A Simple Synthesis of a 1*H*-1,2,4-Triazepine

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Synthesis of 1,2,4-triazepines is a growing[1-12] research area owing, in part, to the presence of the related 1,4-diazepine ring system in some widely-sold, prescription tranquilizers for humans.

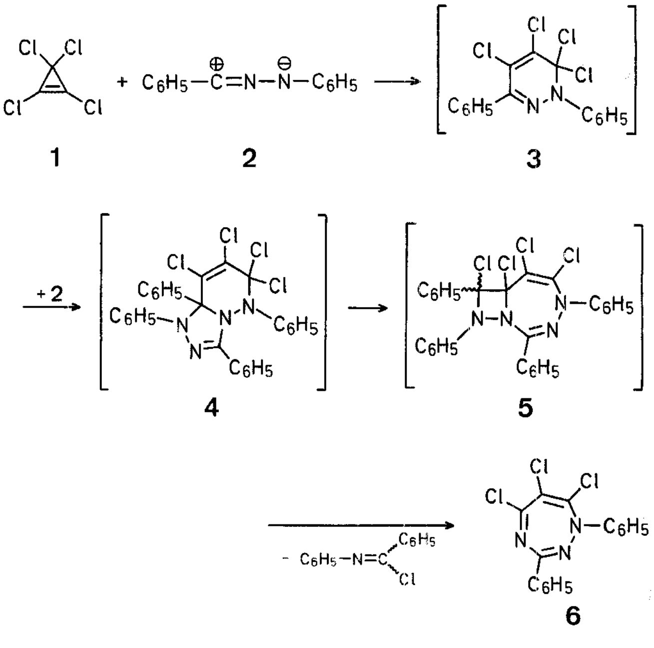
We report the prototype procedure for synthesis of a non-condensed 1*H*-1,2,4-triazepine from tetrachlorocyclopropene (**1**). Other, tautomeric and fully-unsaturated 1,2,4-triazepines (benzo-1*H*-, -2*H*-, -4*H*-, and -6*H*-1,2,4-triazepines) are known to arise in fair-to-excellent yields from three general preparative procedures which are given below.

(a) Intramolecular migration of electrons from nitrogen to a doubly- or triply-bonded nucleus initiates cyclization and the formation of numerous benzo-1*H*-1,2,4-triazepines[1], partially saturated 1,2,4-triazepines[2], and oxo- and thioxo-1,2,4-triazepines[3-7].

(b) Subsequent alkylation of oxo- and thioxo-1,2,4-triazepines [from (a) above] yields 4*H*-1,2,4-triazepines[8].

(c) Rearrangement of a triazanorcaradiene system (or of a corresponding diradical) leads directly to 2*H*-[9,10,11], 6*H*-[10], or 4*H*-1,2,4-triazepines[12].

In the present method, the 1*H*-1,2,4-triazepine (**6**) is formed from two quite different precursors: tetrachlorocyclopropene (**1**), which functions as both a reactant and reaction solvent, and diphenylnitrilimine (**2**), which is generated *in situ*[13] (from triethylamine and *N*-phenylbenzenecarbohydrazonoyl chloride). Compounds **1** and **2** react at room temperature to form 1,3-diphenyl-5,6,7-trichloro-1*H*-1,2,4-triazepine (**6**) in 93% yield.



Tetrachlorocyclopropene (**1**) is a useful reagent for synthesis[14,15] and is readily available. The chlorine atoms of **1** can be displaced from its products to give numerous analogous products. With 1,3-dipoles, tetrachlorocyclopropene (**1**) offers the extra advantage of a facile reaction. It undergoes cycloaddition reactions with 1,3-dipoles such as diphenylnitrilimine, diazoalkanes[16,17], azides[17], isobenzofuran[15,18], and 2,4-diphenyl-3-methyloxazolium 5-oxide[19]. Extension of the reaction of tetrachlorocyclopropene to nitrilimines other than diphenylnitrilimine was not at-

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Table. Metastable Processes Observed in the Mass Spectrum of **6**

Metastable Process	m/e	
	m^* found	m^* calc.
$^{351}M \rightarrow [^{351}M - C_6H_5CN]$	175.4	175.2
$^{349}M \rightarrow [^{349}M - C_6H_5CN]$	173.4	173.4
$[^{349}M - Cl] \rightarrow [^{349}M - Cl - C_6H_5NH]$	156.9	157.0[a]
$[^{351}M - Cl] \rightarrow [^{351}M - Cl - C_6H_5N_2]$	140.95	140.9
$[^{349}M - C_6H_4] \rightarrow [^{349}M - C_6H_4 - C_6H_5NH]$	120.1	120.0
$[^{349}M - C_6H_5NCl] \rightarrow [^{349}M - C_6H_5NCl - 2\,Cl]$	104.9	104.95
$[^{351}M - C_6H_5NCl] \rightarrow [^{351}M - C_6H_5NCl - {}^{35}Cl - {}^{37}Cl]$	103.9	104.0

[a] Compare with Ref.[26].

tempted in our laboratory; other cyclopropenes (cyclopropene, 3,3-dimethylcyclopropene) are known[20] to react with some *C*-phenyl-*N*-arylnitrilimines to form 1:1 adducts.

