The Acylation of 5*H*-2,3-Benzodiazepines and 4*H*-Thieno[2,3-*d*]- and 8*H*-Thieno-[3,2-*d*]-[1,2]diazepines. Reactions with Acid Anhydrides and Nucleophiles to give Fused 7-Substituted 1-Acyl-1,2-diazepines

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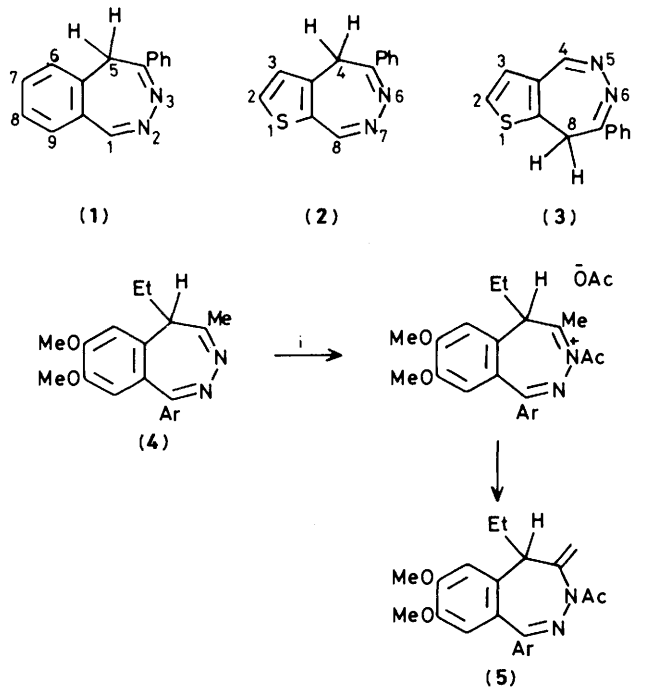
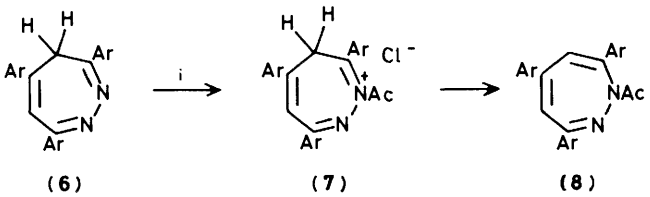
The acylation of 4-phenyl-5*H*-2,3-benzodiazepine (**1**) and its thieno analogues (**2**) and (**3**) with acetic anhydride takes a different course from other 2,3-benzodiazepines having a hydrogen atom or a methyl group at position 4. The latter react at N-3 to give the 3-acyl derivatives (**11**) but 4-phenyl-2,3-benzodiazepine is acylated at N-2 to give the iminium acetate (**12**) which reacts with alcohols and thiols to give the derivatives (**15**) in high yield. The reaction of (**12**) with hydrogen chloride induces rearrangement to an isoquinoline *N*-imide (**18**).

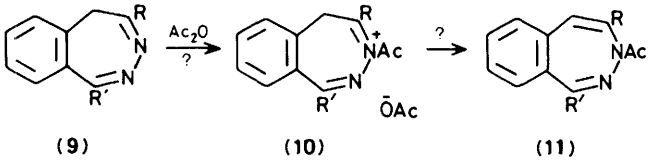
Recent developments in the synthesis of fully unsaturated 1,2-diazepines have made a range of 5*H*-2,3-benzodiazepines accessible for study.[1-7] This paper is concerned with the acylation reactions of the 4-phenyl derivative (**1**) and its thieno analogues (**2**) and (**3**). At the start of this work the only report on the acylation of this ring system was that concerned with the tranquilliser Grandaxin (**4**).[8] This molecule reacts with both acid anhydrides and acyl halides *via* acylation at N-3 and subsequent loss of a proton from the 4-methyl group to give the methylene derivative (**5**) (Scheme 1). This contrasts with the acylation of the analogous monocylic system (**6**) (Scheme 2) in which a similar intermediate (**7**) reacts *via* loss of a ring proton to give the fully unsaturated derivative (**8**).[9] We were interested in preparing the analogous, but then unknown, 3-acyl-3*H*-2,3-benzodiazepine system (**11**) in connection with another project[10] and thought it likely that if the 4-position in (**9**) were substituted with a group (R) not carrying hydrogen atoms on the α-carbon, so blocking the pathway in Scheme 1, then acylation would lead to (**11**) *via* a route similar to that in Scheme 2. Subsequent work carried out elsewhere,[7] discussed later, has shown that this is so in some cases. However, in our initial work on the reactions of diazepines carrying a phenyl group at position 4, *e.g.* (**1**), compounds of type (**11**) were obtained in only one instance. It was found that the course of the reaction depended strongly on the nature of the acylating reagent and on the reaction conditions. This paper deals with the reactions with acid anhydrides which are straightforward; the reactions with acyl halides, which are more complex, will be described in a later paper.[11]



