Studies of Heterocyclic Analogues of Azulenes. Part 9.[1] Regioselective Cycloadditions of 2*H*-Cycloheptathiazol-2-one with Acetylenic Esters and Electron-deficient Olefins

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Cycloadditions of 2*H*-cycloheptathiazol-2-one with acetylenic esters and electron-deficient olefins have been found to proceed regioselectively, producing 2-oxo-3*H*-1-thia-2a-azacyclopent[*cd*]azulenes by 1,10-dipolar cyclisation, and 2-oxo-3*H*-1-thia-2a-azacyclopenta[*ef*]heptalenes.

Cycloadditions of nitrogenous heterocycles with alkynes constitute a versatile synthetic method.[2] In particular, extended dipolar cycloadditions now offer a new route for heterocyclic synthesis;[3] our reactions of both cyclohepta[*b*]-pyrroles and cycloheptimidazole with dialkyl acetylenedicarboxylates[4a] and electron-deficient olefins,[4b] involving a 1,8-dipolar cyclisation, provide other examples of the usefulness of such cycloadditions for heterocyclic syntheses. Benzothiazole is known to give 1*H*-pyrido[2,1-*b*]benzothiazole, 2,3-dihydro-1,4-benzothiazine, and 4a*H*-pyrido-[2,1-*b*]benzothiazole derivatives upon reaction with dimethyl acetylenedicarboxylate (DMAD), depending on the solvent used.[5] To investigate the extension of such pericyclic reactions to other aza-azulenes, and to provide a comparison with benzothiazole, we have studied the cycloaddition reactions of 2*H*-cycloheptathiazol-2-one (1).[6]

When compound (1) and DMAD were heated under reflux in acetonitrile, dimethyl 2-oxo-3*H*-1-thia-2a-azacyclopent-[*cd*]azulene-3,4-dicarboxylate (2a) and tetramethyl 2-oxo-3*H*-1-thia-2a-azacyclopenta[*ef*]heptalene-3,4,5,6-tetracarboxylate (3a) were isolated in 49 and 16% yield, respectively; their structures were assigned on the basis of spectroscopic evidence. The ^{13}C n.m.r. spectrum (Table) of the aza-azulene (2a) has a doublet at δ_C 63.8 p.p.m., assignable to C-3, and nine other ring-carbon signals, besides the signals attributable to CO_2Me groups. The ^1H n.m.r. spectrum contains a one-proton singlet (3-H) at δ_H 5.68 and signals due to the four protons of the seven-membered ring at δ_H 6.13 (ddd, *J* 12, 8, and 1 Hz, 6-H), 6.27 (dd, *J* 13 and 1 Hz, 8-H), 6.52 (ddd, *J* 13, 8, and 1 Hz, 7-H), and 7.50 (dd, *J* 12 and 1 Hz, 5-H). The ^1H n.m.r. spectrum of the azaheptalene (3a) displays four singlets (CO_2Me) at δ_H 3.70, 3.73, 3.80, and 3.83, a methine proton at δ_H 6.42 (3-H), and a multiplet for the four protons of the seven-membered ring at δ_H 6.45—6.55 (4 H, m). Similarly, the reaction of compound (1) with diethyl acetylenedicarboxylate (DEAD) gave the aza-azulene (2b) (76%) and the azaheptalene (3b) (18%). The ^{13}C n.m.r. spectra of the aza-azulenes (2a) and (2b) are given in the Table.

The regiochemistry of the cycloaddition was confirmed from the reactions of compound (1) with electron-deficient olefins. Prolonged heating with ethyl acrylate in xylene afforded ethyl 2-oxo-3*H*-1-thia-2a-azacyclopent[*cd*]azulene-4-carboxylate (2c) in 30% yield. The aza-azulene (2c) showed the 3-protons as a two-proton singlet at δ_H 5.45, the resonance being comparable with that of the 3-protons of ethyl 3*H*-1,2a-diazacyclopent[*cd*]azulene-4-carboxylate (δ_H 5.07),[4b] and the protons of the seven-membered ring at δ_H 6.25—6.8 (m, 6-, 7-, and 8-H) and 7.88 (dd, *J* 12 and 1 Hz, 5-H). The reactions with acrylonitrile, dimethyl maleate, or dimethyl fumarate similarly gave the aza-azulenes (2d) and (2a) in 2, 49, and 18% yields, respectively. All reactions with olefins were extremely sluggish, >50% of the starting material (1) being recovered in all three cases. It is clear that the cyclo-adduct with the olefin has undergone dehydrogenation during the course of the reaction or subsequent work-up.

