Polyaza-azulenes. Part 1. Synthesis and Reactions of Some 2,3,3a,6-Tetrahydropyrazolo[3,4-*d*][1,2]diazepines

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The reactions of 2,3,3a,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepines (2) with methanolic sodium carbonate have been investigated. 4-Vinylpyrazoles (3) and (4), 2,4,5,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepines (5), 1(2),4,5,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepines (6), and 1(2),6-dihydropyrazolo[3,4-*d*][1,2]diazepines (7) are obtained, the nature of the product being dependent upon the way in which (2) is substituted. The mechanism by which the above compounds are formed is discussed.

THE synthesis of polyaza-azulenes is of interest when studying the effect of methine group replacement by nitrogen atoms upon the properties of azulene. Along these lines Hafner,[1] in his elegant work in the field of heterocyclic aromatic systems, synthesised some mono- and di-aza-azulene systems and showed the similarities

[1] K. Hafner, *J. Heterocyclic Chem.*, 1975, **12**, Suppl. vol. 3, S-33.

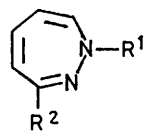
of their electronic spectra with those of azulene. We describe here our first results obtained in the field of polyaza-azulene synthesis.

The photochemically accessible 1*H*-[1,2]diazepines (1) [2,3] were chosen as starting materials for our synthetic work since these compounds, as recently reported,[4] undergo ready cycloaddition with diazomethane to afford unstable tetrahydro-1,2,6,7-tetra-aza-azulene derivatives (2; R^3 = H) (hereafter referred to as 2,3,3a,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepines). As reported earlier [4] the cycloaddition reaction affords initially the expected 1-pyrazoline in the first step; however this rapidly isomerises to the more conjugated 2-pyrazoline (2). These unstable adducts (2) may be stabilized by acetylation, methoxymethylation, or tosylation at the N-2 nitrogen atom. Acetylation and tosylation of the adducts (2; R^3 = H) were carried out using standard procedures. Attempted N-2 methylation of (2; R^1 = Ts, R^2 = R^3 = H) using methanolic formaldehyde and sodium borohydride [5] led unexpectedly to the 2-methoxymethyl derivative (2f). Formation of this compound may be visualized as occurring *via* attack by methoxide anion upon the immonium ion-Mannich type intermediate which is presumably initially formed in this reaction.

Thus, starting from the diazepines (1a—d) we obtained in good overall yield the stable crystalline adducts (2a—f) (see Table 1). ^{1}H N.m.r. data (see Table 2) and an *X*-ray structure for a related compound [6,7] show quite clearly that diazomethane adds site-specifically and regiospecifically to the Δ^4-double bond of diazepines (1).

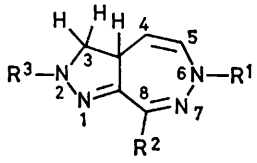
Having achieved the synthesis of stable 2,3,3a,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepine derivatives we next turned our attention to the chemistry of these novel heterocycles. We now report that on treatment with methanolic sodium carbonate the 2,3,3a,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepines (2a—f) afford a series of products the nature of which depends upon the way in which the bicyclic molecules (2) are substituted.

When the tetrahydropyrazolo[3,4-*d*][1,2]diazepines (2a—c), which all bear arylsulphonyl groups at N-6 and acetyl groups at N-2, are treated with methanolic sodium carbonate the corresponding 4-vinylpyrazole-3(5)-carb-



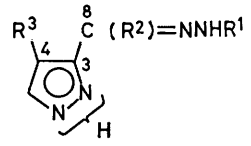
(1)

a; R^1 = Ts, R^2 = H
b; R^1 = SO_2Ph, R^2 = H
c; R^1 = SO_2Ph, R^2 = Me
d; R^1 = Bz, R^2 = Me



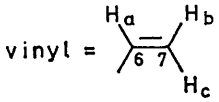
(2)

a; R^1 = Ts, R^2 = H, R^3 = Ac
b; R^1 = SO_2Ph, R^2 = H, R^3 = Ac
c; R^1 = SO_2Ph, R^2 = Me, R^3 = Ac
d; R^1 = Bz, R^2 = Me, R^3 = Ac
e; R^1 = Bz, R^2 = Me, R^3 = Ts
f; R^1 = Ts, R^2 = H, R^3 = $MeOCH_2$



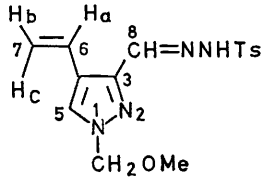
(3)

a; R^1 = Ts, R^2 = H, R^3 = vinyl (*Z*-isomer)
b; R^1 = SO_2Ph, R^2 = H, R^3 = vinyl
c; R^1 = SO_2Ph, R^2 = Me, R^3 = vinyl
d; R^1 = Ts, R^2 = H, R^3 = vinyl (*E*-isomer)
e; R^1 = Ts, R^2 = H, R^3 = Et



