

## REACTIONS OF ISOTHIOCYANATES AND ISOCYANATES WITH SOME SILYLATED NITROGEN-CONTAINING NUCLEOPHILES

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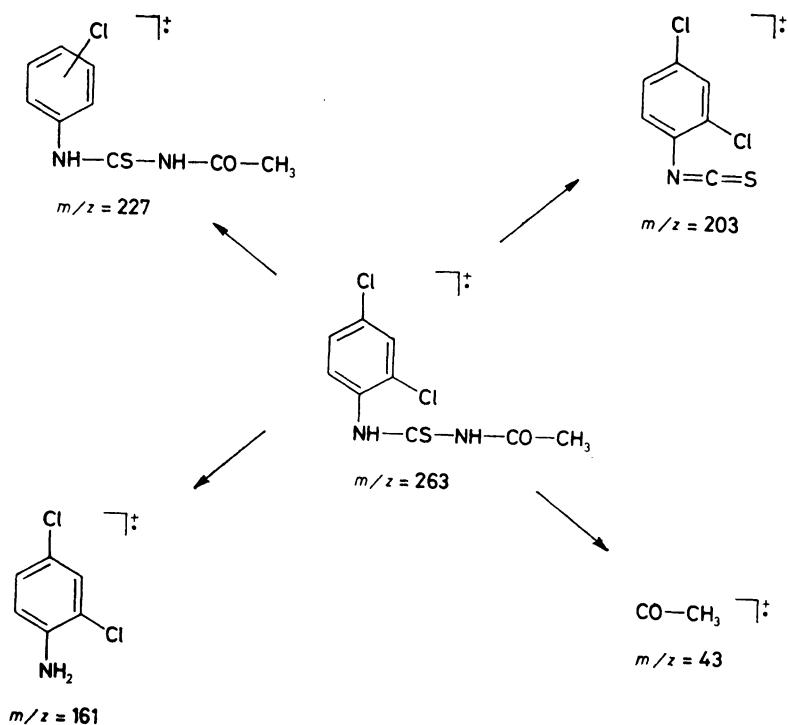
Aryl isothiocyanates and arylisocyanates react with N,O-bis(trimethylsilyl)acetamide to give N-methyl-N'-arylthioureas and ureas. Also nucleophilic additions of other aprotic nucleophiles (e.g. N-trimethylsilylimidazole, N-trimethylsilylpiperidine and N-trimethylsilylmorpholine) to the  $N=C=X$  ( $X = O, S$ ) group were investigated.

Additions of protic nucleophiles and anions to the  $N=C=X$  ( $X = O, S$ ) group of isocyanates and isothiocyanates are well known<sup>1</sup>. Nevertheless, only few examples of additions with aprotic nucleophiles have been reported, as e.g. those of halogens or acid anhydrides to isothiocyanates; the products are, however, unstable and undergo further transformations<sup>2,3</sup>.

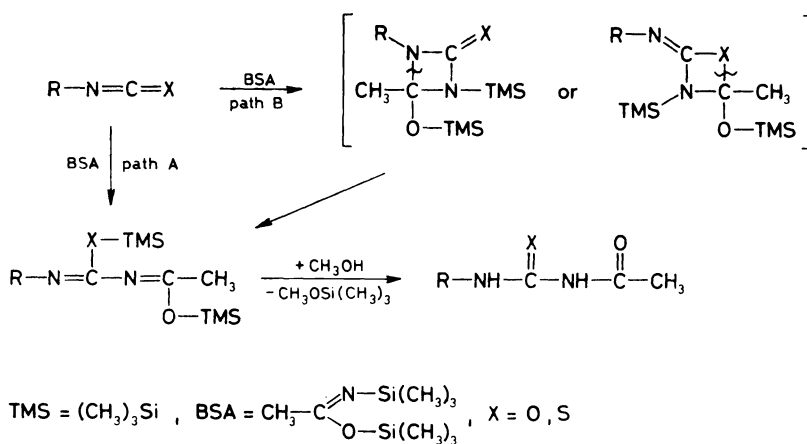
This contribution is aimed to examine additions of silylated aprotic nitrogen-containing nucleophiles to isothiocyanates and isocyanates. An analogous reaction was investigated by Japanese authors<sup>4,5</sup> who found that the strongly basic hexamethyldisilylmethylamine reacted with phenyl isothiocyanates and isocyanates at 150°C to afford N-aryl-N'-methylcarbodiimides. Hexamethyldisilazane adds to aryl isocyanates to form N-aryl-N',N'-bis(trimethylsilyl)ureas; surprisingly, in contrast to addition of dialkylamines, rupture of the Si—N bond took place<sup>6</sup>. Therefore, we investigated this type of reaction using aprotic silylated nitrogen-containing nucleophiles. Thus, phenyl isothiocyanate (*Ia*) and the commercially available N,O-bis(trimethylsilyl)acetamide (*II*) gave N-acetyl-N'-phenylthiourea (*IIIa*) in a quantitative yield by heating the components to 70–80°C (Scheme 1). The mixture was then methanolysed after standing for 24 h. The same conditions were also applied for preparation of substituted thioureas *IIIa–III m* in 72–99% yield (Scheme 1, Table I).