Scheme 1*. Ar = 3,4-dimethoxyphenyl. *Reagents:* i, Ac_2O



Scheme 2. *Reagents:* i, AcCl

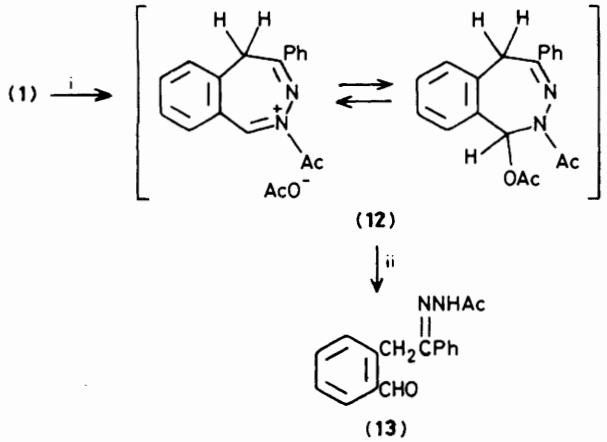


Results and Discussion

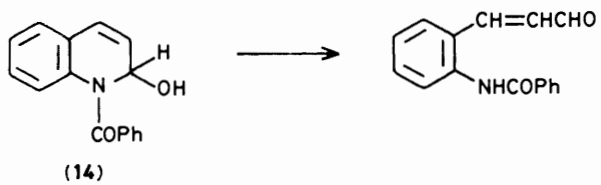
The benzodiazepine (**1**) reacted rapidly with acetic anhydride at room temperature in either pyridine or benzene as solvent to give an unstable compound formulated as (**12**). This compound could not be isolated but on reaction with water gave phenyl 2-formylbenzyl ketone acetylhydrazone (**13**) (Scheme 3). This product was identified from its analytical and spectroscopic properties and from the similarity of this reaction to the known cleavage of the 'pseudobase' (**14**).[12,13]

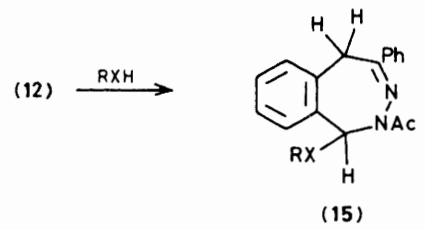
Reaction of the intermediate (**12**) with alcohols, phenol, ethanethiol, and thiophenol gave the benzodiazepine derivatives (**15**) derived by nucleophilic attack at the 1-position. They were all produced in good yields (62—92%) and were stable enough for isolation by chromatography and/or distillation. Similar results were obtained using propionic anhydride, but compound (**1**) did not react with benzoic anhydride even in refluxing benzene. The structures of the products (**15**) follow from their n.m.r. spectra, exemplifed for (**1a**) in structure (**16**).

* *Note*: The numbering of compounds (**2**) and (**3**) differs from that given in ref. 2. This earlier numbering was not compatible with the IUPAC rules of nomenclature.