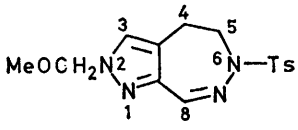
vinyl =

Et =

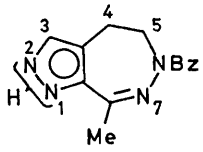


(4)

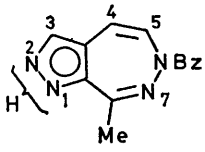
(numbering of the side-chains is non-systematic)



(5)



(6)



(7)

[2] J. Streith and J. M. Cassal, *Angew. Chem. Internat. Edn.*, 1968, **7**, 129.
[3] M. Nastasi, *Heterocycles*, 1976, **4**, 1509.
[4] G. Kiehl, J. Streith, and G. Taurand, *Tetrahedron*, 1974, **30**, 2851.
[5] B. L. Sondengam, J. Hentchoya Hémo, and G. Charles, *Tetrahedron Letters*, 1973, 261.
[6] R. Allmann and T. Debaerdemaecker, *Cryst. Struct. Comm.*, 1974, **3**, 205.
[7] J. Streith, G. Kiehl, and H. Fritz, *Tetrahedron Letters*, 1974, 631.

TABLE 1

Elemental analyses and physical data for compounds (2)—(7)

Compd.	Cryst. solvent	M.p. (°C)	Yield (%)	Found (%) C	H	N	Formula	Requires (%) C	H	N
(2a)	EtOH–H_2O	178	60	54.1	5.0	16.7	$C_{15}H_{16}N_4O_3S$	54.2	4.85	16.9
(2b)	EtOH–H_2O	179—180	56	52.8	4.5	17.6	$C_{14}H_{14}N_4O_3S$	52.8	4.4	17.6
(2c)	MeOH	147	49	54.15	4.85	16.9	$C_{15}H_{16}N_4O_3S$	54.2	4.85	16.9
(2d)	EtOH	167—168	57	65.1	5.3	19.0	$C_{16}H_{16}N_4O_2$	64.85	5.4	18.9
(2e)	EtOH	161	52	61.9	4.9	13.7	$C_{21}H_{20}N_4O_3S$	61.75	4.9	13.7
(2f)	EtOH	144—145	39	54.0	5.3	17.1	$C_{15}H_{18}N_4O_3S$	53.9	5.4	16.75
(3a)	EtOH–H_2O	143	58	53.6	5.0	19.4	$C_{13}H_{14}N_4O_2S$	53.8	4.9	19.3
(3b)	EtOH–H_2O	142	56	52.3	4.4	20.2	$C_{12}H_{12}N_4O_2S$	52.2	4.4	20.3
(3c)	EtOH	138	30	53.7	4.7	19.3	$C_{13}H_{14}N_4O_2S$	53.8	4.9	19.3
(3d)	EtOH–H_2O	159—161	100	53.8	4.9	19.2	$C_{13}H_{14}N_4O_2S$	53.8	4.9	19.3
(3e)	EtOH	149	75	53.3	5.5	19.3	$C_{13}H_{16}N_4O_2S$	53.4	5.5	19.2
(4)			53	53.7	5.6	16.8	$C_{15}H_{18}N_4O_3S$	53.9	5.4	16.75
(5)	EtOH	154—155	21	54.1	5.5	16.8	$C_{15}H_{18}N_4O_3S$	53.9	5.4	16.75
(6)	MeOH	248	24	66.25	5.6	21.8	$C_{14}H_{14}N_4O$	66.1	5.55	22.0
(7)	C_6H_6	179—180	78	66.65	4.9	22.1	$C_{14}H_{12}N_4O$	66.7	4.8	22.2

TABLE 2

^{1}H N.m.r.,* i.r., and u.v. spectra of compounds (2a—f)

Compd.	^{1}H N.m.r. R^1	R^2 (s)	R^3	H-3 and H-3a (m)	H-4 (dd) ‡	H-5 (dd) ‡	I.r. $\nu_{max.}$/cm^{-1}	U.v. $\lambda_{max.}$(EtOH)/nm ($\log_{10}\varepsilon$)
(2a)	2.44 (s), 7.38 and 7.88 †	7.62	2.24 (s)	3.70—4.40	5.17	6.90	1 670	328 (4.22)
(2b)	7.55—8.12 (m)	7.70	2.25 (s)	3.70—4.50	5.18	6.91	1 677	328 (4.19)
(2c)	7.50—8.10 (m)	2.22	2.25 (s)	3.80—4.35	5.22	6.81	1 650	323 (4.21)
(2d)	7.35—7.80 (m)	2.20	2.30 (s)	3.80—4.40	5.36	7.24	1 660	331 (4.26)
(2e)	7.20—7.93 (m)	2.20	2.50 (s) 7.33 and 7.90 †	3.60—4.23	5.23	7.20	1 675	328 (4.13)
(2f)	2.43 (s), 7.30, and 7.83 †	7.48	3.30 (s) 3 H 4.60 (s) 2 H	3.06—4.83	5.06	6.71	1 599	336 (4.10)

* Determined for $CDCl_3$ solutions. † AA'BB' system J = 8 Hz. ‡ $J_{3a,4} = J_{3a,5}$ *ca.* 2 Hz, $J_{4,5}$ *ca.* 8 Hz.

