Synthesis of 1,3-Dichloro-1,5-diazapenta-1,4-dienes

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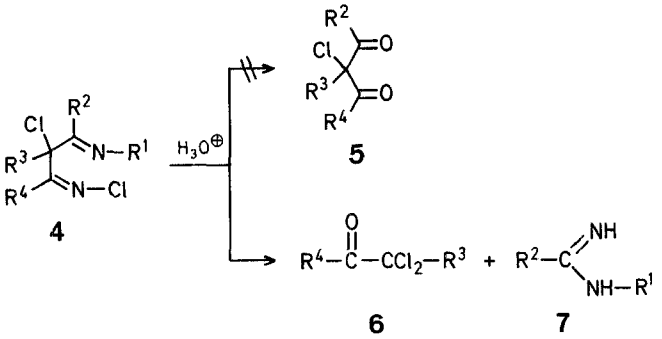
In an earlier paper we have reported the reaction of 1-azabutadienes (**1**, 3-amino-2-alkenimines) with *N*-chlorosuccinimide (**2**) in stoichiometric ratio leading exclusively to the 2-halogenated derivatives **3**. These compounds were found to be useful precursors of chloro-substituted heterocycles[1]. On the other hand, *N*-chloroamidines[2] and *N*-chloro-4- and -5-alkenamines[3] show special reactivity due to the N – Cl bond and can therefore be used for the preparation of a variety of azaheterocycles, some of them with an alkaloid partial structure. Accordingly, we focused our attention on the *N*-chlorination of azabutadienes **1**. *N*-Chlorosuccinimide cannot only be used for the preparation of halogenated enamines[4] but also for the *N*-chlorination of imine groups such as in amidines[5]. Here we report the preparation of 1,3-dichloro-1,5-diazapenta-1,4-dienes (**4**) starting from either **1** or **3** as well as their rearrangement-cleavage reaction upon acid hydrolysis.

When 4-amino-1-azabutadienes (**1**) or 2-chloroalkane-1,3-diimines (**3**) are allowed to react with *N*-chlorosuccinimide (**2**) in a molar ratio of 1 : 2 or 1 : 1, respectively, in toluene at 60 °C, dichloro derivatives (**4**) are obtained in high yields.

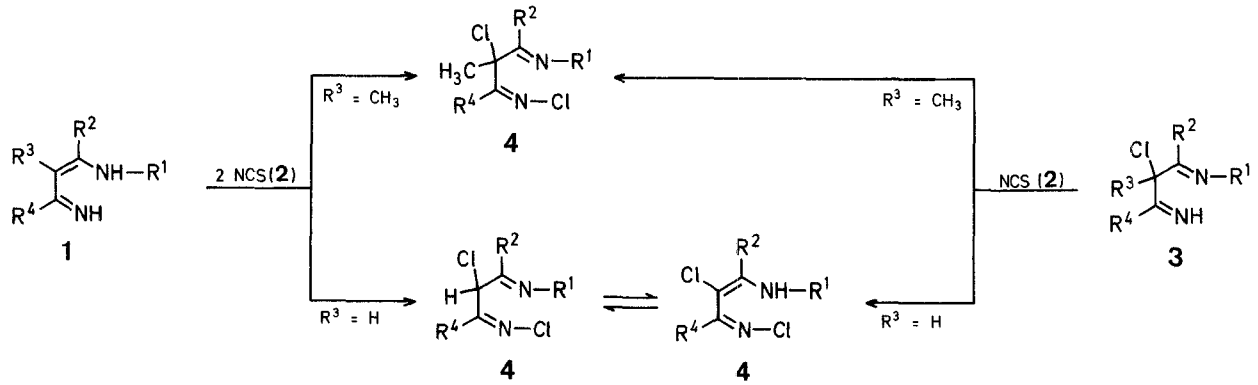


By the above-described method, *N*, 2-dichloroalkane-1,3-diimines (**4**) can be prepared in a regioselective manner. The high yields reached in all instances combined with the easy preparation of the starting materials make this synthesis a convenient route to compounds **4**.

The 1-azabutadienes **1**[6] and the monohalogenated diimines **3**[1] were prepared as previously reported. Dichloroketones **6**[7] and amidines **7**[8] are known compounds.