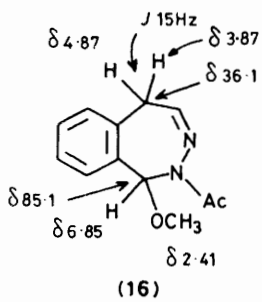
Scheme 3. *Reagents:* i, Ac_2O; ii, H_2O

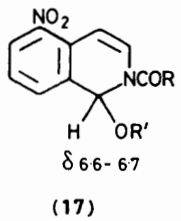


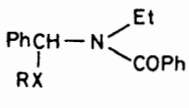


	RX	Yield (%)
(15) a;	MeO	88
b;	EtO	81
c;	PhO	92
d;	EtS	62
e;	PhS	64

The strong deshielding of the C-1 proton is similar to that observed for the analogous proton in 1-alkoxy-2-benzoylisoquinolines[14] (**17**) and the model compounds (**18a**) and (**18b**).



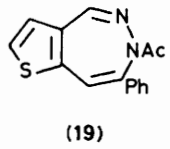


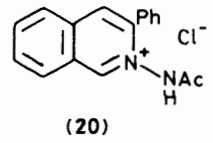


(18)

a; RX = MeO

b; RX = PhS





The latter were prepared from *N*-benzylidene-*N*-ethylamine by the method of Böhme and Hartke.[15] The ^1H n.m.r. spectra of both varied with temperature owing to restricted rotation about the C(O)–N bond, and for (**18a**) the methine proton gave two sharp peaks (δ 5.79 and 6.99 in the ratio 2.4:1) at −24 °C while the analogous proton in (**18b**) was more deshielded giving peaks at δ 6.28 and 7.75 at −31 °C. This parallels the greater deshielding of the C-1 proton in (**15d**) and (**15e**) than (**15a—c**).

The reactions of alcohols and thiols with simple *N*-acyliminium salts[15] and with those derived, for example, from isoquinoline[14] are well known, but as far as we are aware the formation of (**15**) is the first application of this type of reaction to the carbon–nitrogen double bond of an azine.[16] The reaction of (**12**) with some other nucleophiles was not productive; diethylamine reacted by deacylation and regeneration of the original diazepine, lithium diethylamide gave a complex mixture, and the sodium salt of malonic ester again regenerated the diazepine.

The thienodiazepines (**2**) and (**3**) having a substitution pattern identical with that of (**1**) showed similar reactions when acylated with acetic anhydride in benzene and quenched with ethanol. However, compound (**3**), when acetylated in pyridine and quenched with water, gave (**19**) (37%), the only 3-acyl derivative obtained in this work. It is clear from these results that in compounds (**1**) and (**2**), the diazepine N-2 is more nucleophilic than the N-3. Both imine moieties have aromatic conjugation but apparently the nucleophilic character of the diazepine N-3 is reduced by the steric hindrance of the 4-phenyl group in (**1**) and the 2-phenyl in (**2**). After completion of this work it was reported[7] that the acylation of the 2,3-benzodiazepines (**9**; R = H or Me), which have either a hydrogen atom or a methyl group at C-4, takes place at N-3 and follows a path similar to that in Scheme 2 to give the 3-acyl derivatives (**11**).

Treatment of the intermediate (**12**) with dry hydrogen chloride induced a rapid rearrangement to give the isoquinoline *N*-acetylimine hydrochloride (**20**), a reaction path which parallels one of those observed in the reactions of compound (**1**) with acyl halides; this will be discussed in a later paper.[11]

Experimental

N.m.r. spectra were obtained on Varian HA 100 (^1H) (100 MHz) and CFT20 (^{13}C) (20 MHz) instruments. Chemical shifts are reported as δ values. Mass spectra were obtained using an AEI MS902 instrument with electron ionisation at 70 eV. Chromatographic separations were carried out by the medium pressure technique[17] using either 1 000 × 15 or 1 000 × 25 mm columns packed with Merck Kieselgel 60.

Pyridine was dried, distilled, and stored over potassium hydroxide pellets; all alcohols and thiols were either AnalaR grade or were dried and distilled before use. Light petroleum refers to the fraction with b.p. 40—60 °C and ether refers to diethyl ether. All reactions were carried out under dry nitrogen.

