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REACTION OF DIAZOMETHANE WITH 2-METHYL-6,7-METHYLENEDIOXY-3,4-DIHYDRO-ISOQUINOLINIUM PERCHLORATE

RING EXPANSION TO 3-BENZAZEPINE AND 3-BENZAZOCINE DERIVATIVES*

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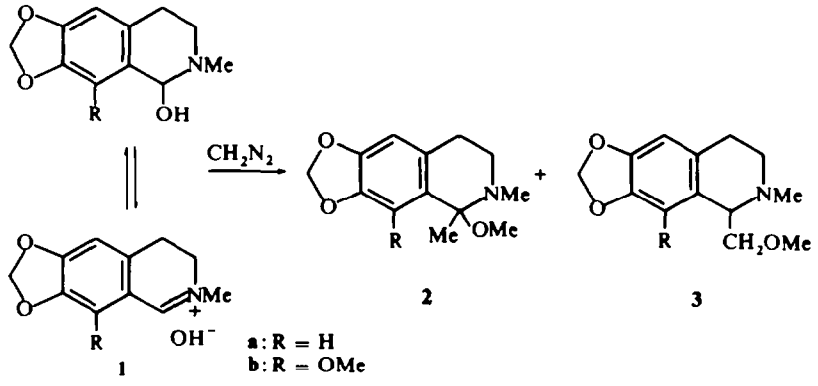
Abstract—Treatment of 2-methyl-6,7-methylenedioxy-3,4-dihydroisoquinolinium perchlorate (**7**) with diazomethane afforded a mixture of aziridinium salts (**8** + **9**) which underwent reaction with MeOH to produce the 1,2,4,5-tetrahydro-3*H*-3-benzazepine (**10a**) and 1,2,4,5,6-pentahydro-3*H*-3-benzazocine (**11a**) derivatives. Similar treatment of **8** + **9** with water gave **10b** and **11b**. LAH reduction of **8** + **9** gave **12** and **13b**. Compound **10a** was converted to **13a** and both **13a** and **13b** were synthesized by a route (**14** → **15** → **16** → **13**) involving a photocyclization reaction as the key step.

DURING an investigation dealing with alkaloid structural elucidation, Pfeifer *et al.* observed that treatment of hydrastinine (**1a**) and cotarnine (**1b**) with diazomethane produced the tetrahydroisoquinoline derivatives **2a**, **3a** and **2b**, **3b** respectively.[1] Furthermore, the Czech–German group was able to extend the reaction to other diazoalkanes (diazoethane, diazopropane, diazoisopropane and phenyl diazomethane) except that in each of these cases only one major product of the structural type **3** was isolated. All of these reactions also yielded two or more minor products which were not characterized. We wish to report that the reaction of 2-methyl-6,7-methylene-dioxy-3,4-dihydroisoquinolinium perchlorate (**7**) with diazomethane takes an entirely



1 **2** **3**

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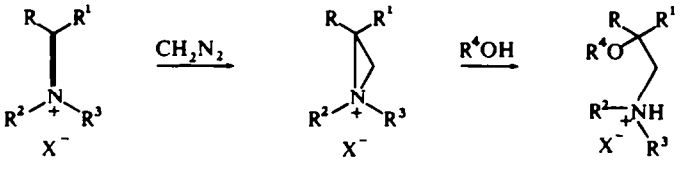
different course from that described by Pfeifer and leads to the aziridinium salts **8** and **9**. Additionally, we present results concerning the ring expansion reactions of these salts under mild solvolytic conditions to yield 3-benzazepine and 3-benzazocine derivatives, **10** and **11** respectively.