Table ^{13}C N.m.r. chemical shifts (δ_C/p.p.m.) and multiplicities (in parentheses) of dialkyl 2-oxo-3*H*-1-thia-2a-azacyclopent[*cd*]-azulene-3,4-dicarboxylates (2a) and (2b)

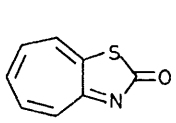
	Compound	
Carbon	(2a)	(2b)
2	167.1 (s)	166.7 (s)
3	63.8 (d)	64.1 (d)
4	112.5 (s)	112.9 (s)
4a	117.1 (s)	116.8 (s)
5	127.7 (d)	127.7 (d)
6	128.9 (d)	128.8 (d)
7	126.4 (d)	126.3 (d)
8	135.3 (d)	135.1 (d)
8a	135.1 (s)	134.9 (s)
8b	142.6 (s)	142.6 (s)
CO_2R	163.6 (s)	163.2 (s)
	166.9 (s)	166.6 (s)
OMe	51.4 (q)	
	53.2 (q)	
OCH_2		60.3 (t)
		62.4 (t)
Me		14.1 (q)
		14.3 (q)

As in our earlier studies,[4a] one would expect the aza-azulene (2) to be formed by the 1,10-dipolar cyclisations of the species (4) and (5), and the reaction indicates that extended dipolar cycloaddition is an important and useful principle for the construction of condensed aza-azulene rings.

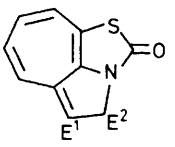
Experimental

M.p.s were determined in a capillary tube. ^1H N.m.r. (60 MHz) and ^{13}C n.m.r. spectra were recorded on Hitachi R-24B and Varian FT-80A spectrometers, respectively; all spectra were taken for solutions in $CDCl_3$ with Me_4Si as internal reference. Mass spectra were taken with an Hitachi M-80 spectrometer by means of the field-desorption method. U.v. spectra were measured for solutions in ethanol and i.r. spectra were determined as Nujol mulls. Petroleum L refers to the fraction of boiling range 70—120 °C and petroleum E to the fraction of boiling range 30—60 °C. Kieselgel 60 was used for chromatography. Yields are based on starting material consumed.

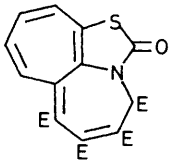
Reaction of 2H-*Cycloheptathiazol-2-one* (1) *with DMAD.*—A mixture of compound (1) (0.326 g, 2 mmol) and the acetylene (0.574 g, 4 mmol) in acetonitrile (30 ml) was heated under



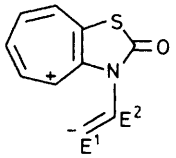
(1)



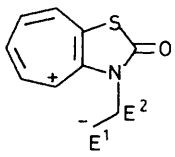
(2) a; $E^1 = E^2 = CO_2Me$
b; $E^1 = E^2 = CO_2Et$
c; $E^1 = CO_2Et$, $E^2 = H$
d; $E^1 = CN$, $E^2 = H$



(3) a; $E = CO_2Me$
b; $E = CO_2Et$



(4)



(5)

reflux for 3 h and evaporated to dryness under reduced pressure. Chromatography of the residue with benzene as eluant gave *dimethyl* 2-*oxo*-3H-1-*thia*-2a-*azacyclopent*[cd]-*azulene*-3,4-*dicarboxylate* (2a) (0.126 g, 49%) which crystallised as red prisms from cyclohexane–methylene dichloride and had m.p. 164—165 °C (Found: C, 55.2; H, 3.7; N, 4.55; S, 10.3%; M^+, 305. $C_{14}H_{11}NO_5S$ requires C, 55.1; H, 3.6; N, 4.6; S, 10.5%; *M*, 305); $\lambda_{max.}$ 225 (log ε 4.23), 253 (4.22), 268 (4.22), 385 (4.22), 401 (4.20), 457 (3.51), 491 (3.41), 528 (3.17), and 565 nm (2.66); $\nu_{max.}$ 1 740, 1 690, and 1 665 cm^{-1}; δ_H 3.75 (3 H, s, Me), 3.82 (3 H, s, Me), 5.68 (1 H, s, 3-H), 6.13 (1 H, ddd, *J* 12, 8, and 1 Hz, 6-H), 6.27 (1 H, dd, *J* 13 and 1 Hz, 8-H), 6.52 (1 H, ddd, *J* 13, 8, and 1 Hz, 7-H), and 7.50 (1 H, dd, *J* 12 and 1 Hz, 5-H).

