Synthesis of Trithiadiazepines from Tetrasulphur Tetranitride and Alkynes

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The reaction of S_4N_4 with cyano- and trifluoromethyl-substituted alkynes gives trithiadiazepines (**1b—d**) in good yield; with less reactive alkynes the yields of trithiadiazepines (**1**) are greatly improved by titanium(IV) chloride catalysis, making a range of functional derivatives of this ring system readily available.

We have shown that 1,3λ⁴δ²,5,2,4-trithiadiazepines are minor products in the complex reactions of acetylenedicarboxylate esters with S_4N_4 but the yields are too low to be practically useful.[1,2] The parent 1,3λ⁴δ²,5,2,4-trithiadiazepine (**1a**) and its 6,7-dihydro- and benzo-derivatives can be synthesised in practical quantities by high dilution cyclisation of bis-sulphenyl chlorides with bis(trimethylsilyl)sulphur diimide,[2] but this route lacks the simplicity and potential versatility of the S_4N_4 reaction.

We now show that S_4N_4 and the alkynes NC–C≡C–CN, NC–C≡C–CF_3, and CF_3–C≡C–CF_3, which are highly reactive in cycloadditions, give the corresponding trithiadiazepines in much higher yield, and that with other alkynes the trithiadiazepine yield is much improved either at higher reaction temperatures (150—160 °C) or, better, by the addition of titanium(IV) chloride (Table 1).

Butynedinitrile (**2**) and S_4N_4 gave 6,7-dicyano-1,3λ⁴δ²,5,2,4-trithiadiazepine (**1b**) and 3,4-dicyano-1,2,5-thiadiazole (**3**) in almost quantitative yield. The structure of (**1b**) was assigned by comparison of its spectroscopic properties with those of other trithiadiazepines[1,2] and confirmed by *X*-ray diffraction.[3] The stoicheiometry of this reaction suggests a simple cycloaddition–cycloreversion mechanism *via* the 2 : 1 adduct (**4**); this could be formed by 1,3-cycloaddition of the alkyne across nitrogen and 1,5-cycloaddition across sulphur, and could dissociate directly into the aromatic products observed. Hexafluorobut-2-yne and 4,4,4-trifluorobutynonitrile were less reactive than butynedinitrile but still gave the corresponding trithiadiazepines (**1b**) and (**1c**) in about 10 times the yield obtained with dimethyl acetylenedicarboxylate (DMAD).

Dicyanotrithiadiazepine (**1b**) and bis(trifluoromethyl)trithiadiazepine (**1c**) had previously been isolated from the same reactions but assigned the incorrect structures (**5a,b**),[4] which are inconsistent with the thermal stability and spectroscopic properties of the compounds.

For less reactive alkynes with substituents such as formyl, acetyl, or diethoxymethyl, the S_4N_4 reaction gave several products in very low yield, similar to that with DMAD.[1] However, the yield of trithiadiazepine from these could be increased by activating the S_4N_4, either by thermolysis or by Lewis acid catalysis. In either case the tight S_4N_4 cage structure is disrupted by thermal dissociation into S_4N_2, S_3N_3, and S_2N_2,[5a] or by formation of a 1 : 1 Lewis acid adduct;[5b] the latter are known to have an approximately planar S_4N_3 unit with the remaining nitrogen atom and co-ordinated catalyst above the plane.

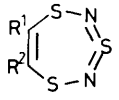
When S_4N_4 was added to DMAD in boiling bromobenzene the yield of trithiadiazepine (**1e**) increased nearly 5-fold (Table 1). Increases in the yield of trithiadiazepines (**1f—h**) were also observed with 4,4-diethoxybut-2-ynal, ethyl 4,4,4-trifluorobut-2-ynoate, and monocyanoacetylene. However, the very low yield of trithiadiazepine (**1i**) from di-t-butyl acetylenedicarboxylate, like that from DMAD, was not improved at 156 °C since the acetylenic ester was decomposed; we therefore turned to catalysed reactions.

