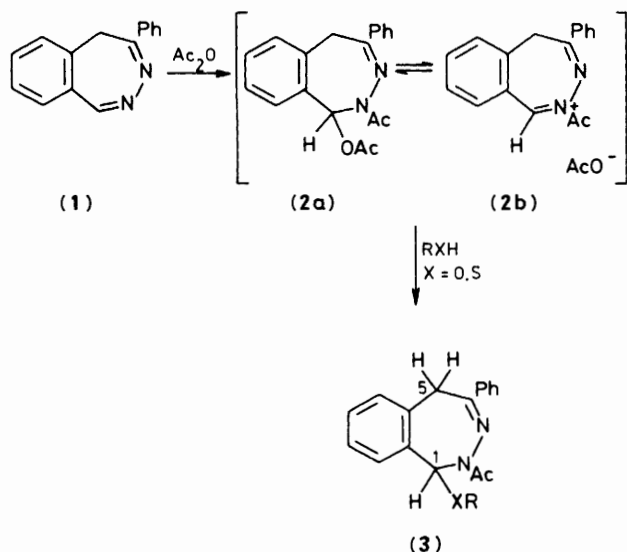


The Acylation of 5*H*-2,3-Benzodiazepines. Reactions of 4-Phenyl-5*H*-2,3-benzodiazepine with Acyl Chlorides to give *N*-Acylaminoisoquinolines and/or Acylated Dimers.¹ X-Ray Molecular Structure of 5,14-Diacetyl-4,5,8,9-tetrahydro-2,7-diphenyl-4,8-*o*-benzeno-3,9-imino-3*H*-3,5,6-benzotriazacycloundecine

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The acylation of 4-phenyl-5*H*-2,3-benzodiazepine (1) with acyl halides in benzene or toluene takes either or both of two reaction paths depending on the nature of the acylating reagent, the order of mixing, and the reaction temperature. One pathway leads to the formation of 2-acylamino-3-phenylisoquinolinium chlorides (4) and the other to the formation of either or both of the acylated dimers (6) and (7) together with the benzodiazepine hydrochloride (8). These results are rationalised on the basis of the mechanism in Scheme 4 which involves the generation of the reactive intermediate (12) by the dehydrochlorination of the iminium chloride (11). Acylations in pyridine took a different path, similar to that followed in the acetic anhydride acylation of (1) in benzene or pyridine, and were used to prepare 1-alkoxy-2-benzoyl derivatives (10).

In an earlier paper² it was reported that 4-phenyl-5*H*-2,3-benzodiazepine (1) reacts with acetic anhydride by acylation at N-2 to give the iminium acetate (2). This intermediate was not isolated but was stable in pyridine or benzene at room temperature and reacted with alcohols, thiols, phenol, and thiophenol at C-1 to give compounds (3), Scheme 1. This paper is concerned with the reactions of (1) with acyl chlorides, chloroformic esters, and toluene-*p*-sulphonyl chloride, all of which follow paths which differ from that in Scheme 1 and which proved to be dependent on the nature of the reagent, the order of mixing of the reactants, the nature of the solvent, and the reaction temperature.

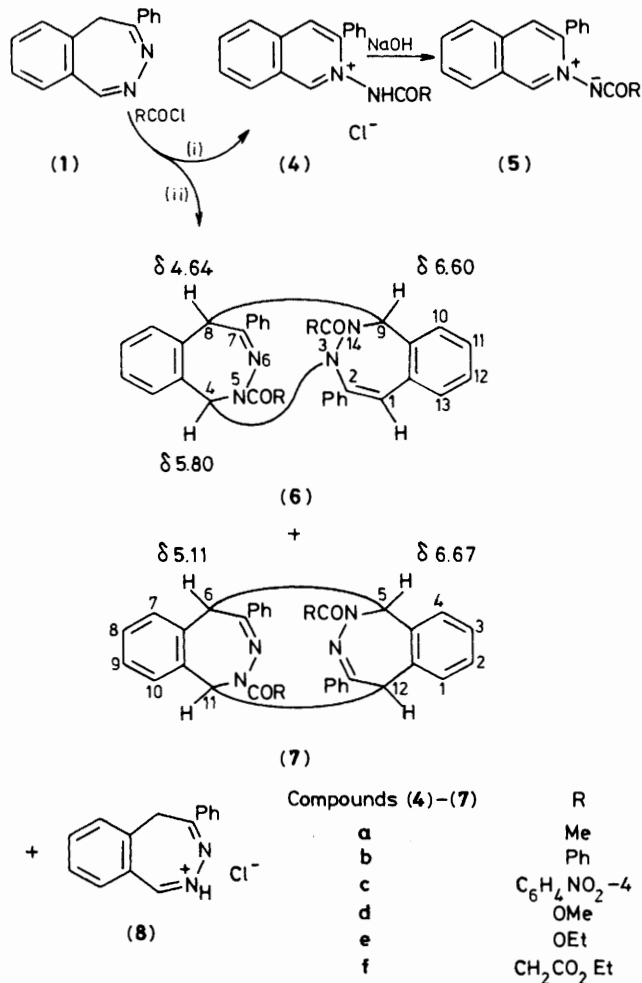


Scheme 1.

Results

(i) *Reactions in Benzene and Toluene.*—The acylation of (1) in benzene as solvent followed either or both of the two courses shown in Scheme 2: (i) precipitation of the 2-acylamino-3-phenylisoquinolinium chloride (4), and/or (ii) formation of

either or both of the acylated dimers (6) and (7) together with the diazepine hydrochloride (8). With one exception the modes of reaction of the acylating reagents fell into two general



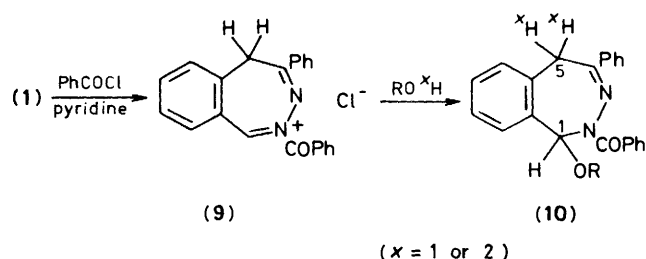
Scheme 2.

patterns which seemed to depend primarily on their reactivity to nucleophilic attack. The first pattern was shown by the more reactive reagents, e.g. acetyl and benzoyl chlorides, and with these the path taken depended greatly on temperature. When added to a solution of the diazepine in benzene at room temperature the reagents produced an immediate precipitation of the 2-acylamino-3-phenylisoquinolinium chlorides (**4a–c**) in high yield. However, if the same reactions were carried out at lower temperatures they were diverted partially or completely into pathway (ii) (Scheme 2) with the formation of (**6**) and/or (**7**) together with (**8**). Thus the reaction with acetyl chloride at room temperature gave (**4a**) (67%) but when the reagent was added to an ice-cooled slurry of (**1**) in benzene a deep red-brown colour was generated which faded during *ca.* 5 min to give a white precipitate of (**8**), and the unsymmetrical dimer (**6a**) (56%). When the reaction was performed in toluene at -45°C the red colour was more persistent and both dimers (**6a**) (26%) and (**7a**) (27%) were obtained. Similarly the reaction with benzoyl chloride at room temperature gave (**4b**) (89%) but in this case there was a lower tendency for dimer formation in the low-temperature reactions. At 0°C the red-brown colour faded during *ca.* 1 h but the product was (**4b**) (90%) as at room temperature; however, at -70°C in toluene the reaction gave (**6b**) (30%) and a trace of (**7b**).

