 71.28; H, 6.60; N, 4.82.

Run 9. Chromatography (40×4) with toluene/$MeCO_2Et$ (10:1) provided 2.294 g of a mixture of hydrocarbons and PhSH, 135 mg of **4a** and 54 mg of a mixt. consisting (H-NMR, 200 MHz) of 6 mg (total 141 mg equal to 10%) of **4a** and 46 mg of **3a**. Elution with toluene/$MeCO_2Et$ (2:1) yielded 943 mg (total 989 mg equal to 69%) of **3a**.

Run 10. Chromatography (40×4, CH_2Cl_2) provided 514 mg of a mixture of hydrocarbons and PhSH, 14 mg (3%) of **4c**, 236 mg of **3c** and 18 mg of a mixture consisting (H-NMR, 90 MHz) of 6 mg (total 242 mg equal to 48%) of **3c** and 12 mg (3%) of **7c**. Recrystallization from MeOH provided a small amount of **7c** sufficient for m.p., IR, MS and elementary analysis.

N-(2-Methyl-2-phenylthiopropyl)-3,4-dichlorobenzamide (**3c**). M.p. 88-90°C; IR ν 3260, 1644, 1550/cm; H-NMR (90 MHz) δ 1.30 (s, 6H, 2 Me), 3.40 (d, 5.9 Hz, 2H, CH_2), 6.09 (s br, 1H, NH), 7.30-7.62 (m, 5H, PhS), 7.55 (m_c, 2H, 5-H + 6-H of ArCO), 7.87 (m_c, 1H, 2-H of ArCO); MS (120°C), e/m (r. i.) 355 (5, M), 353 (7, M), 246 (12, M - PhS), 244 (20, M - PhS), 175 (36, ArCO), 173 (57, ArCO), 151 (100, $PhSCMe_2$). Anal. Calcd. for $C_{17}H_{17}Cl_2NOS$: C, 57.63; H, 4.84; N, 3.95. Found: C, 57.88; H, 4.63; N, 3.99.

N-(1,1-Dimethyl-2-phenylthioethyl)-3,4-dichlorobenzamide (**4c**). M.p. 88-90°C; IR ν 3310, 1640, 1538/cm; H-NMR (90 MHz) δ 1.54 (s, 6H, 2 Me), 3.45 (s, 2H, CH_2), 6.10 (s br, 1H, NH), 7.00-7.47 (m, 5H, PhS), 7.34 (m_c, 2H, 5-H + 6-H of ArCO), 7.58 (m_c, 2H, 2-H of ArCO); MS (140°C), e/m (r. i.) 355 (2, M), 353 (4, M), 232 (14, M - $PhSCH_2$), 230 (21, M - $PhSCH_2$), 175 (49, ArCO), 173 (77, ArCO), 164 (100, M - ArCO), 145 (21). Anal. Calcd. for $C_{17}H_{17}Cl_2NOS$: C, 57.63; H, 4.84; N, 3.95. Found: C, 57.72; H, 4.81; N, 4.04.

N-Methallyl-3,4-dichlorobenzamide (**7c**). M.p. 84-85°C; IR ν 3320, 1655, 1565/cm; H-NMR (90 MHz) δ 1.78 (s, 3H, Me), 3.99 (d, 5.8 Hz, 2H, NCH_2), 4.89 (m_c, 2H, $C=CH_2$), 6.42 (s br, 1H, NH), signals of ArCO overlapped with signals of **3c**; MS (79°C), e/m (r. i.) 245 (12, M), 243 (19, M), 177 (10, ArCO), 175 (64, ArCO), 173 (100, ArCO), 147 (15, Ar), 145 (25, Ar). Anal. Calcd. for $C_{11}H_{11}Cl_2NO$: C, 53.90; H, 4.93; N, 5.71. Found: C, 54.00; H, 4.67; N, 5.60.

Run 11. Chromatography (30×3, CH_2Cl_2/$MeCO_2Et$ 9:1) provided a small forerun of hydrocarbons and PhSH, 54 mg of mixture a, 477 mg of **3d** and 43 mg of mixture b. Mixture a consisted (H-NMR, 250 MHz) of 48 mg (6%) of **4d** and 6 mg of **3d**. Mixture b consisted (H-NMR, 90 MHz) of 21 mg (total 504 mg equal to 68%) of **3d** and 17 mg (3%) of **7d**. Recrystallization of mixture a from MeOH/ether gabe a small amount of **4d** sufficient for m.p., IR, MS and elementary analysis. **7d** was charaterized by H-NMR only.