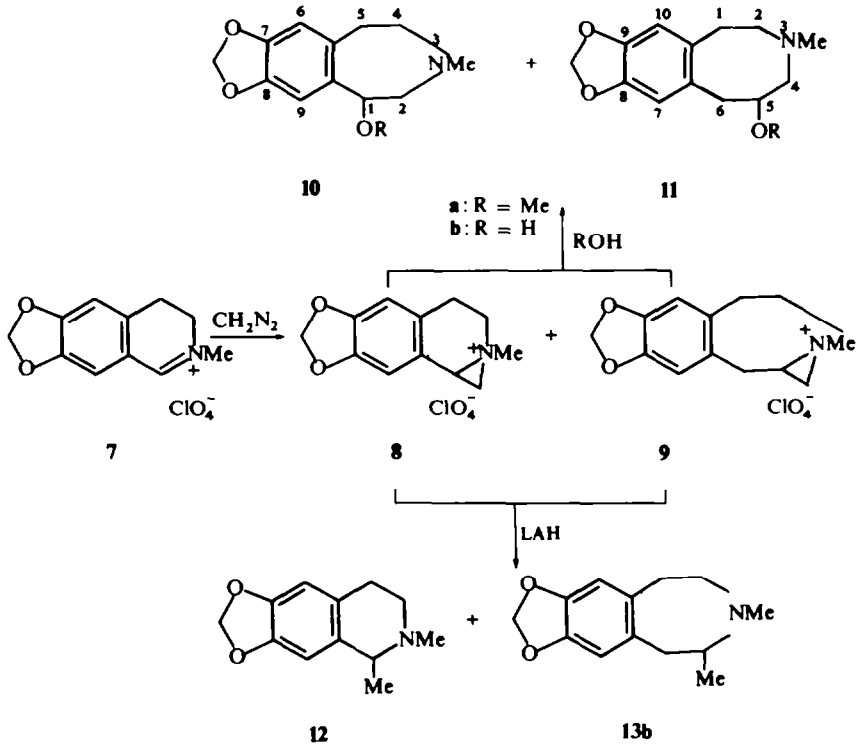
Some time ago, Leonard and his students reported that the reaction of simple imminium perchlorates (**4**) with diazomethane yielded the corresponding aziridinium salts (**5**).[2] Furthermore, these workers found that in non-nucleophilic media these aziridinium salts underwent ring opening to yield products which may be interpreted as resulting from the most stable carbonium ion (e.g., **5** → **6** when R = R^1 = alkyl group). We became interested in effecting a similar reaction sequence with a 3,4-dihydroisoquinolinium salt (**7**) as a means of producing 3-benzazepine systems (**10**). Motivation for this proposal was derived from the following considerations: (a) the 3-benzazepine skeleton forms an important part of the rhoeadine[3] and of the cephalotaxine[4] alkaloids; and (b) among the isomeric benzazepines, the type represented by **10** appears to be most lacking in general preparatory methods.[5]



4 **5** **6**

Treatment of a benzyl alcohol solution of **7** with excess ethereal diazomethane gave a yellow perchlorate salt. This material lacked C=N absorption in the IR spectrum and showed an 89% aziridinium ion activity by standard thiosulfate titration.[2a] Attempts to recrystallize this substance failed and analytical data on partially purified material gave values which were intermediate for the incorporation of one to two moles of diazomethane into **7**. By fractional crystallization, a substance was obtained whose elemental analysis corresponded to the molecular formula of compound **9**. We therefore assumed that the yellow substance was a mixture of aziridinium salts **10a** and **11a** (Scheme I) and we were forced to attempt the ring expansion reactions[2] on this mixture with the expectation that the resulting tertiary amines would be more amenable to separation procedures.

Brief exposure of the crude product from the reaction of **7** with diazomethane to absolute methanol gave a mixture of two oily substances in the approximate ratio of 1:1 (32% overall yield) which were shown to have structures **10a** and **11a** on the basis of the following spectral and chemical evidence. Compound **10a** formed a crystalline methiodide which showed analysis consistent with the formula $C_{14}H_{20}INO_3$. It had an uninformative IR spectrum and its UV spectrum was simply characteristic of a methylenedioxybenzene derivative. However, its NMR spectrum was particularly revealing in that it showed absorption at τ 5·77 (t, 1H, J = 5 Hz) assignable to the X portion of an ABX pattern. The alternate and less likely[2a] mode of ring cleavage of the presumed aziridinium salt **8** would have produced the tetrahydroisoquinoline derivative **3a** which was in fact reported by Pfeifer.[1] The published NMR spectrum of **3a** did not show any signals at lower field than 6 τ and was otherwise