The IR spectra of compounds *IIIa–III m* showed absorption bands of NH ( $3\ 360\text{--}3\ 425\text{ cm}^{-1}$ ) and CO ( $1\ 640\text{--}1\ 690\text{ cm}^{-1}$ ) groups; in <sup>1</sup>H NMR spectra signals of the CH<sub>3</sub>CO and NH groups appeared at  $\delta\ 2.05\text{--}2.53$  and above 9.05, respectively (Table II). The structure of final products was verified by the mass



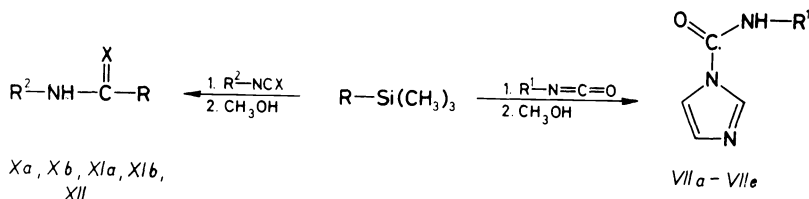


SCHEME 2








SCHEME 3

silylpiperidine<sup>7</sup>, substances unable to enter cycloaddition according to path B and found that aryl isothiocyanates do not react with N-trimethylsilylimidazole, whilst isocyanates afforded 1-(arylamino-carbonyl)imidazoles VIIa – VIIe in 57–78% yield (Scheme 4, Tables V and VI). Nevertheless, the corresponding addition products were obtained on reaction of N-trimethylsilylmorpholine or N-trimethylsilylpiperidine with aryl isocyanates or isothiocyanates (Scheme 4, Tables VII and VIII).



In formulae Xa, Xb, Xla, Xlb, XII:

	R	R <sup>2</sup>	X
a		C <sub>6</sub> H <sub>5</sub>	O
b		4-ClC <sub>6</sub> H <sub>4</sub>	O
c		C <sub>6</sub> H <sub>5</sub>	O
d		4-ClC <sub>6</sub> H <sub>4</sub>	O
e		C <sub>6</sub> H <sub>5</sub>	S

In formulae VIIa – VIIe:

	R <sup>1</sup>
a	C <sub>6</sub> H <sub>5</sub>
b	4-ClC <sub>6</sub> H <sub>4</sub>
c	4-BrC <sub>6</sub> H <sub>4</sub>
d	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>
e	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>

SCHEME 4

It could be, therefore, concluded that these silylated nitrogen-containing nucleophiles underwent nucleophilic additions to isothiocyanates and isocyanates analogously as their not silylated counterparts. In some cases the silylated nucleophiles were more reactive, e.g. N,O-bis(trimethylsilyl)acetamide (II) reacted with isothiocyanates even at a gently elevated temperature, whilst acetamide did not. This procedure has constituted a new approach to N-acetyl-N'-aryleureas and thioureas. Experiments with N-trimethylsilylimidazole, N-trimethylsilylmorpholine and N-trimethylsilylpiperidine indicated that their reactivity towards isothiocyanates and isocyanates corresponded to the stability of the Si—N bond in line with<sup>6</sup> thus favouring our conception expressed by path A.