The other pattern of reactivity was shown by the less reactive reagents, *i.e.* the chloroformic esters and toluene-*p*-sulphonyl chloride. When these were treated in the same way at room temperature, *i.e.* by addition to a solution of (**1**) in benzene, they strongly favoured pathway (ii). Methyl chloroformate gave (**6d**) (28%) and (**8**) (37%) while ethyl chloroformate gave (**6e**) (25%), (**7e**) (13%), (**8**) (27%) and (**4e**) (27%). However, it was found that the course of the reaction could be changed by reversing the order of mixing. Thus when a dilute solution of (**1**) in benzene was added slowly to the chloroformic ester the *N*-acylaminoisoquinoline salts were formed in high yield: (**4d**) (88%) and (**4e**) (85%). A similar but less pronounced diversion of the reaction path was also achieved by raising the reaction temperature. Addition of ethyl chloroformate to (**1**) in refluxing benzene gave (**4e**) (56%) as the only identifiable product.

The exception to this pattern was provided by ethyl malonyl chloride which did not react *via* path (i) as expected for a reactive acylating reagent, but gave only the symmetrical dimer (**7f**) (56%).

(ii) *Reactions in Pyridine.*—The use of pyridine as solvent in the acylation with benzoyl chloride had a dramatic effect in inhibiting the rearrangement to the *N*-acylaminoisoquinoline salt (**4b**) which was very fast in benzene. This was observed for reactions carried out at -20°C and at room temperature, and in both cases quenching the reaction mixture with alcohols, Scheme 3, gave the 1-alkoxy-2-benzoyl derivatives (**10**) in good yield, presumably *via* the intermediate (**9**). This therefore parallels the anhydride acylation shown in Scheme 1 and provides a route to the 2-benzoyl derivatives (**10**) which were not previously accessible because of the low reactivity of (**1**) to benzoic anhydride.



Scheme 3.

(iii) *Structures of the Reaction Products.*—The *N*-acylaminoisoquinoline salts (**4**) were in all cases subsequently converted into the parent amidates (**5**) by treatment with base. In one case, the product (**5b**) was identified by comparison with an authentic sample prepared *via* the *o*-mesitylenesulphonylhydroxylamine amination of 3-phenylisoquinoline. The analogues (**4** and **5**; **a** and **c–e**) showed the expected similarity of ^1H n.m.r. and i.r. spectroscopic properties.

The formulation of the dimers (**6**) and (**7**) is based on an X-ray crystallographic determination of the structure of (**6a**) and on n.m.r. and mass spectroscopic data for (**7**).

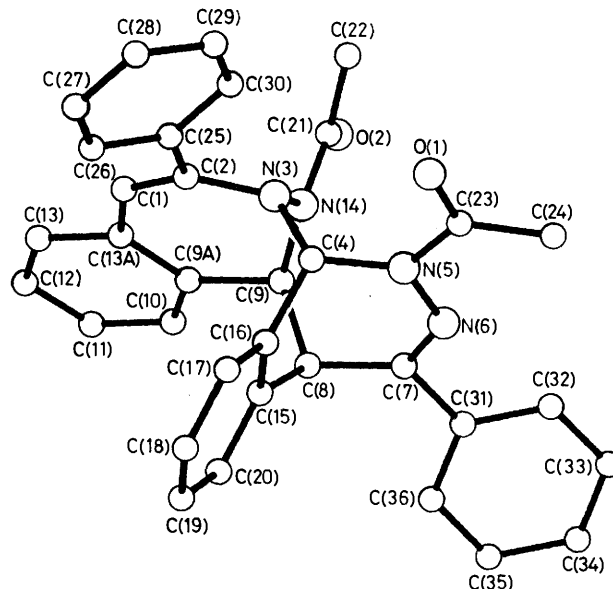


Figure. X-Ray molecular structure of compound (**6a**). The crystallographic numbering system is given

The structure of (**6a**) is shown in the Figure, the atomic coordinates in Table 1, and the bond lengths and angles in Table 2. All bond lengths are within the expected ranges. Because of the unsymmetrical coupling there are no exactly chemically equivalent bonds in the bridged ring system. For example, $\text{N}(5)\text{--N}(6)^* = 1.377(8)$ Å is shorter than $\text{N}(3)\text{--N}(14) = 1.391(5)$ Å because of the effect of the adjacent $\text{N}(6)\text{--C}(7)$ double bond. It may be significant that the longest C–N and C–C bonds [$\text{N}(3)\text{--C}(4) = 1.473(6)$ and $\text{C}(9)\text{--C}(8) = 1.532(7)$ Å] are the two bonds formed by the coupling of the two diazepine rings. All H–C bond lengths from the experimentally determined hydrogen positions lie between 1.14 and 1.02 Å.

There are a number of significant deviations from the ideal trigonal geometry [e.g. $\text{C}(13\text{A})\text{--C}(1)\text{--C}(2) = 133.3(5)^{\circ}$] and tetrahedral geometry [e.g. $\text{C}(15)\text{--C}(8)\text{--C}(9) = 118.9(4)^{\circ}$] expected for sp^2 - and sp^3 -hybridised carbon atoms. Both $\text{N}(5)$ and $\text{N}(14)$ show essentially planar trigonal geometry while $\text{N}(3)$ adopts a more pyramidal co-ordination with the three subtended angles summing to 346.8° .

The conformations of the two diazepine rings are defined by the intra-ring torsion angles in Table 2. An alternative description is given by the interplanar angles between the fused benzene ring and the remaining five atoms in the ring. One of the diazepine rings is only slightly puckered with the angle between the best planes through $\text{C}(1)\text{--C}(13\text{A})\text{--C}(9\text{A})\text{--C}(9)$ and $\text{C}(1)\text{--C}(2)\text{--N}(3)\text{--N}(14)\text{--C}(9)$ equal to 8° . The other ring is V-shaped with the angle between the best planes through $\text{C}(4)\text{--C}(16)\text{--C}(15)\text{--C}(8)$ and $\text{C}(4)\text{--N}(5)\text{--N}(6)\text{--C}(7)\text{--C}(8)$ equal

* Crystallographic numbering as shown in the Figure.

Table 1. Fractional co-ordinates of non-H atoms with standard deviations in parentheses^a

	x	y	z
C(1)	-0.3271(3)	-0.7077(5)	0.414 58(24)
C(13A)	-0.2948(3)	-0.7687(5)	0.481 51(24)
C(13)	-0.3296(4)	-0.9074(5)	0.4900(3)
C(12)	-0.3084(4)	-0.9746(6)	0.5502(3)
C(11)	-0.2496(4)	-0.9105(6)	0.6048(3)
C(10)	-0.2128(4)	-0.7767(6)	0.5982(3)
C(9A)	-0.2354(3)	-0.7040(5)	0.538 24(24)
C(9)	-0.1883(3)	-0.5592(5)	0.538 45(22)
N(14)	-0.176 68(24)	-0.5300(4)	0.475 38(18)
C(21)	-0.1045(4)	-0.5874(6)	0.4637(3)
O(2)	-0.050 18(25)	-0.6578(5)	0.505 90(20)
C(22)	-0.0968(4)	-0.5567(8)	0.3968(3)
N(3)	-0.247 02(24)	-0.4786(4)	0.421 67(18)
C(2)	-0.3133(3)	-0.5818(6)	0.388 63(22)
C(25)	-0.3639(3)	-0.5381(6)	0.319 71(23)
C(26)	-0.4517(4)	-0.5804(7)	0.2907(3)
C(27)	-0.4982(4)	-0.5442(8)	0.2251(3)
C(28)	-0.4572(5)	-0.4672(8)	0.1888(3)
C(29)	-0.3723(5)	-0.4208(7)	0.2175(3)
C(30)	-0.3255(4)	-0.4581(7)	0.281 97(25)
C(4)	-0.2817(3)	-0.3325(5)	0.430 31(22)
C(16)	-0.3463(3)	-0.3339(5)	0.466 24(22)
C(15)	-0.3217(3)	-0.3862(5)	0.530 78(23)
C(8)	-0.2271(3)	-0.4288(5)	0.565 21(22)
C(20)	-0.3821(4)	-0.3826(6)	0.564 44(25)
C(19)	-0.4668(4)	-0.3314(6)	0.5330(3)
C(18)	-0.4925(4)	-0.2808(7)	0.4684(3)
C(17)	-0.4318(3)	-0.2833(6)	0.434 79(25)
N(5)	-0.2083(3)	-0.2331(4)	0.458 93(18)
C(23)	-0.1844(4)	-0.1394(6)	0.4176(3)
C(24)	-0.1121(5)	-0.0346(8)	0.4477(3)
O(1)	-0.2227(3)	-0.1499(5)	0.357 54(19)
N(6)	-0.162 54(23)	-0.2118(4)	0.525 46(18)
C(7)	-0.1701(3)	-0.2923(5)	0.571 52(22)
C(31)	-0.117 43(22)	-0.2380(4)	0.638 52(13)
C(32)	-0.045 77(22)	-0.1440(4)	0.644 95(13)
C(33)	-0.000 04(22)	-0.0810(4)	0.706 44(13)
C(34)	-0.025 80(22)	-0.1118(4)	0.761 51(13)
C(35)	-0.097 46(22)	-0.2057(4)	0.755 08(13)
C(36)	-0.143 27(22)	-0.2688(4)	0.693 59(13)
* O(91)	-0.3096(7)	-0.4571(8)	0.7286(3)
* C(92)	-0.3441(10)	-0.6492(22)	0.7102(8)
* C(93)	-0.2664(19)	-0.6558(23)	0.7548(10)
* O(94)	-0.2318(13)	-0.562(5)	0.7502(9)

