The Synthesis of 3*H*-1,2-Diazepines by the Base-induced Elimination of Toluene-*p*-sulphinic Acid from 3,4-Dihydro-2-tosyl-1,2-diazepines, and some Observations on Sigmatropic Hydrogen Shifts in the 3*H*-1,2-Diazepine System [1]

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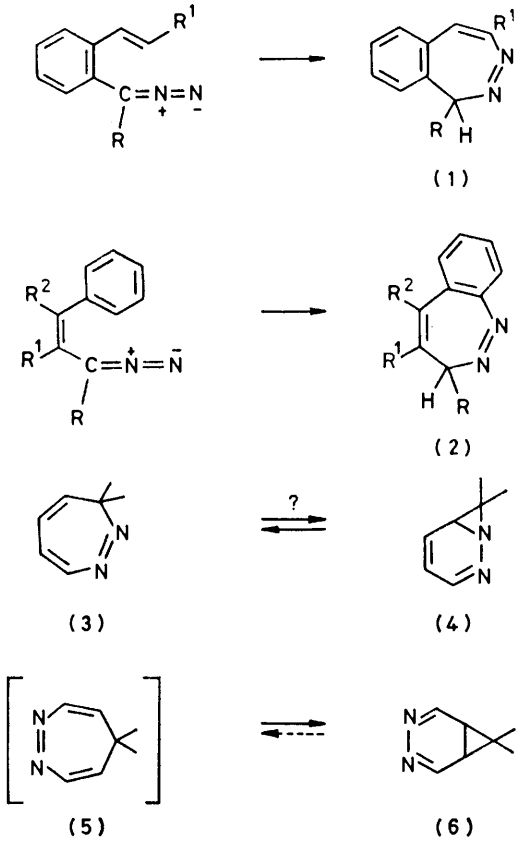
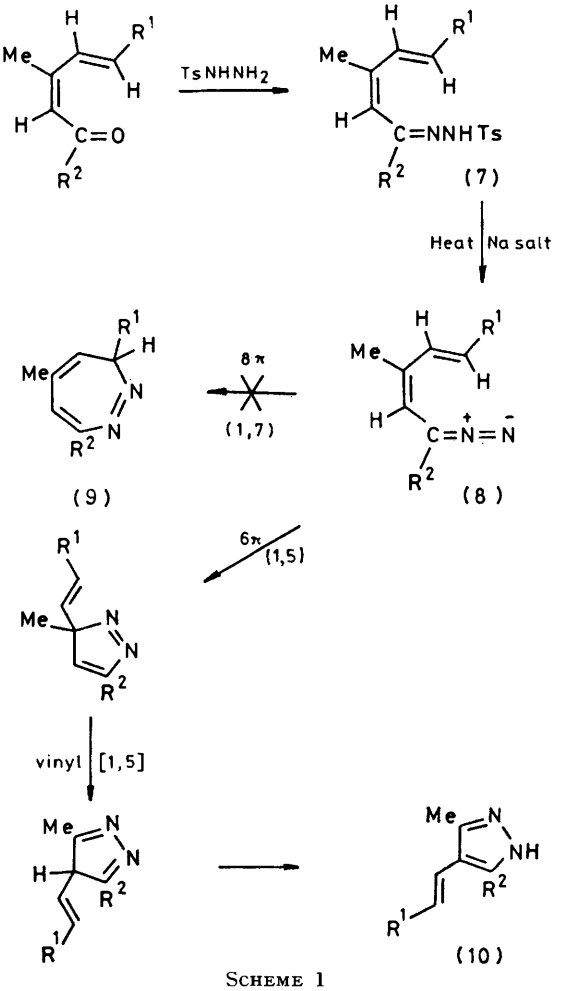
The reaction of 3,4-dihydro-2-tosyl-1,2-diazepines (13) with sodium ethoxide provides the first general synthesis of 3*H*-1,2-diazepines (9). The ^1H and ^{13}C n.m.r. spectra of the products show that they exist as diazepines (3) rather than as the diazanorcaradiene valence tautomers (4). In some cases the synthesis produced mixtures of isomeric 3*H*-1,2-diazepines *via* a rapid [1,5]sigmatropic hydrogen shift in the primary product. A preliminary kinetic study of the isomerisation of 3,5-dimethyl-3*H*-1,2-diazepine (14c) to 5,7-dimethyl-3*H*-1,2-diazepine (9c) at 0 °C has shown that the hydrogen shift is *ca.* 10^{10} faster than in an analogous cycloheptatriene.