TABLE 3

^{1}H N.m.r.,* i.r. and u.v. spectra of compounds (3a—e)

Compd.	^{1}H N.m.r. R^1	R^2/H-5 (s)	R^3	NHbr (s, exchangeable)	I.r. $\nu_{max.}$/cm^{-1}	U.v. $\lambda_{max.}$(EtOH)/nm ($\log_{10}\varepsilon$)
(3a)	2.40 (s), 7.34, and 7.85 †	7.48	6.68 H_a	12.32	3 150, 1 630	268 (4.24)
		7.80	5.24 H_b (dd) ‡	13.46		
			5.52 H_c			
(3b)	7.23—8.06 (m)	7.23—8.06	6.64 H_a	12.40	3 160, 1 629	263 (4.23)
			5.13 H_b (dd) ‡	13.10		
			5.48 H_c			
(3c)	7.30—7.95 (m)	2.23	6.60 H_a	12.20	3 140, 1 630	262 (4.11)
		7.65	5.10 H_b (dd) ‡	13.00		
			5.30 H_c			
(3d)	2.40 (s), 7.27, and 7.82 †	7.62	6.90 H_a	11.07	3 260, 3 150,	284 (4.41)
		8.00	5.15 H_b (dd) ‡	12.60	1 632	
			5.55 H_c			
(3e)	2.40 (s), 7.40, and 7.80 †	7.46	1.14 (t) §	12.37	3 295, 3 050,	273 (4.13)
		7.73	2.57 (q)	13.77	1 612	

* Determined for $(CD_3)_2SO$–$CDCl_3$ solutions. † AA'BB' system J = 8 Hz. ‡ J_{ab} = 11 Hz, J_{ac} = 18 Hz, J_{bc} = 2 Hz. § J = 8 Hz.

TABLE 4

^{13}C N.m.r. spectra of compounds (3a, b, d, e) and (4)

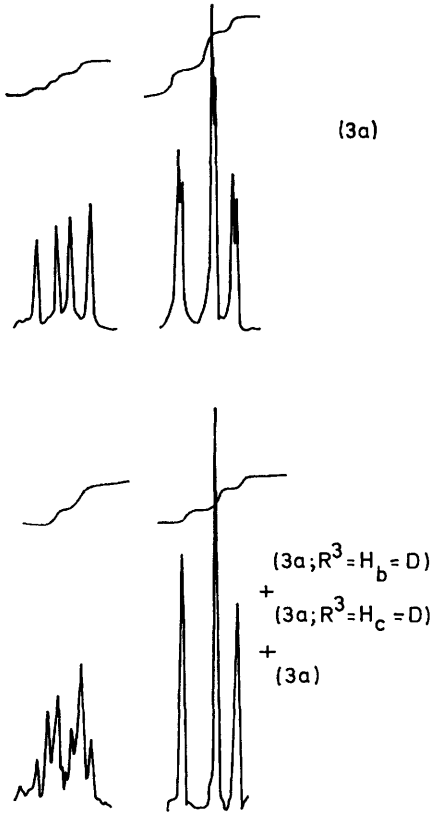
Compd.	C-3	C-4	C-5	C-6	C-7	C-8	C-8 ^1J(CH)	Ar s	Ar *o*	Ar *m*	Ar *p*	ArMe
(3a)	142.18	120.30	127.14	124.97	115.22	132.29	182	135.84	127.14	129.29	143.80	20.92
(3b)	142.34	120.48	127.22	125.12	115.47	132.59	182	138.97	127.22	129.41	133.41	
(3d)	140.03	118.57	129.90	126.82	113.81	141.45	164	135.61	127.36	129.64	143.81	20.89
(3e)	142.82	123.57	127.71	15.55	15.15	132.83	182	135.96	127.11	129.76	143.86	20.97
(4) *	142.43	120.76	*ca.* 128	124.75	114.28	131.95	181	135.68	126.94	129.95	143.71	20.99

* Also signals at 82.12 (N–CH_2–O) and 56.43 (MeO).

aldehyde tosyl and phenylsulphonylhydrazones (3a—c) were obtained. Compounds (3a—c) exhibited characteristic ^{1}H n.m.r. chemical shifts and coupling constants for the three protons of the vinyl moiety (see Table 3). In the case of compound (3a) the presence of a vinyl function was further confirmed by its catalytic hydrogenation to the 4-ethylpyrazole (3e). The stereochemistry of the hydrazone function in these molecules follows from the ^{13}C n.m.r. ^1J(C,H) coupling constant for C-8 (see Table 4). Values of ^1J(C,H) for C-8 of *ca.* 180 Hz

correspond to *Z*-isomers whereas values of *ca.* 160 Hz correspond to *E*-isomers.[8] The stereochemistry of the hydrazone function of compound (3c) could not be determined since this compound bears a methyl group at C-8. When the *Z*-tosylhydrazone (3a) was set aside in $(CD_3)_2SO$ containing deuterium oxide and water for three weeks it isomerised quantitatively (^{13}C n.m.r.) to the *E*-isomer (3d).