4-Phenyl-5*H*-2,3-benzodiazepine (**1**), 2-phenyl-1*H*-thieno[2,3-*d*][1,2]diazepine (**2**), and 4-phenyl-5*H*-thieno[3,2-*d*][1,2]diazepine (**3**) were prepared as described previously.[2]

N-Ethyl-N-(α-methoxybenzyl)benzamide (**18a**).—Benzoyl chloride (10.7 g, 0.076 mol) in ether (30 ml) was added dropwise with stirring to a solution of *N*-benzylidene-*N*-ethylamine[18]

(10.0 g) in ether (25 ml). The reaction mixture was stirred for 2 h at room temperature, cooled to 0 °C, and a solution of triethylamine (10.0 g, 0.099 mol) in ether (20 ml) was added, followed by a solution of methanol (10 ml, 0.25 mol) in ether (10 ml). The triethylamine hydrochloride was filtered off, the filtrate was evaporated, and the residue distilled to give a clear oil which solidified and was crystallised to give N-*ethyl*-N-(α-*methoxybenzyl*)*benzamide* (15.1 g, 75%), m.p. 76—77 °C (from light petroleum, b.p. 60—80 °C) (Found: C, 75.8; H, 7.1; N, 5.1. $C_{17}H_{19}NO_2$ requires C, 75.8; H, 7.1; N, 5.2%); δ_H (100 MHz; −24 °C) 1.14 (3 H, t, *J* 7 Hz, CH_2CH_3), 2.95—3.63 (2 H, m, CH_2CH_3), 3.29 and 3.57 (3 H, 2 s in ratio 2.4:1, OMe), 5.79 and 6.99 (1 H, 2 s in ratio 2.4:1, NCH), and 7.2—7.7 (10 H, m, aromatic); $\nu_{max.}$(Nujol) 1 640 cm^{-1} (C=O).

N-*Ethyl*-N-(α-*phenylthiobenzyl*)*benzamide* (**18b**).—A similar reaction quenched with a solution of thiophenol (15 ml, 0.127 mol) in ether (15 ml) gave N-*ethyl*-N-(α-*phenylthiobenzyl*)-*benzamide* (20.2 g, 78%), b.p. 190 °C at 0.25 mmHg (Found: C, 76.2; H, 6.1; N, 4.2. $C_{22}H_{21}NOS$ requires C, 76.1; H, 6.1; N, 4.0%); δ_H (100 MHz; −31 °C) 1.12 (3 H, br t, *J* 7 Hz, CH_2CH_3), 3.12 and 3.73 (2 H, 2 m in ratio 1:3, CH_2CH_3), 6.28 and 7.75 (1 H, 2 s in ratio *ca.* 3:1, CHN), and 6.6—7.7 (15 H, m, aromatic); $\nu_{max.}$(film) 1 640 cm^{-1} (C=O).

Acylation Reactions

(1) 4-*Phenyl*-5H-2,3-*benzodiazepine* (**1**).—The acylation step in the reactions below was carried out using the general method described in (i); reactions (i)—(iii) utilised pyridine as solvent while (iv)—(viii) were carried out in benzene.

(i) *Acetic anhydride–water.* The anhydride (0.6 ml, 6.3 mmol) was added with stirring to a solution of the diazepine (0.22 g, 1.0 mmol) in pyridine (3 ml) at room temperature. The mixture was stirred at room temperature for 26 h and then poured into ice–water (25 ml), extracted with ether, washed with water, dried, and evaporated under reduced pressure to give a brown oil. Chromatography (silica, 60 vol % ether in petroleum) gave *phenyl 2-formylbenzyl ketone acetylhydrazone* (**13**) (0.118 g, 42%), m.p. 150—152 °C (from propan-2-ol) (Found: C, 72.9; H, 5.8; N, 9.9. $C_{17}H_{16}N_2O_2$ requires C, 72.8; H, 5.8; N, 10.0%); $\nu_{max.}$(Nujol) 1 695 (C=O amide) and 1 660 cm^{-1} (C=O); δ_H 100 MHz) 2.38 (3 H, s, CH_3), 4.56 (2 H, s, CH_2), 6.95—8.06 (9 H, m, aromatic), 9.25 (1 H, br s, NH), and 10.35 (1 H, s, CHO); δ_C (20 MHz) 20.5 (CH_3), 29.9 (CH_2), 126.2, 127.6, 128.5, 129.4, 133.5 (tert.), 134.2, 135.6 (tert.), 135.9, 137.4 (tert.), 147.5 (tert.), 173.6 (C=N), and 193.9 p.p.m. (C=O).