We have recently described routes to benzo-annelated 3*H*-1,2-diazepines, *e.g.* (1) and (2), *via* the 8π-electron electrocyclisation reactions of unsaturated diazo-compounds.[2-4] Another route to 3*H*-1,2-benzodiazepines has also been recently devised [5] but before the present work no general route † to the parent 3*H*-1,2-diazepine system (3) had been reported. This was an attractive synthetic target, not only because it was the only 1,2-diazepine isomer so far unstudied, but particularly to compare its properties with those of the 5*H*-1,2-diazepine (5) which is the only other isomer containing an azo-group. Since the 5*H*-isomer is so destabilised by the low bond energy of the azo-group that it exists entirely as its diazanorcaradiene tautomer (6), it was of interest to determine whether the 3*H*-isomer would be similarly destabilised and tautomerise to (4). In the benzo-diazepines (1) and (2) such isomerisations are not ob-





Scheme 1

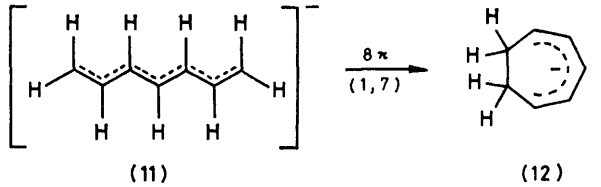
† There is one previous note [6] of the formation of a 3*H*-1,2-diazepine *via* the thermal rearrangement of a diazanorcaradiene, but little information is given about its spectra or properties.

served but would not be expected in these systems due to the double-bond fixation effect of the benzene ring.[7]

RESULTS

It seemed possible that the synthetic method used for the benzodiazepines (1) and (2) above might be capable of extension to provide a route to the 3*H*-1,2-diazepines (9) from the αβ,γδ-unsaturated diazo-compounds (8) (Scheme 1). However, in all cases so far studied, the ring closure of (8) has proceeded *via* a 6π-electron mode to give eventually the vinylpyrazoles (10).[1,8] This contrasts with the reaction of the hydrocarbon analogue, the heptatrienyl anion (11), which reacts only *via* an 8π-electron closure to give (12).[9,10] This work on the reactions of (8) is still in progress and will be reported in full later.

During this investigation, however, it was found that some of the *p*-tosylhydrazones (7), which had been used as precursors to the diazo-compounds (8), could be cyclised under acid conditions to give the 3,4-dihydro-2-tosyl-1,2-diazepines (13).[1,11] These compounds react rapidly with sodium ethoxide in toluene at *ca.* 100 °C (Scheme 2) to provide a high-yielding route to the 3*H*-1,2-diazepines (9). In these reactions the primary product (9) was, however, not always the only compound isolated; in two cases the product was an equilibrium mixture of the two isomers (9) and (14). These isomers interconvert by [1,5]sigmatropic hydrogen shifts, very rapidly at the reaction temperature and fast enough at room temperature to make the isolation of pure samples of each isomer impossible. The isomers



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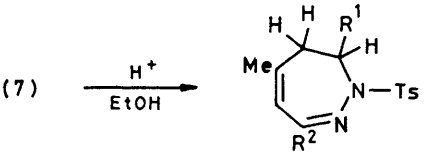
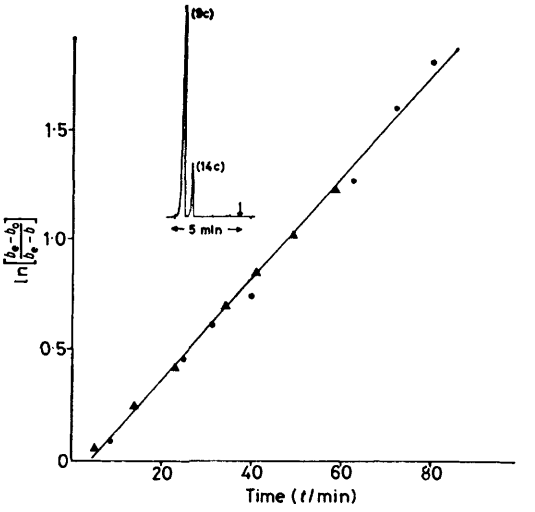


(13)

could, however, be separated on a sub-microgram scale by high-speed, high-resolution analytical liquid chromatography using the column at 0 °C (see Figure inset). After collection, the solutions of the separated isomers (>90% isomeric purity) showed no change in the isomer ratio when kept at −80 °C but each reverted back to the equilibrium ratio over *ca.* 2 h at 0 °C and more rapidly at room temperature.

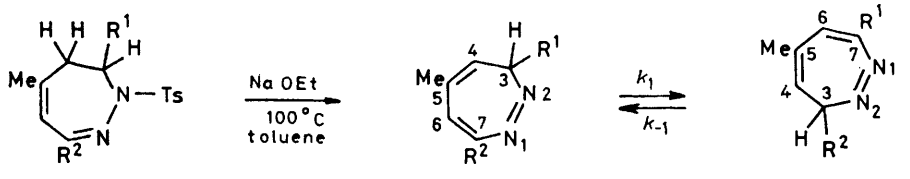


Graph of rate data for the isomerisation of (14c) to (9c) at 0 °C for two runs (● and ▲). The inset shows the h.p.l.c. trace for the system at equilibrium

A preliminary kinetic study of the conversion of (14c) into (9c) at 0 °C was carried out using h.p.l.c. to determine the isomer ratio over *ca.* 90 min during which time the proportion of (14c) decreased from *ca.* 95 to 25%. In this experiment it had to be assumed that both isomers gave an equal molar response on the h.p.l.c. u.v. detector since no calibration was possible, it not being possible to obtain the individual isomers pure. That this is at least approximately true was confirmed by the ^{1}H n.m.r. spectrum of the equilibrium mixture which showed the same *ca.* 85 : 15 ratio as did the h.p.l.c. analysis. The graph in the Figure was obtained using the following integrated rate equation:

$$\ln\left[\frac{b_e - b_o}{b_e - b}\right] = \left[\frac{a_o + b_o}{b_e}\right] k_{-1}t$$

where a_o and b_o are the initial concentrations of (14c) and (9c), b_e is the equilibrium concentration of (9c), and b is its concentration at time t. From this $k_{-1} = 3.3 \times 10^{-4}$ s^{-1} and since the equilibrium constant $K = 5.9$ then $k_1 = 0.56 \times 10^{-4}$ s^{-1}. The failure of the graph to extrapolate back to the origin is probably due to the time required for the reaction solution to warm up from −80 to 0 °C at the start of the experiment.



