Acid-catalysed Cyclisation of αβ,γδ-Unsaturated *p*-Tolylsulphonylhydrazones to 3,4-Dihydro-2-tolylsulphonyl-1,2-diazepines [1]

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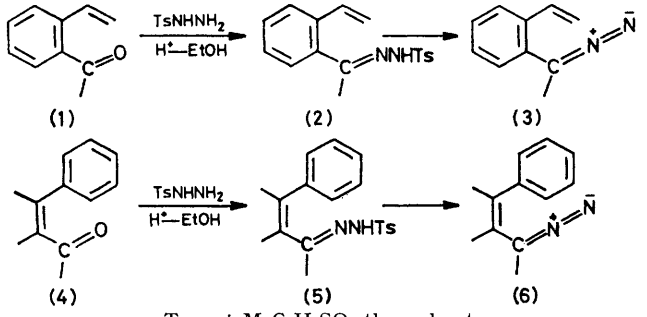
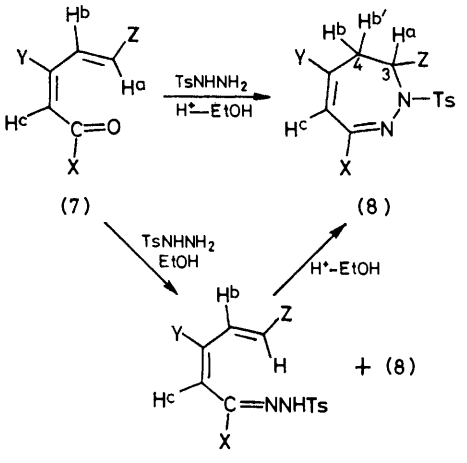
The acid-catalysed reactions of some substituted 2,4-dienones with *p*-tolylsulphonylhydrazine give 3,4-dihydro-2-tosyl-1,2-diazepines (8); other 2,4-dienones give only the *p*-tolylsulphonylhydrazones. The dependence of the mode of reaction on the substituents on the dienone, and the role of the acid in promoting the cyclisation have been investigated.

Our recent syntheses of 3*H*-1,2-benzodiazepines [2] and 1*H*-2,3-benzodiazepines [3] *via* the 8π-electron cyclisations of the αβ,γδ-unsaturated diazo-compounds (3) and (6) have utilised the tosylhydrazones (2) and (5) as the



Ts = *p*-$MeC_6H_4SO_2$ throughout

precursors of the diazo intermediates. These tosylhydrazones were prepared by the usual reaction of the aldehyde or ketone (1) and (4) with *p*-tolylsulphonylhydrazine in ethanol in the presence of hydrochloric or sulphuric acid as catalyst. In an extension of this work

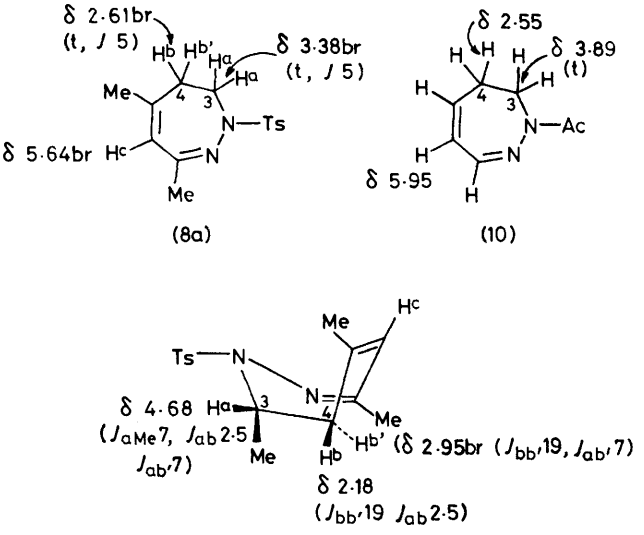


a; X = Y = Me, Z = H
b; X = Y = Z = Me
c; X = Ph, Y = Me, Z = H
d; X = Et, Y = Z = Me

Scheme 1

to the dienones (7) and (14) having only olefinic unsaturation we now report that some of these dienones (7a—d) react under the same conditions to give the 3,4-dihydro-2-tosyl-1,2-diazepines (8) rather than tosylhydrazones. This reaction provides an easy and direct route to these 3,4-dihydro-1,2-diazepines previously only accessible either *via* base induced deacylation of 2,3-dihydro-1*H*-1,2-diazepines [4] or the bromination–dehydrobromination of 2,3,4,5-tetrahydro-1*H*-1,2-diazepines.[5]

The structures of the dihydrodiazepines (8) follow from their analytical and spectroscopic data. Their i.r. spectra lack the N–H stretching band observed in analogous tosylhydrazones and the ^1H n.m.r. spectrum