## EXPERIMENTAL

The IR spectra of chloroform solutions or KBr pellets were measured with a Specord 75 (Zeiss, Jena) spectrophotometer in the 880–4 000 cm<sup>-1</sup> range, the <sup>1</sup>H NMR spectra of deuteriochloroform, deuteriochloroform-hexadeuterodimethyl sulfoxide or hexadeuterodimethyl sulfoxide

solutions containing tetramethylsilane as an internal reference or hexamethyldisiloxane as an external standard were recorded with a Tesla BS 487 A apparatus operating at 80 MHz. The mass spectra were taken with an AEI MS 902 S instrument at 70 eV ionizing electron energy. The reaction course and purity of products were monitored by thin-layer chromatography on Silufol 254 (Kavalier, Czechoslovakia) sheets.

TABLE I  
Characteristic data for N-aryl-N'-acetylthioureas *IIIc*—*III m*

Compound	Formula M.w.	Yield, % M.p., °C	Calculated/Found		
			% C	% H	% N
<i>IIIa</i>	C <sub>9</sub> H <sub>10</sub> N <sub>2</sub> OS	99	55.65	5.18	14.43
	194.2	173—175	55.63	5.22	14.46
<i>IIIb</i>	C <sub>9</sub> H <sub>9</sub> FN <sub>2</sub> OS	93	50.93	4.22	13.20
	212.2	198—200	50.93	4.22	13.34
<i>IIIc</i>	C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> OS	98	47.26	3.94	12.25
	228.7	185—188	47.34	4.01	12.35
<i>III d</i>	C <sub>9</sub> H <sub>9</sub> BrN <sub>2</sub> OS	87	39.57	3.32	10.25
	273.1	117—118	39.66	3.29	10.33
<i>IIIe</i>	C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O <sub>3</sub> S	88	45.18	3.79	17.56
	239.2	188—191	45.34	3.78	17.14
<i>III f</i>	C <sub>10</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub> S	95	53.55	5.39	12.49
	224.2	189—192	53.59	5.45	12.52
<i>III g</i>	C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> OS	87	47.26	3.96	12.25
	228.7	190—193	47.19	4.00	12.24
<i>III h<sup>a</sup></i>	C <sub>9</sub> H <sub>8</sub> Cl <sub>2</sub> N <sub>2</sub> OS	80	41.08	3.06	10.65
	263.1	218—200	41.34	2.97	10.61
<i>III i</i>	C <sub>11</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub> S	72	55.91	5.12	11.86
	236.2	230—233	54.53	5.01	11.40
<i>III j<sup>b</sup></i>	C <sub>10</sub> H <sub>10</sub> N <sub>2</sub> O <sub>2</sub> S	77	54.04	4.53	12.60
	222.2	135—138	53.24	4.51	12.61
<i>III k</i>	C <sub>11</sub> H <sub>15</sub> N <sub>3</sub> OS	83	55.67	6.37	17.71
	237.3	127—128	55.33	6.17	18.62
<i>III l</i>	C <sub>12</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub> S	88	58.08	4.87	11.28
	248.3	173—175	57.98	4.72	10.50
<i>III m</i>	C <sub>14</sub> H <sub>14</sub> N <sub>2</sub> OS	86	65.08	5.45	10.85
	258.3	148—150	65.12	5.50	10.91

<sup>a</sup> Mass spectrum, *m/z* (%): 229 (31), 227 (83), 205 (18), 203 (29), 187 (30), 185 (79), 163 (60), 161 (29), 43 (100); <sup>b</sup> mass spectrum, *m/z* (%): 222 (26), 105 (100), 86 (60), 77 (39), 59 (31), 30 (63).

N-Aryl-N'-acetylthioureas *IIIa—III m*

Aryl isothiocyanate *Ia—Im* (10 mmol) was added to N,O-bis(trimethylsilyl)acetamide (2.03 g, 10 mmol) under exclusion of air moisture at 70–80°C during 1 h. The mixture was left to stand for 24 h, a little amount of methanol was added (c. 10 ml) and the separated crystals were filtered off and recrystallized from ethanol. Yields and characteristic data are given in Table I, the spectral values are listed in Table II.