In order to elucidate the mechanism of this base-promoted ring cleavage compound (2a) was treated with sodium carbonate at reflux in monodeuteriomethanol. The n.m.r. spectrum of the product clearly showed that deuterium had been incorporated into the vinyl moiety affording a *ca.* 1 : 1 mixture of monodeuteriated vinyl pyrazoles (3a; H_b = D) and (3a; H_c = D) together with



a little undeuteriated material. The Figure shows the n.m.r. spectrum of the mixture in the range δ 5.0—7.2. The ^1H n.m.r. spectrum of compound (3a) is also reproduced over the same range of chemical shift for comparison purposes. It will be noted that the ^1H n.m.r. spectrum of the mixture lacks the geminal coupling (J_{bc} = 2 Hz) between protons H_b and H_c. These protons now appear as sharp doublets having coupling constants of 11 and 18 Hz respectively. Proton H_a in the mixture appears essentially as two superimposed doublets having coupling constants of 11 and 18 Hz. From this data we conclude that deuterium has been incorporated at C-7 of compound (3a) *via* the intermediacy of anion (9) (Scheme) in a non-stereospecific manner. The mechanism depicted in the Scheme accounts for these findings provided that the first step in the reaction is a base-catalysed deprotonation of the doubly allylic H-3a of compound (2). That this is indeed the case was shown by the following ^1H n.m.r. experiment with compounds (2a).

Treatment of a tetradeuteriomethanol solution of compound (2a) contained in an n.m.r. tube with a small piece of metallic sodium resulted in the loss of the vicinal and allylic couplings, $J_{3a,4}$ and $J_{3a,5}$ = 2 Hz at H-4 and H-5 respectively (see Table 2). Signals due to these protons now appear as sharp doublets, $J_{4,5}$ = 8 Hz, showing that H-3a of compound (2a) had been removed.

It will be noticed that the acetyl stabilizing group is lost when (2a—c) are treated with methanolic sodium carbonate. Although it is not clear at which stage along the reaction path this group is removed it has been reported [9] that *N*-acetylpyrazoles would be easily solvolysed under the reaction conditions employed. Methyl acetate formed from the solvolysis of the acetyl function was detected by v.p.c. in the distilled reaction solvent residues.

Treatment of the methoxymethyl derivatives (2f) with methanolic sodium carbonate afforded the corresponding vinylpyrazole (4) (53%) together with compound (5) (21%). This result prompted a careful re-examination of the reaction of compound (2a) with methanolic sodium carbonate. Chromatography on preparative plates afforded a small quantity (4%) of what we believe to be the corresponding 1(2),4,5,6-tetrahydropyrazolo-[3,4-*d*][1,2]diazepine [(5), $MeOCH_2$ replaced by H)] which was identified by ^1H n.m.r. spectroscopy only.

Compound (2d) on treatment with methanolic sodium carbonate afforded the pyrazolo[3,4-*d*]diazepine (6) albeit in low yield. Methyl benzoate and methyl acetate were also formed during this reaction indicating that solvolysis occurred at both the N-2 and N-6 positions of compounds (2d). Other products were formed in this reaction but these could not, in our hands, be isolated in a pure form.