J values in Hz

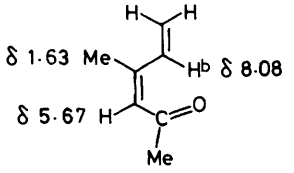
of (8a) shows chemical shifts for the C-3 and C-4 methylene groups similar to those reported for (10).[4] In compounds of this type with no substituent on C-3, *e.g.* (8a) and (8c), the two protons on C-4 have the same chemical shift, absorbing as a broad triplet (*J* 5 Hz). This equivalence suggests that ring flexing is fast on the n.m.r. time scale at room temperature: both this triplet and that due to the C-3 methylene group were much broadened by cooling the sample to −60 °C but a lower temperature study was not possible because of low solubility. In compounds (8b) and (8d) which do have a substituent on C-3, a type not previously prepared, the chemical shifts of the protons on C-4 differ; the geminal coupling constant of 19 Hz and vicinal coupling constants to the C-3 proton are consistent with the conformation (11). In a Dreiding model with minimum angle strain the dihedral angles between H^a and H^b and $H^{b'}$ re-

spectively are *ca.* 45 and 160° but in the molecule some flattening of the boat might be expected which would produce a more completely staggered conformation about the C-3–C-4 bond. The ^{13}C n.m.r. spectra (Table) with assignments based on single-frequency off-resonance decoupling are also consistent with the proposed formulation.

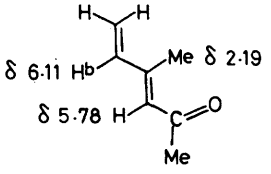
^{13}C N.m.r. data (p.p.m. from Me_4Si; $CDCl_3$ solvent) of 3,4-dihydro-2-tosyl-1,2-diazepines

Compound	
(8a)	C-3, 49.7; C-4, 39.1; C-5, 133.5; C-6, 121.1; C-7, 152.8; aromatic, 152.2 (tert.), 143.8 (tert.), 129.2, and 128.8; CH_3(X), CH_3(Y), and CH_3(Ts), 26.1, 25.8, and 21.6
(8b)	C-3, 52.1; C-4, 45.1; C-5, 135.4; C-6, 121.6; C-7, 153.5; aromatic, 149.6 (tert.), 143.6 (tert), 129.2, and 128.7; CH_3(X), CH_3(Y), CH_3(Z), and CH_3(Ts), 26.7, 25.4, 21.5, and 13.2
(8c)	C-3, 50.3; C-4, 39.0; C-5, 133.6; C-6, 119.2; C-7, 153.9; aromatic, 152.5 (tert.), 144.0 (tert.), 139.5 (tert.), 129.3, 128.2, 128.9, and 127.3; CH_3(Y) and CH_3(Ts), 26.5 and 21.5
(8d)	C-3, 52.0; C-4, 45.0; C-5, 135.1; C-6, 121.1; C-7, 157.5; aromatic, 149.7 (tert.), 143.6 (tert.), 129.2, and 128.8; CH_2Me, 32.4; CH_3(X), CH_3(Y), CH_3(Z), and CH_3(Ts), 26.9, 21.6, 13.0, and 12.0

In the cyclisation (Scheme 1) it is notable that both the *E*- and *Z*-dienones react to give the diazepine. For (7a) the dienone consisted of a *ca.* 2.2 : 1 ratio of the *E*- (13) to *Z*- (12) isomers as shown by the ^1H n.m.r. spectrum



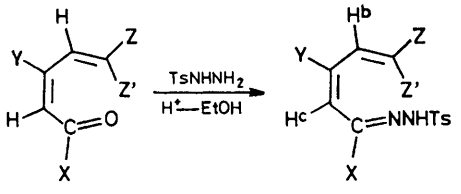
(*Z*)-(7a) (12)



(*E*)-(7a) (13)

of the mixture. The assignments in (12) and (13), and in the spectra of the new dienones, are based on the assumption that H^b will be more deshielded by the carbonyl group in the *Z*-isomer and that the C-4 methyl group will similarly be more deshielded in the *E*-isomer, as reported for related systems.[6,7] The intermediacy of the tosylhydrazones (9) in the cyclisation has been demonstrated in one case: reaction of the dienone (7a) with tosylhydrazine for 18 h in the absence of acid caused conversion mainly into the tosylhydrazone (9a) (mixed *E*- and *Z*-isomers) together with a little (13%) of the diazepine (8a). The tosylhydrazone, dissolved in ethanol, was then rapidly converted into the diazepine by the addition of a little sulphuric acid. Thus there appear to be two mechanisms for diazepine formation: a slow cyclisation of the *Z* tosylhydrazone occurring in the absence of acid, and a fast acid-catalysed reaction in which protonation of the tosylhydrazone allows *E* ⟶ *Z*-conversion before ring closure.

Although the cyclisation is successful for a variety of dienones (7) the reaction has failed to produce diazepines in several cases. Reactions of the dienones (14) with tosylhydrazine under identical acid-catalysed conditions gave only the tosylhydrazones (15) which could not be induced to cyclise although a variety of acid–solvent–temperature combinations were tried. The failure of (15a) and (15b) to cyclise is notable since they differ



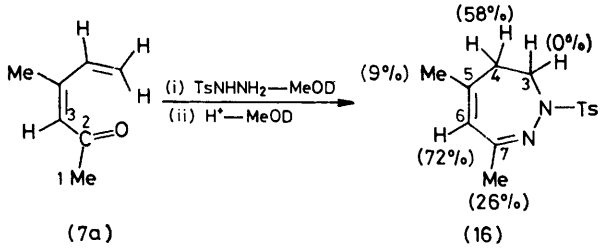
(14) (15)

a; X = Z = Me, Y = H, Z′ = H
b; Y = Z = Me, X = H, Z′ = H
c; X = H, Y = Me, Z = Ph, Z′ = H
d; X = Y = Me, Z = Ph, Z′ = H
e; X = Y = Z′ = Me, Z = Ph

from (9b) only in the absence of methyl groups at C-4 and C-2 respectively. The failure of (15c—e) to cyclise is perhaps less surprising since all have large (phenyl) groups attached to the terminus of the diene, and Michael type additions are known to be sensitive to steric hindrance.