TABLE II  
Spectral data of N-aryl-N'-acetylthioureas *IIIa—III m*

Com- pound	IR (cm <sup>-1</sup> ) <sup>a</sup>			<sup>1</sup> H NMR (ppm, δ) <sup>b</sup>			Other protons
	ν(NH)	ν(C=O)	ν(NHCS)	CH <sub>3</sub>	H <sub>ar</sub>	NH	
<i>IIIa</i>		1 680	1 520	2.2	7.25—7.68	9.83 12.4	
<i>IIIb</i>	3 405	1 680	1 505	2.5	7.28—7.98	11.58	
<i>IIIc</i>		1 670	1 540	2.18	7.08—7.65	9.23 12.33	
<i>III d</i>	3 405	1 680	1 535	2.48	7.7—7.98	11.75	
<i>IIIe</i>	3 360	1 675	1 537	2.53	8.25—8.58	11.83 13.2	
<i>III f</i>		1 680	1 520	2.43	7.13—7.8	11.63	4.05 s, 3 H (CH <sub>3</sub> O)
<i>III g</i>	3 425	1 670	1 580	2.15	7.05—7.5	9.05 9.4	
<i>III h</i>	3 400	1 685	1 570	2.48	7.5—8.55	11.93 12.93	
<i>III i</i>		1 665 1 590	1 530	2.33	7.95—8.23	11.78	2.73 s, 3 H (CH <sub>3</sub> CO)
<i>III j</i>	3 390	1 690	1 534	2.33	7.48—8	10.53 12.5	
<i>III k</i>	3 405	1 680	1 541	2.18	6.55—7.35	9.73 12.35	2.95 s, 6 H (CH <sub>3</sub> )
<i>III l</i>		1 640	1 539	2.45			
<i>III m</i>	3 410	1 680	1 544	2.05	7.38—8.05	9.65 10.85	5.25 d, 2 H (CH <sub>2</sub> )

<sup>a</sup> Compounds *IIIa*, *III d*, *III f*, *III i*, *III l* were measured in KBr, *III b*, *III c*, *III g*, *III h*, *III j*, *III k*, *III m* in CHCl<sub>3</sub>; <sup>b</sup> compounds *IIIa*, *III c*, *III g*, *III j*, *III k*, *III m* were measured in CDCl<sub>3</sub>, *III i*, *III l* in (CD<sub>3</sub>)<sub>2</sub>SO, *III d*, *III f*, *III h* in CDCl<sub>3</sub>-(CD<sub>3</sub>)<sub>2</sub>SO (1 : 1), *III b* in CDCl<sub>3</sub>-(CD<sub>3</sub>)<sub>2</sub>SO (3 : 1), *III e* in CDCl<sub>3</sub>-(CD<sub>3</sub>)<sub>2</sub>SO (5 : 1).

TABLE III  
Characteristic data for N-aryl-N'-acetylureas *Va*–*Ve*

Compound	Formula M.w.	Yield, % M.p., °C	Calculated/Found		
			% C	% H	% N
<i>Va</i>	C <sub>9</sub> H <sub>10</sub> N <sub>2</sub> O <sub>2</sub> 178.1	99	60.67	5.66	15.12
		172–174	60.69	5.56	15.05
<i>Vb</i> <sup>a</sup>	C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> O <sub>2</sub> 212.6	96	50.84	4.27	13.17
		238–240	50.74	4.19	13.19
<i>Vc</i>	C <sub>9</sub> H <sub>9</sub> BrN <sub>2</sub> O <sub>2</sub> 257.0	97	42.05	3.53	10.90
		213–215	42.12	3.41	10.89
<i>Vd</i> <sup>b</sup>	C <sub>10</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> 208.2	98	57.69	5.81	13.45
		217–220	57.60	5.83	13.43
<i>Ve</i>	C <sub>12</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> 218.2	89	66.04	6.47	12.84
		17–178	66.07	6.49	12.81

<sup>a</sup> Mass spectrum, *m/z* (rel. int., %): 214 (7), 212 (22), 155 (34), 153 (100), 129 (8), 127 (30), 125 (11), 99 (7), 90 (8), 63 (7), 43 (50); <sup>b</sup> mass spectrum, *m/z* (rel. int., %): 208 (19), 149 (100), 134 (27), 123 (5), 122 (6), 108 (29), 106 (7), 78 (6), 52 (6), 43 (24).

