A Simple, Regioselective Synthesis of 5,6-Dihydro-1,3,5-triazine-2,4(1*H*,3*H*)-dione Derivatives from *N*-Trimethylsilyl Imines via 1,3-Diazabutadienes

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2-Trimethylsiloxy- and 2-trimethylsilylthio-1,3-diaza-1,3-butadienes, formed on reaction of trimethylsilylimines with isocyanates and isothiocyanates R^2-N=C=X (X=O, S), react with isocyanates to give high yields of substituted 5,6-dihydro-1,3,5-triazine-2,4(1*H*,3*H*)-dione and 4-thioxo-3,4,5,6-tetrahydro-1,3,5-triazin-2(1*H*)-one derivatives.

Cycloaddition reactions of heterodienes have been shown to be of great potential in heterocyclic synthesis.[1] While the chemistry of 1- and 2-azabutadienes has been investigated in the last years, the utility of simple 1,3-diazabutadienes remains much less exploited.[1,2,3] Some years ago it was reported that *N*-trimethylsilyl(diphenylmethylene)amine adds to isocyanates and isothiocyanates to give substituted 4,4-diphenyl-1,3-diazabutadienes;[4] moreover, a few 6,6-diphenyl-5,6-dihydro-1,3,5-triazine-2,4(1*H*,3*H*)-diones were synthesized from the isocyanate adducts.[4,5] However, *N*-trimethylsilyl imines derived from aromatic aldehydes are easily available[6] and their usefulness has been demonstrated.[2,6,7] On the other hand, there exist no general methods for preparing 1,3,5-triazines with oxo and/or thioxo functions at 2- and 4-positions.[8] We report here that conveniently substituted 5,6-dihydro-1,3,5-triazine-2,4(1*H*,3*H*)-dione derivatives are formed by reaction of *N*-trimethylsilyl imines with isocyanates and isothiocyanates.[9]

Thus, *N*-trimethylsilyl imines **1**[6] were treated with one equivalent of isocyanates or isothiocyanates **2** in methylene chloride for 8 h; the resulting tautomer mixture **3**,[4] which could be isolated and characterized (see experimental part for compound **3a**), was allowed to react overnight with isocyanates **4** and then stirred with methanol to afford the 1,3,5-triazine cycloadducts **5**, as solid compounds in almost pure form (Scheme); the overall yield from **1** was in all instances higher than 84% (Table 1). The addition reaction of **1** to the isocyanate **2** (X=O) takes place at room temperature, while heating at reflux is required in the case of isothiocyanates **2** (X=S); on the other hand, the cycloaddition step occurs in methylene chloride at room temperature for both azadienes **3** (X=O,S).[10]

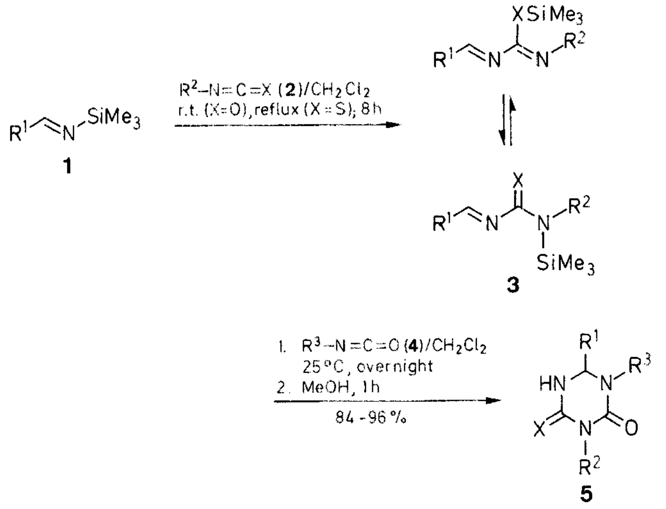
Table 1. 1,3,5-Triazines **5** Prepared[a]