In an attempt to understand better the failure of compounds (15) to cyclise and to clarify the role of the acid catalyst in promoting the cyclisations of (9), the reactions of (7a) with tosylhydrazine in deuteriomethanol were carried out in the presence and absence of acid.

In the acid-catalysed reactions both the direct and indirect routes (Scheme 1) gave products [*e.g.* (16)] with extensive deuteriation at C-4 and C-6, and some deuterium incorporation into the methyl groups at C-5 and C-7. There was no deuteriation at C-3 but the ^1H n.m.r. absorption for this methylene group was changed from the triplet of the all-proton case to a doublet superimposed on a triplet showing that C-4 was predominantly mono- rather than di-deuteriated.

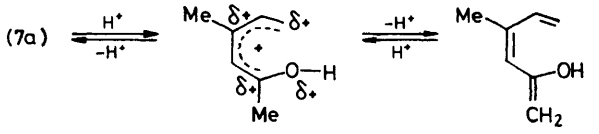


(7a) (16)

% deuterium incorporation into (16)

The degree of deuteriation of these compounds was determined by ^1H n.m.r. spectroscopy assuming no deuteriation of the aromatic ring or the arylmethyl group. A control experiment showed that the product tosyldiazepine (8a) was not deuteriated under the reaction conditions. Another control experiment showed that the ketone (7a) underwent acid-catalysed exchange of its methyl protons (*ca.* 17% deuteriation after 10 min) but not of the C-3 or other vinylic hydrogens. This exchange most likely occurs *via* protonation on oxygen, *e.g.* Scheme 2.[8]

Two possible cyclisation mechanisms which are consistent with the deuteriation study and with the formation of (8) from both the *E*- and *Z*-isomers of (7) are shown in Schemes 3 and 4. The first is the more

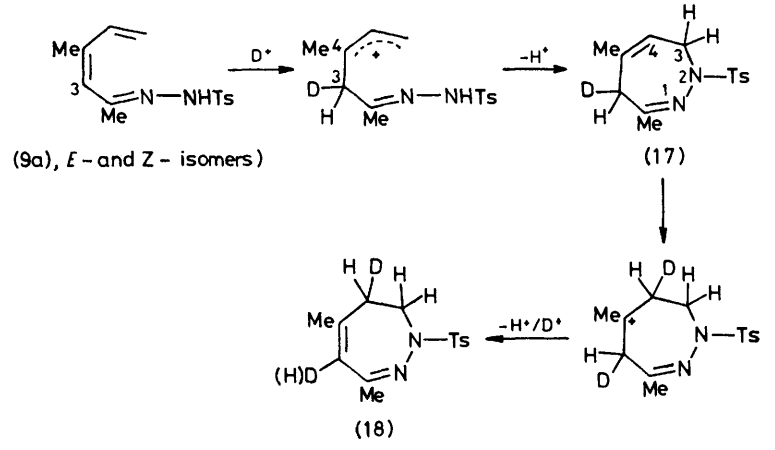


SCHEME 2

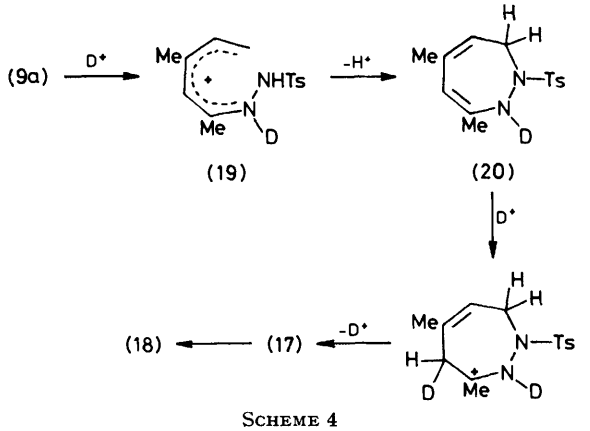
economical and involves primary protonation at C-3 of the tosylhydrazone, allowing rotation about the 3—4 bond, followed by ring closure and loss of the proton on nitrogen to give (17). Further protonation on C-4 of (17) would then allow its isomerisation to the conjugated, and presumably more stable, final product (18). Alternatively, the cyclisation could be initiated by protonation on nitrogen, Scheme 4, to give the extensively delocalised carbonium ion (19) which on cyclisation would give (20). This compound, an ene–hydrazine analogue, would be expected to isomerise to the hydrazone analogue (17) and thence to (18) as in Scheme 3. The results do not allow a conclusive differentiation between these schemes but, since the ketone (7a) is protonated at oxygen rather than at C-3 (Scheme 2), it seems likely that (9a) will similarly be protonated preferentially at nitrogen. That this does occur is supported by the observation that deuterium is incorporated into both the methyl groups, *via* exchange in (19), whereas Scheme 3 would lead to deuteriation only in the 5-methyl group.