(13) (9) (14)

a; $R^1 = R^2 = Me$		77%	
b; $R^1 = H$, $R^2 = Ph$	82%		0%
c; $R^1 = H$, $R^2 = Me$	67%		11%
d; $R^1 = Me$, $R^2 = Et$	27%		35% (see discussion)

SCHEME 2

The formulation of the products (9) and (14) as 3*H*-1,2-diazepines relies mainly on comparison of their properties and spectra with those of the known 3*H*-1,2- and 1*H*-2,3-benzodiazepines (1) and (2). Like both these systems the 3*H*-1,2-diazepines were yellow, either oils (a, c, d) or crystalline solids (b). They were thermally stable enough for the oils to be rapidly distilled without decomposition at *ca.* 100 °C under water-pump vacuum but they decomposed or isomerised to pyrazoles on prolonged heating.[8] Like the 1*H*-2,3-benzodiazepines [12] they were rapidly isomerised by daylight and u.v. irradiation *via* a ring closure of the diazabutadiene unit.[8]

TABLE 1

Mass spectra of 3*H*-1,2-diazepines

Compound	*m/e* (relative abundance %)
(9a)	39 (16), 41 (12), 77 (31), 79 (12), 91 (31), 93 (100), 94 (8), 107 (10), 108 (35), 136 (10)
(9b)	76 (10), 77 (15), 78 (16), 91 (19), 115 (29), 127 (8). 128 (16), 129 (14), 141 (40), 155 (36), 156 (100), 157 (13), 169 (10), 184 (9)
(9c)/(14c)	39 (18), 41 (13), 53 (12), 77 (55), 79 (100), 80 (13), 91 (24), 93 (25), 94 (53), 95 (11), 106 (11), 122 (14)
(9d)/(14d)	39 (17), 41 (20), 77 (24), 79 (34), 91 (56), 92 (17), 93 (24), 105 (17), 107 (100), 108 (15), 122 (34), 123 (10), 135 (10), 150 (15)

The mass spectra of the 3*H*-1,2-diazepines (Table 1) showed major fragmentation pathways *via* loss of N_2 and methyl fragments as previously observed for (1; R = Me, R^1 = H).[2] The most important comparative data, however, derived from their ^{1}H and ^{13}C n.m.r. spectra. The ^{1}H n.m.r. spectra were much like those of similarly substituted 1*H*-2,3-benzodiazepines (1). For example in compounds (9b) and (9c) the chemical shifts of the two protons attached to the saturated ring carbon had characteristically wide chemical-shift separation [2,4] as illustrated in structures (16) and (17), *cf.* (15). In both (9b) and (9c) the multiplet due to the pseudo-axial proton (H_a) was partly obscured by overlapping peaks but for (9c) its chemical shift was confirmed by a ^{13}C n.m.r. single frequency off-resonance proton decoupling (SFORD) study: irradiation at frequencies other than the resonance frequencies of H_a and H_e gave the ^{13}C C-3 absorption as a doublet of doublets whose separations depended on the different residual coupling constants to H_a and H_e,[13] but irradiation at each of the resonance frequencies of H_a and H_e (≡ 2 and 5.8 δ respectively) reduced this to a doublet. Similar effects have previously been reported for compounds with non-equivalent geminal protons.[14] In the non-decoupled ^{13}C spectrum of (9c), H_a and H_e showed slightly different coupling constants to C-3, J = 137 and 148 Hz (with further splitting due to long range coupling). In the ^{13}C n.m.r. spectra (Table 2) C-3, the saturated carbon attached to the azo-group, was strongly deshielded and absorbed in a range (65.7—77.4 p.p.m.) similar to that observed for the benzodiazepines (1), 69—72 p.p.m.; [3] (2) 67—75 p.p.m.[3,4] The assignments in Table 2 are supported by SFORD proton decoupling and/or by running the spectra with no proton decoupling.