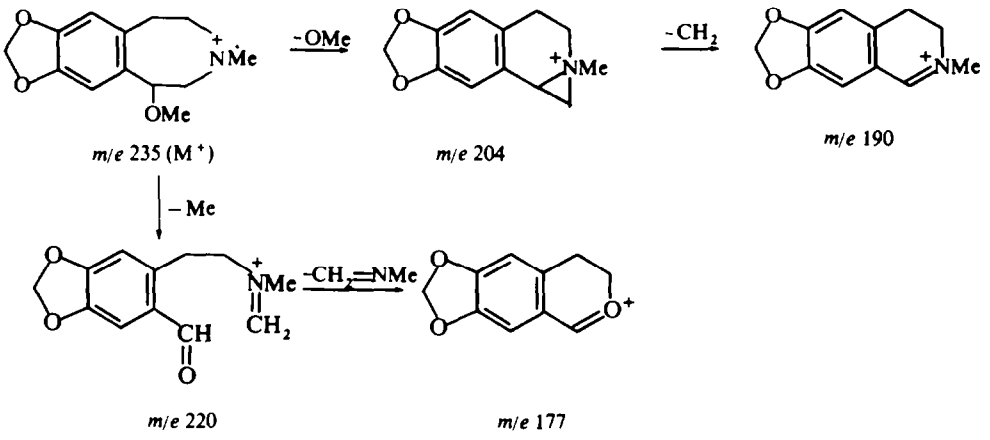


SCHEME 1

substantially different from that observed for **10a**. The mass spectrum showed the correct molecular ion and offered further support for the 3-benzazepine (**10a**) formulation (Scheme II, Table 1). The most intense peak appears at *m/e* 204 (M^+—OMe) with a weak spike at *m/e* 190. Notably, the base peak is at *m/e* 177, explicable by the dihydrobenzisopyrylium ion in Scheme II, which is consistently observed for 3-benzazepines with C-1 oxygen functions.[3,6] On the other hand, extensive studies on the mass spectral behavior of 1-substituted tetrahydroisoquinolines[1,7] have shown that invariably the base peak in these systems appears at *m/e* 190. Clearly, the spectral data for the methanolysis product strongly support structure **10a**.

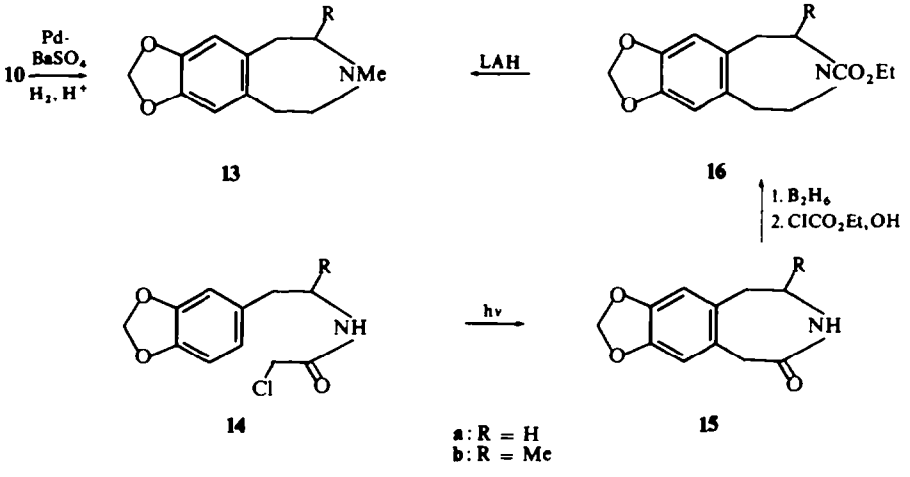
Conclusive chemical evidence for the benzazepine structure **10a** was secured by a simple degradation (Scheme III). Catalytic hydrogenolysis of **10a** gave **13a** which was shown to be identical with an authentic sample prepared from **14a** using the recently discovered photocyclization reaction of α-chloroamides[8] as the key step in the sequence.