As depicted in the Scheme, the simple 1*H*-1,2,4-triazepine (**6**) probably derives from an isomer (**5**) of the 1:2 cycloadduct **4**, upon a retro [2+2] cycloaddition of diphenylnitrilimine with the six-membered 2,3-dihydropyridazine **3**. This reaction between a heterocyclic C=N bond and a nitrilimine to generate intermediate **4** is precedented by the cycloaddition of *N*-methylbenzimidazole and *C*-acetyl-*N*-phenylnitrilimine, which gives a stable cycloadduct[21].

1,3-Diphenyl-5,6,7-trichloro-1*H*-1,2,4-triazepine (**6**) is the prototype 1*H*-1,2,4-triazepine. Its significant stability is inferred from the abundance of metastable fragments in its mass spectrum. The two other isolable *N*-substituted and fully-unsaturated 1,2,4-triazepines are 4*H*-tautomers. In contrast, the systems with unsubstituted nitrogen are exclusively 2*H*-[9,10,11] and 6*H*-1,2,4-triazepines[10]. The remaining 1,2,4-triazepine structures (3*H*-, 5*H*-, and 7*H*-) possess a nitrogen-to-nitrogen double bond and no experimental data exist to substantiate them as stable entities.

The 1*H*-, 2*H*-, and 4*H*-1,2,4-triazepine rings are spectroscopically distinguishable. Only 4*H*-1,2,4-triazepines show a strong $[M-N_2]^{+\cdot}$ mass spectral peak; no $[M-N_2]$ radical ion has been reported for another fully unsaturated 1,2,4-triazepine system, and it was not observed (R.I. < 10%) for the 1*H*-1,2,4-triazepine **6**. The 1*H*- and 2*H*-1,2,4-triazepines exhibit mass spectral similarities; both yield the radical cations $[M]^{+\cdot}$ and $[M-RCN]^{+\cdot}$.

The structure of **6** is confirmed by its I.R. spectrum[9,22-25]. No infra-red evidence exists for C=C, C=N, polysubstituted phenyl groups, or benzo-fused rings in compound **6**. Alternative structures to **6**, which possess fused three- and four-membered rings (and sp^3 carbon atoms) were definitely excluded from consideration; there is no chemical shift value smaller than 121.4 ppm (relative to tetramethylsilane) in the ^{13}C-FT-N.M.R. spectrum of **6**. The extended lifetime of **6** under normal laboratory conditions excludes other heterocycles of limited stability and also *N*-chloramine structures.

The specific atomic array in **6** is consistent with the observed metastable processes (Table) and an alternative 1,2,3-triazepinoid structure is disregarded for the following reason. A 1,2,3-triazepine would facilely extrude diatomic nitrogen following loss of phenyl nitrene upon electron impact[27,28] on the parent molecule to give a pyridazine (which are known to loose nitrogen readily[27,28]). No evidence exists in the M.S. of **6** for the sequence $[\text{a pyridazine}]^{+\cdot} \rightarrow [\text{a pyridazine} - N_2]^{+\cdot}$.

1,3-Diphenyl-5,6,7-trichloro-1*H*-1,2,4-triazepine (6):
Triethylamine (0.137 ml, 0.98 mmol) is added slowly to stirred *N*-phenylbenzenecarbohydrazonoyl chloride[13] (0.44 g, 1.91 mmol) in tetrachlorocyclopropene (**1**; 1.00 ml, 8.7 mmol). Gas and heat are readily evolved. After six to seven days at room temperature, the heterogeneous dark brown reaction mixture is evacuated. The residue (1.15 g) in chloroform (< 1.50 ml) is applied to an activated P.L.C. plate (silica gel). Developed (1:4 ether/30–60 °C petroleum ether) and dried P.L.C. regions are leached with benzene, then chloroform, and finally in some cases, with acetone. N-*Phenylbenzenecarbohydrazonoyl chloride* (6% recovery) and *2,3-dichloropropenoic acid* are identified in appropriate leaches by comparison (U.V. and I.R. spectra, m.p.) with authentic samples.

Leaches of another region of the developed P.L.C. plate give **6**; yield: 0.16 g (48% based on nitrilimine **2**, 93% based on triethylamine). Recrystallization from hexane yields a white-yellow powder (24% recovery): m.p. 97.0–99.7 °C.

$C_{16}H_{10}Cl_3N_3$	calc.	C 54.81	H 2.87	Cl 30.33	N 11.98
(350.6)	found	54.99	2.77	29.97	11.94

I.R. (CHCl$_3$): $\nu = 1589$; 1500; 1457; 1445; 1351; 1341; 709; 686 cm^{-1}; compare with Refs.[9,22-25].

U.V. (ethanol): $\lambda_{max} = 255$ (O.D. 0.709); 222 (sh, 0.937) nm.

^{13}C-FT-N.M.R. (CDCl$_3$): $\delta = 157.3$; 154.5; 137.7; 130.4; 129.3; 129.1; 128.8; 128.4; 127.1; 125.4; 124.6; 121.4 ppm.

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