Tetrahedron Letters No. 35, pp 3069 - 3072, 1974. Pergamon Press. Printed in Great Britain.

REGIOSPECIFIC SYNTHESIS OF 1,3-DIAZAAZULENES

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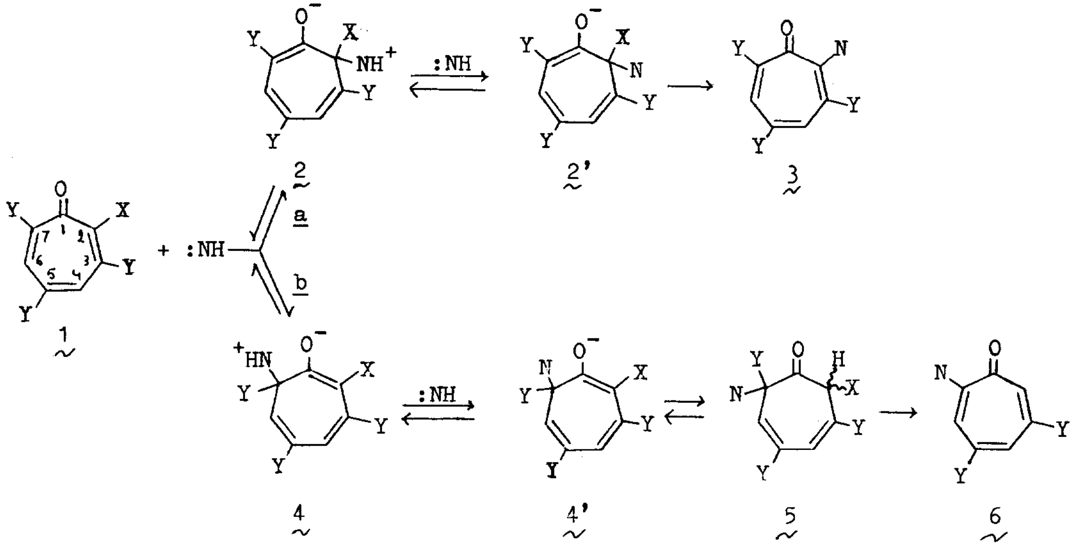
(Received in UK 10 July 1974; accepted for publication 18 July 1974)

Recently it has become possible to functionalize the cycloheptatrienone nucleus specifically at either C(2) or C(7).[1] Briefly, cycloheptatrienones carrying a displaceable group at C(2) react with nucleophiles by competitive paths a and b (Scheme).[1] Path a is favoured by both mesomerically electron repelling X groups and strong nucleophiles :NH.[1] Conversely, electron attracting X groups activate the cycloheptatrienone nucleus for attack at C(7), substitution being favoured by weak nucleophilic reagents :NH, provided a protonating agent is available.[1]

SCHEME

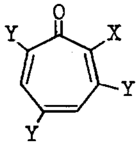
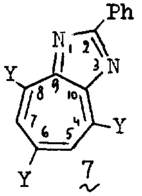
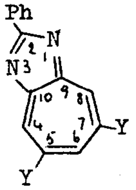
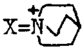


We have now discovered that (Table, reactn no. 1),using an amidine as nucleophilic reagent, cycloheptatrienones carrying a displaceable group at C(2) do not merely undergo replacement of X by nitrogen, but the reaction is completed by carbonyl condensation with the other amidine ''tooth'', leading to 1,3-diazaazulenes (7, 8),[3] which constitute a novel case of Nozoe's azulenoid synthesis.[4] We report here that complete regiospecificity in the five membered ring closure can be achieved in such syntheses, using our new reaction above as a model.

Thus, deuterium labeling of the starting cycloheptatrienone (**1**, Y = D) shows that when X is as strongly electron attracting as a quaternary ammonium group (Table, reactn no. 3) attack by the amidine on **1** occurs at C(7), together with carbonyl condensation to give exclusively **8** (Y = D).[5]

TABLE

Synthesis of 2-Phenyl-1,3-diazaazulene with Benzamidine and 2-Substituted Cycloheptatrienones (in dried dimethyl sulphoxide at room temperature, when not otherwise stated)

REAGENTS		REACTION TIME (h)	PRODUCTS				REACTN no.
 **1**	Benzamidine ($\underline{M}$)		 **7**		 **8**		
				yield[a]		yield[a]	
X=Cl; Y=H; 0.07$\underline{M}$[b]	0.30	1	Y=H	60(100)			1
X=Cl; Y=D; 0.13$\underline{M}$	0.64	2	Y=D	- -	Y=D	50(80)	2
X= ;Y=D;0.064$\underline{M}$	0.13	2	Y=D	- -	Y=D	30(60)	3
X=OCH_3; Y=D;0.15$\underline{M}$	0.30	14	Y=D	20	Y=D	- -	4

[a] isolated yields and, within parentheses, spectroscopic yields are given;

[b] in dried benzene as solvent.