N-(2-Methyl-2-phenylthiopropyl)-1-naphthamide (**3d**). M.p. 130-131°C; IR ν 3260, 1633, 1530/cm; H-NMR (90 MHz) δ 1.36 (s, 6H, 2 Me), 3.50 (d, 5.9 Hz, 2H, CH_2), 6.58 (t br, ca. 6 Hz, 1H, NH), 7.25-7.71 (m, 9H, PhS, 3-H + 5-H + 6-H + 7-H of ArCO), 7.80-8.02 (m, 2H, 2-H + 4-H of ArCO), 8.29-8.45 (m, 1H, 8-H of ArCO); MS (190°C), m/e (r. i.) 335 (19, M), 226 (29, M - PhS), 155 (100, ArCO), 151 (86, $PhSCMe_2$), 127 (65, Ar). Anal. Calcd. for

$C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.17. Found: C, 74.96; H, 6.45; N, 4.07.
N-(1,1-Dimethyl-2-phenylthioethyl)-1-naphthamide (**4d**). M.p. 88-89°C; IR ν 3300, 1636, 1540/cm; H-NMR (90 MHz) δ 1.58 (s, 6H, 2 Me), 3.62 (s, 2H, CH_2), 5.98 (s br, 1H, NH), 7.10-7.63 (m, 9H, PhS, 3-H + 5-H + 6-H + 7-H of ArCO), 7.73-7.93 (m, 2H, 2-H + 4-H of ArCO), 8.20-8.34 (m, 1H, 8-H of ArCO); MS (180°C), e/m (r. i.) 335 (7, M), 212 (11, M - $PhSCH_2$), 164 (100, M - $ArCONH_2$), 155 (100, ArCO), 127 (93, Ar), 77 (14, Ph). Anal. Calcd. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.17. Found: C,75.32; H, 6.27; N, 4.22.
N-Methallyl-1-naphthamide (**7d**). Only in mixture with **3d**. H-NMR (90 MHz) δ 1.74 (s, 3H, Me), 3.93 (d, 5.1 Hz, 2H, NCH_2), 4.83 (m, 2H, $C=CH_2$), 6.48 (s br, 1H, NH), signals of ArCO overlapped with signals of **3d**.

Run 12. Chromatography (30×3) with CH_2Cl_2 removed the major part of hydrocarbons and of PhSH. Elution with $CH_2Cl_2/MeCO_2Et$ (9:1) gave a small fore-run of hydrocarbons and PhSH, then 37 mg of **4e**, 300 mg of a mixture and 242 mg of **3e**. The mixture consisted (H-NMR, 250 MHz) of 9 mg (total 46 mg equal to 6%) of **4d** and 291 mg (total 533 mg equal to 72%) of **3e**.
N-(2-Methyl-2-phenylthiopropyl)-2-naphthamide (**3e**). M.p. 108-109°C; IR ν 3420, 1645, 1550/cm; H-NMR (250 MHz) δ 1.36 (s, 6H, 2 Me), 3.49 (d, 5.8 Hz, 2H, CH_2), 6.94 (t br, ca. 6 Hz, 1H, NH), 7.33-7.48 (m, 3H, o-H + p-H of PhS), 7.53-7.62 (m, 4H, m-H of PhS, 6-H + 7-H of ArCO), 7.85-8.01 (m, 3H, 3-H + 5-H + 8-H of ArCO), 7.92 (d, 8.2 Hz, 1H, 4-H of ArCO), 8.34 (s br, 1H, 1-H of ArCO); MS (120°C), m/e (r. i.) 335 (19, M), 226 (34, M - PhS), 155 (100, ArCO), 151 (92, $PhSCMe_2$), 127 (72, Ar). Anal. Calcd. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.17. Found: C, 75.09; H, 6.19; N, 3.95.
N-(1,1-Dimethyl-2-phenylthioethyl)-2-naphthamide (**4e**). M.p. 80-82°C; IR ν 3300, 1640, 1545/cm; H-NMR (250 MHz) δ 1.62 (s, 6H, 2 Me), 3.55 (s, 2H, CH_2), 6.28 (s br, 1H, NH), 7.09-7.17 (m, 1H, p-H of PhS), 7.21-7.28 (m, 2H, o-H of PhS), 7.41-7.46 (m, 2H, m-H of PhS), 7.54 (m, 2H, 6-H + 7-H of ArCO), 7.64 (dd, 8.2 Hz/2.2 Hz, 1H, 3-H of ArCO), 7.84 (d, 8.2 Hz, 1H, 4-H of ArCO), 7.87 (m, 2H, 5-H + 8-H of ArCO), 8.08 (s br, 1H, 1-H of ArCO); MS (150°C), m/e (r. i.) 335 (8, M), 212 (9, M - $PhSCH_2$) 164 (81, M - ArCO), 155 (100, ArCO), 127 (68, Ar). Anal. Calcd. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.17. Found: C, 75.12; H, 6.44; N, 3.98.