^a Atoms indicated with an asterisk are those of disordered ethanol**Table 2.** Bond lengths (Å), bond angles (°), and selected torsion angles

C(1)-C(13A)	1.457(7)	C(4)-N(5)	1.433(6)
C(1)-C(2)	1.321(7)	C(16)-C(15)	1.384(7)
C(13A)-C(13)	1.413(7)	C(16)-C(17)	1.382(7)
C(13A)-C(9A)	1.394(7)	C(15)-C(8)	1.491(7)
C(13)-C(12)	1.360(8)	C(15)-C(20)	1.378(7)
C(12)-C(11)	1.359(9)	C(8)-C(7)	1.517(7)
C(11)-C(10)	1.377(8)	C(20)-C(19)	1.373(8)
C(10)-C(9A)	1.377(8)	C(19)-C(18)	1.378(8)
C(9A)-C(9)	1.514(7)	C(18)-C(17)	1.380(8)
C(9)-N(14)	1.441(6)	N(5)-C(23)	1.366(7)
C(9)-C(8)	1.532(7)	N(5)-N(6)	1.377(6)
N(14)-C(21)	1.358(7)	C(23)-C(24)	1.467(9)
N(14)-N(3)	1.391(5)	C(23)-O(1)	1.227(8)
C(21)-O(2)	1.204(7)	N(6)-C(7)	1.262(6)
C(21)-C(22)	1.498(8)	C(7)-C(31)	1.481(6)
N(3)-C(2)	1.414(6)	C(31)-C(32)	1.395(5)
N(3)-C(4)	1.473(6)	C(31)-C(36)	1.395(5)
C(2)-C(25)	1.477(7)	C(32)-C(33)	1.395(5)
C(25)-C(26)	1.382(8)	C(33)-C(34)	1.395(5)
C(25)-C(30)	1.370(8)	C(34)-C(35)	1.395(5)
C(26)-C(27)	1.389(9)	C(35)-C(36)	1.395(5)

Table 2. (continued)

C(27)-C(28)	1.359(10)	O(91)-O(94)	1.51(3)
C(28)-C(29)	1.353(10)	C(92)-C(93)	1.29(3)
C(29)-C(30)	1.372(9)	C(93)-O(94)	1.03(4)
C(4)-C(16)	1.472(7)		
C(13A)-C(1)-C(2)	133.3(5)	N(3)-C(4)-N(5)	109.4(4)
C(1)-C(13A)-C(13)	116.0(4)	C(16)-C(4)-N(5)	113.2(4)
C(1)-C(13A)-C(9A)	127.4(5)	C(4)-C(16)-C(15)	120.2(4)
C(13)-C(13A)-C(9A)	116.6(5)	C(4)-C(16)-C(17)	119.4(4)
C(13A)-C(13)-C(12)	122.4(5)	C(15)-C(16)-C(17)	120.4(4)
C(13)-C(12)-C(11)	120.1(6)	C(16)-C(15)-C(8)	119.1(4)
C(12)-C(11)-C(10)	119.1(6)	C(16)-C(15)-C(20)	119.5(5)
C(11)-C(10)-C(9A)	122.0(5)	C(8)-C(15)-C(20)	121.0(4)
C(13A)-C(9A)-C(10)	119.8(5)	C(9)-C(8)-C(15)	118.9(4)
C(13A)-C(9A)-C(9)	124.2(4)	C(9)-C(8)-C(7)	111.3(4)
C(10)-C(9A)-C(9)	115.9(4)	C(15)-C(8)-C(7)	108.0(4)
C(9A)-C(9)-N(14)	112.0(4)	C(15)-C(20)-C(19)	119.7(5)
C(9A)-C(9)-C(8)	114.4(4)	C(20)-C(19)-C(18)	121.3(5)
N(14)-C(9)-C(8)	113.4(4)	C(19)-C(18)-C(17)	119.1(5)
C(9)-N(14)-C(21)	118.6(4)	C(16)-C(17)-C(18)	120.0(5)
C(9)-N(14)-N(3)	120.8(4)	C(4)-N(5)-C(23)	118.5(4)
C(21)-N(14)-N(3)	118.5(4)	C(4)-N(5)-N(6)	127.0(4)
N(14)-C(21)-O(2)	120.6(5)	C(23)-N(5)-N(6)	114.3(4)
N(14)-C(21)-C(22)	116.4(5)	N(5)-C(23)-C(24)	117.9(5)
O(2)-C(21)-C(22)	123.0(5)	N(5)-C(23)-O(1)	118.4(5)
N(14)-N(3)-C(2)	116.8(4)	C(24)-C(23)-O(1)	123.6(6)
N(14)-N(3)-C(4)	115.7(4)	N(5)-N(6)-C(7)	124.5(4)
C(2)-N(3)-C(4)	114.3(4)	C(8)-C(7)-N(6)	127.9(4)
C(1)-C(2)-N(3)	124.5(5)	C(8)-C(7)-C(31)	119.3(4)
C(1)-C(2)-C(25)	122.5(5)	N(6)-C(7)-C(31)	112.8(4)
N(3)-C(2)-C(25)	112.9(4)	C(7)-C(31)-C(32)	118.8(3)
C(2)-C(25)-C(26)	120.5(5)	C(7)-C(31)-C(36)	120.9(3)
C(2)-C(25)-C(30)	121.6(5)	C(32)-C(31)-C(36)	120.0(3)
C(26)-C(25)-C(30)	117.9(5)	C(31)-C(32)-C(33)	120.0(3)
C(25)-C(26)-C(27)	120.5(6)	C(32)-C(33)-C(34)	120.0(3)
C(26)-C(27)-C(28)	119.9(6)	C(33)-C(34)-C(35)	120.0(3)
C(27)-C(28)-C(29)	120.0(7)	C(34)-C(35)-C(36)	120.0(3)
C(28)-C(29)-C(30)	120.4(6)	C(31)-C(36)-C(35)	120.0(3)
C(25)-C(30)-C(29)	121.2(5)	C(92)-C(93)-O(94)	107.6(28)
N(3)-C(4)-C(16)	114.4(4)	O(91)-O(94)-C(93)	98.1(27)
C(2)-C(1)-C(13A)-C(9A)	-1.4(9)		
C(1)-C(13A)-C(9A)-C(9)	-4.7(8)		
C(13)-C(9A)-C(9)-N(14)	-27.3(7)		
C(9A)-C(9)-N(14)-N(3)	78.1(5)		
C(9)-N(14)-N(3)-C(2)	-75.3(5)		
N(14)-N(3)-C(2)-C(1)	19.8(7)		
N(3)-C(2)-C(1)-C(13A)	11.2(9)		
C(7)-C(8)-C(15)-C(16)	62.9(6)		
C(8)-C(15)-C(16)-C(4)	5.2(7)		
C(15)-C(16)-C(4)-N(5)	-65.7(6)		
C(16)-C(4)-N(5)-N(6)	41.6(6)		
C(4)-N(5)-N(6)-C(7)	10.7(7)		
N(5)-N(6)-C(7)-C(8)	1.6(8)		
N(6)-C(7)-C(8)-C(15)	-59.4(6)		

to 120°. The interplanar angle between the benzene rings of the two monomer subunits is 72°.

