Synthesis of Functionally Substituted 1,3-Diaza-1,3-butadienes

S.N. Mazumdar, M.P. Mahajan

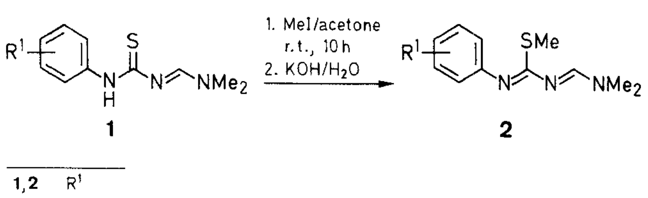
Department of Chemistry, North-Eastern Hill University, Shillong 793 003, Meghalaya, India

Three methods for the synthesis of various stable 1,3-diaza-1,3-butadienes from easily available thiourea derivatives are reported.

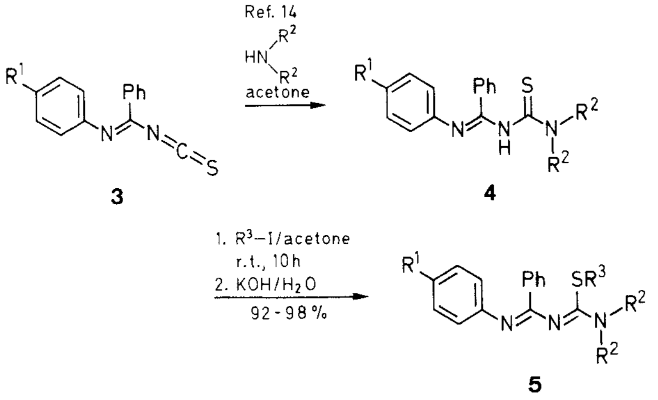
Heterodienes are of large potentiality as regards the synthesis of heterocyclic compounds.[1,2] Thus, 1,2- and 1,4-diaza-1,3-butadienes have been extensively used for this purpose; on the other hand, reports on comparable reactions of 1,3-diaza-1,3-butadienes are rare,[1-6] probably due to difficulties encountered in the preparation of stable 1,3-diaza-1,3-butadienes.[1] These heterodienes have been postulated as reactive intermediates,[7,8] and hemicyclic 1,3-diaza-1,3-butadienes such as 2-(aminomethylenamino)-*N*-heterocycles have been used as N=C−N=C units in ring-closure reactions.[9] Relatively easy access to some substituted 1,3-diaza-1,3-butadienes is possible by reaction of *N*-silylimines with imidoyl halides[5,6] and by the condensation of suitable *N*′-arylbenzamidines with dimethylformamide acetals.[10] Our interest in 1,3-diaza-1,3-butadienes[11,12] made us work out some general methods for the preparation of 1,3-diaza-1,3-butadienes (more particularly: 1,3,5-triaza-1,3-pentadienes) of various types.

The preparation of various 1-aryl-4-dimethylamino-2-methylthio-1,3-diaza-1,3-butadienes [methyl *N*′-aryl-*N*-(dimethylaminomethylene)carbamimidothioates, **2**], described briefly in our earlier communication,[12] was achieved by *S*-alkylation of *N*-aryl-*N*′-(dimethylaminomethylene)thioureas **1**, which were, in turn, prepared by condensation of *N*-arylthioureas with dimethylformamide dimethyl acetal according to Lit.[13]. Thus, treatment of thioureas **1** with methyl iodide in dry acetone afforded the hydroiodides of **2**, which were converted into the desired free compounds **2** in good yields by treatment with aqueous potassium hydroxide. Most 1,3-diaza-1,3-butadienes **2** were isolated as crystalline solids, some as a viscous mass. The identities of products **2** were established by analytical and spectral data. For example, the 1,3-diazabutadiene **2a** exhibited the molecular ion peak at $m/z = 221$. Its ^{1}H-NMR spectrum showed three singlets at $\delta = 2.30$ (3H), 2.90 (6H), and 8.20 (1H), which were assigned to the SCH_3 and $N(CH_3)_2$ protons and the olefinic proton, respectively. The aromatic protons appeared as multiplet at $\delta = 7.01-7.40$ (5H).