Compound	Yield[b] (%)	mp (°C)	Molecular Formula[c] or Lit. mp (°C)
5a	93	213-215	$C_{23}H_{21}N_3O_2$ (371.4)
5b	96	201-203	$C_{22}H_{19}N_3O_2$ (357.4)
5c	92	212-213	214[9]
5d	90	190-192	$C_{22}H_{25}N_3O_2$ (363.4)
5e	92	150-152	$C_{21}H_{23}N_3O_2$ (349.4)
5f	96	196-197	$C_{21}H_{15}Cl_2N_3O_2$ (412.3)
5g	89	170-172	$C_{19}H_{15}N_3O_2S$ (349.4)
5h	91	217-219	$C_{20}H_{17}N_3O_2S$ (363.4)
5i	93	158-160	$C_{19}H_{21}N_3O_2S$ (355.4)
5j	88	168-170	$C_{21}H_{17}N_3OS$ (359.4)
5k	86	222-224	$C_{22}H_{19}N_3OS$ (373.5)
5l	84	199-201	$C_{19}H_{15}N_3OS_2$ (365.5)

[a] All reactions were carried out at room temperature, except those involving isothiocyanates **2** which were run at reflux.

[b] Overall yield based on **1**.

[c] Satisfactory microanalyses obtained: C ±0.27, H ±0.16, N ±0.18.



3	X	R^1	R^2	3	X	R^1	R^2
a	O	Ph	4-$CH_3C_6H_4$	**e**	O	2-thienyl	Ph
b	O	Ph	Ph	**f**	O	2-thienyl	*c*-C_6H_{11}
c	O	Ph	*c*-C_6H_{11}	**g**	S	Ph	Ph
d	O	Ph	3-ClC_6H_4	**h**	S	2-thienyl	Ph

5	X	R^1	R^2	R^3
a	O	Ph	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$
b	O	Ph	4-$CH_3C_6H_4$	Ph
c	O	Ph	Ph	Ph
d	O	Ph	*c*-C_6H_{11}	4-$CH_3C_6H_4$
e	O	Ph	*c*-C_6H_{11}	Ph
f	O	Ph	3-ClC_6H_4	3-ClC_6H_4
g	O	2-thienyl	Ph	Ph
h	O	2-thienyl	Ph	4-$CH_3C_6H_4$
i	O	2-thienyl	*c*-C_6H_{11}	Ph
j	S	Ph	Ph	Ph
k	S	Ph	Ph	4-$CH_3C_6H_4$
l	S	2-thienyl	Ph	Ph

Compounds **5** were characterized on the basis of microanalytical, spectroscopic (IR, ^1H-, and ^{13}C-NMR), and mass spectrometric data (Table 2).

We conclude that a great variety of 1,3,5-triazines **5** (X=O,S; R^2: aliphatic, aromatic) are easily available in a one-pot, regioselective fashion. The starting *N*-trimethylsilyl imines are made from aldehydes in multigram quantities following a well established method.

Substituted 1,3,5-Triazines 5; General Procedure:

To a solution of *N*-trimethylsilyl imine (**1**; 5.4 mmol) in dry CH_2Cl_2 (10 mL) is added the heterocumulene (**2**, 5.4 mmol); the resulting mixture is stirred for 8 h, at r.t. for isocyanates (X=O) or at reflux for isothiocyanates (X=S). The isocyanate (**4**, 5.4 mmol) is then added at 25°C, and stirring is continued overnight at r.t. The reaction mixture is treated at 25°C with MeOH (5 mL) for 1 h, and the solvents are removed at reduced pressure to give compounds **5** in almost pure form; they are further purified by recrystallization from hexane/$CHCl_3$ (3:1).

When compounds **5** having $R^2=R^3$ and X=O (**5a**, **5c**, **5f**, **5g**) are to be synthesized the above procedure is also applied, except that a mixture of the imine (5.4 mmol) and isocyanate (12 mmol, 2.2 equiv) is stirred overnight.