Tetramethyl 2-*oxo*-3H-1-*thia*-2a-*azacyclopenta*[ef]*heptalene*-3,4,5,6-*tetracarboxylate* (3a) (0.059 g, 16%) was eluted with benzene–chloroform (3 : 1) and crystallised as red prisms from petroleum L–methylene dichloride, m.p. 181—182 °C (Found: C, 53.65; H, 3.9; N, 3.1; S, 6.9%; M^+, 447. $C_{20}H_{17}NO_9S$ requires C, 53.7; H, 3.8; N, 3.1; S, 7.2; *M*, 447); $\lambda_{max.}$ 247 (log ε 4.23), 272sh (3.95), 282sh (3.89), 334 (3.55), 353 (3.54), 373 (3.59), 393 (3.62), 420sh (3.65), 437 (3.69), 457 (3.64), 490sh (3.42), and 532sh nm (2.84); $\nu_{max.}$ 1 750, 1 710, and 1 670 cm^{-1}; δ_H 3.70 (3 H, s, Me), 3.73 (3 H, s, Me), 3.80 3 H, s, Me), 3.83 (3 H, s, Me), 6.42 (1 H, s, 3-H), and 6.45—6.55 (total 4 H, m, 7-, 8-, 9-, and 10-H).

Elution with chloroform then gave the starting material (1) (0.189 g recovery).

Reaction of 2H-*Cycloheptathiazol*-2-*one* (1) *with DEAD*.—A mixture of compound (1) (0.326 g, 2 mmol) and the acetylene (1.367 g, 4 mmol) in acetonitrile (30 ml) was heated under reflux for 3 h and worked up as described above. Elution with benzene afforded *diethyl* 2-*oxo*-3H-1-*thia*-2a-*azacyclopent*-[cd]*azulene*-3,4-*dicarboxylate* (2b) (0.144 g, 76%) which crystallised as red prisms from cyclohexane–methylene dichloride and had m.p. 137—139 °C (Found: C, 57.8; H, 4.7; N, 4.2; S, 9.9. $C_{16}H_{15}NO_5S$ requires C, 57.65; H, 4.5; N, 4.2; S, 9.6%); $\lambda_{max.}$ 225 (log ε 4.20), 255 (4.18), 268 (4.20), 385 (4.22), 402 (4.20), 458 (3.58), 491 (3.48), 528 (3.24), and 568 nm (2.73); $\nu_{max.}$ 1 740, 1 705, and 1 665 cm^{-1}; δ_H 1.29 (3 H, t, *J* 7 Hz, Me), 1.31 (3 H, t, *J* 7 Hz, Me), 4.23 (2 H, q, *J* 7 Hz, OCH_2), 4.28 (2 H, q, *J* 7 Hz, OCH_2), 5.67 (1 H, s, 3-H), 6.18 (1 H, ddd, *J* 12, 8, and 1 Hz, 6-H), 6.30 (1 H, dd, *J* 13 and 1 Hz, 8-H), 6.52 (1 H, ddd, *J* 13, 8, and 1 Hz, 7-H), and 7.50 (1 H, dd, *J* 12 and 1 Hz, 5-H).

Tetraethyl 2-*oxo*-3H-1-*thia*-2a-*azacyclopenta*[ef]*heptalene*-3,4,5,6-*tetracarboxylate* (3b) (0.045 g, 18%) was eluted with benzene–chloroform (2 : 1) and crystallised as red prisms from petroleum E, m.p. 73—77 °C (Found: C, 57.1; H, 4.85; N, 2.9; S, 6.5. $C_{24}H_{25}NO_9S$ requires C, 57.25; H, 5.0; N, 2.8; S, 6.4%); $\lambda_{max.}$ 248 (log ε 4.57), 273 (4.18), 282sh (3.90), 335 (3.74), 352 (3.74), 371 (3.80), 392 (3.79), 418sh (3.67), 437 (3.76), 465 (3.75), 495 (3.57), and 530sh nm (3.09); $\nu_{max.}$ 1 740, 1 725, 1 700, and 1 675 cm^{-1}; δ_H 1.30 (6 H, t, *J* 7 Hz, 2 × Me), 1.33 (3 H, t, *J* 7 Hz, Me), 1.40 (3 H, t, *J* 7 Hz, Me), 4.27 (2 H, q, *J* 7 Hz, OCH_2), 4.33 (2 H, q, *J* 7 Hz, OCH_2), 4.37 (4 H, q, *J* 7 Hz, 2 × OCH_2), 6.46 (1 H, s, 3-H), and 6.3—6.8 (total 4 H, m, 7-, 8-, 9-, and 10-H).