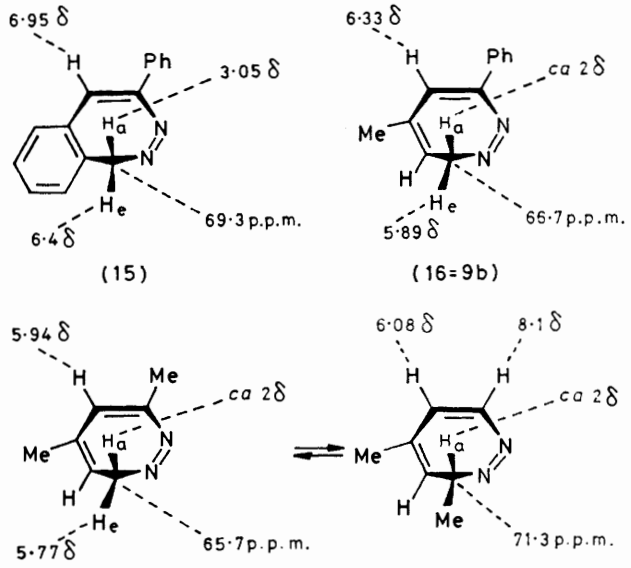


TABLE 2

^{13}C N.m.r. data (as p.p.m. from Me_4Si) of 3*H*-1,2-diazepines *

Compound	Chemical shift
(9a)	C-3 70.9; C-4 and C-6 117.4, 118.1; C-5 135.9; C-7 154.5; 3-Me 18.5; 5-Me 20.4; 7-Me 21.0
(9b)	C-3 66.7; C-4 and C-6 111.3, 115.7; C-5 138.6; C-7 156.3; aromatic 137.0 (tert.), 126.0, 128.5, 128.7; Me 21.0
(9c)	C-3 65.7; C-4 and C-6 110.5, 117.8; C-5 138.0; C-7, 154.4; 2 × Me 21.1, 20.6
(14c)	C-3 71.3; C-4 and C-6 119.3, 121.2; C-5 138.0 [coincident with C-5 in (9c)]; C-7, 144.8; 2 × Me 18.6, 20.3
(9d)/(14d)	C-3 71.2, 77.4; C-4 and C-6 116.0, 116.9, 117.3, 118.5; C-5 136.0, 136.3; C-7 154.5, 160.8; CH_2 26.0, 28.5; Me's 10.7, 13.8, 18.6, 20.6, 21.1

* $CDCl_3$ as solvent.

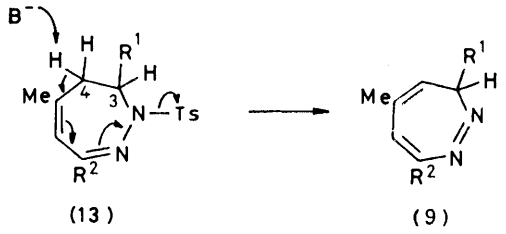
In the equilibrium mixture of (9c) and (14c) the formulation of the minor isomer as (14c) was supported by the ^{13}C n.m.r. spectrum which showed six peaks separate from, and smaller than those due to (9c); only that of C-5 was not observed and is probably coincident with the C-5 peak of (9c). In the ^{1}H spectrum of the mixture the only peaks which could be clearly distinguished from those of (9c) were two doublets at 6.08 and 8.1 δ (J 9 Hz), these were assigned to the vinyl protons on C-6 and C-7 as shown in structure (18) on the basis of the similarity of their chemical shifts and coupling constants to the analogous protons in (19).[3]

DISCUSSION

The formation of the 3*H*-1,2-diazepines is likely to be *via* either an *E*1cB or *E*2 elimination mechanism as depicted in Scheme 3. That the elimination follows this course to give (9) *via* base-attack at the C-4 methylene group is at first sight rather surprising, since the alter-

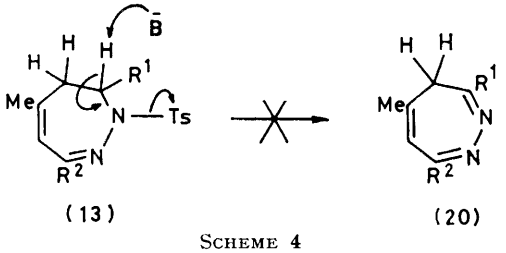
native elimination, Scheme 4, would have produced the 4*H*-1,2-diazepine (20) which, by comparison with the analogous 1*H*- and 5*H*-2,3-benzodiazepines [2] would be expected to be the more thermodynamically stable isomer. The preference for the observed reaction may simply be due to the higher acidity of the C-4 than the C-3 protons, or it may be due in part to the steric inaccessibility of the antiperiplanar conformation in (13) which would be required for a rapid β-elimination.

It is clear from their n.m.r. spectra that the products are 3*H*-1,2-diazepines rather than diazanorcaradienes (4) and, at least for the compounds studied so far, the tautomeric equilibrium is so strongly biassed in favour of the diazepine structure that the diazanorcaradiene form is undetectable. This contrasts with the 5*H*-1,2-diazepine (5) case in which the equilibrium is as strongly



(13) (9)

SCHEME 3



(13) (20)