We further synthesised alkyl *N,N*-dialkyl-*N*′-(α-aryliminobenzyl)carbamimidothioates **5**, i.e., 1,3-diaza-1,3-butadienes having two polarising functions at position 4. This was realised in high yields by reaction of α-aryliminobenzyl isothiocyanates **3** with secondary amines[14] and *S*-alkylation of the resultant thioureas **4** with alkyl iodides, followed by treatment with aqueous potassium hydroxide.

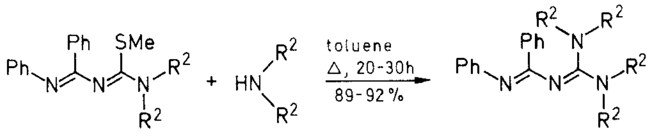


1,2	R¹
a	H
b	4-Me
c	2-Me
d	4-Cl
e	4-OMe



5	R¹	R²	R²	R³
a	H	$(CH_2)_2O(CH_2)_2$		Me
b	H	$(CH_2)_3$		Me
c	H	$(CH_2)_2$		Me
d	H	Me	Me	Me
e	H	$(CH_2)_2O(CH_2)_2$		Et
f	H	$(CH_2)_3$		Et
g	H	$(CH_2)_2$		Et
h	H	Me	Me	Et
i	Me	$(CH_2)_2O(CH_2)_2$		Me
j	Me	$(CH_2)_3$		Me
k	Me	$(CH_2)_2$		Me
l	Me	Me	Me	Me
m	Cl	$(CH_2)_2O(CH_2)_2$		Me
n	Cl	$(CH_2)_3$		Me
o	Cl	$(CH_2)_2$		Me
p	Cl	Me	Me	Me

The 1,3-diaza-1,3-butadienes **5** react with secondary amines in boiling toluene (20−30 h) to give a different type of 1,3-diaza-1,3-butadienes, i.e. **6**, having two amino groups at position 4.



In the ^{1}H-NMR spectra of **5** and **6**, the signals of the *ortho* protons of the phenyl group on C-2 appear around $\delta = 8.00$, possibly because of deshielding due to conjugation with the C=N unit. For the preferred stereochemistry of 1,3-diaza-1,3-butadienes as based on theoretical calculations. see Lit.[15]