The failure of the tosylhydrazones (15a—e) to undergo acid-catalysed cyclisation must obviously be due either to their failure to be protonated under the reaction conditions or, if protonation does occur, to a charge distribution and/or stereochemistry in the delocalised cation which does not facilitate ring closure. In an attempt to differentiate between these possibilities some deuterium exchange experiments under the cyclisation conditions have been carried out on the two crystalline tosylhydrazones (15d) and (15a).

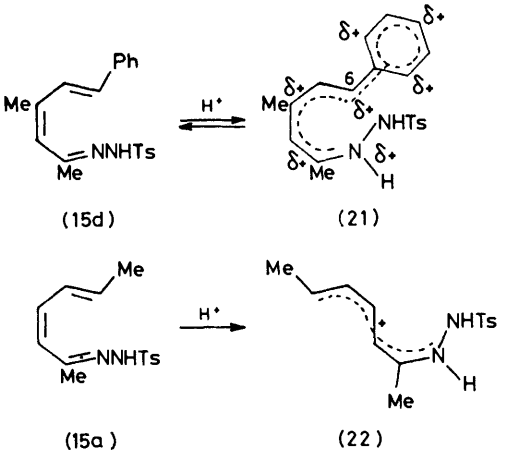
Compound (15d), only sparingly soluble in the acidified deuteriomethanol, was recovered in 77% yield after 18 h and found to be deuteriated in both methyl groups (*ca.* 20%) indicating some protonation at nitrogen, structure (21). The non-cyclisation of (21) may be due either to the conjugating effect of the phenyl group in reducing the positive charge density at C-6 or to steric inhibition of ring closure. Further work on related compounds to clarify this point is in progress.



SCHEME 3



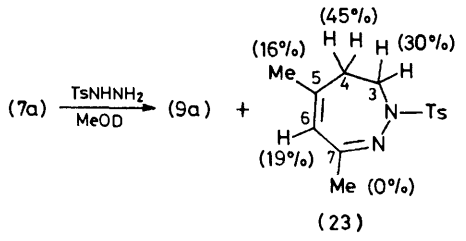
SCHEME 4



The tosylhydrazone (15a) was also sparingly soluble in

acidified deuteriomethanol but was consumed more rapidly, only 37% being recovered after 1 h. In this case the recovered material showed no deuterium incorporation and it seems possible here that protonation gives a species (22) which, since it lacks the methyl group on the β-carbon atom possessed by all the cyclisable ketones (7), has a stereochemistry unfavourable to cyclisation and reacts rapidly by some other pathway, probably polymerisation.

In the slow, non-acid-catalysed cyclisation of (9a) (Scheme 5), the use of deuteriomethanol as solvent did not produce any positive mechanistic information. Then product (23) was extensively deuteriated possibly owing to the operation of several ring closure–ring opening equilibria preceding product formation.



(23)

SCHEME 5 % deuterium incorporation into (23)

The cyclisation in Scheme 1 thus provides a useful addition to the synthetic routes to the 1,2-diazepine system, particularly so since the base-induced elimination of toluene-*p*-sulphinic acid from the products (8) provides the only route yet devised to 3*H*-1,2-diazepines.[1,9] Further extensions of this work to the synthesis of other *N*-substituted 1,2-diazepines by the reactions of a variety of substituted hydrazines with αβ,γδ-unsaturated carbonyl compounds are in progress.

EXPERIMENTAL

^{1}H N.m.r. spectra were obtained with a Varian HA100 spectrometer and ^{13}C n.m.r. spectra with either Varian XL100 or CFT20 spectrometers. Mass spectra were obtained with an A.E.I. MS902 instrument (70 eV) using a direct insertion probe.

Preparations of the αβ,γδ-Unsaturated Aldehydes and Ketones.—The following were prepared by the literature routes indicated and had correct characteristics: 3-methyl-5-phenylpenta-2,4-dienal,[10] hepta-3,5-dien-2-one,[11] 4-methylhexa-3,5-dien-2-one,[12] 4-methylhepta-3,5-dien-2-one,[12] 3-methyl-1-phenylpenta-2,4-dien-1-one,[13] 4-methyl-6-phenylhepta-3,5-dien-2-one.[12]

3-Methylhexa-2,4-dienal. This was prepared by the oxidation of 3-methylhexa-2,4-dien-1-ol (see below) (7.7 g) with active manganese dioxide [14] (24 g) in petroleum–ether for 20 h at room temperature. After filtration and evaporation, the residue was distilled to give 3-methylhexa-2,4-dienal (4.95 g, 66%) as a pale yellow liquid, b.p. 73—78 °C at 12 mmHg (Found: M^+, 110.073 089. $C_7H_{10}O$ requires *m/e*, 110.073 161); ^{1}H n.m.r. ($CDCl_3$) δ 10.14 and 10.07 (overlapping d, *J* 8 Hz, aldehyde H), 7.11br (d, *J* 16 Hz, 0.4 H), 6.0—6.5 (m, 1.6 H), 5.77br and 5.85br (overlapping d, *J* 8 Hz, 1 H), 2.23 (d, *J* 1.5 Hz, 0.6 Me), and 2.04 (d, *J* 1.5 Hz, 0.4 Me), 1.8—2.0 (m, 3 H); i.r. (film) 1 660 and 1 630 cm^{-1} (C=O); *E,E* to *Z,E* ratio 1.5 : 1. The 2,4-dinitrophenylhydrazone derivative had m.p. 197.5 °C (Found: C, 53.6; H, 4.8; N, 19.1. $C_{13}H_{14}N_4O_4$ requires C, 53.8; H, 4.9; N, 19.3%).