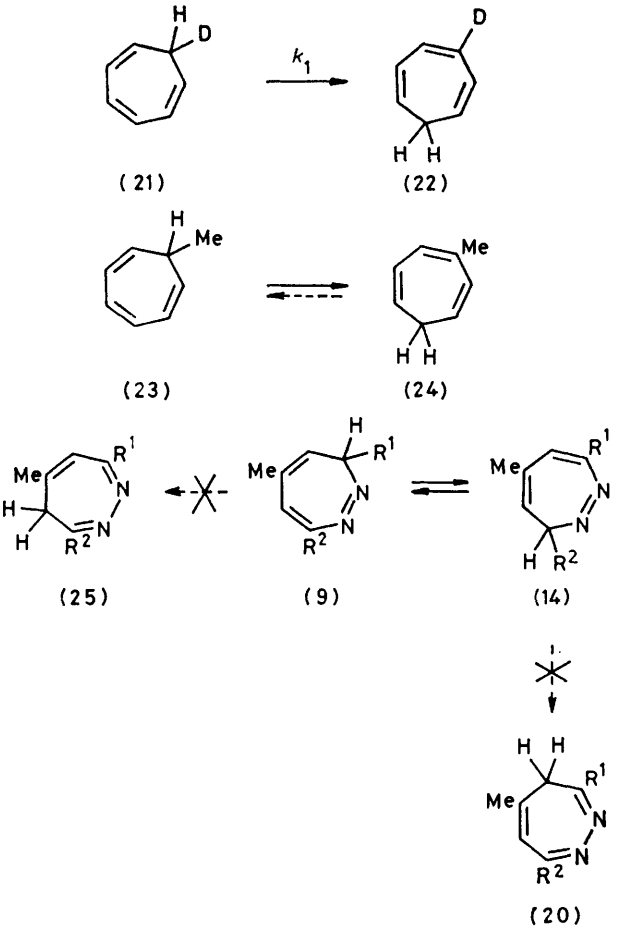
SCHEME 4

biased in the opposite direction.[15] This crossover in thermodynamic stability is broadly explicable in terms of bond energies. The average bond energies of C=N (607) and C=C (613) bonds are much higher than for N=N (385) bonds while for the single bonds C–C (348) > C–N (302) > N–N (168 kJ mol^{-1}). Thus although both the 5*H*- and the 3*H*-1,2-diazepines are similarly destabilised by having an azo-group, in the diazanorcaradienes (4) is destabilised relative to (6) by having two C–N bonds where (6) has the stronger C–C bonds. So apparently for the 5*H*-isomer the gain in bonding energy on its conversion into the diazanorcaradiene (6) more than offsets the increased ring strain,[15] but for the 3*H*-isomer it does not and the diazepine structure is favoured. In the analogous hydrocarbon case, the equilibrium between cycloheptatriene and norcaradiene is affected by substituents on the ring.[16] We have not yet been able to prepare 3*H*-1,2-diazepines with conjugating groups on C-3 to see if the same effects are observed.

The formation of two isomeric diazepines in some of these reactions is of much interest. *A priori* the formation of the second isomer (14) could have been due to either the base-catalysed isomerisation of the primary product (9), since a two-fold excess of base was used in the synthesis to achieve the rapid conversion of (13), or *via* a [1,5] sigmatropic hydrogen shift. That it was the latter mechanism which was operating was shown by the h.p.l.c. isolation technique described in the Results section—solutions of each of the isomers (9c)/(14c) and (9d)/(14d) in hexane–ether were found to revert readily to the equilibrium isomer ratio at both room temperature and 0 °C in the absence of base but to be stable when kept at −80 °C. Both the very high rate of this sigmatropic hydrogen shift and its specificity are remarkable.

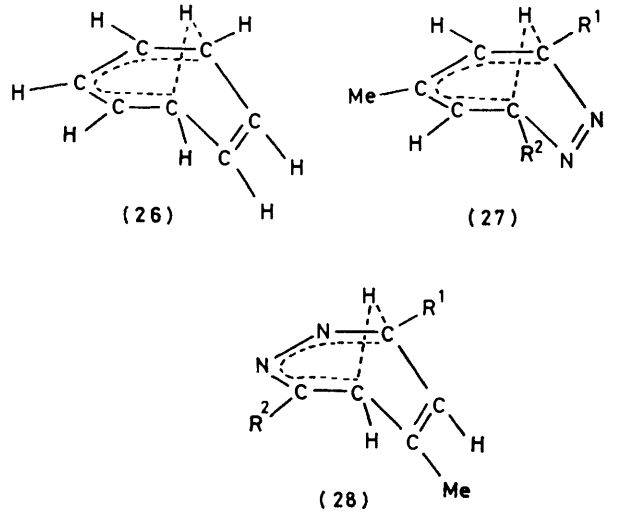
In the equilibrium of (9c) and (14c) the rate constants at 0 °C ($k_1 = 0.56 \times 10^{-4}$ s^{-1}, $k_{-1} = 3.3 \times 10^{-4}$ s^{-1}) are very much higher than would be expected for similar cycloheptatrienes at this temperature. For example in the liquid-phase isomerisation of (21) to (22) the rate constant k_1 is 4.8×10^{-8} s^{-1} at 98 °C, 6.6×10^{-7} s^{-1} at 121 °C, and 3.2×10^{-6} s^{-1} at 140 °C which gives an activation enthalpy for the reaction of 126 kJ mol^{-1} and an activation entropy of −48.2 J K^{-1} mol^{-1}.[17] From this data calculation of the rate constant at 0 °C gives $k_1 = ca.\ 1 \times 10^{-14}$ s^{-1}. The substitution of a methyl group at the departure site is known to accelerate the reaction by *ca.* 9-fold [18] so, allowing for the statistical factor of 2, the rate constant for the conversion of (23) to (24) into the liquid phase at 0 °C would be expected to be *ca.* 4×10^{-14} s^{-1}. Thus the rate constant for the hydrogen shift converting (14c) into (9c) is *ca.* 10^{10} greater than for an analogous cycloheptatriene. The activation energies for the (9c)/(14c) equilibrium, calculated *via* the Eyring equation, are $\Delta G_1^{\ddagger} = 85$ kJ mol^{-1}, $\Delta G_{-1}^{\ddagger} = 89$ kJ mol^{-1} and are both lower than the value of *ca.* 96 kJ mol^{-1} normally recognised as the minimum for the isomers to be stable at room temperature.[19] Thus the isolation of pure samples of each was expected to be difficult and was, in practice, found to be impossible. The rapid analytical h.p.l.c. technique at 0 °C is ideal for very small-scale separations but attempts at scaling-up encountered not only the usual problems due to the conflicting requirements for high sample loading and high column efficiency but also the additional problem of keeping the analysis time short. Increasing the resolving power at preparative scale by using longer columns was, therefore, of limited value because of the increased analysis time and consequent band-broadening due to on-column isomerisation. Attempts to minimise this by lowering the column temperature caused loss of resolution due to higher solvent viscosity.