(ii) *Acetic anhydride–methanol.* After addition of the anhydride the mixture was stirred for 10 min and methanol (AnalaR grade; 25 ml) was added. The solvent was removed by evaporation under high vacuum to leave a green oil which was chromatographed (silica, 80 vol % ether in petroleum) to give 2-*acetyl*-1-*methoxy*-2,5-*dihydro*-4-*phenyl*-1H-2,3-*benzodiazepine* (**15a**) (0.26 g, 88%) as an oil, b.p. 140 °C at 0.15 mmHg (Found: C, 73.3; H, 6.2; N, 9.3. $C_{18}H_{18}N_2O_2$ requires C, 73.45; H, 6.2; N, 9.5%); $\nu_{max.}$(film) 1 680 cm^{-1} (C=O); δ_H (100 MHz) 3.40 (3 H, s, $COCH_3$), 2.41 (3 H, s, OCH_3), 3.87 (1 H, d, *J* 15 Hz, 5-H), 4.87 (1 H, d, *J* 15 Hz, 5-H), 6.85 (1 H, s, 1-H), 7.00—7.50 (7 H, m, aromatic), and 7.71 (2 H, m, aromatic). A similar experiment quenched with monodeuteriomethanol gave the same product (83%) with no incorporation of deuterium. (^{13}C N.m.r. data are in the Table.)

(iii) *Acetic anhydride–ethanol.* A reaction similar to (ii) gave 2-*acetyl*-1-*ethoxy*-2,5-*dihydro*-4-*phenyl*-1H-2,3-*benzodiazepine* (**15b**) (0.25 g, 81%), as an oil, b.p. 150 °C at 0.2 mmHg (Found: C, 73.8; H, 6.6; N, 9.3. $C_{19}H_{20}N_2O_2$ requires C, 74.0; H, 6.5; N, 9.1%); $\nu_{max.}$(film) 1 670 cm^{-1} (C=O); δ_H (100 MHz) 1.21 (3 H, t, *J* 7 Hz, CH_3), 2.42 (3 H, s, CH_3CO), 3.62 (2 H, q, *J* 7 Hz, CH_2), 3.85 (1 H, d, *J* 15 Hz, 5-H), 4.95 (1 H, d, *J* 15 Hz, 5-H), 6.90 (1 H, s, 1-H), 7.00—7.50 (7 H, m, aromatic), and 7.72 (2 H, m, aromatic). (^{13}C N.m.r. data are in the Table.)

Table. ^{13}C N.m.r. data of the 1-substituted- 2-acetyl-2,5-dihydro-4-phenyl-1*H*-2,3-benzodiazepines (**15**)

Compound	δ_C/p.p.m.
(**15a**)	22.4 (Me), 36.1 (C-5), 55.6 (OMe), 85.1 (C-1), 126.3, 127.1, 128.2, 128.6, 128.8, 129.4, 134.0 (tert.), 134.9 (tert.), 140.1 (tert.), 147.8 (C=N), 174.5 (C=O)
(**15b**)	14.8 (CH_3CH_2), 22.4 (Me), 36.2 (C-5), 63.3 (CH_3CH_2), 83.5 (C-1), 126.3, 127.0, 127.8, 128.1, 128.6, 129.2, 134.3 (tert.), 134.8 (tert.), 140.2 (tert.), 147.3 (C=N), 174.3 (C=O)
(**15c**)	22.3 (Me), 36.7 (C-5), 82.9 (C-1), 117.5, 122.7, 126.4, 127.2, 128.1, 128.3, 129.0, 129.5, 129.7, 133.6 (tert.), 134.9 (tert.), 140.1 (tert.), 155.6 (tert.), 148.1 (C=N), 173.6 (C=O)
(**15d**)	14.4 (CH_3CH_2), 22.3 (Me), 26.1 (CH_3CH_2), 37.7 (C-5), 60.1 (C-1), 126.4, 127.4, 128.0, 128.2, 128.8, 129.1, 134.3 (tert.), 135.3 (tert.), 139.8 (tert.), 149.5 (C=N), 173.3 (C=O)
(**15e**)	21.8 (Me), 37.6 (C-5), 64.7 (C-1), 126.5, 127.3, 128.3, 128.7, 129.0, 129.3, 129.5, 135.1, 132.0 (tert.), 134.0 (tert.), 134.5 (tert.), 139.3 (tert.), 153.1 (C=N), 172.9 (C=O)