Run 13. Chromatography (32×3) with toluene removed the major amount of hydrocarbons and PhSH. Toluene/$MeCO_2Et$ (10:1) eluted a small fore-run of hydrocarbons and PhSH, 156 mg of **4f**, 108 mg of a mixture, 884 mg of **3f** and 75 mg (8%) of **7f** (authentic **7f** and its characterization were provided by Dr. Werry[21,5]). The mixture consisted (H-NMR, 90 MHz) of 18 mg (total 174 mg equal to 11%) of **4f** and 90 mg (total 974 mg equal to 63%) of **3f**.
N-(2-Methyl-2-phenylthiopropyl)cinnamamide (**3f**). M.p. 117-119°C; IR ν 3320, 1642, 1545/cm; H-NMR (90 MHz) δ 1.24 (s, 6H, 2 Me), 3.37 (d, 5.9 Hz, 2H, CH_2), 6.63 (d, 15.6 Hz, 1H, COC=CH), 6.69 (t br, ca, 6 Hz, 1H, NH), 7.26-7.51 (m, 10H, 2 Ph), 7.64 (d, 15.6 Hz, 1H, COCH=C); MS (110°C), e/m (r. i.) 311 (17, M), 202 (40, M - PhS), 161 (24, M - $PhSCMe=CH_2$), 151 (92, $PhSCMe_2$), 131 (100, PhCH=CHCO), 103 (36, PhCH=CH), 77 (18, Ph). Anal. Calcd. for $C_{19}H_{21}NOS$: C, 73.27; H, 6.80; N, 4.50. Found: C, 73.05; H, 6.81; N, 4.50.
N-(1,1-Dimethyl-2-phenylthioethyl)cinnamamide (**4f**). M.p. 102-103°C; IR ν 3300, 1627, 1532/cm; H-NMR (90 MHz) δ 1.49 (s, 6H, 2 Me), 3.47 (s, 2H, CH_2), 5.79 (s br, 1H, NH), 6.27)d, 15.7 Hz, 1H, COC=CH), 7.05-7.58 (m, 10H, 2 Ph), 7.61 (d, 15.6 Hz, 1H, COCH=C); MS (100°C), e/m (r. i.) 311 (4, M), 188 (11, M - $PhSCH_2$), 164 (100, M - PhCH=CHCO), 131 (85, PhCH=CHCO), 103 (29, PhCH=CH), 77 (13, Ph). Anal. Calcd. for $C_{19}H_{21}NOS$: C, 73.27; H, 6.80; N, 4.50. Found: C, 73.06; H, 6.73; N, 4.19.
N-Methallylcinnamamide (**7f**)[21,5]. M.p. 84°C; IR ν 3285, 3275, 1659, 1621, 1618, 1553/cm; H-NMR (250) δ 1.77 (s, 3H, Me), 3.95 (d, 6.1 Hz, 2H, NCH_2), 4.85-4.90 (m, 2H, $C=CH_2$), 5.99 (s br, 1H, NH), 6.47 (d, 15.6 Hz, 1H, COCH=C) 7.31-7.40 (m, 3H, m-H + p-H of Ph), 7.45-7.53 (m, 2H, o-H of Ph), 7.65 (d, 15.6 Hz, 1H, COC=CH). Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.58; H,

7.51; N, 6.96. Found: C, 77.27; H, 7.66; N, 6.97.

Run 14. Chromatography (40×4, toluene/$MeCO_2Et$ 10:1) provided 2.437 g of hydrocarbons and PhSH, 159 mg of **4f**, 370 mg of a mixt., 558 mg of **3f** and 30 mg (3%) of **7f**. The mixture consisted (H-NMR, 200 MHz) of 24 mg (total 183 mg equal to 12%) of **4f** and 346 mg (total 904 mg equal to 57%) of **3f**.

Stability of **3a**

(a) 347 mg 1.22 mmol) of **3a** were added to a stirred solution of 28 mg (1.22 mmol) of sodium in 30 ml of MeOH; stirring was continued for 8 days; evaporation yielded 331 (95%) of crude **3a** (H-NMR, 90 MHz). - (b) 74 mg (0.3 mmol) of **3a** were added to a stirred solution prepared from 23 ml of MeOH, 6 mg (0.3 mmol) of sodium and 29 mg (0.3 mmol) of PhSH; stirring was continued for 9 days; evaporation yielded 74 mg of crude **3a** (H-NMR, 90 MHz).