The second product isolated from methanolysis of the mixture of aziridinium salts (**8** and **9**) also gave a crystalline methiodide, $C_{15}H_{22}INO_3$. It was assigned the 3-benzazocine structure **11a** on the basis of the following evidence. The NMR spectrum of the free base showed, besides the characteristic peaks due to aromatic, methylenedioxy, O-Me, and N-Me functions, absorption of τ 6·66–7·73 (br m, 9H, aliphatic protons). The absence of signals at lower field than that for the OMe



SCHEME II

function allowed assignment of the OMe function at C-5 rather than at C-4 or C-7. Additional evidence against the C_4-OMe formulation was the fact that the compound did not behave like a carbinol amine ether. The mass spectral data offered further support for the proposed structure (**11a**) (Table I). The fragmentation pattern is seen to be very similar to that observed for the benzazepine system **10a** except that each major peak is displaced by 14 units to higher mass values. Therefore a similar fragmentation pattern may be operating which is triggered by the ready loss of the OMe function due to its location β to the nitrogen.*



SCHEME III

* No mass spectral data on benzazocine systems is available although a compound closely related to **11** has been recently prepared.[9] H.O.B. thanks Professor M. Hesse for comments regarding the mass spectral data.

We sought to obtain corroborative evidence for the structures **8** and **9** by an alternate chemical method. Leonard had reported that LAH reduction of simple aziridinium salts (**5**) generally leads to S_N2-like ring opening at the least substituted carbon.[10] On this basis, we expected that like reduction of the mixture **8** + **9** would lead to compounds **12** and **13b** respectively (Scheme I). In the event, the two predicted tertiary bases were obtained in 62% overall yield. The major product (42%) was shown to be 1,2-dimethyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (**12**) by spectral evidence and by the preparation of the known crystalline methiodide (Experimental).

The second product showed an NMR spectrum which was equally compatible with the isomeric benzazepines **13b** and **17**. Furthermore, the mass spectrum did not offer an unambiguous assignment (Table I). Therefore, even though the formation of **17** by LAH reduction of **9** would be mechanistically obscure, it was decided to confirm structure (**13b**) by synthesis. This was achieved by an analogous set of reactions to that employed for the preparation of **13a** (Scheme III, series *b*).

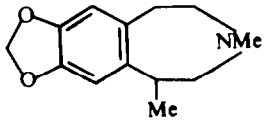


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TABLE 1. MASS SPECTRAL DATA OF 3-BENZAZEPINE AND 3-BENZAZOCINE DERIVATIVES*

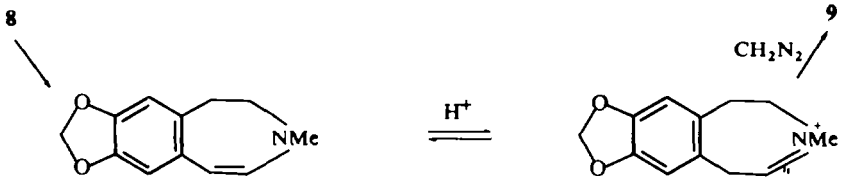
Compound	*m/e* (% relative abundance)
10a	235 (M^+, 25), 220 (25), 204 (100), 203 (28), 190 (30), 177 (80), 162 (30), 161 (68), 149 (28).
10b	221 (M^+, 100), 204 (82), 190 (37), 177 (62), 163 (36), 162 (50), 161 (36), 149 (50).
11a	249 (M^+, 100), 234 (25), 218 (61), 217 (30), 191 (40), 190 (60), 182 (55), 166 (39), 165 (30), 163 (75), 161 (60), 149 (35), 148 (50), 147 (35).
11b	235 (M^+, 90), 204 (75), 190 (35), 163 (25), 161 (40), 149 (100), 148 (40).
13a	205 (M^+, 75), 204 (25), 203 (100), 162 (40), 161 (30), 149 (90).
13b	219 (M^+, 100), 204 (70), 163 (95), 162 (61), 161 (30), 149 (25).