3-Methylhexa-2,4-dien-1-ol. Lithium aluminium hydride (3.05 g, 0.084 mol) in dry ether (50 ml) was added slowly to a stirred solution of ethyl 3-methylhexa-2,4-dienoate [15] (10.2 g, 0.066 mol) in dry ether (60 ml), keeping the temperature below 20 °C. The mixture was then treated with wet ether (50 ml) followed by dilute sulphuric acid (1M; 50 ml). The organic layer was washed with dilute sulphuric acid (2 × 40 ml), aqueous potassium hydroxide (3%, 2 × 50 ml), and water (2 × 50 ml), and then dried and evaporated, and the residue was distilled to give the alcohol (5.4 g, 73%), b.p. 82—84 °C at 16 mmHg (lit.,[16] 82 °C at 15 mmHg); i.r. (film) 3 300 cm^{-1} (O–H).

5-Methylocta-4,6-dien-3-one. A Grignard reagent prepared from ethyl bromide (6.23 g, 0.057 mol) and magnesium (1.27 g, 0.052 mol) in ether (40 ml) was cooled to 0 °C and anhydrous cadmium chloride (5.07 g, 0.026 mol) was added in one batch. After rapid mechanical stirring for 30 min, 3-methylhexa-2,4-dienoyl chloride [17] in ether (20 ml) was added slowly. The mixture was boiled under reflux for 3 h and then hydrolysed with aqueous ammonium chloride (10%; 100 ml). The organic layer was washed with water (2 × 50 ml), dried, and evaporated to give a yellow liquid (3.9 g). Short-path distillation gave the product as a yellow oil (2.3 g, 59%), b.p. 77—79 °C at 10 mmHg (Found: M^+, 138.103 697. $C_7H_{14}O$ requires *m/e*, 138.104 459); ^{1}H n.m.r. ($CDCl_3$) δ 7.6br (d, *J* 16 Hz, 0.3 H), 6.1—6.4 (m, 1.7 H), 6.03br (s, 0.7 H), 5.95br (s, 0.3 H), 2.44 and 2.46 (overlapping q, *J* 7.5 Hz, CH_2), 2.23 (d, *J* 1.5 Hz, 0.7 Me), 1.96 (d, *J* 1.5 Hz, 0.3 Me), and 1.06 (t, *J* 7.5 Hz, Me); i.r. (film) 1 680 cm^{-1} (C=O); *E,E* to *Z,E* ratio 2.3 : 1. The 2,4-dinitrophenylhydrazone derivative had m.p. 121—123 °C (Found: C, 56.4; H, 5.8; N, 17.6. $C_{15}H_{18}N_4O_4$ requires C, 56.6; H, 5.7; N, 17.2%).

4-Methyl-6-phenylhexa-3,5-dien-2-one. This was prepared in a similar reaction of 3-methyl-5-phenylpenta-2,4-dienoyl chloride [18,19] (see below) (11.0 g, 0.053 mol) and methyl iodide (15.8 g, 0.111 mol). The ketone was obtained as a yellow oil (5.4 g, 55%), b.p. 101—103 °C at 0.15 mmHg (lit.,[20] 79—85 °C at 0.03 mmHg); i.r. (film) 1 675 cm^{-1} (C=O); ^{1}H n.m.r. ($CDCl_3$) δ 8.4 (d, *J* 16 Hz, 0.4 H), 7.2—7.7 (m, 6.6 H), 7.10br (d, *J* 16 Hz, 1 H), 6.75br (d, *J* 16 Hz, 1 H), 6.32br (s, 0.6 H), 6.15br (s, 0.4 H), 2.40 (d, *J* 1.5 Hz, 0.4 Me), 2.13 (d, *J* 1.5 Hz, 0.6 Me), and 2.29 (s, Me); *E,E* to *Z,E* ratio 1.5 : 1.