TABLE IV  
Spectral data of N-aryl-N'-acetylureas *Va*–*Ve*

Compound	IR (cm <sup>-1</sup> ) <sup>a</sup>		<sup>1</sup> H NMR (ppm, δ) <sup>b</sup>			Other protons
	ν(NH)	ν(CO)	CH <sub>3</sub>	H <sub>ar</sub>	NH	
<i>Va</i>	3 410	1 675	2.4	7.25–7.80	—	
<i>Vb</i>	3 385	1 680	2.3	7.50–7.83	10.78	
					10.93	
<i>Vc</i>	—	1 665	2.4	7.40–8.05	10.88	
<i>Vd</i>	—	1 675	2.28	7.05–7.76	10.58	3.93 s, 3 H (OCH <sub>3</sub> )
					10.80	
<i>Ve</i>	3 420	1 700	2.53	7.63–7.70	10.65	2.3 s, 3 H (CH <sub>3</sub> CO)
					10.78	6.05 s, 1 H (—CH—)

<sup>a</sup> Compounds *Va*–*Vd* were measured in KBr, *Ve* in CHCl<sub>3</sub>; <sup>b</sup> compounds *Va*, *Vc*, *Ve* were measured in CDCl<sub>3</sub>–(CD<sub>3</sub>)<sub>2</sub>SO (1 : 1), *Vb*, *Vd* in (CD<sub>3</sub>)<sub>2</sub>SO.

N-Aryl-N'-acetylureas *Va*—*Vm*

N,O-Bis(trimethylsilyl)acetamide (2.03 g, 10 mmol) was added to aryl isocyanate (10 mmol) at an ambient temperature. The exothermic reaction rose the temperature to 35–40°C which was maintained for 2 h. Methanol (5 ml) was then added to the cooled (0°C) mixture and the

TABLE V  
Characteristic data for 1-(arylaminoacetyl)imidazoles *VIIa*—*VIIe*

Compound	Formula M.w.	Yield, % M.p., °C	Calculated/Found		
			% C	% H	% N
<i>VIIa</i>	C <sub>10</sub> H <sub>9</sub> N <sub>3</sub> O	78.8	64.11	4.84	22.44
	183.1	237	64.10	4.76	22.48
<i>VIIb</i>	C <sub>10</sub> H <sub>8</sub> ClN <sub>3</sub> O	72.3	54.19	3.64	18.96
	221.6	189	54.14	3.84	18.36
<i>VIIc</i>	C <sub>10</sub> H <sub>8</sub> BrN <sub>3</sub> O	50	45.14	3.03	15.79
	266.0	224	43.04	3.11	15.64
<i>VIIId</i>	C <sub>10</sub> H <sub>8</sub> N <sub>4</sub> O <sub>3</sub>	66.8	51.73	3.47	24.13
	232.1	255	51.66	3.55	24.29
<i>VIIe</i> <sup>c</sup>	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	52.5	60.81	5.10	19.34
	217.2	211	60.79	5.19	19.46

<sup>a</sup> Mass spectrum, *m/z* (rel. int., %): 149 (100), 143 (50), 121 (8), 106 (49), 80 (8), 78 (29), 68 (84).

TABLE VI  
Spectral data of 1-(arylaminoacetyl)imidazoles *VIIa*—*VIIe*

Compound	IR (cm <sup>-1</sup> ) <sup>a</sup>			<sup>1</sup> H NMR (ppm, δ) <sup>b</sup>			
	ν(NH)	ν(C=N)	ν(C=O)	H <sub>im</sub> (2 H)	H <sub>ar</sub> + H <sub>im</sub> (1 H)	NH	Other protons
<i>VIIa</i>	3 370	1 675	1 720	7.25	7.61—7.88	—	
<i>VIIb</i>	3 340	1 680	1 715	7.25	7.63—7.83	9.50	
<i>VIIc</i>	3 380	1 680	1 710	7.25	7.55—8.00	8.75	
<i>VIIId</i>	3 365	1 670	1 720	7.23	7.88—8.93	—	
<i>VIIe</i>	3 374	1 700	1 750	7.25	7.03—7.63	8.63	3.93 s, 3 H (CH <sub>3</sub> O)

<sup>a</sup> Compound *VIIa* was measured in CHCl<sub>3</sub>, compounds *VIIb*—*VIIe* in KBr; <sup>b</sup> compound *VIIa* was measured in CDCl<sub>3</sub>, compounds *VIIb*—*VIIe* in (CD<sub>3</sub>)<sub>2</sub>SO.



separated crystals were filtered off and recrystallized from ethanol. Yields and characteristic data are presented in Table III, spectral data are seen in Table IV.