1-(4-Methylphenyl)-2-trimethylsilyloxy-4-phenyl-1,3-diaza-1,3-butadiene (3a; R^1=Ph, R^2=4-$CH_3C_6H_4$):

A solution of *N*-trimethylsilylbenzylideneamine (**1a**, 960 mg, 5.4 mmol) in dry CH_2Cl_2 (10 mL) is treated at r.t. with 4-methylphenyl isocyanate

Table 2. Spectral Data of Compounds **5**

5	IR (Nujol)[a] ν(cm^{-1})	^{1}H-NMR (300 MHz, $CDCl_3$/TMS)[b] δ, J(Hz)	^{13}C-NMR (75 MHz, $CDCl_3$/TMS)[b] δ	MS (70 eV)[c] m/z (M^+)
a	3300, 1710, 1670	2.0 (s, 3H, CH_3); 2.1 (s, 3H, CH_3); 5.7 (d, 1H, J = 3.8, CH); 6.9–7.3 (m, 13H_{arom}); 7.9 (br, 1H, NH)	153.56 (s); 151.58 (s); 138.73 (s); 137.98 (s); 136.74 (s); 136.50 (s); 132.17 (s); 129.46–125.43 (CH_{arom}); 68.79 (d); 20.92 (q); 20.74 (q)	371
b	3310, 1700, 1680	2.3 (s, 3H, CH_3); 5.9 (d, 1H, J = 3.8, CH); 7.1–7.5 (m, 15H, 14H_{arom} + NH)	153.43; 151.60; 139.34; 138.60; 138.06; 132.08; 129.37–125.41 (CH_{arom}); 68.66; 20.90	357
c	3280, 1720, 1670	5.9 (d, 1H, J = 3.9, CH); 7.0–7.2 (m, 15H_{arom}); 7.9 (br, 1H, NH)	155.45 (s); 151.51 (s); 139.31 (s); 138.50 (s); 134.79 (s); 129.18 (d); 129.11 (d); 129.02 (d); 128.97 (d); 128.82 (d); 128.37 (d); 126.89 (d); 125.90 (d); 125.74 (d); 69.03 (d)	343
d	3300, 1720, 1670	1.0–1.9 (m, 10H, 5CH_2); 2.1 (s, 3H, CH_3); 4.1 (m, 1H, CH); 5.9 (d, 1H, J = 3.6, CH); 7.0–7.2 (m, 9H_{arom}); 8.0 (br, 1H, NH)	154.12 (s); 152.10 (s); 138.87 (s); 137.31 (s); 136.39 (s); 129.80 (d); 129.39 (d); 128.78 (d); 126.10 (d); 125.99 (d); 69.15 (d); 54.89 (d); 29.70 (t); 29.45 (t); 26.41 (t); 25.35 (t); 20.95 (q)	
e	3310, 1690, 1660	1.0–2.5 (m, 10H, 5CH_2); 4.2 (m, 1H, CH); 5.8 (d, 1H, J = 3.8, CH); 7.1–7.3 (m, 11H, 10H_{arom} + NH)	153.97 (s); 151.89 (s); 139.79 (s); 136.61 (s); 128.84–125.57 (CH_{arom}); 68.75 (d); 54.78 (d); 29.51 (t); 29.24 (t); 26.22 (t); 25.16 (t)	
f	3280, 1720, 1670	5.9 (d, 1H, J = 3.7, CH); 7.1–7.5 (m, 14H, 13H_{arom} + NH)	152.66 (s); 151.09 (s); 140.06 (s); 137.62 (s); 135.63 (s); 134.65 (s); 134.33 (s); 130.04 (d); 129.90 (d); 129.76 (d); 129.61 (d); 129.31 (d); 128.87 (d); 127.49 (d); 127.43 (d); 126.33 (d); 125.91 (d); 124.06 (d); 69.24 (d)	411
g	3330, 1720, 1670	6.2 (d, 1H, J = 3.7, CH); 7.0–7.9 (m, 13H_{arom} + NH)	153.20; 150.84; 142.50; 138.73; 134.74; 129.08; 128.93; 128.66; 128.21; 127.10; 126.72; 126.07; 125.98; 65.69	
h	3300, 1710, 1670	2.3 (s, 3H, CH_3); 6.1 (d, 1H, J = 3.7, CH); 7.0–7.6 (m, 12H_{arom} + NH)	153.27 (s); 150.93 (s); 142.48 (s); 137.46 (s); 136.20 (s); 134.83 (s); 129.70 (d); 129.12 (d); 128.77 (d); 128.33 (d); 126.79 (d); 126.44 (d); 126.36 (d); 126.26 (d); 66.33 (d); 20.98 (q)	363
i	3320, 1700, 1660	1.1–2.2 (m, 10H, 5CH_2); 4.2 (m, 1H, CH); 6.0 (d, 1H, J = 4.0, CH); 7.0–7.3 (m, 8H_{arom}); 7.9 (br, 1H, NH)	153.82 (s); 151.35 (s); 142.80 (s); 139.42 (s); 129.04 (d); 127.09 (d); 126.64 (d); 126.31 (d); 126.19 (d); 125.96 (d); 65.91 (d); 55.05 (d); 29.56 (t); 29.32 (t); 26.33 (t); 25.27 (t)	355
j	3300, 1710	5.7 (d, 1H, J = 3.6, CH); 6.9–7.2 (m, 15H_{arom}); 8.0 (br, 1H, NH)	180.10 (s); 153.60 (s); 139.98 (s); 139.10 (s); 134.42 (s); 129.32–124.52 (CH_{arom}); 70.56 (d)	359
k	3300, 1700	2.2 (s, 3H, CH_3); 5.9 (d, 1H, J = 3.7, CH); 7.0–7.4 (m, 14H_{arom}); 7.9 (br, 1H, NH)	180.44 (s); 149.04 (s); 138.20 (s); 137.36 (s); 137.23 (s); 136.19 (s); 129.76–125.78 (CH_{arom}); 71.11 (d); 20.94 (q)	373
l	3310, 1690	6.2 (d, 1H, J = 3.8, CH); 7.0–7.5 (m, 13H_{arom} + NH)	180.71 (s); 148.36 (s); 140.72 (s); 138.45 (s); 138.20 (s); 129.52 (d); 129.36 (d); 128.87 (d); 128.78 (d); 127.85 (d); 127.29 (d); 127.09 (d); 127.02 (d); 126.35 (d); 67.79 (d)	365