1,3-Dichloro-3-methyl-5-phenyl-4-(4-chlorophenyl)-2-(4-methylphenyl)-1,5-diazapenta-1,4-diene (4e); Typical Procedure:

N-Chlorosuccinimide (1.67 g, 20 mmol) is added to a stirred solution of 3-methyl-5-phenyl-4-(4-chlorophenyl)-2-(4-methylphenyl)-1,5-diazapenta-1,3-diene (**1e**; 3.26 g, 10 mmol) in toluene (60 ml). The resultant mixture is heated at 50 °C for 3 h, then cooled, and treated with aqueous 3 normal potassium hydroxide (150 ml). The organic layer is washed with water (50 ml) and dried with sodium sulfate. Removal of the solvent leaves a solid which is purified by recrystallization from hexane to give **4e**; yield: 3.44 g (87%); m.p. 115–117 °C.



Compounds **4** were characterized by microanalyses and spectroscopic data. Thus, the ^{13}C-N.M.R. spectra of **4** show characteristic signals at $\delta \approx 167$ (s), 157 (s), and 86 (s) ppm which are assignable to the imine C-atoms and to the C-atom bearing the Cl-atom, respectively.

In the case of R^3 = H there is spectroscopic evidence of an equilibrium between the tautomeric forms **4** and **4'**. Whereas the form **4'** is present according to the I. R. (Nujol) and ^{1}H-N.M.R. ($CDCl_3$) spectra (see Table 2, entries **g**, **h**, **i**), the form **4** is found almost exclusively in the ^{13}C-N.M.R. ($CDCl_3$) spectrum since the C-3 atom appears as a doublet at ~ 68.5 ppm. Low- and high-temperature N.M.R. studies on the tautomerism **4** ⇌ **4'** as well as studies on the mechanism of the reaction are in progress.

Unlike the monochloro derivatives **3**[1], compounds **4** are not converted into the 2-chloro-1,3-diketones **5** upon treatment with 2 normal sulfuric acid in tetrahydrofuran; instead, a rearrangement-cleavage process takes place to afford a ~ 1/1 mixture of α,α-dichloroketones **6** and amidines **7**, the yields ranging from 80–90%.

$C_{23}H_{19}Cl_3N_2$ (429.8) calc. C 64.28 H 4.55 Cl 24.65 N 6.52 found 64.41 4.46 24.75 6.46

I. R. and ^{1}H-N.M.R., see Table 2.

^{13}C-N.M.R. ($CDCl_3$/TMS_{int}): δ = 167.71 (s), 157.11 (s), 147.83 (s), 139.84 (s), 137.09 (s), 134.06 (s), 130.55 (s), 86.12 (s), 35.46 (q), 21.12 (q) ppm.

The preparation of compounds **4** from **3** is carried out in an analogous manner, except for the use of equimolecular amounts of **3** and *N*-chlorosuccinimide.

Table 1. 1,3-Dichloro-1,5-diazapenta-1,4-dienes(**4**) from 4-Amino-1-azabutadienes (**1**)

4	R^1	R^2	R^3	R^4	Yield [%]	m.p. [°C] (hexane)	Molecular Formula[a]	M.S. *m/e* (M^+)
a	C_6H_5	C_6H_5	CH_3	C_6H_5	89	128–130°	$C_{22}H_{18}Cl_2N_2$ (381.3)	380
b	C_6H_5	C_6H_5	CH_3	4-H_3C—C_6H_4	91	120–122°	$C_{23}H_{20}Cl_2N_2$ (395.3)	394
c	4-H_3C—C_6H_4	C_6H_5	CH_3	C_6H_5	83	83–85°	$C_{23}H_{20}Cl_2N_2$ (395.3)	
d	4-H_3C—C_6H_4	C_6H_5	CH_3	4-H_3C—C_6H_4	86	104–106°	$C_{24}H_{22}Cl_2N_2$ (409.4)	
e	C_6H_5	4-Cl—C_6H_4	CH_3	4-H_3C—C_6H_4	87	115–117°	$C_{23}H_{19}Cl_3N_2$ (429.8)	
f	C_6H_5	C_6H_5	CH_3	4-Cl—C_6H_4	90	127–129°	$C_{22}H_{19}Cl_3N_2$ (415.7)	
g	C_6H_5	C_6H_5	H	C_6H_5	74	86–88°	$C_{21}H_{16}Cl_2N_2$ (366.3)	
h	C_6H_5	C_6H_5	H	4-H_3C—C_6H_4	79	120–122°	$C_{22}H_{18}Cl_2N_2$ (381.3)	380
i	4-H_3C—C_6H_4	C_6H_5	H	C_6H_5	80	92–94°	$C_{22}H_{18}Cl_2N_2$ (381.3)	