TABLE VII

Characteristic data for 1-(arylamino-carbonyl)morpholines *Xa*, *Xb*; 1-(arylamino-carbonyl)piperidines *XIa*, *XIb* and 1-(arylaminothio-carbonyl)morpholine *XII*

Compound	Formula M.w.	Yield, % M.p., °C	Calculated/Found		
			% C	% H	% N
<i>Xa</i>	$C_{11}H_{14}N_2O_2$	94	64.06	6.85	13.58
	206.2	154–157	63.55	6.95	13.69
<i>Xb</i>	$C_{11}H_{13}ClN_2O_2$	96	54.89	5.44	11.64
	240.6	199–202	54.96	5.56	11.72
<i>XIa</i>	$C_{12}H_{16}N_2O$	97	70.58	7.90	13.71
	204.2	125–127	69.07	7.56	13.89
<i>XIb</i>	$C_{12}H_{15}ClN_2O$	91	60.38	6.33	11.73
	238.7	142–144	59.48	6.48	11.28
<i>XII</i>	$C_{11}H_{14}N_2OS$	97	59.43	6.35	12.60
	222.3	127–128	59.41	6.50	12.92

TABLE VIII

Spectral data of 1-(arylamino-carbonyl)morpholines *Xa*, *Xb*, 1-(arylamino-carbonyl)piperidines *XIa*, *XIb* and 1-(arylaminothio-carbonyl)morpholine *XII*

Compound	IR (cm <sup>-1</sup> ) <sup>a</sup>		<sup>1</sup> H NMR (ppm, δ) <sup>b</sup>		
	ν(NH)	ν(C=O)	H <sub>arom</sub>	NH	Other protons
<i>Xa</i>	3 340	1 640	7.28–7.83	8.58	3.80–3.88 m, 8 H (CH <sub>2</sub> )
<i>Xb</i>	3 345	1 635	7.40–7.83	8.83	3.73–3.85 m, 8 H (CH <sub>2</sub> )
<i>XIa</i>	3 335	1 635	6.95–7.48	6.30	1.83–2.00 m, 6 H (CH <sub>2</sub> )
					3.33–3.50 m, 4 H (NCH <sub>2</sub> )
<i>XIb</i>	3 365	1 645	7.45–7.88	9.98	2.00–2.18 m, 6 H (CH <sub>2</sub> )
					3.45–3.68 m, 4 H (NCH <sub>2</sub> )
<i>XII</i>	3 385	<sup>c</sup>	7.43–7.70	9.55	4.03–4.28 m, 8 H (CH <sub>2</sub> )

<sup>a</sup> Measured in KBr; <sup>b</sup> compounds *Xa*, *Xb* were measured in CDCl<sub>3</sub>-(CD<sub>3</sub>)<sub>2</sub>SO (1 : 1.5), *XIb* in (1 : 1), *XII* in (2 : 1) and *XIa* in CDCl<sub>3</sub>; <sup>c</sup> ν(NHCS) 1 590 cm<sup>-1</sup>.

1-(N-Arylamino-carbonyl)imidazoles *VIIa—VIIe*

N-Trimethylsilylimidazole (1.40 g, 10 mmol) was added to aryl isocyanate (10 mmol) under exclusion of air moisture. Due to exothermic reaction the temperature rose to 35–40°C at which it was kept for 2 h. The mixture was cooled to 0°C, methanol was added and the separated crystals were filtered off. Yields and characteristic data are listed in Table V, spectral data are presented in Table VI.

1-(Arylamino-carbonyl)morpholines *Xa, Xb*; 1-(Arylamino-carbonyl)piperidines *XIa, XIb* and 1-(Phenylaminothio-carbonyl)morpholine (*XII*)

Applying the same procedure, starting from isocyanate or isothiocyanate (10 mmol) and N-trimethylsilylmorpholine<sup>7</sup> (1.59 g, 10 mmol) or N-trimethylsilylpiperidine (1.57 g, 10 mmol) at a temperature range from 45–50°C and 1 h reaction time the title products were prepared in yields listed in Table VII together with their analytical data. Spectral values are given in Table VIII.

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