[a] Recorded on a Philips PU 9716.
[b] Recorded on a Bruker AC-300.
[c] Recorded on a Hewlett-Packard 5987A spectrometer.

(**2**, 718 mg, 5.4 mmol). After stirring the mixture for 8 h, the solvents are removed at reduced pressure, and the solid obtained is washed with dry hexane to give **3a** as a white solid; yield: 1.62 g (97 %); mp 180–182 °C.

$C_{18}H_{22}N_2OSi$ calc. C 69.64 H 7.14 N 9.02
(310.5) found 69.43 7.25 8.90

MS (70 eV): m/z = 310 (M^+).

^{1}H-NMR (80 MHz, $CDCl_3$): δ = 0.1, 0.2 (2 s, 9 H, $Si(CH_3)_3$); 2.2, 2.3 (2 s, 3 H, CH_3); 6.8–8.1 (m, 9 H_{arom}); 9.15 (br, 1 H, CH).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.5–168 (br); 155.30 (s); 151.92 (s); 139.45–127.15 (m, C_{arom}); 125.65 (d); 125.32 (d); 20.17 (q); 2.2 (br q).

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(10) The treatment of **3** with phenyl isothiocyanate or cyclohexyl isocyanate in refluxing toluene for 3 days gave back the starting diazadiene.