(iv) *Acetic anhydride–phenol.* After addition of the anhydride the mixture was stirred for 1 h, a solution of phenol (0.60 g, 6.4 mmol) in benzene (3 ml) was added, and the mixture stirred for a further 20 min. Benzene (25 ml) was added and the solution was washed with sodium hydrogen carbonate solution (20% w/v; 2 × 50 ml) and water (50 ml) and dried. Evaporation and chromatography of the residue (silica, 50 vol % ether in light petroleum) gave phenol and 2-*acetyl*-2,5-*dihydro*-1-*phenoxy*-4-*phenyl*-1H-2,3-*benzodiazepine* (**15c**) (0.33 g, 92%), m.p. 115.5—116.5 °C (from ethanol) (Found: C, 77.3; H, 5.6; N, 7.8. $C_{23}H_{20}N_2O_2$ requires C, 77.5; H, 5.7; N, 7.9%); $\nu_{max.}$(Nujol) 1 670 cm^{-1} (C=O); δ_H (100 MHz) 2.12 (3 H, s, CH_3), 4.02 (1 H, d, *J* 15 Hz, 5-H), 5.15 (1 H, d, *J* 15 Hz, 5-H), 6.85—7.50 (13 H, m, aromatic), 7.64 (1 H, s, 1-H), and 7.70 (2 H, m, aromatic). (^{13}C N.m.r. data are in the Table.)

(v) *Acetic anhydride–ethanethiol.* A reaction similar to (ii) but using the diazepine (0.44 g, 2.0 mmol), acetic anhydride (0.4 ml, 4.2 mmol), and after stirring for 1 h, ethanethiol (5 ml), gave after chromatography (silica, 80 vol % ether in light petroleum) (a) 2-*acetyl*-1-*ethylthio*-2,5-*dihydro*-4-*phenyl*-1H-2,3-*benzodiazepine* (**15d**) (0.40 g, 62%), as a yellow oil, b.p. 190 °C at 0.4 mmHg (Found: C, 70.6; H, 6.2; N, 8.8. $C_{19}H_{20}N_2OS$ requires C, 70.35; H, 6.2; N, 8.6%); $\nu_{max.}$(film) 1 675 cm^{-1} (C=O); δ_H (100 MHz) 1.35 (3 H, t, *J* 7 Hz, CH_3CH_2), 2.45 (3 H, s, CH_3), 2.55 (2 H, q, *J* 7 Hz, CH_3CH_2), 4.02 (1 H, d, *J* 17 Hz, 5-H), 5.03 (1 H, d, *J* 17 Hz, 5-H), 7.05—7.60 (8 H, m, aromatic and 1-H), and 7.72 (2 H, m, aromatic) (^{13}C n.m.r. data in Table); and (b) phenyl 2-formylbenzyl ketone acetylhydrazone (0.17 g, 30%), m.p. 150—152 °C (from ethanol), identical with that prepared in (i) above.