[a] Satisfactory microanalyses obtained: C ±0.30; H ±0.23; N ±0.17; Cl ±0.25.

Table 2. Spectral Data of Compounds **4**

4	I.R. (Nujol) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm]
a	1650, 1620	2.4 (s, 3H, CH_3); 6.3–8.0 (m, 15H_{arom})
b	1655, 1625	2.2 (s, 3H, CH_3); 2.4 (s, 3H, CH_3); 6.7–8.0 (m, 14H_{arom})
c	1660, 1620	2.3 (s, 3H, CH_3); 2.4 (s, 3H, CH_3); 6.6–8.0 (m, 14H_{arom})
d	1650, 1610	2.2 (s, 3H, CH_3); 2.3 (s, 3H, CH_3); 2.45 (s, 3H, CH_3); 6.5–8.0 (m, 13H_{arom})
e	1650, 1615	2.3 (s, 3H, CH_3); 2.4 (s, 3H, CH_3); 6.5–7.9 (m, 13H_{arom})
f	1650, 1600	2.4 (s, 3H, CH_3); 6.6–7.9 (m, 14H_{arom})
g	3350, 1620, 1590	6.3–6.5 (br., 1H, NH); 6.8–7.6 (m, 15H_{arom})
h	3450, 1630, 1600	2.2 (s, 3H, CH_3); 6.4 (br., 1H, NH); 6.8–7.7 (m, 14H_{arom})
i	3450, 1645, 1620	2.2 (s, 3H, CH_3); 6.9 (br., 1H, NH); 6.9–7.5 (m, 14H_{arom})

Hydrolysis of Compounds 4e; Typical Procedure:

A solution of compound **4e** (1.97g, 5 mmol) in tetrahydrofuran (30 ml) is stirred with 2 normal sulfuric acid (25 ml) for 4 h at room temperature. The resultant mixture is extracted with ether (3 × 40 ml). The organic extract is washed with saturated sodium chloride solution (40 ml), and dried with sodium sulfate. The solvent is removed and the residue distilled in vacuo to afford *2,2-dichloro-1-(4-methylphenyl)-propanone* (**6**, $R^3 = CH_3$, $R^4 = 4\text{-}H_3C\text{—}C_6H_4$); yield: 0.93 g (86%); b.p. 76°C/0.05 torr.

$C_{10}H_{10}Cl_2O$	calc.	C 55.33	H 4.64	Cl 32.66
(217.1)	found	55.06	4.41	32.82

M.S.: *m/e* = 216 (M^+).

I.R. (neat): ν = 1680 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 2.35 (s, 3H, CH_3); 2.4 (s, 3H, CH_3); 7.2 (d, 2H_{arom}); 8.1 ppm (d, 2H_{arom}).

^{13}C-N.M.R. ($CDCl_3$/TMS_{int}): δ = 187.96 (s), 145.37 (s), 132.39 (d), 129.89 (d), 129.65 (s), 84.08 (s), 35.27 (q), 22.53 (q) ppm.

The aqueous layer is made alkaline with aqueous 6 normal potassium hydroxide and extracted with ether (3 × 40 ml). The organic extract is dried with sodium sulfate, the solvent is removed, and the residue is recrystallized from hexane to give N-*phenyl-4-chlorobenzamidine* (**7**, $R^1 = C_6H_5$, $R^2 = 4\text{-Cl—}C_6H_4$); yield: 1.01 g (88%); m.p. 138–140°C (Ref.[9], m.p. 140–141°C).

I.R. (Nujol): ν = 3450, 3300, 1620 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 4.7 (br., 2H, NH); 6.8–7.8 ppm (m, 9H_{arom}).

Received: December 28, 1983

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