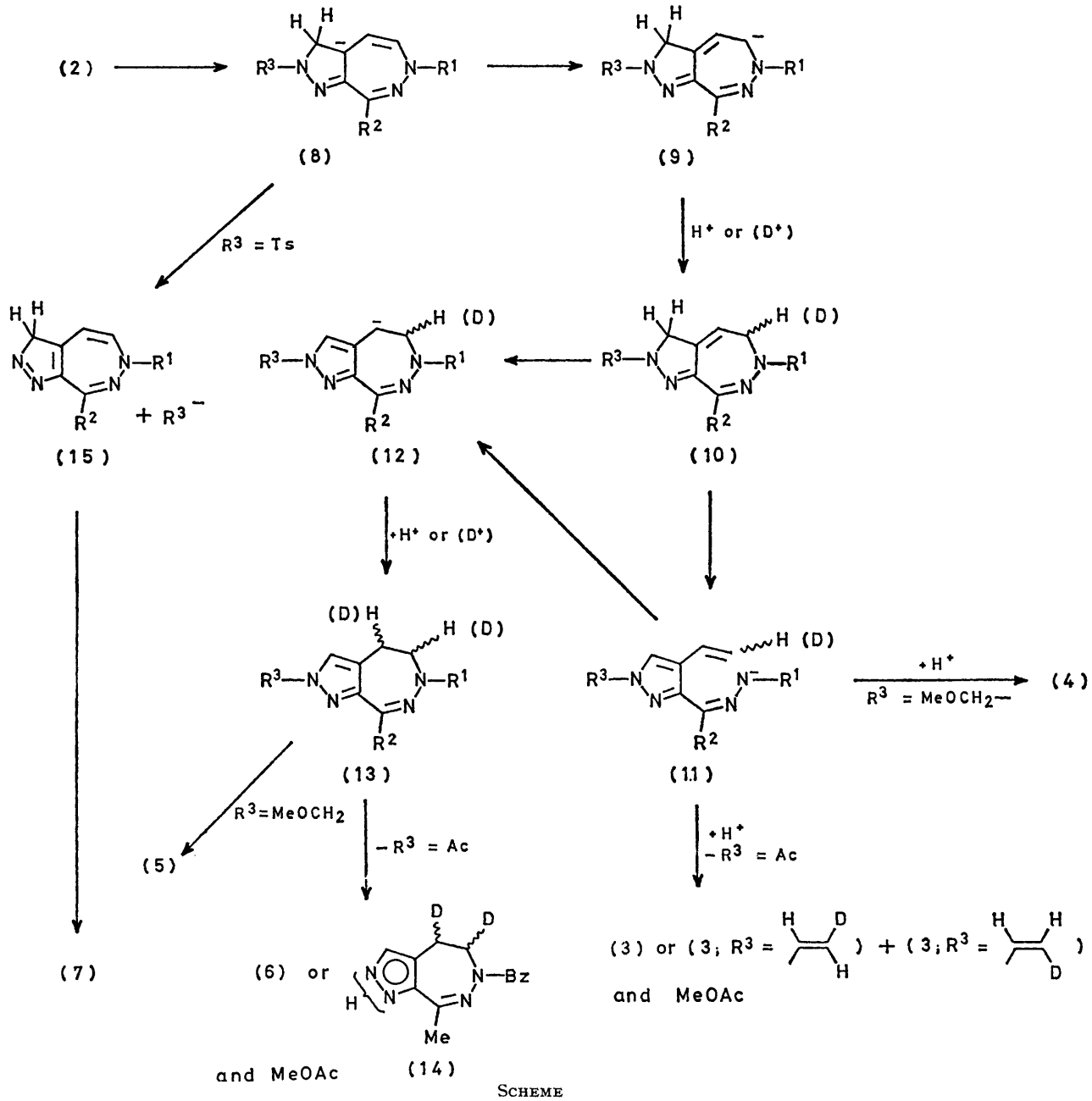
In order to explain the formation of these pyrazolo-[3,4-*d*]diazepines (5) and (6) we assume that the initial steps in the reaction sequence are the same as those shown in Scheme for vinylpyrazole formation. If instead of ring-opening intermediate (10) undergoes aromatisation leading to anion (12) *via* a base-induced double-bond migration or (12) is formed by recyclisation of the proposed intermediate (11) then compounds of type (5) and (6) may be obtained as depicted in the Scheme. That anion (12) is most likely to be involved in the formation of compounds of type (5) and (6) was shown by a second deuterium incorporation experiment.

Thus reaction of compound (2d) with sodium carbonate in tetradeuteriomethanol resulted in the formation of compound (14) (Scheme). Integration of the ^1H n.m.r. spectrum of (14) indicated that one deuterium had been

[8] N. Naulet, M. L. Filleux, G. J. Martin, and J. Pornet, *Org. Magnetic Resonance*, 1975, **7**, 326.
[9] H. A. Staab, *Angew. Chem. Internat. Edn.*, 1962, **1**, 351.

incorporated at *both* C-4 and C-5 in a non-stereospecific manner.

An understanding of the mechanistic pathways leading to compounds (3)—(6) enabled us to design suitably substituted tetrahydropyrazolo[3,4-*d*]diazepines of type (2) which could undergo elimination affording 1(2),6-dihydropyrazolo[3,4-*d*][1,2]diazepines. These compounds are potentially tetra-aza-azulene precursors. Along these lines we synthesised the N-2 tosyl derivative (2e). On treatment with methanolic sodium carbonate at reflux this compound afforded the 1(2),6-dihydropyrazolo[3,4-*d*][1,2]diazepine (7), presumably *via* the intermediacy of (8) and (15) (see Scheme). The design of suitably substituted compounds of type (2) with a view to achieving the synthesis of 1,2,6,7-tetra-aza-azulene is continuing in this laboratory.