* Only those fragment ions of 25% or higher relative abundance above *m/e* 140 are listed.

The success of the solvolytic ring expansion **8** + **9** → **10a** + **11a** in methanol solution encouraged us to attempt a similar reaction in aqueous medium. Indeed, brief treatment of the aziridinium salt mixture with hot water yielded the corresponding 1-hydroxy-3-benzazepine and 5-hydroxy-3-benzazocine derivatives, **10b** and **11b** (1:1, 37% yield). The structures are assigned by analogy to the products of the methanolysis reaction and are supported by analytical and spectral data (Experimental).

The difference between our results and those of Pfeifer[1] may be explained in terms

of the nature of the starting material. Whereas Pfeifer's cases involve a reaction of diazomethane with an equilibrating mixture of the imminium salt and the corresponding carbinol amine (**1**), our example (**7**), whose use was dictated by Leonard's wide experience with aziridinium perchlorates,[2] ensured that reaction with diazomethane would take place only with the imminium salt species. Therefore, different mechanisms are operative and give rise to different observed products.* The formation of compound **9** may be explained by diazomethane addition to **19** which, in turn, could arise *via* a rearrangement-protonation sequence **8** → **18**. Leonard has shown that in the case of simple azirdinium salts such a process occurs albeit at higher temperatures.[2b] In our case, this process is no doubt facilitated by the modest energy requirement for the initial ring opening of **8**.



18 **19**

The synthetic utility of the ring expansion reactions is limited by the formation of mixtures of products. Finally, we note that attempts to carry out the reaction of **7** with phenyl diazomethane resulted in the recovery of the starting material.

EXPERIMENTAL

Microanalyses were performed by Microtech Laboratories, Inc., Skokie, Ill. and Dr. F. Pascher, Bonn, West Germany. Mps were measured on a Fisher–Johns apparatus and are uncorrected. IR spectra were determined on a Beckmann IR-5A instrument in $CHCl_3$ soln unless otherwise stated. UV spectra were recorded on a Cary Model 14 spectrophotometer in EtOH soln. NMR spectra were obtained with Varian T-60 and HA-100 spectrometers using TMS as internal standard in $CDCl_3$ soln unless otherwise indicated. Mass spectra were determined with a Hitachi–Perkin–Elmer RMU-6E spectrometer. Chromatography was carried out with silica gel obtained from Brinkmann (Canada) Ltd. Thick-layer separations were effected in a benzene-methanol-acetone (5:3:1) mixture[1]. Photochemical reactions were carried out with a 200-W Hanovia mercury discharge tube in a water-cooled quartz immersion well.

Preparation of 2-methyl-6,7-methylenedioxy-3,4-dihydroisoquinolinium perchlorate (**7**) N-(3,4-Methylenedioxyphenethyl)formamide[11] (5·6 g, 29 mmol) was mixed with 55 g polyphosphate ester[12] and heated in an oil bath at 80° for 11 hr. Normal isolation procedure gave 3·64 g (72%) 6,7-methylenedioxy-3,4-dihydroisoquinoline (norhydrastinine) which was directly converted in 80% yield into its methiodide salt, mp 230–232° (lit[13] mp 234°). The methiodide was then treated with anhyd silver perchlorate using the procedure of Leonard[14] to give a 87·5% yield of **7**, mp 178–181°; IR (nujol) 1680 (C=$\overset{+}{N}$<) cm^{-1}; UV (max) 250 (16,000), 294 (4900), 363 (2500) mμ; NMR (acetonitrile d-3) τ 1·50 (s, 1, H_1), 2·83 (s, 1, H_9), 3·05 (s, 1, H_6), 3·85 (s, 2, $-OCH_2O-$), 6·10 (t, 2, J = 5 Hz, $-CH_2N$), 6·35 (s, 3, NCH_3), 6·84 (t, 2, J = 5 Hz, $-\underline{C}H_2CH_2N$). Found: C, 46·11; H, 4·22; Cl, 12·02; N, 4·83. Calcd. for $C_{11}H_{12}ClNO_6$: C, 45·61; H, 4·15; Cl, 12·24; N, 4·84%).