Table. 1,3-Diaza-1,3-butadienes **2**, **5**, and **6** Prepared

Product	Yield[a] (%)	mp (°C) (solvent)[b]	Molecular Formula[c]	MS (70 eV) m/z (M^+)	IR (KBr) ν (cm^{-1})	^1H-NMR (Solvent/TMS)[d] δ, J (Hz)
2a	86	viscous oil	$C_{11}H_{15}N_3S$ (221.3)	221	3050, 2960, 1640, 1600	2.30 (s, 3H, SCH_3), 2.92 [s, 6H, $N(CH_3)_2$], 7.01–7.4 (m, 5H_{arom}), 8.08 (s, 1$H_{olefinic}$)
2b	90	78–80 (PE)	$C_{12}H_{17}N_3S$ (235.3)	235	3040, 2950, 1640, 1610	2.20 (s, 3H, CH_3), 2.28 (s, 3H, SCH_3), 2.92 [s, 6H, $N(CH_3)_2$], 7.03–7.43 (m, 4H_{arom}), 8.10 (s, 1$H_{olefinic}$)
2c	70	viscous oil	$C_{12}H_{17}N_3S$ (235.3)	235	3050, 2950, 1640, 1595	2.16 (s, 3H, CH_3), 2.28 (s, 3H, SCH_3), 2.90 [s, 6H, $N(CH_3)_2$], 6.92–7.26 (m, 4H_{arom}), 8.10 (s, 1$H_{olefinic}$)
2d	82	54–55 (PE)	$C_{11}H_{14}ClN_3S$ (255.7)	255	3100, 2950, 1640, 1595	2.31 (s, 3H, SCH_3), 2.92 [s, 6H, $N(CH_3)_2$], 7.02–7.38 (m, 4H_{arom}), 8.10 (s, 1$H_{olefinic}$)
2e	86	viscous oil	$C_{12}H_{17}N_3OS$ (251.4)	251	3050, 2960, 1600, 1570	2.28 (s, 3H, SCH_3), 3.10 [s, 6H, $N(CH_3)_2$], 3.62 (s, 3H, OCH_3), 7.06–7.42 (m, 4H_{arom}), 8.10 (s, 1$H_{olefinic}$)
5a	98	108 (benzene/PE)	$C_{19}H_{21}N_3OS$ (339.5)	339	3050, 2960, 1600, 1570	2.10 (s, 3H, SCH_3), 3.30–3.34 (m, 4H, CH_2NCH_2), 3.40–3.48 (m, 4H, CH_2OCH_2), 6.80–6.90 (m, 2H_{arom}), 6.94–7.26 (m, 6H_{arom}), 7.94–8.08 (m, 2H_{arom})
5b	95	44–46[e]	$C_{20}H_{23}N_3S$ (337.5)	337	3100, 2960, 1590, 1560	1.10–1.43 (m, 6H, $CH_2CH_2CH_2$), 2.12 (s, 3H, SCH_3), 2.97–3.16 (m, 4H, CH_2NCH_2), 6.68–6.78 (m, 2H_{arom}), 6.97–7.23 (m, 6H_{arom}), 7.81–7.95 (m, 2H_{arom})
5c	97	106 (benzene/PE)	$C_{19}H_{21}N_3S$ (323.5)	323	3100, 2960, 1590, 1560	1.60–1.74 (m, 4H, CH_2CH_2), 2.25 (s, 3H, SCH_3), 2.97–3.14 (m, 4H, CH_2NCH_2), 6.88–6.80 (m, 2H_{arom}), 7.00–7.30 (m, 6H_{arom}), 7.94–8.07 (m, 2H_{arom})
5d	96	78–80[e]	$C_{17}H_{19}N_3S$ (297.4)	297	3050, 2960, 1600, 1550	2.01 (s, 3H, SCH_3), 2.68 [s, 6H, $N(CH_3)_2$], 6.63–6.88 (m, 2H_{arom}), 7.02–7.33 (m, 6H_{arom}), 7.95–8.10 (m, 2H_{arom})
5e	94	88 (benzene/PE)	$C_{20}H_{23}N_3OS$ (353.5)	253	3050, 2920, 1600, 1560	0.98–1.07 (t, 3H, CH_3, $J = 8$), 2.48–2.73 (q, 2H, SCH_2, $J = 10$), 3.23–3.34 (m, 1H, CH_2NCH_2), 3.38–3.48 (m, 4H, CH_2OCH_2), 6.80–6.93 (m, 2H_{arom}), 7.04–7.34 (m, 6H_{arom}), 7.87–8.03 (m, 2H_{arom})
5f	94	viscous oil	$C_{21}H_{25}N_3S$ (351.5)	351	3050, 2940, 1600, 1560	0.94–1.12 (t, 3H, CH_3, $J = 8$), 1.27–1.53 (m, 6H, $CH_2CH_2CH_2$), 2.45–2.71 (q, 2H, SCH_2, $J = 10$), 3.17–3.33 (m, 4H, CH_2NCH_2), 6.76–6.91 (m, 2H_{arom}), 7.10–7.40 (m, 6H_{arom}), 7.90–8.03 (m, 2H_{arom})