(vi) *Acetic anhydride–thiophenol.* A reaction similar to (v) but using thiophenol (2 ml) was worked up by evaporation of the solvent under reduced pressure, distillation at 0.4 mmHg to remove thiophenol, and chromatography (silica, 50 vol % ether in light petroleum) to give 2-*acetyl*-2,5-*dihydro*-4-*phenyl*-1-*phenylthio*-1H-2,3-*benzodiazepine* (**15e**) (0.55 g, 74%), as an oil, b.p. 150 °C at 0.15 mmHg (Found: C, 74.0; H, 5.4; N, 7.5. $C_{23}H_{20}N_2OS$ requires C, 74.2; H, 5.4; N, 7.5%); $\nu_{max.}$(film) 1 685 cm^{-1} (C=O); δ_H (100 MHz) 2.12 (3 H, s, CH_3), 4.09 (1 H, d, *J* 14 Hz, 5-H), 4.99 (1 H, d, *J* 14 Hz, 5-H), 7.00—7.60 (12 H, m, aromatic), 7.48 (1 H, s, 1-H), and 7.76 (2 H, m, aromatic). (^{13}C N.m.r. data are given in the Table.)

(vii) *Acetic anhydride–hydrogen chloride.* A reaction similar to (ii) using the diazepine (0.05 g, 0.23 mmol) and acetic anhydride (0.1 ml, 1.0 mmol) was quenched by adding a solution of hydrogen chloride in benzene (0.29M; 1 ml). After the mixture had been stirred for 10 min at room temperature, the white precipitate was filtered off and crystallised from ethanol to give 2-acetylimino-3-phenylisoquinolinium hydrochloride (**20**) (0.04 g, 60%), m.p. 249—252 °C (lit.,[11] 252—254 °C), with i.r. and n.m.r. spectra identical with those reported.

(viii) *Propionic anhydride–methanol.* A solution containing the diazepine (0.22 g, 1.0 mmol) and propionic anhydride (0.25 ml, 2.0 mmol) was stirred at room temperature for 30 min, and methanol (5 ml) was added. Evaporation of the solvent and distillation of the residue gave 2,5-*dihydro*-1-*methoxy*-4-*phenyl*-2-*propionyl*-1H-2,3-*benzodiazepine* (0.2 g, 62%) as an oil, b.p. 140 °C at 0.15 mmHg (Found: C, 73.9; H, 6.6; N, 9.1. $C_{19}H_{20}N_2O_2$ requires C, 74.0; H, 6.5; N, 9.1%); $\nu_{max.}$(Nujol) 1 675 cm^{-1} (C=O); δ_H (100 MHz) 1.20 (3 H, t, *J* 7 Hz, CH_2CH_3), 2.86 (2 H, m, CH_2CH_3), 3.40 (3 H, s, OCH_3), 3.86 (1 H, d, *J* 15 Hz, 5-H), 4.88 (1 H, d, *J* 15 Hz, 5-H), 6.84 (1 H, s, 1-H), 7.06—7.56 (7 H, m, aromatic), and 7.71 (2 H, m, aromatic).

(2) 5-*Phenyl*-4H-*thieno*[2,3-d][1,2]*diazepine* (**2**).—(i) *Acetic anhydride–water.* Acetic anhydride (0.6 ml, 6.3 mmol) was added with stirring to a solution of the diazepine (0.23 g, 1.0 mmol) in pyridine (3 ml). The solution was immediately poured into ice–water (25 ml) and the product extracted with ether (3 × 25 ml). The ether solution was washed, dried, and evaporated to give a brown oil. Chromatography (silica, 85 vol % ether in light petroleum) gave *phenyl* 2-*formyl*-3-*thienylmethyl ketone acetylhydrazone* (0.205 g, 72%), m.p. 154—155 °C (from ethanol) (Found: C, 62.8; H, 4.9; N, 9.8. $C_{15}H_{14}N_2O_2S$ requires C, 62.9; H, 4.9; N, 9.8%); $\nu_{max.}$(Nujol) 1 695 (C=O amide), 1 660 cm^{-1} (C=O); δ_H (100 MHz) 2.35 (3 H, s, CH_3), 4.50 (2 H, s, CH_2), 6.72—7.90 (7 H, m, aromatic), 9.74 (1 H, br s, NH), and 10.10 (1 H, s, CHO); δ_C (20 MHz) 20.5 (CH_3), 26.7 (CH_2), 126.3, 128.6, 129.5, 130.3, 135.1 (tert.), 137.0 (tert.), 141.5 (tert.), 146.1 (tert.), 173.8 (C=N), and 183.0 p.p.m. (C=O).