The only notable intermolecular contacts are O(91) ... O(1) = 2.81 Å and O(94) ... O(1) = 2.96 Å, which are both likely to be due to hydrogen bonds to the disordered ethanol molecules. The gross disorder in the solvent of crystallisation results from the way in which the dimer packs to give large unfilled channels the length of the *b* axis. Some of the n.m.r. absorptions of this compound are shown in structure (6).

The dimeric nature of (7) was demonstrated by mass spectrometry but in this case its ¹H and ¹³C n.m.r. spectra showed it to have a symmetrical structure with chemical shift equivalence of the two acylated diazepine moieties. Its formulation as (7), the head-to-tail 1,5':5,1* dimer of (12) is

based on this and on the similarity of the chemical shift values of the protons on C-5 and C-6 as shown in structure (7) to those at the similar linkage between C-8 and C-9 in the unsymmetrical dimer (6). The large vicinal coupling (10–11 Hz) between 5-H and 6-H in (7) is consistent with the very small dihedral angle required by the structure.

The unsymmetrical dimers (6) had a strong tendency to occlude solvent molecules, particularly alcohols, in their crystals. This made it difficult to obtain good analytical data and m.p.s so in most cases the determination of molecular formula relied on accurate mass data rather than combustion analysis.

Discussion

The rearrangement to give (4) can be rationalised by the mechanism shown in Scheme 4. Acylation at N-2 to give the iminium chloride (11a and b) parallels that previously observed in the anhydride reaction, Scheme 1. The lower stability of 11a and b compared with that of (2a and b) must be largely due to the greater electronegativity of Cl than OAc which will result in the equilibrium between (11a) and (11b) lying further to the right than that between (2a) and (2b). In consequence the diazepine ring in (11) will have a more fully developed cationic character and will undergo deprotonation at C-5 to give an intermediate which can be represented as an azomethine imine with extended conjugation (12a) or by the *o*-quinonoid structure (12b). Ring contraction of this intermediate by a 6π electron electrocyclicisation gives the diazanocaradiene (13) which then undergoes acid-catalysed ring opening to give the isolated product (4). There is precedent for the last two steps in the acid-catalysed rearrangement of monocyclic 1*H*-1,2-

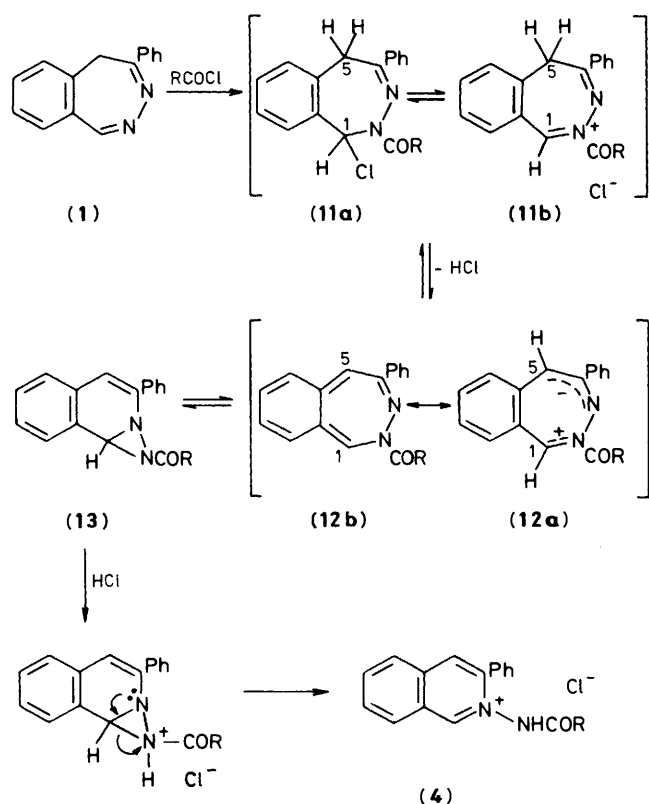
diazepines and -diazepinones to pyridine *N*-amine salts.³ The observation² that the treatment of a solution of (2) in benzene with dry hydrogen chloride causes the rapid precipitation of (4a) is consistent with this mechanism.

The question then arises as to why this rearrangement is the dominant reaction path at room temperature when the more reactive acylating agents are added to (1) but is only favoured for the less reactive chloroformic esters when the order of addition is reversed. This can be understood if it is accepted that the successful operation of the rearrangement sequence in Scheme 4 is dependent on the availability of the hydrogen chloride eliminated in step two for the catalysis of the final step. If the hydrogen chloride were to be scavenged by some other reactant in the system then the conversion of (13) into (4) would be inhibited and the concentration of the intermediate (12) would build up to an extent where the formation of the dimers (6) and (7) would become the major reaction path. This could arise when the less reactive acylating reagents are added to a solution of the diazepine in benzene. Their relatively slow reaction with the diazepine (see below) leads to a situation in which the intermediate (12) is generated in the presence of an excess of the unchanged diazepine which acts as a base and competes successfully with (13) for the hydrogen chloride eliminated in step two. This has two consequences: (i) the inhibition of the (13) \rightarrow (4) conversion and the consequent diversion into dimer formation as discussed above, and (ii) the precipitation of much of the diazepine as its hydrochloride which is less reactive to the acylating reagent than the parent diazepine. In support of this explanation it was found that the reversal of the order of addition, *i.e.* the slow addition of a dilute solution of the diazepine to the chloroformic ester so that the diazepine concentration in the reaction mixture was kept low, led to a high yield of (4d and e). This rationalisation depends on the assertion that the chloroformic esters are significantly less reactive than acetyl and benzoyl chlorides. It has been reported that this is so in bimolecular hydrolysis reactions⁴ and in this work we have confirmed by a competition reaction, that benzoyl chloride is > 50 times more reactive than ethyl chloroformate towards (1). The competition was carried out using a 2.5 times excess of both benzoyl chloride and ethyl chloroformate over the diazepine and under conditions where the individual acylating agents both gave a *ca.* 90% yield of (4). The competition reaction gave a virtually quantitative conversion of (1) into a mixture of (4b) and (4e) which was shown by ¹H n.m.r. spectrometry to contain < 2% of (4c).

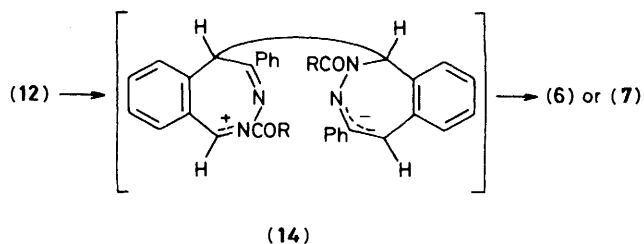
The effect of temperature on the acylation with acetyl and benzoyl chlorides can also be explained by the same argument. At room temperature the rates of acylation and of the (12) \rightarrow (13) ring contraction are fast so that the whole of (1) is converted rapidly into (11) and thence into (4). At lower temperatures the rate of acylation will be lower and the course of the reaction will parallel that of the chloroformic esters at room temperature.

This rationalisation highlights the effect on the course of the reaction of the reactivity of the acylating reagent to nucleophilic attack but other factors must also be important. For example the nature of the R group in (13) will affect the ease of protonation at nitrogen and hence the rate of ring opening. The nature of R may also affect the partitioning of (12) between ring contraction and dimerisation and account for the lesser tendency to dimerisation in (12; R = C₆H₅) compared with (12; R = COMe).