SCHEME

EXPERIMENTAL

^{1}H N.m.r. spectra were determined at 60 MHz with tetramethylsilane as internal reference. ^{13}C N.m.r. spectra were determined at 20.1 and 25 MHz for $(CD_3)_2SO$ solutions with tetramethylsilane as internal reference. Unless otherwise stated i.r. spectra were determined for KBr discs and column chromatography was carried out with Merck Kieselgel 60, 70—230 mesh ASTM using a mixture of ethyl acetate and cyclohexane 8 : 2 (v/v) as eluant. Preparative t.l.c. was carried out on 20 × 20 cm plates coated with

Merck Kieselgel HF_{254} (type 60). A Girdel 75 gas chromatograph (N_2 carrier gas, flame ionisation detector, column packed with FFAP on Chromosorb WHMDS) was used for analytical v.p.c.; i.v. refers to evaporation under water-pump vacuum.

2,3,3a,6-Tetrahydropyrazolo[3,4-d][1,2]*diazepines* (2a—f).—To ice-cold ethereal diazomethane (prepared from 43 g of *p*-tosylmethylnitrosamide [10]) was added a saturated chloroform solution of the appropriate 1*H*-1,2-diazepine (2.0 g).[11,12,*] The reactants were maintained at 0 °C for 18 h after which time the solvent was removed by i.v. evaporation and the residual oil, crude (2; R^3 = H), was treated as described under (i)—(iii) below.

(i) It was treated with a mixture of acetic anhydride (2 ml) and pyridine (20 ml) at 50 °C for 18 h. The reaction mixture was poured onto crushed ice (*ca.* 100 g) and the resulting mixture was extracted with chloroform (3 × 100 ml). Evaporation of the chloroform extracts i.v. afforded an oil which was freed from residual pyridine by warming at 50 °C and 0.1 mmHg and finally column chromatographed † to give 2-*acetyl*-2,3,3a,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepines* (2a—d); see Tables 1 and 2.

(ii) It was treated with *p*-toluenesulphonyl chloride (4.0 g) in pyridine (12 ml) at reflux for 15 min. The reaction mixture was cooled, poured into water (*ca.* 100 ml), and extracted with chloroform (3 × 75 ml). Evaporation of the chloroform extracts i.v. afforded a brown oil which was freed from pyridine at 50 °C and 0.1 mmHg and finally column chromatographed to give 6-*benzoyl*-8-*methyl*-2-*tosyl*-2,3,3a,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepine* (2e); see Tables 1 and 2.

(iii) It was treated with methanolic formaldehyde (35—40%; 9 ml) in methanol (25 ml) at reflux for 30 min. The reaction mixture was cooled and sodium borohydride (1.04 g) was added portionwise with cooling. On stirring for *ca.* 1 h a pale yellow solid precipitated and this was filtered off and crystallized to afford 2-*methoxymethyl*-6-*tosyl*-2,3,3a,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepine* (2f); see Tables 1 and 2.

4-*Vinylpyrazole*-3(5)-*carbaldehyde Phenylsulphonyl- and Tosyl-hydrazones* (3a—c).—The appropriate tetrahydropyrazolo[3,4-*d*][1,2]diazepine [(2a), (0.98 g); (2b), (0.99 g); and (2c), (0.77 g)] was heated at reflux in methanol [50 ml per g of (2)] containing sodium carbonate [1 g per g of (2)] for 3 h. Filtration and evaporation of the solvent i.v. afforded a residue which was column chromatographed to give 4-vinylpyrazole-3(5)-carbaldehyde phenylsulphonyl- and tosyl-hydrazones (3a—c); see Tables 1, 3, and 4. An investigation (v.p.c.) of the reaction solvent obtained from the evaporation of the above reaction indicated the presence of methyl acetate.

Suspected 6-*Tosyl*-1(2),4,5,6-*tetrahydropyrazolo*[3,4-d][1,2]-*diazepine*.—Compound (3a) (0.97 g) was heated at reflux in methanolic sodium carbonate for 2.5 h under identical conditions to those described above. The residue obtained from evaporation of the reaction filtrate was applied to eighteen preparative t.l.c. plates. Elution with ethyl acetate–cyclohexane (8 : 2 v/v) gave compound (3a) (0.59 g, 69%) and a mixture (0.095 g) which was re-chromatographed on preparative t.l.c. plates. Two elutions with the same solvent mixture afforded crude suspected 6-*tosyl*-1(2),4,5,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepine* (0.036 g, 4%) which was identified from the following ^{1}H n.m.r. spectrum only, δ[$CDCl_3$–$(CD_3)_2SO$] 2.41 (s), 7.33 and 7.86 (AA′BB′, Ts), 2.90—3.2 (m, 2 × H-4) and 3.46—3.66 (m, 2 × H-5), 7.43 (s, H-3), and 7.73 (s, H-8), and 8.0br (s, NH).