(ii) *Acetic anhydride–ethanol.* A similar reaction using benzene as solvent was quenched with ethanol (25 ml). Evaporation of the solvent and chromatography (silica, 50 vol % ether in petroleum) gave 7-*acetyl*-8-*ethoxy*-5,8-*dihydro*-5-*phenyl*-4H-*thieno*[2,3-d][1,2]*diazepine* (0.16 g, 51%), m.p. 119—120 °C (from ethanol) (Found: C, 65.1; H, 5.6; N, 8.9. $C_{17}H_{18}N_2O_2S$ requires C, 65.0; H, 5.8; N, 8.9%); $\nu_{max.}$(Nujol) 1 665 cm^{-1} (C=O); δ_H (100 MHz) 12.3 (3 H, t, *J* 7 Hz, CH_2CH_3), 2.28 (3 H, s, CH_3), 3.68 (2 H, q, *J* 7 Hz, CH_2CH_3), 3.95 (1 H, d, *J* 15 Hz, 4-H), 4.21 (1 H, d, *J* 15 Hz, 4-H), 6.76 (1 H, d, *J* 5 Hz, 3-H), 7.18 (1 H, d, *J* 5 Hz, 2-H), 7.23 (1 H, s, 8-H), 7.29—7.48 (3 H, m, aromatic), and 7.75 (2 H, m, aromatic).

(3) 7-*Phenyl*-8H-*thieno*[3,2-d][1,2]*diazepine* (**3**).—(i) *Acetic anhydride–water.* A reaction carried out as in section (2,i) but for a period of 2 h gave on chromatography (silica, 60 vol % ether in light petroleum) 6-*acetyl*-7-*phenyl*-6H-*thieno*[3,2-d][1,2]*diazepine* (**19**) (0.10 g, 37%), m.p. 186—187 °C (from propan-2-ol) (Found: C, 67.25; H, 4.5; N, 10.5. $C_{15}H_{12}N_2OS$ requires C, 67.1; H, 4.5; N, 10.4%); δ_H (100 MHz; C_2D_6SO) 2.24 (3 H, s, Me), 7.36—7.58 (5 H, m, aromatic), 7.75 (1 H, d, *J* 6 Hz, 2-H), 8.09—8.18 (2 H, m, aromatic), and 8.45 (1 H, s, CH=N); $\nu_{max.}$(Nujol) 1 668 cm^{-1} (C=O); *m/z* 268 (63), 253 (13), 226 (100), and 43 (13%).

(ii) *Acetic anhydride–ethanol.* A reaction similar to that in section (2,ii) using the diazepine (0.11 g, 0.5 mmol), acetic anhydride (0.1 ml), and ethanol (15 ml) gave after chromatography (silica, 50 vol % ether in light petroleum) 5-*acetyl*-4-*ethoxy*-5,8-*dihydro*-7-*phenyl*-4H-*thieno*[3,2-d]-[1,2]*diazepine* (0.05 g, 31%), m.p. 87—88 °C (from ethanol) (Found: C, 64.8; H, 5.7; N, 8.8. $C_{17}H_{18}N_2O_2S$ requires C, 65.0; H, 5.8; N, 8.9%); $\nu_{max.}$(Nujol) 1 670 cm^{-1} (C=O); δ_H (100 MHz) 1.21 (3 H, t, *J* 7 Hz, CH_2CH_3), 2.30 (3 H, s, CH_3), 3.64 (2 H, d, *J* 7 Hz, CH_2CH_3), 4.08 (1 H, d, *J* 15 Hz, 8-H), 4.36 (1 H, d, *J* 15 Hz, 8-H), 7.13 (1 H, s, 4-H), 6.90—7.50 (5 H, m, aromatic), and 7.76 (2 H, m, aromatic).

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