Reaction of 2-methyl-6,7-methylenedioxy-3,4-dihydroisoquinolinium perchlorate (**7**) *with diazomethane*

The formation of aziridinium salts **8** *and* **9**. To a soln of **7** (435 mg; 1·5 mmol) in abs benzyl alcohol (20 ml)

* It is noteworthy that structure **10a** was considered by Pfeifer[1] and, in fact, may have been one of the uncharacterized minor constituents of his reaction mixture (based on a comparison of R_f values in the same solvent system).

was added with stirring at 0–5° a 0·17 molar soln of ethereal diazomethane (12 ml; 2 mmol). After gas evolution ceased, the soln was diluted with 200 ml abs ether and the resulting ppt was collected to yield 420 mg of solid, mp 102–104° whose IR spectrum (nujol) showed the absence of the 1680 cm^{-1} band. Rapid repeated recrystallization from acetone-benzene gave an analytical sample of **9**, mp 166–169°. Found: C, 49·69; H, 5·09; Cl, 10·31; N, 4·33. Calcd. for $C_{12}H_{14}ClNO_6$: C, 49·14; H, 5·08; Cl, 11·16; N, 4·41%).

Methanolysis of the aziridinium perchlorate mixture (**8**, **9**)

1-*Methoxy*-3-*methyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* (**10a**) *and* 3-*methyl*-6-*methoxy*-8,9-*methylenedioxy*-1,2,4,5,6-*pentahydro*-3H-3-*benzazocine* (**11a**). A soln of the mixture **8** + **9** (200 mg) in abs MeOH (4 ml) was refluxed for 2 hr. The soln was concentrated *in vacuo* and the residue was dissolved in methylene chloride and washed with 5% $NaHCO_3$ aq. The methylene chloride soln was taken to dryness *in vacuo* to give an oil which was subjected to thick-layer chromatography. Two fractions were isolated:

Fraction 1 yielded 29 mg (19%) of **10a** as a yellow oil which gave a crystalline methiodide salt, mp 192–196°; (ethanol–ether), UV (max) 223 (13,400), 290 (3600) mμ. (Found: C, 45·29; H, 5·30; I, 33·44; N, 3·54. Calcd. for $C_{14}H_{20}INO_3$: C, 44·58; H, 5·34; I, 33·64; N, 3·71%).

Fraction 2 gave 36 mg (23%) of **11a** as a yellow oil which furnished a methiodide, mp 162–165° (acetone-ether); UV (max) 223 (13,500), 290 (3700) mμ. (Found: C, 45·82; H, 5·43; I, 31·57; N, 3·56. Calcd. for $C_{15}H_{22}INO_3$: C, 46·05; H, 5·67; I, 32·43; N, 3·58%).

Catalytic reduction of 1-*methoxy*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* (**10a**)

A soln of **10a** (20 mg) in glacial AcOH (2 ml) containing 2 drops 70% perchloric acid was hydrogenated over 5% Pd on $BaSO_4$ at atm press and 70° for 2·5 hr.[15] The catalyst was removed by filtration, the filtrate was basified with 20% NaOH aq. and extracted with ether to give 14 mg of **13a** whose methiodide was found to be identical by mp and mixture mp determinations to authentic material prepared below.

Lithium aluminum hydride reduction of the aziridinium perchlorate mixture (**8** + **9**)

1,2-*Dimethyl*-6,7-*methylenedioxy*-1,2,3,4-*tetrahydroisoquinoline* (**12**) *and* 2,3-*dimethyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* (**13b**). To a soln of the mixture **8** + **9** (310 mg, *ca* 1 mmol) in dry THF (15 ml) was added LAH (114 mg, 3 mmol). The soln was refluxed for 24 hr and processed by a standard method to yield 170 mg of an oil which was subjected to thick-layer chromatography. Two fractions were isolated:

Fraction 1 gave 43 mg (42%) of **12** as an oil whose methiodide derivative was shown to be identical to an independently synthesized sample (see below).