The high specificity of the hydrogen migration in the 3*H*-1,2-diazepine system is also notable. Although the interconversion of the two 3*H*-isomers (9) and (14) is rapid there is no leakage *via* the alternative [1,5] hydrogen shifts (Scheme 5) to the 4*H*-isomers (20) and (25) which, lacking the azo-group, would be expected to be more stable. The transition state for hydrogen migration in cycloheptatriene has recently been calcu-



SCHEME 5

lated [20] and is shown in (26); it has a virtually planar pentadienyl unit with an ethene unit out-of-plane and virtually out-of-conjugation. If the transition states for the two possible migrations in the diazepine system are similar to (26) then that for the observed shift (27), which has the azo-group out-of-plane, must be of lower



energy than that for the not-observed shift (28) which has the azo-group as part of the pentadienyl unit. This alternative [1,5] shift is not observed even at higher temperatures since the diazepine then reacts *via* ring ontraction and nitrogen extrusion as reported elsewhere.[8]

The equilibrium isomer ratios of (9) : (14) are qualitatively similar to those reported for similarly substituted cycloheptatrienes,[18] the isomer (9c) being favoured by the conjugation of the electron-donating methyl group (R^2) with the unsaturated bonds of the ring and (9b) being strongly favoured by the conjugation of the phenyl group. For the (9c)/(14c) pair, the h.p.l.c. shows a 1.3 : 1 peak area ratio but it is not possible to determine from the spectra which is the major product.

EXPERIMENTAL

^{1}H N.m.r. spectra were obtained on a Varian HA 100 spectrometer and ^{13}C n.m.r. spectra on either Varian XL 100 or CFT 20 spectrometers. The high performance liquid chromatography (h.p.l.c.) analysis utilised a 15 × 0.5 cm column packed with Spherisorb (S5Y) silica (6 500 plates), used with an A.R.L. constant pressure pump and an L.D.C. 1205 u.v. monitor operated at 254 nm.

Preparation of the 3,4-*Dihydro*-2-*tosyl*-1,2-*diazepines* (13).—These were prepared by the reactions of conjugated dienones with *p*-tosylhydrazine.[1,11]

Synthesis of 3H-1,2-*Diazepines* (9)/(14).—The general method was to heat the 3,4-dihydro-2-tosyl-1,2-diazepine with a two-fold molar excess of sodium ethoxide in dry toluene, as described below for 3,5,7-trimethyl-3*H*-1,2-diazepine. At *ca.* 100 °C precipitation of sodium toluene-*p*-sulphinate occurred; heating was continued until t.l.c. (alumina; benzene–ether, 1 : 1) showed that all the starting material had been consumed. The mixture was filtered, the filtrate was washed with water, dried, and evaporated under reduced pressure to leave the crude product which was purified by distillation or recrystallisation.

3,5,7-*Trimethyl*-3H-1,2-*diazepine* (9a) ≡ (14a).—Sodium (0.16 g, 6.96 g-atom) was dissolved in dry ethanol (20 ml) and 3,4-dihydro-3,5,7-trimethyl-2-tosyl-1,2-diazepine (1.00 g, 3.42 mmol) was added. The ethanol was then evaporated off on a rotary evaporator at room temperature and the residual solid was dried, in the flask, at *ca.* 0.1 mmHg in a desiccator over phosphorus pentaoxide overnight. Dry toluene (20 ml) was added and the mixture was boiled under reflux for 15 min. The precipitated sodium toluene-*p*-sulphinate was filtered off and the filtrate washed with water (2 × 50 ml), dried, and the solvent removed under reduced pressure to leave a yellow oil. This was distilled to give 3,5,7-trimethyl-3*H*-1,2-diazepine (0.36 g, 77%) as a yellow oil, b.p. 75—78 °C at 10 mmHg (Found: C, 70.3; H, 8.7; N, 20.7. $C_8H_{12}N_2$ requires C, 70.55; H, 8.9; N, 20.6%). Mass spectrum: *m/e* $M^{+\cdot}$ 136.099 912, $(M - 28)^{+\cdot}$ 108.093 493; $C_8H_{12}N_2$ requires *m/e* 136.100 043, C_8H_{12} requires *m/e* 108.093 896; ^{1}H n.m.r. ($CDCl_3$) δ 5.92br (s, H-6), 4.88br (d, *J* 5 Hz, H-4), 2.36br (s, 7-Me), 1.99 (d, *J* 6 Hz, 3-Me), 1.94 (m, 5-Me), 1.77br (quintet, *J ca.* 6 Hz, H-3); in [$^2H_6$]benzene δ 5.52br (s, H-6), 4.64br (d, *J* 5 Hz, H-4), 2.16 (d, *J* 1.5 Hz, 7-Me), 1.89 (d, *J* 6 Hz, 3-Me), and 1.62br (s, 5-Me) superimposed on 1.5—1.7 (m, H-3).