However, specific attack at C(2) and carbonyl condensation on **1** was obtained for a strongly deactivating substituent as the methoxy group at C(2) (Table, reactn no. 4).[6]

The surprising result of reaction no. 2 (Table) indicates that previously established rules for monofunctionalization of the cycloheptatrienone ring[1] need a basic reelaboration when cyclization reactions are to be dealt with, as in the present case. We propose that the type-**4** intermediate of amidine attack on 1 is more rapidly transformed into 8 (Y = D) than it can be driven back along the paths at the Scheme to give 7 (Y = D) because both of rapid carbonyl condensation occurring in type-5 species owing to proximity effects,[7] and scarce aptitude of the type-4 intermediate to revert to 1 owing to charge stabilisation by the amidinium moiety.[8]

With 2-methoxytropone only substitution at C(2) is observed because the cycloheptatrienone ring is completely inhibited toward attack at C(7),[9] thus the only reaction having chances to occur, albeit at slow rate (Table), is replacement of the methoxy group by attack at C(2).

REFERENCES AND NOTES

1) G. Biggi, F. Del Cima, and F. Pietra, J. Amer. Chem. Soc., 95, 7101 (1973).

2) G. Biggi, A. J. de Hoog, F. Del Cima, and F. Pietra, J. Amer. Chem. Soc., 95, 7108 (1973).

3) The structure of product 7 (Y = H), m.p. 161°, is supported by satisfactory elemental analysis, mass spectrum [M^+, 100%; $(M - 26)^+$, 24%; $(M - 101)^+$, 28%; $(M - 129)^+$, 33%; $(M - 130)^+$, 23%], and proton n. m.r. spectrum in deuterochloroform which shows three complex multiplets at δ_{TMS} 8.65 (for the two protons at C(8) and C(10) and the two ortho phenyl protons), 7.95 (for the other four protons at the seven-membered ring), and 7.50 p. p. m. (for the other three phenyl protons). Such spectral assignment is based on the proton n. m. r. spectra of the deuteriated azulenoids discussed below.

4) F. Pietra, Chem. Rev., 73, 293 (1973), p 350.

5) The structure of product 8 (Y = D), m.p. 160°, is supported both by the mass spectrum, which shows that 7 (Y = D) is absent [$(M + 1)^+ = 209$, 15%; $M^+ = 208$, 100%] and by the proton n. m. r. spectrum in deuterochloroform (δ_{TMS} 8.8, s, 2H; 8.63, m, 2H; 8.00, s, 1H; and 7.50 p.p.m., m, 3H. On deuterium decoupling[1,2] only the two singlets at δ_{TMS} 8.8 and 8.0 p.p.m. sharpen, thus proving that such signal arise from, respectively, the C(8) + C(4) and C(6) protons of the seven-membered ring

6) The structure of product 7 (Y = D), m.p. 160°, is supported by both the mass spectrum [$M^+ = 209$, 100%; $(M - 1)^+ = 208$, 16%) and the proton

n. m. r. spectrum in deuterochloroform which shows, besides the phenyl proton resonances (see notes 3 and 5 above), a singlet at δ_{TMS} 7.92 p. p. m. for the two protons at C(5) and C(7) of the seven-membered ring which is the only one undergoing sharpening on deuterium decoupling.[1,2]

7) Protonation of 4' to give 5 is expected to occur in a fast step on the basis of previous kinetic work.[1]

8) R. L. Shriner and F. W. Neumann, <u>Chem. Rev.</u>, 35, 351 (1944).

9) G. Biggi, C. A. Veracini, and F. Pietra, <u>Chem. Comm.</u>, 523 (1973).

10) It can be ruled out that formation of azulenoids 7 and 8 occurs by initial carbonyl condensation of the amidine with 1 followed by substitution at either C(2) or C(7). In fact, cycloheptatrienones are known to be resistant to carbonyl reactions , certainly too much to account for the reaction at the Table (ref. 4 above, p 348) which proceed rapidly under mild conditions.

Financial support by C. N. R., Roma, is acknowledged.