3-Methyl-5-phenylpenta-2,4-dienoyl chloride. 3-Methyl-5-phenylpenta-2,4-dienoic acid [18,19] (17.2 g, 0.091 mol) and thionyl chloride (21.5 g, 0.18 mol) in benzene (100 ml) were stirred at room temperature overnight and then boiled under reflux for 1.3 h. The benzene and excess of thionyl chloride were evaporated off under reduced pressure to leave a brown solid (20.0 g) which on crystallisation from petroleum gave yellow crystals (6.3 g, 33%), m.p. 86—87 °C, of the *Z,E*-isomer; ^{1}H n.m.r. ($CDCl_3$) δ 7.3—7.6 (m, 5 H), 7.10 (d, *J* 16 Hz, 1 H), 6.74 (d, *J* 16 Hz, 1 H), 6.17br (s, 1 H), and 2.32 (d, *J* 1.5 Hz, Me). From the mother liquor, a yellow oil was distilled (5.4 g, 29%), b.p. 128—130 °C at 0.09 mmHg (Found: C, 70.0; H, 5.7. $C_{12}H_{10}ClO$ requires C, 69.7; H, 5.3%). This was shown by ^{1}H n.m.r. spectroscopy to consist of the *Z,E*- and the *E,E*-isomers in the ratio 1.4 : 1; by subtraction the ^{1}H n.m.r. spectrum of the *E,E*-isomer was δ 7.3—7.6 (m, 5 H), 7.00 (d, *J* 16 Hz, 1 H),

6.78 (d, *J* 16 Hz, 1 H), 5.93br (s, 1 H), and 2.41 (d, *J* 1.5 Hz, Me).

Reactions of the Unsaturated Aldehydes and Ketones with p-*Tosylhydrazine*.—(a) *To give* 3,4-*dihydro*-2-*tosyl*-1,2-*diazepines*. The general method was to stir equimolar quantities of the dienone and *p*-tosylhydrazine in ethanol containing concentrated hydrochloric or sulphuric acid, under nitrogen, overnight, at room temperature. The tosyldiazepine was then filtered off and recrystallised. The ^{1}H n.m.r. assignments refer to structure (8).

4-*Methylhexa*-3,5-*dien*-2-*one* (7a). (i) The ketone (7a) (2.93 g, 0.026 mol), *p*-tosylhydrazine (4.96 g, 0.026 mol), and hydrochloric acid (1.5 ml) in ethanol (30 ml) gave 3,4-*dihydro*-5,7-*dimethyl*-2-*tosyl*-1,2-*diazepine* (8a) as needles (5.5 g, 75%), m.p. 185 °C (from ethyl acetate) (Found: C, 60.7; H, 6.7; N, 10.0. $C_{14}H_{18}N_2O_2S$ requires C, 60.4; H, 6.5; N, 10.1%); ^{1}H n.m.r. ($CDCl_3$) δ 1.89br [s, Me(Y)], 2.00 [s, Me(X)], 2.41 [s, Me(Ts)], 2.61br (t, *J* 5 Hz, H^b and H$^{b'}$), 3.38 (t, *J* 5 Hz, 2 H^a), 5.64br (s, H^c), and 7.30 and 7.86 (A_2M_2, *J* 8 Hz, 4 × ArH). (ii) In a similar reaction in the absence of hydrochloric acid the yield of the diazepine (8a) was 13%. After the diazepine had been filtered off the solvent was evaporated off leaving 4-methylhexa-3,5-dien-2-one tosylhydrazone (9a) as a yellow oil which could not be induced to crystallise: i.r. (film) 3 200 cm^{-1} (N–H); *M*$^+$, 278; ^{1}H n.m.r. ($CDCl_3$) δ 8.50br (s, NH), 7.7—8.0 (m, 2 H, ArH), 7.1—7.4 (m, 2 H, ArH), 6.28 and 6.31 (d of d, *J* 18, *J'* 10.5 Hz, H^b), 5.09 and 5.27br (d, *J* 18 Hz, =CHZ), 5.09 and 4.89 [d, *J* 10.5 Hz, H(Z)], 5.62br and 5.73br (s, H^c), 2.35br [s, Me(Ts)], and 1.8—2.0 (m, 2 × Me). This tosylhydrazone (0.272 g, 0.98 mmol) was stirred overnight in methanol (3 ml) containing concentrated sulphuric acid (10μl) to give the diazepine (8a) (0.12 g, 44%).

4-*Methylhepta*-3,5-*dien*-2-*one* (7b) (with Mr. R. S. Strathdee). The ketone (7b) (0.56 g, 4.5 mmol), *p*-tosylhydrazine (0.85 g, 4.5 mmol), and hydrochloric acid (0.25 ml) in ethanol (10 ml) gave 3,4-*dihydro*-3,5,7-*trimethyl*-2-*tosyl*-1,2-*diazepine* (8b) as needles (0.87 g, 66%), m.p. 164—166 °C (from ethanol) (Found: C, 61.5; H, 6.9; N, 9.5. $C_{15}H_{20}N_2O_2S$ requires C, 61.6; H, 6.9; N, 9.6%); ^{1}H n.m.r. ($CDCl_3$) δ 0.48 [d, *J* 7 Hz, Me(Z)], 1.87br [s, Me(Y)], 2.06 [s, Me(X)], 2.41 [s, Me(Ts)], 2.18 (d of d, *J* 19, *J'* 2 Hz, H^b), 2.95br (d of d, *J* 19, *J'* 7 Hz, H$^{b'}$), 4.68 (quintet of d, *J* 7, *J'* 2 Hz, H^a), 5.69br (s, H^c), and 7.28 and 7.68 (A_2M_2, *J* 8 Hz, 4 × ArH).