5-*Methyl*-7-*phenyl*-3H-1,2-*diazepine* (9b).—A similar reaction (5 min) of 3,4-dihydro-5-methyl-7-phenyl-2-tosyl-

1,2-diazepine (2.00 g, 5.88 mmol) gave the crude product as a yellow oil (1.1 g). This was recrystallised at *ca.* −30 °C from light petroleum–diethyl ether (b.p. 40—60 °C) to give 5-methyl-7-phenyl-3*H*-1,2-diazepine (0.89 g, 82%) as yellow crystals, m.p. 64—65 °C (Found: C, 78.5; H, 6.5; N, 15.4. $C_{12}H_{12}N_2$ requires C, 78.5; H, 6.6; N, 15.2%); ^{1}H n.m.r. ($CDCl_3$) δ 7.6—7.9 (m, 2 H, aromatic), 7.1—7.5 (m, 3 H, aromatic), 6.33br (s, H-6), 5.89 [d of d, J_{gem} 8.5 Hz, J_{vic} 7 Hz, H-3 (quasi-eq)], 5.22 (t of q, J_{vic} 7 Hz, J^4 1.2 Hz, H-4), and 2.01br (5-Me) superimposed on 1.9—2.1 [m, H-3 (quasi-ax)].

5,7-Dimethyl-3H-1,2-*diazepine* (9c) *and* 3,5-*Dimethyl*-3H-1,2-*diazepine* (14c).—A similar reaction (15 min) of 3,4-dihydro-5,7-dimethyl-2-tosyl-1,2-diazepine (1.164 g, 4.19 mmol) gave a yellow oil (0.53 g) as the crude product. This was distilled to give a yellow oil (0.40 g, 78%), b.p. 80 °C at 12 mmHg (Found: C, 69.0; H, 8.4; N, 22.9. $C_7H_{10}N_2$ requires C, 68.8; H, 8.25; N, 22.9%) which consisted of 5,7-dimethyl-3*H*-1,2-diazepine (9c) and 3,5-dimethyl-3*H*-1,2-diazepine (14c); mass spectrum: *m/e* $M^{+\cdot}$ 122. 084 493, $(M - 28)^{+\cdot}$ 94.078 046; $C_7H_{10}N_2$ requires *m/e* 122.084 394, C_7H_{10} requires *m/e* 94.078 247; ^{1}H n.m.r. ($CDCl_3$) for (9c) δ 5.94br (s, H-6), 5.77 [d of d, J_{gem} 8.5 Hz, J_{vic} 7.5 Hz, H-3 (quasi-eq)], 5.13br (t, *J ca.* 7—8 Hz, H-4), 2.38br (s, 7-Me), and 1.95 (m, 5-Me) superimposed on 1.8—2.2 [m, H-3 (quasi-ax)]: for (14c) δ 8.1 (d, *J* 9 Hz, H-7), 6.08 (d, *J* 9 Hz, H-6), and 5.0br (d, *J* 8 Hz, H-4); the absorptions for the 5-Me, 3-Me, and H-3 all under the 1.8—2.2 multiplet. H.p.l.c. analysis with the column of 0 °C and using a mixture of dry diethyl ether (10 vol %) and 50% water-saturated hexane (90 vol %) as eluant at a flow rate of 2.5 ml min^{-1} gave the (9c) : (14c) peak area ratio of 5.9 : 1.

Kinetic Study of the Isomerisation of 3,5-*Dimethyl*-3H-1,2-*diazepine* (14c) *to* 5,7-*Dimethyl*-3H-1,2-*diazepine* (9c).—The isomers were separated using the column and conditions as above and 2 μl injections of a *ca.* 0.06 molar solution of the mixture. About 0.5—1 ml of the eluant was collected in a sample vial around each peak maximum and the vials were closed with Suba-seals and immediately cooled to −80 °C. These solutions were subsequently analysed for the (9c) : (14c) ratio by h.p.l.c. using a Spectra-Physics Minigrator integrator to measure the peak areas. Both sampling and h.p.l.c. injection were done with a 100 μl syringe pre-cooled to −20 °C using an injection size of *ca.* 50 μl and a detector absorbance range of 0.08. The first sample was taken at −80 °C to determine the initial (9c) : (14c) ratio. The solution was then kept at 0 °C in an ice–water bath and sampled repeatedly over *ca.* 1½ h. Two experiments were carried out; in the first the initial mixture contained 96% (14c), in the second 91% (14c). The proportion of (14c) decreased to *ca.* 20% after 1½ h at 0 °C and after being set aside overnight the equilibrated mixture contained 14.5% of (14c). The treatment of the data is described in the Results section and the results are shown in the Figure.