The mechanism of the formation of the dimers is uncertain. The unsymmetrical dimer (6) could be formed *via* a concerted ($6\pi + 4\pi$) electron dimerisation of (12), but a concerted mechanism for the symmetrical dimer (7) is unlikely in view of the necessarily different symmetries of the HOMO and LUMO. Both may be formed stepwise *via* the common intermediate



Scheme 4. R as in Scheme 2.



(14). Attempts to trap (12; R = COMe) using a range of electron-rich and electron-poor alkenes were wholly unsuccessful.

The strong inhibition of the rearrangement reaction to give (4) when the benzoylation reaction was carried out in pyridine as solvent is also consistent with the Scheme 4 mechanism. The pyridine would scavenge the hydrogen chloride produced in step two and so inhibit the (13) \rightarrow (4) conversion. However, this cannot be the only role played by the pyridine because dimer formation is also inhibited and either the iminium chloride (11) or the intermediate (12) is stabilised to such a degree that it can be trapped by quenching the reaction mixture with alcohols (Scheme 3). Since no red-brown colour is observed in these reactions, which indicates the absence of (12), we suggest that the pyridine strongly solvates (11) so stabilising it and swinging the (11) \rightleftharpoons (12) equilibrium to the left. That this equilibrium still exists in pyridine when the counterion is Cl^- but not when it is AcO^- was shown by quenching experiments with MeOD. In these, solutions of (1) in pyridine were treated with benzoyl chloride or acetic anhydride² and then quenched with MeOD. The first gave (10; R = Me), fully deuteriated at position 5, while the second gave (3; R = Me, X = O) containing no deuterium.

Experimental

The spectroscopic and chromatographic techniques, reagents, and preparation of 4-phenyl-5*H*-2,3-benzodiazepine (1) were described in an earlier paper.² Light petroleum refers to the fraction boiling in the range 40–60 °C.

N-(3-Phenyl-2-isoquinolinio)benzamidate (5b).—To a stirred solution of 3-phenylisoquinoline⁵ (1.6 g, 7.8 mmol) in dichloromethane (10 ml) was added dropwise a solution of *o*-mesitylenesulphonylhydroxylamine⁶ (1.8 g, 8.3 mmol) in dichloromethane (10 ml). After 30 min ether (50 ml) was added and the *N*-amino-3-phenylisoquinolinium mesitylenesulphonate (2.03 g, 60%) separated as a brown oil and was washed with ether (3 \times 30 ml) but could not be crystallised. A solution of this product (0.9 g, 2.2 mmol) in water (15 ml) was made alkaline with aqueous sodium hydroxide (15 ml; 20% w/v), benzoyl chloride (2.3 g, 0.016 mol) was added, and the reaction mixture was shaken vigorously overnight. The precipitate (0.88 g) was filtered off and chromatographed (silica; 50 vol% ethyl acetate in ethanol) to give *N*-(3-phenyl-2-isoquinolinio)benzamidate (0.28 g, 49%), m.p. 181–182 °C (from ethyl acetate), identical with a sample prepared by the reaction of (1) with benzoyl chloride.

Acylation Reactions.—1. *Acetyl chloride.* (i) *Benzene, room temperature.* Acetyl chloride (0.2 ml, 2.8 mmol) was added to a stirred solution of the diazepine (1) (0.22 g, 1.0 mmol) in benzene (3 ml) at room temperature. A white precipitate came down immediately and was crystallised from methanol by an extractive technique to give 2-acetamido-3-phenylisoquinolinium chloride (0.20 g, 67%), m.p. 252–254 °C (Found: C, 68.4; H, 4.9; N, 9.3. $\text{C}_{17}\text{H}_{15}\text{ClN}_2\text{O}$ requires C, 68.3; H, 5.1; N, 9.4%). ν_{max} (Nujol) 3 450 (NH) and 1 695 cm^{-1} (C=O); δ_{H} [100 MHz;

(CD_3)₂SO] 1.92 (3 H, s, Me), 7.42–8.62 (11 H, m, ArH and NH), 8.69 (1 H, s, 4-H), and 10.29 (1 H, s, CH=N). Treatment of this salt with aqueous sodium hydroxide (2M) followed by extraction into dichloromethane gave *N*-(3-phenylisoquinolinio)acetamidate (5a) (84%), m.p. 88–89 °C (from ethyl acetate) (Found: C, 78.0; H, 5.6; N, 10.4. $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}$ requires C, 77.8; H, 5.8; N, 10.7%); ν_{max} (Nujol) 1 560 cm^{-1} (C=O); δ_{H} (100 MHz) 1.94 (3 H, s, Me), 7.28–8.10 (10 H, m, ArH) and 9.21 (1 H, s, CH=N).

(ii) *Benzene, 0 °C.* A solution of the diazepine (1) (0.22 g, 1.0 mmol) in benzene (5 ml) was cooled and stirred in an ice-bath until the contents were a thick slurry. Acetyl chloride (0.2 ml, 2.8 mmol) was added slowly by syringe through a septum. A dark red-brown colour developed immediately and faded during ca. 5–10 min to give a white precipitate. The mixture was stirred at 0 °C for 1.5 h and then ethanol (2.5 ml) was added to destroy the excess of acetyl chloride. The mixture was stirred at room temperature for 1.5 h and then the solvents were evaporated to leave a light brown solid (0.29 g). Soxhlet extraction of this with methanol gave white crystals of 5,14-diacetyl-4,5,8,9-tetrahydro-2,7-diphenyl-4,8-*o*-benzeno-3,9-imino-3*H*-3,5,6-benzotriazacycloundecine (6a) (0.164 g, 56%), which softened with evolution of gas at 168–175 °C, solidified, and then melted at 257–259 °C (Found: M^+ , 524.224 002. $\text{C}_{34}\text{H}_{28}\text{N}_4\text{O}_2$ requires M , 524.221 214); ν_{max} (Nujol) 1 665 (C=O) and 1 680 cm^{-1} (C=O); δ_{H} (360 MHz) 2.36 (3 H, s, Me), 2.53 (3 H, s, Me), 4.64 (1 H, d, J 5 Hz, 8-H), 5.80 (1 H, s, 4-H), 6.60 (1 H, d, J 5 Hz, 9-H), 6.53 (1 H, m, aromatic), 6.78 (1 H, m, aromatic), 7.07 (1 H, s, 1-H), and 7.0–7.8 (16 H, m, ArH); δ_{C} (90 MHz) 21.4 (Me), 22.3 (Me), 53.4 (C-8), 57.7 (C-4), 71.0 (C-9), 116.3 (C-1), 126.1, 126.5, 127.4, 127.5, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 129.2, 129.3, 129.4, 132.6, 133.6, 134.3, 135.7, 136.6, 136.7, 139.0, 145.2, 147.0, 173.7 (C=O), and 173.8 p.p.m. (C=O).

(iii) *Toluene, -45 °C.* Acetyl chloride (0.43 ml) was added slowly to a solution of the diazepine (1) (0.469 g, 2.13 mmol) in toluene (10 ml) at -45 °C. The mixture was stirred at -45 °C for 3.5 h and then ethanol (5 ml) was added. On being kept overnight the solution deposited crystals of 15,16-diacetyl-5,6,11,12-tetrahydro-13,18-diphenyl-5,12:11,6-bis(hydrazin-1'-yl-2'-ylidene)metheno)dibenzo[a,e]cyclo-octene (7a) (0.163 g, 29%), m.p. > 360 °C (Found: M^+ , 524.222 998. $\text{C}_{34}\text{H}_{28}\text{N}_4\text{O}_2$ requires M , 524.221 214); δ_{H} (200 MHz) 2.10 (6 H, s, 2 \times Me), 5.11 (2 H, d, J 11 Hz, 6- and 12-H), 6.67 (2 H, d, J 11 Hz, 5- and 11-H), and 6.95–7.60 (18 H, m, ArH); δ_{C} 22.1 (Me), 50.0 (C-6 and -12), 60.7 (C-5 and -11), 126.4, 128.4, 128.7, 129.1, 130.5, 130.7, 134.5, 137.8, 140.2, 143.6, and 174.0 p.p.m.; ν_{max} (Nujol) 1 665 cm^{-1} (C=O). The filtrate was evaporated and the residue separated by chromatography on silica to give the unsymmetrical dimer (6a) (0.147 g, 26%) and recovered starting material (0.035 g, 7%).