3-*Methyl*-1-*phenylpenta*-2,4-*dien*-1-*one* (7c). The ketone (7c) (5.00 g, 0.029 mol), *p*-tosylhydrazine (5.39 g, 0.029 mol), and sulphuric acid (2.5 ml) in ethanol (50 ml) gave 3,4-*dihydro*-5-*methyl*-7-*phenyl*-2-*tosyl*-1,2-*diazepine* (8c) (5.4 g, 55%), m.p. 169—171 °C (from ethanol) (Found: C, 66.9; H, 5.9; H, 8.3. $C_{19}H_{20}N_2O_2S$ requires C, 67.05; H, 5.9; N, 8.2%); ^{1}H n.m.r. ($CDCl_3$) δ 1.98 [d, *J* 1 Hz, Me(Y)], 2.36 [s, Me(Ts)], 2.70br (t, *J* 5 Hz, H^b and H$^{b'}$), 3.49 (t, *J* 5 Hz, 2 H^a), 6.16 (q, *J* 1 Hz, H^c), 7.1—7.7 (m, 7 H, ArH), and 7.86 (d, *J* 8 Hz, 2 H, ArH).

5-*Methylocta*-4,6-*dien*-3-*one* (7d). The ketone (7d) (0.583 g, 4.22 mmol), *p*-tosylhydrazine (0.786 g, 4.22 mmol), and hydrochloric acid (5 drops) in ethanol (5 ml) gave 7-*ethyl*-3,4-*dihydro*-3,5-*dimethyl*-2-*tosyl*-1,2-*diazepine* (8d) as plates (0.67 g, 52%), m.p. 126 °C (from ethanol) (Found: C, 62.6; H, 7.2; N, 9.1. $C_{16}H_{22}N_2O_2S$ requires C, 62.7; H, 7.2; N, 9.1%); ^{1}H n.m.r. ($CDCl_3$) δ 0.47 [d, *J* 7 Hz, Me(Z)], 1.08 (t, *J* 8 Hz, CH_2*Me*), 2.2—2.5 (m, CH_2Me), 1.88br [s, Me(Y)], 2.40 [s, Me(Ts)], 2.0—2.4 (m, overlapping with CH_2Me, H^b), 2.96br (d of d, *J* 18, *J'* 7 Hz, H$^{b'}$), 4.70 (quintet of d, *J* 7, *J'* 2 Hz, H^a), 5.69br (s, H^c), and 7.26 and 7.87 (A_2M_2, *J* 8 Hz, ArH).

(b) *To give tosylhydrazones*. The following were prepared by stirring equimolar quantities of the dienone and *p*-tosylhydrazine in ethanol, in the dark, under nitrogen, overnight, when completion of the reaction was confirmed by t.l.c. (alumina–benzene). In cases where the tosylhydrazones were crystalline they were filtered off and recrystallised from ethanol. The tosylhydrazones (15b) and (15e) could not be crystallised. All were shown by ^{1}H n.m.r. spectroscopy to be mixtures of *E,E*- and *Z,E*-isomers. The n.m.r. assignments refer to structure (15).

3-Methyl-5-phenylpenta-2,4-dienal tosylhydrazone (15c) (71%) had m.p. 148—149 °C (Found: C, 66.8; H, 5.9; N, 8.2. $C_{19}H_{20}N_2O_2S$ requires C, 67.05; H, 5.9; N, 8.2%); i.r. (Nujol) 3 170 cm^{-1} (N–H); ^{1}H n.m.r. ($CDCl_3$) δ 8.45br (s, NH), 7.1—7.5 (m, 7 H, ArH), 7.7—8.0 (m, 2 H, ArH), 6.82 and 6.63 [AB, *J* 16 Hz, H(Z') and H^b], 6.26br and 6.16br (s, H^c), 2.38 [s, Me(Ts)], and 1.96 and 2.04 [s, Me(Y)].

4-Methyl-6-phenylhexa-3,5-dien-2-one tosylhydrazone (15d) (70%) had m.p. 136—137.5 °C (Found: C, 67.5; H, 6.3; N, 7.95. $C_{20}H_{22}N_2O_2S$ requires C, 67.8; H, 6.3; N, 7.9%); i.r. (Nujol) 3 180 cm^{-1} (N–H); ^{1}H n.m.r. ($CDCl_3$) δ 8.18br (s, NH), 7.1—7.5 (m, 7 H, ArH), 7.7—8.0 (m, 2 H, ArH), 6.60 and 6.79 [AB, *J* 16 Hz, H^b and H(Z')], 5.87br and 5.71br (s, H^c), 2.38 [s, Me(Ts)], 2.01br [s, Me(Y)], and 1.90 and 1.77 [s, Me(X)].

Hepta-3,5-dien-2-one tosylhydrazone (15a) (74%) had m.p. 147—149 °C (Found: C, 60.3; H, 6.6; N, 9.9. $C_{14}H_{18}N_2O_2S$ requires C, 60.4; N, 6.5; N, 10.1%); ^{1}H n.m.r. ($CDCl_3$) δ 8.29br (s, N–H), 7.27 and 7.85 (A_2M_2, *J* 8 Hz, ArH), 5.7—6.6 (m, 4 H, olefinic), 2.38 [s, Me(Ts)], 1.86 and 1.99 [s, Me(X)], and 1.77 [d, *J* 6 Hz, Me(Z)].