As a control experiment a similar solution containing (14c) 93% was kept at −80 °C and sampled over 2 h at the same frequency as the experiment above: the proportion of (14c) remained unchanged throughout (±2%).

7-Ethyl-3,5-*dimethyl*-3H-1,2-*diazepine* (9d) and 3-*Ethyl*-5,7-*dimethyl*-3H-1,2-*diazepine* (14d).—A similar reaction (5 min) of 7-ethyl-3,4-dihydro-3,5-dimethyl-2-tosyl-1,2-diazepine (1.15 g, 3.76 mmol) gave after distillation a yellow oil (0.35 g, 62%), b.p. 94—96 °C at 10 mmHg, which consisted of a mixture of the two diazepines (9d) and (14d). Mass spectrum: *m/e* $M^{+\cdot}$ 150.115 300, $(M - 28)^{+\cdot}$ 122.109 601; $C_9H_{14}N_2$ requires *m/e* 150.115 693, C_9H_{14} requires *m/e* 122.109 545. ^{1}H N.m.r. ($CDCl_3$) δ 5.90br [s, 6H in both isomers], 4.90br [overlapping triplets, 4 H in both isomers], 2.38 [s, 7-Me in (14d)] superimposed on 2.1—3.0 [twelve-peak multiplet, CH_2 in both isomers], 2.01 [d, *J* 6 Hz, 3-Me in (9d)], 1.94br [5-Me in both isomers], 1.4—1.9br [m, H-3 in both isomers], and 1.4 and 1.7 [overlapping triplets, *J* 8 Hz (ethyl CH_3)].

H.p.l.c. analysis with the column at 0 °C and using a mixture of dry diethyl ether (2 vol %) and 50% water-saturated hexane (98%) as eluant at a flow rate of 2.6 ml min^{-1} gave a peak area ratio of 1.3 : 1. The isomers were separated using the technique described above for (9c) and (14c) using a 2 μl injection of a *ca.* 0.08 molar solution of the mixture. H.p.l.c. analysis of the solutions kept at −80 °C showed >90% isomeric purity. The solutions of each isomer were then kept at room temperature for 1 h when h.p.l.c. analysis showed that the isomer ratio had returned to 1.3 : 1 in both.

[8/1499 *Received*, 15*th August*, 1978]

REFERENCES

[1] Preliminary report, C. D. Anderson, J. T. Sharp, H. R. Sood, and R. S. Strathdee, *J.C.S. Chem. Comm.*, 1975, 613.
[2] A. A. Reid, J. T. Sharp, H. R. Sood, and P. B. Thorogood, *J.C.S. Perkin I*, 1973, 2543.
[3] J. T. Sharp, R. H. Findlay, and P. B. Thorogood, *J.C.S. Perkin I*, 1975, 102.
[4] K. L. M. Stanley, J. Dingwall, J. T. Sharp, and T. W. Naisby, *J.C.S. Perkin I*, 1979, 1433.
[5] J. Kurita and T. Tsuchiya, *J.C.S. Chem. Comm.*, 1974, 936.
[6] J. Sauer and G. Heinrichs, *Tetrahedron Letters*, 1966, 4979.
[7] G. Maier, *Angew. Chem. Internat. Edn.*, 1967, **6**, 402.
[8] C. D. Anderson, J. T. Sharp, E. Stefaniuk, and R. S. Strathdee, *Tetrahedron Letters*, 1976, 305.
[9] H. Kloosterziel and J. A. A. van Drunen, *Rec. Trav. chim.* 1969, **88**, 1084.
[10] R. D. Bates, W. H. Deines, D. A. McCombs, and D. E. Potter, *J. Amer. Chem. Soc.*, 1969, **91**, 4608.
[11] C. D. Anderson, P. N. Anderson, and J. T. Sharp, *J.C.S. Perkin I*, 1979, 1640.
[12] A. A. Reid, H. R. Sood, and J. T. Sharp, *J.C.S. Perkin I*, 1976, 362.
[13] B. Birdsall, N. J. M. Birdsall, and J. Feeney, *J.C.S. Chem. Comm.*, 1972, 316.
[14] E. W. Hagaman, *Org. Magnetic Resonance*, 1976, **8**, 389.
[15] A. Steigel, J. Sauer, D. A. Kleier, and G. Binsch, *J. Amer. Chem. Soc.*, 1972, **94**, 2770.
[16] S. W. Staley, M. A. Fox, and A. Cairncross, *J. Amer. Chem. Soc.*, 1977, **99**, 4524 and papers cited therein.
[17] A. P. ter Borg, H. Kloosterziel, and N. van Meurs, *Rec. Trav. chim.*, 1963, **82**, 717.
[18] A. P. ter Borg, E. Razenberg, and H. Kloosterziel, *Rec. Trav. chim.*, 1965, **84**, 1230.
[19] H. Kessler, *Angew. Chem. Internat. Edn.*, 1970, **9**, 219.
[20] J. R. de Dobbelaere, J. M. F. van Dijk, J. W. de Haan, and H. M. Buck, *J. Amer. Chem. Soc.*, 1977, **99**, 392.