4-*Vinylpyrazole*-3(5)-*carbaldehyde* (E)-*Tosylhydrazone* (3d).—4-Vinylpyrazole-3(5)-carbaldehyde (*Z*)-tosylhydrazone (3a) was set aside in $(CD_3)_2SO$ containing deuterium oxide and water for 3 weeks whence it was observed by ^{13}C n.m.r. to isomerise quantitatively to its (*E*)-isomer (3d). Addition of the $(CD_3)_2SO$ solution to water gave a white precipitate which was filtered off and crystallised to afford 4-vinylpyrazole-3(5)-carbaldehyde (*E*)-tosylhydrazone (3d); see Tables 1, 3, and 4.

4-*Ethylpyrazole*-3(5)-*carbaldehyde* (Z)-*Tosylhydrazone* (3e).—Hydrogen was bubbled through a solution of the vinylpyrazole (3a) (0.18 g) in ethanol (100 ml) containing 10% palladium charcoal (0.1 g) until all the starting material had been consumed (*ca.* 2 h t.l.c.). The reaction mixture was filtered and the filtrate evaporated i.v. to yield a white solid which was crystallized to afford 4-*ethylpyrazole*-3(5)-*carbaldehyde* (Z)-*tosylhydrazone* (3e); see Tables 1, 3, and 4.

1-*Methoxymethyl*-4-*vinylpyrazole*-3-*carbaldehyde* (Z)-*Tosylhydrazone* (4) *and* 2-*Methoxymethyl*-6-*tosyl*-2,4,5,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepine* (5).—2-Methoxymethyl-6-tosyl-2,3,3a,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepine (2f) (0.33 g) was heated under reflux in methanol (12.5 ml) containing sodium carbonate (0.3 g) for 3 h. The reaction mixture was cooled, filtered, and evaporated i.v. to afford an oil which was applied to ten preparative t.l.c. plates. Elution with ethyl acetate–cyclohexane (6 : 4 v/v) afforded 1-methoxymethyl-4-vinylpyrazole-3-carbaldehyde (*Z*)-tosylhydrazone (4) (see Tables 1 and 4) [R_F 0.7; i.r. $\nu_{max.}$ (liq. film) 3 120 and 1 630 cm^{-1}; ^{1}H n.m.r. δ($CDCl_3$) 2.39 (s), 7.25 (d) and 7.83 (d) (AA′BB′, Ts), 7.30 (s, H-5), 7.63 (s, H-8), 6.53 (dd, H_a), 5.21 (dd, H_b), 5.46 (dd, H_c), 11.83br (s, NH exchangeable), 3.38 (s, OMe), 5.40 (s, OCH_2N) (J_{ab} = 11 Hz, J_{ac} = 17, J_{bc} = 1.5 Hz)] and 2-*methoxymethyl*-6-*tosyl*-2,4,5,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepine* (5) (see Table 1) [R_F 0.46; i.r. $\nu_{max.}$ 1 620 cm^{-1}; ^{1}H n.m.r. δ($CDCl_3$) 2.41 (s), 7.30 (d) and 7.90 (d) (AA′BB′, Ts), 2.90—3.20 (m, 2 × H-4) and 3.50—3.80 (m, 2 × H-5), 7.44 (s, H-3) and 7.70 (s, H-8), 3.30 (s, OMe), and 5.33 (s, $O-CH_2-N$).

6-*Benzoyl*-8-*methyl*-1(2),4,5,6-*tetrahydropyrazolo*[3,4-d]-[1,2]*diazepine* (6).—2-Acetyl-6-benzoyl-8-methyl-2,3,3a,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepine (2d) (1.00 g) was heated at reflux in methanol (50 ml) containing sodium carbonate (1.0 g) for 2 h. The reaction mixture was cooled, filtered, and the filtrate evaporated i.v. to afford

* The diazepine (1d) was prepared by photolysis of the corresponding *N*-iminopyridinium ylide in toluene and had a m.p. of 73 °C.[13]

† For compounds (2a—c) a small quantity of yellow material was eluted first in each case. This was identified spectroscopically as the corresponding 2-acetyl-2,6-dihydropyrazolo[3,4-*d*][1,2]-diazepine. For example, the preparation of (2a) afforded 2-acetyl-6-tosyl-2,6-dihydropyrazolo[3,4-*d*][1,2]diazepine (1.5%), m.p. 205—215 °C (decomp.) (xylene) (Found: C, 54.5; H, 4.3; N, 17.0. $C_{15}H_{14}N_4O_3S$ requires C, 54.5; H, 4.3; N, 17.0%), i.r. $\nu_{max.}$ 3 160, 1 742, and 1 675 cm^{-1}; u.v. $\lambda_{max.}$($CHCl_3$) 289 nm ($\log_{10}\varepsilon$ = 3.93); M^+ = 330; ^{1}H n.m.r. δ($CDCl_3$) 2.47 (s, Me), 2.57 (s, Me), 5.28 (d, *J* = 9.6 Hz, H-4), 6.40 (d, *J* = 9.6 Hz, H-5), 7.28 (s, H-3), 7.61 (s, H-8), 7.37 (d) and 7.87 (d) (AA′BB′ system, Ts).