5g	94	viscous oil	$C_{20}H_{23}N_3S$ (337.5)	337	3050, 2940, 1600, 1550	1.15–1.31 (t, 3H, CH_3, $J = 8$), 1.56–1.73 (m, 4H, CH_2CH_2), 2.73–3.00 (q, 2H, SCH_2, $J = 10$), 3.03–3.30 (m, 4H, CH_2NCH_2), 6.73–6.88 (m, 2H_{arom}), 7.06–7.33 (m, 6H_{arom}), 8.00–8.13 (m, 2H_{arom})
5h	97	viscous oil	$C_{18}H_{21}N_3S$ (311.5)	–	3050, 2950, 1600, 1550	1.03–1.22 (t, 3H, CH_3, $J = 8$), 2.63–2.82 (q, 2H, SCH_2, $J = 10$), 2.78 [s, 6H, $N(CH_3)_2$], 6.78–6.88 (m, 2H_{arom}), 7.08–7.34 (m, 6H_{arom}), 7.97–8.06 (m, 2H_{arom})
5i	98	105–106 (benzene/PE)	$C_{20}H_{23}N_3OS$ (353.5)	353	3050, 2920, 1590, 1530	2.02 (s, 3H, CH_3), 2.31 (s, 3H, SCH_3), 3.28–3.42 (m, 4H, CH_2NCH_2), 3.47–3.66 (m, 4H, CH_2OCH_2), 6.78–6.97 (m, 2H_{arom}), 7.26–7.38 (m, 5H_{arom}), 7.85–8.03 (m, 2H_{arom})
5j	97	viscous oil	$C_{21}H_{25}N_3S$ (351.5)	–	3050, 2940, 1598, 1540	1.43–1.68 (m, 6H, $CH_2CH_2CH_2$), 2.15 (s, 3H, CH_3), 2.33 (s, 3H, SCH_3), 3.35–3.50 (m, 4H, CH_2NCH_2), 6.9–7.1 (m, 2H_{arom}), 7.30–7.48 (m, 5H_{arom}), 7.98–8.10 (m, 2H_{arom})
5k	97	72–74[e]	$C_{20}H_{23}N_3S$ (337.5)	337	3050, 2940, 1600, 1540	1.52–1.70 (m, 4H, CH_2CH_2), 2.26 (s, 6H, CH_3, SCH_3), 2.92–3.12 (m, 4H, CH_2NCH_2), 6.63–7.00 (m, 2H_{arom}), 7.20–7.34 (m, 5H_{arom}), 7.97–8.13 (m, 2H_{arom})
5l	94	viscous oil	$C_{18}H_{21}N_3S$ (311.5)	311	3050, 2920, 1590, 1540	2.13 (s, 3H, CH_3), 2.25 (s, 3H, SCH_3), 2.75 [s, 6H, $N(CH_3)_2$], 6.68–7.02 (m, 2H_{arom}), 7.20–7.33 (m, 5H_{arom}), 7.90–8.03 (m, 2H_{arom})
5m	94	136–138 (benzene/PE)	$C_{19}H_{20}ClN_3OS$ (373.9)	373	3050, 2980, 1600, 1550	2.12 (s, 3H, SCH_3), 3.34–3.35 (m, 4H, CH_2NCH_2), 3.50–3.64 (m, 4H, CH_2OCH_2), 6.83–6.98 (m, 2H_{arom}), 7.13–7.47 (m, 5H_{arom}), 7.94–8.06 (m, 2H_{arom})
5n	92	66–67[e]	$C_{20}H_{22}ClN_3S$ (371.9)	371	3080, 2970, 1600, 1560	1.32–1.53 (m, 6H, $CH_2CH_2CH_2$), 2.08 (s, 3H, SCH_3), 3.25–3.46 (m, 4H, CH_2NCH_2), 6.78–6.81 (m, 2H_{arom}), 7.07–7.34 (m, 5H_{arom}), 7.87–8.00 (m, 2H_{arom})
5o	93	96 (benzene/PE)	$C_{19}H_{20}ClN_3S$ (357.9)	357	3080, 2980, 1600, 1560	1.68–1.92 (m, 4H, CH_2CH_2), 2.20 (s, 3H, SCH_3), 3.07–3.26 (m, 4H, CH_2NCH_2), 6.82–6.95 (m, 2H_{arom}), 7.15–7.43 (m, 5H_{arom}), 8.02–8.15 (m, 2H_{arom})
5p	94	98–100 (benzene/PE)	$C_{17}H_{18}ClN_3S$ (331.9)	–	3100, 2950, 1600, 1560	2.16 (s, 3H, SCH_3), 2.95 [s, 6H, $N(CH_3)_2$], 6.85–6.95 (m, 2H_{arom}), 7.13–7.32 (m, 5H_{arom}), 7.87–8.02 (m, 2H_{arom})
6a	92	195 (benzene)	$C_{22}H_{26}N_4O_2$ (378.5)	378	3050, 2900, 1610, 1560	2.84–3.02 (m, 8H, CH_2NCH_2), 2.43–3.60 (m, 8H, CH_2OCH_2), 6.91–7.05 (m, 2H_{arom}), 7.17–7.43 (m, 6H_{arom}), 7.87–8.02 (m, 2H_{arom})