2. *Benzoyl chloride.*—(i) *Benzene, room temperature.* Benzoyl chloride (0.3 ml, 2.5 mmol) was added to a stirred solution of the diazepine (1) (0.22 g, 1.0 mmol) in benzene (3 ml) at room temperature. A white precipitate formed immediately and was filtered off and crystallised from ethanol to give 2-benzamido-3-phenylisoquinolinium chloride (4b) (0.32 g, 89%), m.p. 235–238 °C (Found: C, 73.0; H, 4.6; N, 7.6. $\text{C}_{22}\text{H}_{17}\text{ClN}_2\text{O}$ requires C, 73.2; H, 4.7; N, 7.8%); ν_{max} (Nujol) 3 350 (NH) and 1 675 cm^{-1} (C=O); δ_{H} [100 MHz; (CD_3)₂SO] 7.31–8.69 (16 H, m, ArH and NH), 8.85 (1 H, s, 4-H), and 10.58 (1 H, s, CH=N). Treatment with sodium hydroxide solution (2M) gave *N*-(3-phenylisoquinolinio)benzamidate (5b) (85%), m.p. 182–183 °C (from ethyl acetate) (Found: C, 81.3; H, 4.8; N, 8.7. $\text{C}_{22}\text{H}_{16}\text{N}_2\text{O}$ requires C, 81.5; H, 4.9; N, 8.6%); ν_{max} (Nujol) 1 600 cm^{-1} (C=O); δ_{H} (100 MHz) 7.08–8.19 (15 H, m, ArH) and 9.52 (1 H, s, CH=N). This compound was identical with the authentic sample prepared above.

(ii) *Benzene*, 0 °C. A similar reaction in which benzoyl chloride (0.4 ml) was added dropwise to an ice-cooled slurry of the diazepine (1) (0.22 g) in benzene (5 ml) produced an immediate red-brown colour which faded during *ca.* 1 h. The mixture was stirred at 0 °C for 7 h after which the white precipitate (0.36 g) was filtered off. Recrystallisation from ethanol gave 2-benzamido-3-phenylisoquinolinium chloride (4b) (90%), m.p. 236–239 °C, identical with the sample prepared above.

(iii) *Toluene*, –70 °C. A solution of the diazepine (1) (0.19 g, 0.86 mmol) in toluene (5 ml) was cooled to *ca.* –70 °C and benzoyl chloride (0.3 ml, 2.6 mmol) was added slowly. No visible change occurred when the mixture was stirred for 4 h at this temperature but when the mixture was slowly warmed a red colour appeared at *ca.* –65 °C; this colour faded at *ca.* –30 °C to leave a yellow solution. After being kept overnight at room temperature the mixture was filtered and evaporated and chromatography of the residue gave 5,14-dibenzoyl-4,5,8,9-tetrahydro-2,7-diphenyl-4,8-o-benzo-3,9-imino-3H-3,5,6-benzotriazacycloundecine (6b) (0.084 g, 30%), m.p. 254–257 °C (Found: C, 81.2; H, 5.2; N, 8.6. $C_{44}H_{32}N_4O_2$ requires C, 81.5; H, 5.0; N, 8.6%; ν_{\max} (Nujol) 1 660 cm^{-1} (C=O); δ_C (90 MHz) 52.6 (C-8), 58.8 (C-4), 71.3 (C-9), and 116.2 (C-1) p.p.m.; δ_H (200 MHz) 4.84 (1 H, d, *J* 5 Hz, 8-H), 5.93 (1 H, s, 4-H), and 6.55 (1 H, m, ArH), 6.80 [1 H, d, *J* 5 Hz, 9-H (confirmed by decoupling of 8-H)], and 6.80–7.95 (27 H, m, ArH).

(iv) *Benzene*, room temperature, ethanol. A reaction similar to (i) in which the reaction mixture was quenched with ethanol immediately after the addition of the benzoyl chloride gave only the *N*-benzamidochloride (4b) (78%).

(v) *Pyridine*, –20 °C, ethanol. Benzoyl chloride (0.3 ml, 2.5 mmol) was added to a stirred solution of the diazepine (1) (0.22 g, 1.0 mmol) in pyridine (3 ml) at –20 °C and the reaction mixture was stirred for 30 min at that temperature. A yellow colour was seen. Ethanol (25 ml) was added, the mixture was allowed to warm up to room temperature, and the solvents were evaporated to leave a yellow solid. Chromatography (silica; 50 vol% ether in light petroleum) gave 2-benzoyl-1-ethoxy-2,5-dihydro-4-phenyl-1H-2,3-benzodiazepine (10; R = Et, *x* = 1) (0.26 g, 70%), m.p. 126–127.5 °C (from ethanol) (Found: C, 78.0; H, 5.9; N, 7.4. $C_{24}H_{22}N_2O_2$ requires C, 77.8; H, 6.0; N, 7.6%; ν_{\max} (Nujol) 1 660 cm^{-1} (C=O); δ_H (100 MHz) 1.24 (3 H, t, *J* 7 Hz, CH_3CH_2), 3.78 (2 H, q, *J* 7 Hz, CH_3CH_2), 3.92 and 4.92 (each 1 H, d, *J* 16 Hz, 5-H), and 6.95–7.75 (15 H, m, ArH). The silica in the precolumn was extracted (Soxhlet) with hot ethanol to give 2-benzamido-3-phenylisoquinolinium chloride (4b) (0.05 g, 13%) identical with that obtained above.

(vi) *Pyridine*, room temperature, methanol. An experiment similar to (v) but carried out at room temperature and quenched with methanol (0.5 ml) and worked up by distillation* gave 2-benzoyl-2,5-dihydro-1-methoxy-4-phenyl-1H-2,3-benzodiazepine (10; R = Me, *x* = 1) (0.20 g, 58%), b.p. 220 °C at 0.2 mmHg [Found: M^+ , 356.149 207 (30 eV). $C_{23}H_{20}N_2O_2$ requires M , 356.152 469]; δ_H (100 MHz) 3.49 (3 H, s, Me), 3.92 and 4.92 (each 1 H, d, *J* 15 Hz, 5-H), 6.97 (1 H, s, 1-H), and 7.00–7.70 (14 H, m, ArH).

(vii) *Pyridine*, room temperature, deuteriomethanol. An experiment similar to (vi) but quenched with monodeuteriomethanol (MeOD) (0.5 ml) gave the same product (64%) but shown by 1H n.m.r. spectroscopy to be fully deuteriated at position 5 (10; R = Me, *x* = 2).

(viii) *Competition reaction of benzoyl chloride and ethyl chloroformate in benzene*. A solution of the benzodiazepine (1)

(0.22 g, 1.0 mmol) in benzene (10 ml) was added dropwise during 1 h to a vigorously stirred solution of benzoyl chloride (0.35 g, 2.5 mmol) and ethyl chloroformate (0.27 g, 2.5 mmol) in benzene (5 ml) at room temperature. The mixture was stirred for a further 2.5 h and filtered to give a white solid (0.36 g) which was dried under high vacuum. 1H n.m.r. spectroscopy (80 MHz) showed that it was predominantly (>98%) 2-benzamido-3-phenylisoquinolinium chloride (4b), containing <2% of the *N*-ethoxycarbonyl analogue.