Reactions with tosylaziridine **10**

(a) The reaction of **2** with **10** was performed analogously to the General Procedure of Runs of Table 1, variant a, using 116 mg (5mmol) of sodium, 20 ml of MeOH, 770 mg (7 mmol) PhSH and 1.126 g (7 mmol) of **10**, time one day. Chromatography (30×3, toluene/$MeCO_2Et$ 9:1) provided a small fore-run and then a 1.614 g of a mixture consisting (H-NMR, 300 MHz) of 1.533 g (90%) of **11** and 81 mg (6%) of **12**. An authentic sample of **11** was prepared from **9** and tosyl chloride analogously to the synthesis of authentic samples of **4b,g**. For authentic **12** see reaction (b).

N-(1,1-Dimethyl-2-phenylthioethyl)toluene-4-sulfonamide (**11**). M.p. 87-88°C; IR ν 3280, 1325, 1140/cm; H-NMR (300 MHz) δ 1.25 (s, 6H, CMe_2), 2.39 (s, 3H, Me of Ts), 3.09 (s, 2H, CH_2), 5.17 (s br, 1H, NH), 7.10-7.35 (m, 5H, PhS), 7.24 (m, 2H, m-H of Ts), 7.75 (m, 2H, o-H of Ts). Anal. Calcd. for $C_{17}H_{21}NO_2S_2$: C, 60.86; H, 6.31; N, 4.18. Found: C, 60.97; H, 6.30; N, 4.04.

(b) A solution of 1.125 g (5 mmol) of **10** in 4.4 g (40 mmol) of PhSH was stirred under nitrogen for 3 months. The mixture was dissolved in CH_2Cl_2, washed thoroughly with aqueous sodium hydroxide and then washed with water. The organic layer gave in a rotat. evaporator a residue which by chromatography (30×3, toluene/$MeCO_2Et$ 10:1) yielded 43 mg (2%) of **12** followed by a trace of **11** and many unknown products.

N-(2-Methyl-2-phenylthiopropyl)toluene-4-sulfonamide (**12**). M.p. 112-113°C; IR ν 3245, 1325, 1170/cm; H-NMR (300 MHz) δ 1.20 (s, 6H, CMe_2), 2.48 (s, 3H, Me of Ts), 2.74 (d, 6.0 Hz, 2H, CH_2), 5.07 (t br, 1H, NH), 7.10-7.35 (m, 5H, PhS), 7.35 (m, 2H, m-H of Ts), 7.77 (m, 2H, o-H of Ts); MS (121°C), m/e (r. i.) 335 (7, M), 155 (24, Ts), 151 (100, $PhSCMe_2$), 91 (44, tolyl). Anal. Calcd. for $C_{17}H_{21}NO_2S_2$: C, 60.86; H, 6.31; N, 4.18. Found: C, 60.78; H, 6.21; N, 4.18.

Stability of **13** toward **2**.

In analogy to Table 1 and General Procedure (a) a run was performed with 5 mmol of sodium, 50 ml of MeOH, 7 mmol of PhSH and 2.5 mmol of **13**. After 30 days the mixture was evaporated. The residue was washed with petroleum ether to yield 0.77 g (100%) of **13**.

Reactions of **1a,c,g** with MeOH.

(a) A solution of 38 mg of **1a** in 20 ml of MeOH was stirred for 8 days and evaporated. The residue showed H-NMR signals (60 MHz) of **5a** only. - (b) A solution of 59 mg of **1a** in 1 ml of CD_3OD was put aside (NMR tube) for 21 h at 28°C (H-NMR, 60 MHz: 50% **1a** + 50% **5a**) and then for 2 days at room temperature (H-NMR, 60 MHz: 36% **1a** + 64% **5a** deuterated at NH and OMe). The H-NMR spectrum (300 MHz) of the residue obtained by evaporation confirmed the final composition. - (c) 60 mg of **1g** were treated in all details exactly as in experiment (b) and yielded first 10% **1g** + 90% **5g** and finally 100% **5g** (confirmation as in the preceding experiment). - (d) A solution of 59 mg of **1c** in 10 ml of MeOH was stirred for 2 days and evaporated. The residue consisted (H-NMR, 300 MHz) of 17% **1c**, 31% **5c** and 52% **6c**. **5c** was identified by comparison with **5a,b**. H-NMR (300 MHz) for

5c: δ 1.22 (s, 6H, 2 Me), 3.24 (s, 3H, OMe), 3.47 (d, 5.6, 2H, NCH_2), 6.48 (s br, 1H, NH), aromatic signals hidden under signals of **1c** and **6c**.

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