Table. (continued)

Product	Yield[a] (%)	mp (°C) (solvent)[b]	Molecular Formula[c]	MS (70 eV) m/z (M^+)	IR (KBr) ν (cm^{-1})	^1H-NMR (Solvent/TMS)[d] δ, J (Hz)
6b	89	134–135 (benzene/PE)	$C_{24}H_{30}N_4$ (374.5)	374	3050, 2900, 1610, 1560	1.32–1.53 (m, 12H, $CH_2CH_2CH_2$), 2.70–2.93 (m, 8H, CH_2NCH_2), 6.91–7.28 (m, 2H_{arom}), 7.37–7.45 (m, 6H_{arom}), 8.05–8.23 (m, 2H_{arom})
6c	90	144–146 (benzene)	$C_{22}H_{26}N_4$ (346.5)	–	3100, 2950, 1580, 1500	1.56–1.73 (m, 8H, CH_2CH_2), 2.78–3.10 (m, 8H, CH_2NCH_2), 6.73–7.03 (m, 2H_{arom}), 7.30–7.40 (m, 6H_{arom}), 8.06–8.20 (m, 2H_{arom})

[a] Yields of **2**, **5**, and **6** are based on **1**, **4**, and **5**, respectively.

[b] PE = petroleum ether.

[c] Satisfactory microanalyses obtained: C ±0.40, H ±0.30, N ±0.20.

[d] Compounds **2a–e** in CCl_4, all other compounds in $CDCl_3$.

[e] Viscous oil which solidifies very slowly.

The 1,3-diaza-1,3-butadienes (1,3,5-triaza-1,3-pentadienes) described here are stable enough to be stored at room temperature for a few months without any decomposition. They possess polarising functions at positions 2 or 4 which make these dienes highly reactive 4π components in Diels-Alder cycloadditions with various dienophiles (results of these reactions will be presented separately).

Melting points were determined on a Toshniwal melting point apparatus and are uncorrected. Microanalyses and mass spectra were performed by R.S.I.C., C.D.R.I., Lucknow, India. IR spectra were recorded on a Perkin-Elmer model 297 spectrophotometer, ^1H-NMR spectra on a Varian 390 90 MHz spectrometer.

All *N*-arylthioureas[16] dimethylformamide dimethylacetal,[17] *N*-aryl-*N*-(dimethylaminomethylene)thioureas,[13] and *N*-(α-aryliminobenzyl)thioureas[14] were prepared by reported procedures.

1-Aryl-4-dimethylamino-2-methylthio-1,3-diaza-1,3-butadienes [Methyl *N*′-Aryl-*N*-(dimethylaminomethylene)carbamimidothioates] 2; General Procedure:

A solution of the appropriate *N*′ aryl-*N*-(dimethylaminomethylene)thiourea (*N*-arylthiocarbamoylformamidine)[13] **1** (0.1 mol) and MeI (31.23 g, 0.22 mol) in dry acetone (250 mL) is stirred at r.t. for 10 h. The separated hydroiodide of **2** is isolated by suction and treated with 3 N aq KOH (50 mL). The resultant mixture is extracted with benzene (3 x 100 mL). The extract is washed with cold H_2O (3 x 50 mL) and dried ($MgSO_4$). The solvent is removed under reduced pressure to give the product **2**, which is sufficiently pure for use in further reactions.

4-Dialkylamino-4-alkylthio-1-aryl-2-phenyl-1,3-diaza-1,3-butadienes [Alkyl *N*,*N*-Dialkyl-*N*′-(α-aryliminobenzyl)carbamimidothioates] 5; General Procedure:

A solution of the appropriate *N*,*N*-dialkyl-*N*′-(α-aryliminobenzyl) thiourea **4** (0.01 mol) and MeI or EtI (0.023 mol) in dry acetone (250 mL) is stirred at r.t. for 10 h. The separated hydroiodide of **5** is isolated by suction and treated with 3 N aq KOH (50 mL). The resultant mixture is extracted with $CHCl_3$ (3 x 100 mL) and the extract is washed with H_2O (3 x 50 mL), (Na_2SO_4), and evaporated under reduced pressure to the sufficiently pure product **5**; solid products are recrystallised from appropriate solvents.

4,4-Bis(dialkylamino)-1,2-diphenyl-1,3-diaza-1,3-butadienes [*N*,*N*,*N*′,*N*′-Tetraalkyl-*N*″-(α-phenylaminobenzyl)guanidines] 6; General Procedure:

A solution of the 4-dialkylamino-4-methylthio-1,2-diphenyl-1,3-diaza-1,3-butadiene **5a,b,c** (0.01 mol) and the corresponding secondary amine (morpholine, piperidine, pyrrolidine; 0.02 mol) in dry toluene (50 mL) is refluxed for 20–30 h. The solvent is then evaporated under reduced pressure and the remaining product is recrystallised from an appropriate solvent.

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