3. *p-Nitrobenzoyl chloride*. A reaction similar to that with benzoyl chloride in benzene at room temperature gave 2-(4-nitrobenzamido)-3-phenylisoquinolinium chloride (4c) (0.34 g, 84%), m.p. 209–211 °C (from ethanol) (Found: C, 64.9; H, 4.0; N, 10.3. $C_{22}H_{16}ClN_3O_3$ requires C, 65.1; H, 4.0; N, 10.3%; ν_{\max} (Nujol) 3 420 (NH) and 1 685 cm^{-1} (C=O); δ_H [100 MHz; $(CD_3)_2SO$] 7.40–8.60 (15 H, m, ArH), 8.74 (1 H, s, 4-H), and 10.39 (1 H, s, CH=N). Treatment with aqueous sodium hydroxide (2M) gave 4-nitro-*N*-(3-phenyl-2-isoquinolinio)benzamide (5c) (78%), m.p. 202–203 °C (from ethanol) (Found: C, 71.5; H, 4.1; N, 11.2. $C_{22}H_{15}N_3O_3$ requires C, 71.5; H, 4.1; N, 11.4%; ν_{\max} (Nujol) 1 562 cm^{-1} (C=O); δ_H (100 MHz) 7.30–8.20 (14 H, m, ArH) and 9.57 (1 H, s, CH=N).

4. *Methyl chloroformate*. (i) A solution of the diazepine (1) (0.22 g, 1.0 mmol) in benzene (10 ml) was added during 1 h to stirred methyl chloroformate (0.1 ml, 1.2 mmol). The precipitate was filtered off and recrystallised to give 2-methoxyformamido-3-phenylisoquinolinium chloride (4d) (0.28 g, 88%), m.p. 213–215 °C (from ethanol) (Found: C, 64.7; H, 4.8; N, 8.7. $C_{17}H_{15}ClN_2O_2$ requires C, 64.8; H, 4.8; N, 8.9%; ν_{\max} (Nujol) 3 500 (NH) and 1 734 cm^{-1} (C=O); δ_H [100 MHz; $(CD_3)_2SO$] 3.15 (3 H, s, Me), 7.41–8.55 (11 H, m, ArH and NH), 8.54 (1 H, s, 4-H), and 10.13 (1 H, s, CH=N). Treatment with aqueous sodium hydroxide gave *N*-(3-phenyl-2-isoquinolinio)-methoxyformamide (5d) (86%), m.p. 179–180 °C (from ethanol) (Found: C, 73.6; H, 5.1; N, 9.9. $C_{17}H_{14}N_2O_2$ requires C, 73.9; H, 5.1; N, 10.1%; ν_{\max} (Nujol) 1 630 cm^{-1} (C=O); δ_H (100 MHz) 3.60 (3 H, s, Me), 7.25–8.10 (10 H, m, ArH), and 9.51 (1 H, s, CH=N).

(ii) Methyl chloroformate (0.4 ml) was added to a solution of the diazepine (1) (0.44 g, 2.0 mmol) in benzene (20 ml) at room temperature. A precipitate of the diazepine hydrochloride was formed at once and after 5 min was filtered off (0.1923 g, 37%), m.p. 147–148 °C (from propan-2-ol) (Found: C, 70.0; H, 5.1; N, 10.7. $C_{15}H_{13}Cl$ requires C, 70.2; H, 5.1; N, 10.9%; ν_{\max} (Nujol) 1 925, 1 965, 2 075, and 2 280 cm^{-1} (C=NH); δ_H [100 MHz; $(CD_3)_2SO$] 4.35 (2 H, br s, 5-H₂), 7.60–8.60 (9 H, m, ArH), and 9.75 (1 H, s, CH=N). This compound, on treatment with base, gave back 4-phenyl-5H-2,3-benzodiazepine. The filtrate was evaporated and the residue chromatographed (silica; 80 vol% ether in light petroleum) to give 4,5,8,9-tetrahydro-5,14-bis(methoxycarbonyl)-2,7-diphenyl-4,8-o-benzo-3,9-imino-3H-3,5,6-benzotriazacycloundecine (6d) (0.154 g, 28%), m.p. 280–283 °C (from propan-2-ol-dioxane) (Found: M^+ , 556.208 341. $C_{34}H_{28}N_4O_4$ requires M , 556.211 044); ν_{\max} (Nujol) 1 705 br and 1 720 br cm^{-1} (C=O); δ_H (100 MHz) 3.77 (3 H, s, Me), 3.94 (3 H, s, Me), 4.61 (1 H, d, *J* 5 Hz, 8-H), 5.70 (1 H, s, 4-H), 6.24 (1 H, d, *J* 5 Hz, 9-H), and 6.50–7.90 (19 H, m, ArH and 1-H).

5. *Ethyl chloroformate*. (i) A reaction similar to 4(i) above gave 2-ethoxyformamido-3-phenylisoquinolinium chloride (4e) (85%), m.p. 185–188 °C (from propan-2-ol) (Found: C, 65.6; H, 5.0; N, 8.4. $C_{18}H_{17}ClN_2O_2$ requires C, 65.75; H, 5.2; N, 8.5%; ν_{\max} (Nujol) 3 400 (NH) and 1 730 cm^{-1} (C=O); δ_H [100 MHz; $(CD_3)_2SO$] 1.03 (3 H, t, *J* 7 Hz, CH_2CH_3), 4.05 (2 H, q, *J* 7 Hz, CH_2CH_3), 7.45–8.70 (11 H, m, ArH and NH), 8.80 (1 H, s, 4-H), and 10.62 (1 H, s, CH=N). Treatment with aqueous sodium hydroxide gave *N*-(3-phenyl-2-isoquinolinio)ethoxyformamide (5e) (74%), m.p. 140–141 °C (from ethyl acetate) (Found: C, 73.8; H, 5.5; N, 9.5. $C_{18}H_{16}N_2O_2$ requires C, 73.7; H, 5.8; N, 9.5%; ν_{\max} (Nujol) 1 632 cm^{-1} (C=O); δ_H 1.15 (3 H, t, *J* 7

* The product was found to undergo partial decomposition during chromatography on silica gel. The non-chromatographic work-up adopted for experiments (vi) and (vii) avoided this problem and also possible loss of deuterium from the product of reaction (vii).

H_z, CH₂CH₃), 4.02 (2 H, q, *J* 7 Hz, CH₃CH₂), 7.28–8.10 (10 H, m, ArH), and 9.45 (1 H, s, CH=N).

(ii) Ethyl chloroformate (0.2 ml) was added to a solution of the diazepine (1) (0.22 g, 1.0 mmol) in benzene (5 ml) at room temperature and the mixture was stirred for 17 h. The precipitate was filtered off (0.21 g), dissolved in water (15 ml), and basified with aqueous sodium hydroxide (2M; 10 ml). Extraction with dichloromethane gave an oil (0.16 g) which was chromatographed on silica. Elution with 80 vol% ether in light petroleum gave unchanged 4-phenyl-5*H*-2,3-benzodiazepine (0.06 g, 27% recovery), m.p. 148–150 °C, and elution with 20 vol% methanol in ethyl acetate gave *N*-(3-phenyl-2-isoquinolinio)ethoxyformamidine (0.083 g, 27%), m.p. 140–141 °C, identical with that obtained in reaction 5(i). Evaporation of the filtrate gave a solid which, by chromatography (silica; 80 vol% ether in light petroleum) gave (a) 15,16-bis(ethoxycarbonyl)-5,6,11,12-tetrahydro-13,18-diphenyl-5,12:11,6-bis(hydrazin-1'-yl-2'-ylidenemetheno)dibenzo[a,e]cyclo-octene (7e) (0.072 g, 25%), m.p. 275–276 °C (from propan-2-ol-ethyl acetate) (Found: *M*⁺, 584.245 731. C₃₆H₃₂N₄O₄ requires *M*, 584.242 341); *v*_{max}. (Nujol) 1 695 cm⁻¹ (C=O); δ_H (100 MHz) 1.28 (6 H, t, *J* 7 Hz, 2 × CH₂CH₃), 4.25 (4 H, q, *J* 7 Hz, 2 × CH₂CH₃), 5.14 (2 H, d, *J* 12 Hz, 6- and 12-H), 6.37 (2 H, d, *J* 12 Hz, 5- and 11-H), and 6.90–7.60 (18 H, m, ArH); and (b) 5,14-bis(ethoxycarbonyl)-4,5,8,9-tetrahydro-2,7-diphenyl-4,8-*o*-benzeno-3,9-imino-3*H*-3,5,6-benzotriazacycloundecine (6e) (0.039 g, 13%), m.p. 124 °C (Found: *M*⁺, 584.241 123. C₃₆H₃₂N₄O₄ requires *M*, 584.242 341); *v*_{max}. (Nujol) 1 700br and 1 715br cm⁻¹ (C=O); δ_H (100 MHz) 1.32 (3 H, t, *J* 7 Hz, CH₂CH₃), 1.39 (3 H, t, *J* 7 Hz, CH₂CH₃), 4.15 (2 H, m, CH₂CH₃), 4.35 (2 H, q, *J* 7 Hz, CH₂CH₃), 4.60 (1 H, d, *J* 5 Hz, 8-H), 5.68 (1 H, s, 4-H), 6.22 (1 H, d, *J* 5 Hz, 9-H), and 6.50–7.90 (19 H, m, ArH and 1-H).