3-Methylhexa-2,4-dienal tosylhydrazone (15b) was obtained as a red oil which did not crystallise (Found: *M*$^+$, 278.108 888. $C_{14}H_{18}N_2O_2S$ requires *m/e* 278.108 892); i.r. (film) 3 200br cm^{-1} (N–H).

4-Methyl-6-phenylhepta-3,5-dien-2-one tosylhydrazone (15e) was obtained as a red oil; mass spectrum *M*$^{+\cdot}$ 368; i.r. (film) 3 200br cm^{-1} (N–H).

These tosylhydrazones could not be cyclised to 3,4-dihydro-2-tosyl-1,2-diazepines by treatment with hydrochloric acid, acetic acid, boron trifluoride, or silver ion in a variety of solvents at room temperature nor with toluene-*p*-sulphonic acid in benzene at reflux temperature. Reactions of these carbonyl compounds with tosylhydrazine in the presence of hydrochloric or sulphuric acid catalysts also gave only the tosylhydrazones.

Reactions of 4-*Methylhexa*-3,5-*dien*-2-*one* (7a) *with* p-*Tosylhydrazine in Deuteriomethanol* (CH_3OD). (i) *Indirect route*. A mixture of the ketone (7a) (0.50 g, 4.55 mmol) and *p*-tosylhydrazine (0.846 g, 4.55 mmol) in deuteriomethanol (5 ml) was stirred in the dark at room temperature under nitrogen overnight. The precipitated diazepine (8a) (0.082 g) was then filtered off, washed with deuteriomethanol, and dried *in vacuo*. Its ^{1}H n.m.r. spectrum showed deuterium incorporation as shown in structure (23); a repeat experiment gave C-3 (26%), C-4 (46%), C-6 (25%), 5-Me (16%), and 7-Me (0%). To the filtrate, containing the tosylhydrazone of (7a), was added sulphuric acid (25 μl) and the mixture was stirred in the dark under nitrogen at room temperature for 2 h. The precipitated diazepine (8a) (0.325 g) was filtered off, washed with deuteriomethanol, and dried *in vacuo*. Its ^{1}H n.m.r. spectrum showed deuterium incorporation as shown in structure (16); two

repeat experiments gave C-4 (57, 42%), C-6 (62, 60%), 5-Me (11, 5%), and 7-Me (22, 17%).

(ii) *Direct route.* A mixture of the ketone (0.50 g, 4.55 mmol), *p*-tosylhydrazine (0.846 g, 4.55 mmol), and sulphuric acid (25 μl) in deuteriomethanol (5 ml) was stirred in the dark at room temperature under nitrogen for 2 h. The precipitated diazepine (8a) (0.481 g) was filtered off, washed with deuteriomethanol, and dried under high vacuum. Its ^{1}H n.m.r. spectrum showed deuterium incorporation at C-4 (38%), C-6 (64%), 5-Me (11%), and 7-Me (15%); a repeat experiment gave C-4 (36%), C-6 (76%), 5-Me (8%), and 7-Me (18%).

Control experiments. (i) A slurry of the diazepine (8a) (108 mg), sulphuric acid (2.5 μl), and deuteriomethanol (0.5 ml) was stirred at room temperature in the dark under nitrogen for 24 h. The usual work-up gave the diazepine (92 mg) whose ^{1}H n.m.r. spectrum showed no deuterium incorporation. (ii) The ^{1}H n.m.r. spectrum was obtained of a solution of the ketone (7a) (50 mg) in deuteriomethanol (CD_3OD) (0.4 ml) containing cyclohexane (5 μl) as an internal standard. Sulphuric acid (2 μl) was added and the n.m.r. spectrum was recorded again after 10 min, and after 24 h. After 10 min the absorptions of the vinyl protons were not affected but those of the methyl groups had diminished by *ca.* 17%. After 24 h all the absorptions had diminished relative to that of the internal standard, probably owing to acid-catalysed polymerisation.

In a similar experiment a mixture of the ketone (7a) (250 mg), deuteriomethanol (2 ml), and sulphuric acid (10 μl) was kept for 18 h at room temperature. After work-up by distillation at 10 mmHg the ketone (35 mg) was recovered, the residue being polymeric. The ^{1}H n.m.r. spectrum of the product showed *ca.* 25% deuteriation of the methyl groups.

A slurry of the tosylhydrazone (15d) of 4-methyl-6-phenylhexa-3,5-dien-2-one (0.138 g), sulphuric acid (2.5 μl), and deuteriomethanol (0.5 ml) was stirred at room temperature for 18 h. The usual work-up gave the tosylhydrazone (0.10 g) whose ^{1}H n.m.r. spectrum showed *ca.* 20% deuteriation of the 1- and 3-methyl groups.

A slurry of the tosylhydrazone (15a) of hepta-3,5-dien-2-one (0.216 g), sulphuric acid (5μl), and deuteriomethanol (1 ml) was stirred at room temperature for 1 h. The usual work-up gave the tosylhydrazone (0.081 g) whose ^{1}H n.m.r. spectrum showed no deuterium incorporation. In a similar reaction of duration 18 h all the tosylhydrazone had dissolved and no pure product could be obtained.

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