With S_4N_4 and DMAD in boiling toluene, addition of aluminium chloride, boron trifluoride, or iron(III) chloride

Table 1. Yield of trithiadiazepine (**1**) in the reaction of S_4N_4 with alkynes.

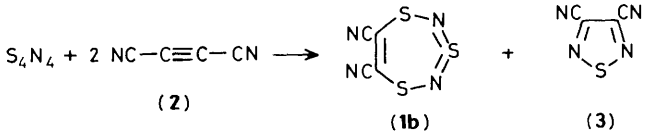
Alkyne	Solvent	Temp. /°C	Thiadiazepine	Uncatalysed/%	With $TiCl_4$/%
NCC≡CCN	C_6H_6	120	(**1b**)	90	—
$CF_3C{\equiv}CCF_3$	CH_2Cl_2	140	(**1c**)	52	—
$CF_3C{\equiv}CCN$	CH_2Cl_2	150	(**1d**)	40	—
$MeO_2CC{\equiv}CCO_2Me$	PhMe	110	(**1e**)	5[a]	40
$MeO_2CC{\equiv}CCO_2Me$	PhBr	156	(**1e**)	23	—
$(EtO)_2CHC{\equiv}CCHO$	PhMe	110	(**1f**)	6	—
$(EtO)_2CHC{\equiv}CCHO$	PhBr	156	(**1f**)	24[b]	—
$CF_3C{\equiv}CCO_2Et$	CH_2Cl_2	120	(**1g**)	4	25
$CF_3C{\equiv}CCO_2Et$	CH_2Cl_2	150	(**1g**)	10	—
HC≡CCN	PhMe	100	(**1h**)	0	—
HC≡CCN	PhMe	140	(**1h**)	10	—
$Bu^tO_2CC{\equiv}CCO_2Bu^t$	PhMe	110	(**1i**)	4[c]	30

[a] Ref. 1. [b] Combined yield of (**1f**) and bicyclic diethoxydihydrofuran isomers readily formed from it. [c] Ref. 2.

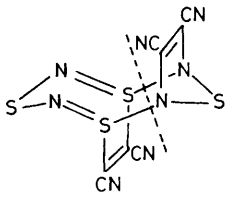


(**1**)

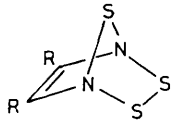
a; $R^1 = R^2 = H$
b; $R^1 = R^2 = CN$
c; $R^1 = R^2 = CF_3$
d; $R^1 = CF_3$, $R^2 = CN$
e; $R^1 = R^2 = CO_2Me$
f; $R^1 = CHO$, $R^2 = CH(OEt)_2$
g; $R^1 = CF_3$, $R^2 = CO_2Et$
h; $R^1 = H$, $R^2 = CN$
i; $R^1 = R^2 = CO_2Bu^t$



(**2**) (**1b**) (**3**)



(**4**)



(**5**) **a**; R = CN
b; R = CF_3

had little effect on the trithiadiazepine yield though the formation of methyl $1,3\lambda^4\delta^2,5,2,4,6$-trithiatriazepine-7-carboxylate[1] was suppressed, showing some selectivity. However, titanium(IV) chloride (0.1 equiv.) caused a marked increase in reaction rate and in trithiadiazepine yield (Table 1), with a compensating reduction in yield of the 1,2,5-thiadiazole and elimination of the trithiatriazepine. The trithiadiazepine (**1e**) and thiadiazole yields were remarkably constant in different solvents (C_6H_6, PhMe, PhBr, MeCN) at temperatures from 80 to 156 °C. Titanium(IV) chloride was almost as beneficial in the reactions of di-t-butyl acetylenedicarboxylate and ethyl 4,4,4-trifluorobut-2-ynoate (Table 1).

Thus alkynes which are highly reactive in cycloadditions, and others at elevated temperatures or with $TiCl_4$, react with S_4N_4 to give the 10π-electron aromatic trithiadiazepines (**1**) in preparatively useful amounts, making a range of these with functional substituents readily available for the first time.

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