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an oil which was column chromatographed giving methyl benzoate (0.155 g, 29%) followed by a pale yellow solid mixture (0.336 g) which afforded 6-*benzoyl*-8-*methyl*-1(2),4,5,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepine* (6) (0.207 g) on crystallisation (see Table 1), i.r. $\nu_{max.}$ 3 160 and 1 620 cm^{-1}, u.v. $\lambda_{max.}$(EtOH) 295 nm ($\log_{10} \varepsilon = 3.95$); ^1H n.m.r. δ[$CDCl_3$–$(CD_3)_2SO$] 2.40 (s, Me), 2.85—3.15 (m, 2 × H-4), and 3.90—4.18 (m, 2 × H-5), 7.20—7.60 (m, Ar*H* + H-3), and 13.2br (s, NH exchangeable). Continued elution with ethyl acetate–cyclohexane followed by ethanol afforded a crude yellow solid (0.434 g) which was not investigated further. An investigation (v.p.c.) of the reaction solvent obtained from the evaporation of the above reaction indicated the presence of methyl acetate.

6-*Benzoyl*-8-*methyl*-1(2),6-*dihydropyrazolo*[3,4-d][1,2]*diazepine* (7).—6-Benzoyl-8-methyl-2-tosyl-2,3,3a,6-tetrahydropyrazolo[3,4-*d*][1,2]diazepine (2e) (1.00 g) was heated at reflux in methanol (50 ml) containing sodium carbonate (1.0 g) for 1 h. The reaction mixture was cooled, filtered, and the filtrate evaporated i.v. The residue was column chromatographed to afford 6-*benzoyl*-8-*methyl*-1(2),6-*dihydropyrazolo*[3,4-d][1,2]*diazepine* (7) (see Table 1), i.r. $\nu_{max.}$ 3 140 and 1 660 cm^{-1}; u.v. $\lambda_{max.}$(EtOH) 237 nm ($\log_{10} \varepsilon = 4.32$); ^1H n.m.r. δ[$CDCl_3$–$(CD_3)_2SO$] 2.40 (s, Me), 6.41 (AB quartet, J_{AB} = 8 Hz, H-4 and H-5), 7.20—7.70 (m, Ar*H* + H-3), and 7.50br (s, NH exchangeable).

Deuteriation Experiments.—(i) *The reaction of* 2-*acetyl*-6-*tosyl*-2,3,3a,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepine* (2a) *with sodium carbonate in monodeuteriomethanol* (CH_3OD). Compound (2a) (0.352 g) was heated at reflux in monodeuteriomethanol (5 ml) containing sodium carbonate (0.3 g) for 2.5 h. The reaction was cooled, filtered, and the filtrate evaporated i.v. to afford a residue which was column chromatographed. Elution with a mixture of ethyl acetate and cyclohexane (6 : 4; v/v) gave a white solid (0.142 g) which on crystallisation from aqueous ethanol afforded a mixture (0.081 g) of vinylpyrazole-3(5)-carbaldehyde tosylhydrazones [(3a; H_b = D) and (3a; H_c = D) *ca.* 1 : 1 major products and (3a) minor product]; M^+ 291; ^1H n.m.r. [$(CD_3)_2SO$] (see Figure).

(ii) *The reaction of* 2-*acetyl*-6-*benzoyl*-8-*methyl*-2,3,3a,6-*tetrahydropyrazolo*[3,4-d][1,2]*diazepine* (2d) *with sodium carbonate in tetradeuteriomethanol* (CD_3OD). Compound (2d) (0.398 g) was heated at reflux in tetradeuteriomethanol (4 ml) containing sodium carbonate (0.4 g) for 3 h. The reaction was set aside overnight at room temperature and then filtered. Evaporation of the filtrate i.v. gave an oil which was applied to eight preparative t.l.c. plates. Elution with a mixture of ethyl acetate and cyclohexane (8 : 2; v/v) gave deuteriomethyl benzoate (0.047 g) and a mixture (0.22 g). A portion of the latter (0.103 g) was rechromatographed over Merck silica gel 60 under pressure (*ca.* 5 bar). Elution with a mixture of ethyl acetate and acetonitrile (95 : 5; v/v) afforded 6-benzoyl-8-methyl-4,5-dideuterio-1(2),6-dihydropyrazolo[3,4-*d*][1,2]diazepine (14) (0.031 g), M^+ 256; ^1H n.m.r. (80 MHz Fourier transform) δ[$(CD_3)_2SO$–$CDCl_3$] 2.45 (s, Me), 3.05 (m, CHD), 4.10 (m, CHD), 7.30—7.65 (m, ArH + H-3), and 12.95br (s, NH).

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