Fraction 2 gave 22 mg (20%) of **13b** as a yellow oil whose methiodide derivative was shown to be identical to authentic material as prepared below.

1,2-*Dimethyl*-6,7-*methylenedioxy*-1,2,3,4-*tetrahydroisoquinoline* (**12**)

Compound **12** was prepared in 69% yield from **7** by a literature method.[21] It was obtained as a homogeneous colorless oil: NMR τ 3·44 and 3·50 (2s, 2, H_5 and H_8), 4·16 (s, 2, —OCH_2O—), 6·50 (q, 1, J = 6 Hz, C_1—H), 6·85–7·44 (m, 4, —CH_2—), 7·56 (s, 3, NCH_3), 8·70 (d, 3, J = 6 Hz, C_1—CH_3); mass spectrum *m/e* (relative intensity) 205 (38), 204 (20), 191 (64), 190 (100), 162 (32). The methiodide derivative was recrystallized from acetone–benzene and showed mp 241–243° (lit[22] mp 229–230°).

N-*Chloroacetyl*-3,4-*methylenedioxyphenethylamine* (**14a**)

To a stirred soln of 3,4-methylenedioxyphenethylamine[16] (8·25 g, 50 mmol) and pyridine (4·34 g, 55 mmol) in dry methylene chloride soln (80 ml) cooled in an ice bath was added dropwise chloroacetyl chloride (6·2 g, 55 mmol) over a period of 30 min. The soln was stirred for 3 hr and washed consecutively with water, 1N HCl, and 5% $NaHCO_3$ aq. The methylene chloride soln was dried (Na_2SO_4) and evaporated to dryness *in vacuo*. The remaining oil was distilled, bp 180–182° (0·1 mm), to give 5·7 g (48% of product. Recrystallization from benzene-light petroleum (35–60°) gave colorless prisms of **14a** mp 70–71°; IR 3400 (NH), 1660 (C=O) cm^{-1}; NMR τ 3·23 (br s, 3, aromatic protons), 3·37 (br s, 1, NH) (NH), 4·10 (s, 2, —OCH_2O—), 5·89 (s, 2, —$COCH_2Cl$), 6·37 (q, 2, J = 7 Hz, —CH_2N), 7·13 (t, 2, J = 7 Hz, —$C\underline{H}_2CH_2N$). (Found: C, 54·79; H, 4·90; Cl, 14·60; N, 5·69. Calcd for $C_{11}H_{12}ClNO_3$: C, 54·67; H, 5·01; Cl, 14·67; N, 5·80%).

N-*Chloroacetyl*-3,4-*methylenedioxyphenylisopropylamine* (**14b**)

β-(3,4-Methylenedioxyphenyl)isopropylamine, bp 148–150° (12 mm) [lit[17] 143–145° (11 mm)] was

prepared in 84% yield from 1-piperonylidinenitroethane[18] according to a literature method.[19] Compound **14b** was obtained in 95% yield in the manner described for the preparation of **14a**. Recrystallization from benzene-light petroleum (35–60°) gave an analytical sample, mp 74–75°; IR 3400 (NH), 1680 (C=O) cm^{-1}; NMR τ 3·3 (m, 3, aromatic protons), 4·08 (s, 2, $-OCH_2O-$), 5·8 (m, 1, $-CH_2CH(N)CH_3$), 6·02 (s, 2, $-COCH_2Cl$), 7·25 (m, 2, $-CH_2CH(N)CH_3$), 8·85 (d, 3, J = 7 Hz, $-CH_3$). (Found: C, 56·53; H, 5·31; Cl, 13·95; N, 5·44. Calcd for $C_{12}H_{14}ClNO_3$: C, 56·37; H, 5·52; Cl, 13·86; N, 5·48%).