Elution with chloroform gave the starting material (1) (0.233 g recovery).

Reaction of 2H-*Cycloheptathiazol*-2-*one* (1) *with Ethyl Acrylate*.—A mixture of compound (1) (0.326 g, 2 mmol) and ethyl acrylate (2.00 g, 20 mmol) in xylene (30 ml) was heated under reflux for 72 h and worked up as described above. Elution with benzene gave *ethyl* 2-*oxo*-3H-1-*thia*-2a-*azacyclopent*[cd]*azulene*-4-*carboxylate* (2c) (0.048 g, 30%) which crystallised as red prisms from ethanol, m.p. 134—135 °C (Found: C, 59.8; H, 4.2; N, 5.2; S, 12.1. $C_{13}H_{11}NO_3S$ requires C, 59.8; H, 4.2; N, 5.4; S, 12.3%); $\lambda_{max.}$ 221 (log ε 4.22), 257 (4.11), 266 (4.11), 384 (4.15), 395 (4.13), 435sh (3.38), 486 (3.35), 503 (3.25), 543 (3.00), and 588 nm (2.44); $\nu_{max.}$ 1 685 and 1 660 cm^{-1}; δ_H 1.44 (3 H, t, *J* 7 Hz, Me), 4.25 (2 H, q, *J* 7 Hz, OCH_2), 5.45 (2 H, s, 3-H_2), 6.25—6.8 (total 3 H, m, 6-, 7-, and 8-H), and 7.88 (1 H, dd, *J* 12 and 1 Hz, 5-H).

Elution with benzene–chloroform (1 : 1) gave, after work-up, a violet powder (not characterised) (0.112 g), m.p. >300 °C; elution with chloroform gave the starting material (1) (0.216 g recovery).

Reaction of 2H-*Cycloheptathiazol*-2-*one* (1) *with Acrylonitrile*.—A mixture of compound (1) (0.815 g, 5 mmol) and acrylonitrile (2.65 g, 50 mmol) in xylene (30 ml) was heated under reflux for 110 h and worked up as described above. Elution with benzene gave 2-*oxo*-3H-1-*thia*-2a-*azacyclopent*-[cd]*azulene*-4-*carbonitrile* (2d) (0.010 g, 2%) which crystallised as red prisms from petroleum L–methylene dichloride, m.p. >300 °C (Found: C, 61.6; H, 2.7; N, 13.2; S, 15.1. $C_{11}H_6N_2OS$ requires C, 61.7; H, 2.8; N, 13.1; S, 15.0%); $\lambda_{max.}$ 225 (log ε 4.01), 256 (3.99), 267 (3.99), 376 (4.01), 389 (3.97), 445 (3.13), 475 (3.12), 512 (3.00), 553 (2.75), and 595 (2.12); $\nu_{max.}$ 2 190 and 1 685 cm^{-1}; δ_H 4.80 (2 H, s, 3-H_2) and 5.65—6.50 (total 4 H, m, 5-, 6-, 7-, and 8-H).

Elution with benzene–chloroform (1 : 1) afforded a violet powder (not characterised), (0.046 g), m.p. >300 °C. Finally, elution with ethyl acetate gave the starting material (1) (0.453 g recovery).

Reaction of 2H-*Cycloheptathiazol*-2-*one* (1) *with Dimethyl Maleate*.—A mixture of compound (1) (0.326 g, 2 mmol) and dimethyl maleate (2.89 g, 20 mmol) in xylene (30 ml) was heated under reflux for 72 h and worked up as described above. Elution with benzene gave the azulene (2a) (0.134 g, 49%). Elution with benzene–chloroform (1 : 1) afforded violet needles (not characterised) (0.075 g), m.p. >300 °C, and chloroform eluted the starting material (1) (0.179 g recovery).

Reaction of 2H-*Cycloheptathiazol*-2-*one* (1) *with Dimethyl Fumarate*.—A mixture of compound (1) (0.326 g, 2 mmol) and dimethyl fumarate (2.89 g, 20 mmol) in xylene (50 ml) was heated under reflux for 72 h and worked up as described above.

Elution with benzene gave the azulene (2a) (0.030 g, 18%). Elution with benzene–chloroform (1 : 1) then afforded violet crystals (not characterised) (0.015 g), m.p. >300 °C, and finally, elution with chloroform gave the starting material (1) (0.235 g recovery).

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