(iii) A reaction similar to 5(ii) but carried out with the solution at reflux temperature gave 2-ethoxyformamido-3-phenylisoquinolinium chloride (4e) (0.176 g, 54%) as a precipitate. The filtrate was evaporated and a ¹H n.m.r. spectrum of the residue showed it to be a complex mixture containing a small amount of (6e) but none of (7e).

6. *Ethyl malonyl chloride* (with D. Skinner*). A solution of the diazepine (1) (0.733 g, 3.33 mmol) in benzene (10 ml) was added to ethyl malonyl chloride (6.0 g, 4.0 mmol). On keeping the mixture overnight crystals were deposited which, on recrystallisation from ethanol-dichloromethane, gave 15,16-bis(ethoxycarbonyl)acetyl-5,6,11,12-tetrahydro-13,18-diphenyl-5,12:11,6-bis(hydrazin-1'-yl-2'-ylidenemetheno)dibenzo[a,e]cyclo-octene (7f) [0.64 g, 56%], m.p. 250 °C (Found: C, 71.6; H, 5.4; N, 8.1. C₄₀H₃₆N₄O₆ requires C, 71.8; H, 5.4; N, 8.4%); *v*_{max}. (Nujol) 1 740 cm⁻¹ (C=O); δ_H (100 MHz) 1.06 (6 H, t, *J* 7 Hz, 2 × CH₃CH₂), 3.32 (2 H, d, *J* 15 Hz, 2 × CHHCO), 3.56 (2 H, d, *J* 15 Hz, 2 × CHHCO), 4.00 (4 H, q, *J* 7 Hz, 2 × CH₃CH₂), 5.14 (2 H, d, *J* 11 Hz, 6- and 12-H), 6.64 (2 H, d, *J* 11 Hz, 5- and 11-H), and 6.90–7.55 (18 H, m, ArH); δ_C (20 MHz) 13.8 (CH₂CH₃), 41.9 (CH₂CO), 50.1 (C-6 and -12), 60.8 (CH₂CH₃), 61.0 (C-5 and -11), 126.5, 128.3, 128.5, 129.0, 129.3, 130.6, 133.8, 137.1, 139.5, 145.0, 167.4, and 169.4 p.p.m.

7. *Toluene-4-sulphonyl chloride*. A solution of the diazepine (1) (0.44 g, 2.0 mmol) in benzene (20 ml) was added during 1 h to a stirred solution of toluene-4-sulphonyl chloride (2.4 g, 12.5 mmol) in benzene (20 ml). The mixture was boiled under reflux for 8 h. Filtration and crystallisation gave 3-phenyl-2-(4-tolylsulphonamido)isoquinolinium chloride (0.51 g, 62%), m.p. 219–220 °C (decomp.) (from ethanol) (Found: C, 64.1; H, 4.7;

N, 6.7. C₂₂H₁₉ClN₂O₂S requires C, 64.3; H, 4.7; N, 6.8%); *v*_{max}. (Nujol) 3 400 (NH), 1 335, and 1 170 cm⁻¹ (SO₂); δ_H [100 MHz; (CD₃)₂SO] 2.31 (3 H, s, Me), 6.95–8.70 (15 H, m, ArH and NH), and 9.93 (1 H, s, CH=N). Treatment with aqueous sodium hydroxide (2*M*) gave *N*-(3-phenyl-2-isoquinolinio)toluene-4-sulphonamidate (79%), m.p. 219–220 °C (from methanol) (Found: C, 70.7; H, 4.9; N, 7.4. C₂₂H₁₈N₂O₂S requires C, 70.6; H, 5.1; N, 7.5%); *v*_{max}. (Nujol) 1 275 and 1 140 cm⁻¹ (SO₂); δ_H (100 MHz) 2.23 (3 H, s, Me), 6.60–8.30 (14 H, m, ArH), and 9.65 (1 H, s, CH=N).

Crystal Data for the Dimer (6a).—C₃₄H₂₈N₄O₂·C₂H₅OH, *M*_r = 570.7, space group *P*2₁/*c*, *a* = 15.924(6), *b* = 9.089(5), *c* = 21.319(6) Å, β = 109.35(6)°, *V* = 2 911 Å³, *Z* = 4, *D*_c = 1.30 g cm⁻³, *F* = 1 208, *t* = 20 °C, Mo-*K*_α radiation, λ = 0.710 69 Å, μ(Mo-*K*_α) = 0.8 cm⁻¹, *R* = 0.079 calculated from 2 802 observed unique reflections.

Well formed, clear, monoclinic crystals were grown from ethanol. Diffraction intensity fell off rapidly with increasing angle, suggesting disorder, and a large crystal of dimensions 0.7 × 0.7 × 0.4 mm was therefore chosen for data collection. Data from layers *h*0*l* through to *h*10*l* (2θ_{max} = 50°) were collected on a Stoe two-circle diffractometer. Of the 4 600 unique reflections collected, 2 800 had *I* > 3σ(*I*). The positions of all non-hydrogen atoms were determined by direct methods using MULTAN.⁷ Subsequent structural refinement was carried out using SHELX 76.⁸ Most of the hydrogen atoms were located on difference Fourier maps and were included in the structure factor calculation with fixed positions and fixed isotropic thermal parameters. The hydrogen atoms on the two methyl groups and on one of the phenyl rings were included in idealised calculated positions. All non-hydrogen atoms were refined anisotropically and in the final cycles of full-matrix least-squares refinement the mean shift over estimated error for the 392 parameters was < 0.10. The highest peaks in the final difference map were *ca.* 0.5 e Å⁻³ and were in the vicinity of the badly disordered ethanol molecule. The most reasonable model for the solvent molecule was obtained by refining four atoms with carbon scattering factors and anisotropic thermal parameters. These four atoms approximated to two partially occupied overlapping ethanol molecules O(91)–C(92)–C(93) and C(92)–C(93)–O(94). The weighting scheme which gave the best analysis of variance in ranges of |*F*| and in θ was ω = 1/[σ²(*F*) + 0.0035 *F*²] and gave a final *R* value of 0.079 and *R'* of 0.112. Fractional co-ordinates of all non-H atoms are given in Table 1. Bond lengths and angles and selected torsion angles are given in Table 2. A full list of fractional co-ordinates for H atoms, and co-ordinates and thermal parameters for non-H atoms, along with tables of calculated and observed structure factors have been deposited as a Supplementary Publication [Sup No. 23975 (22 pp)][†]

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† For details of the Supplementary Publications Scheme, see Instructions for Authors (1984), *J. Chem. Soc., Perkin Trans. 1*, 1984, Issue 1.