TABLE 2. NMR SPECTRA OF SOME 3-BENZAZEPINE AND 3-BENZAZOCINE DERIVATIVES

Compound	Chemical shift, τ values $-OCH_2O-$[a]	$-NCH_3$[b]	Other
10a	4·13	7·6	3·22 and 3·45 (2s, 2, H_6 and H_9), 5·77 (t, 1, J = 5 Hz, C_1-H), 6·67 (s, 3, OCH_3), 6·7–7·5 (m, 6, $-CH_2-$)
10b	4·2	7·72	3·29 and 3·5 (2s, 2, H_6 and H_9), 5·5 (d, 1, J = 7 Hz $-CH(OH)CH_2$), 6·12[c] (br s, 1, OH), 6·6–7·76 (m, 6, $-CH_2-$).
11a	4·13	7·6	3·44 (s, 2, H_7, H_{10}), 6·6 (s, 3, OCH_3), 6·66–7·73 (m, 9, $-CH_2-$).
11b	4·13	7·66	3·4 and 3·43 (2s, 2, H_7 and H_{10}), 6·3 (m, 1, $-CH(OH)CH_2$), 6·8[c] (br s, 1, OH), 7·14–7·6 (m, 8, $-CH_2-$).
13a	4·22	7·77	3·35 (s, 2, H_6, H_9), 7·17–7·35 (m, 4, $-CH_2-$), 7·5–7·7 (m, 4, $-CH_2NCO_2Et$).
13b	4·07	7·63	3·52 (s, 2, H_6, H_9), 6·8–7·5 (m, 7, $-CH_2-$), 9·17 (d, 3, J = 6 Hz, $CH(CH_3)$).
15a	4·12		3·4 and 3·43 (2s, 2, H_6 and H_9), 3·87[c] (br s, 1, NH), 6·28 (s, 2, $-CH_2CO$), 6·45 (m, 2, $-CH_2N$), 6·96 (m, 2, $-CH_2-$).
15b[d]	4·08		3·34 and 3·4 (2s, 2, H_6 and H_9), 6·23 (s, 2, $-CH_2CO$), 6·37 (m, 1, $CH(CH_3)$), 7·1 (m, 2, $-CH_2-$), 8·75 (d, 3, J = 7 Hz, $CH(CH_3)$).
16a	4·12		3·4 (s, 2, H_6, H_9), 5·82 (q, 2, J = 7 Hz, $CO_2CH_2CH_3$), 6·43 (t, 4, $-CH_2NCO_2Et$), 7·21 (t, 4, $-CH_2-$), 8·27 (t, 3, J = 7 Hz, $CO_2CH_2CH_3$).
16b	4·1		3·2 and 3·21 (2s, 2, H_6 and H_9), 5·85 (q, 2, J = 7 Hz, $CO_2CH_2CH_3$), 6·8–7·6 (m, 7, $-CH_2-$), 8·75 (t, 3, J = 7 Hz, $CO_2CH_2CH_3$), 8·98 (d, 3, J = 7 Hz, $CH(CH_3)$).

[a] singlet, 2H
[b] singlet, 3H
[c] exchanged with D_2O
[d] NH not detected

7,8-*Methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepin*-2-*one* (**15a**)

A soln of **14a** (241 mg, 1 mmol) in EtOH-water (1:1; 150 ml) was irradiated according to the method of Witkop[20] to yield **15a** (83 mg, 40%). Recrystallization from EtOAc gave an analytical sample, mp 235–237°; IR (nujol) 3200 (NH), 1690 (C=O) cm^{-1}. (Found: C, 64·18; H, 5·34; N, 6·84. Calcd for $C_{11}H_{11}NO_3$: C, 64·38; H, 5·40; N, 6·83%).

4-*Methyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazapin*-2-*one* (**15b**)

Irradiation of **14b** according to the above method afforded **15b** in 13% yield. Recrystallization from EtOAc gave an analytical sample, mp 179–179·5°; IR 3350 (NH), 1660 (C=O) cm^{-1}. (Found: C, 65·53; H, 5·92; N, 6·53. Calcd for $C_{12}H_{13}NO_3$: C, 65·74; H, 5·98; N, 6·39%).

3-*Ethoxycarbonyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* (**16a**)*

The diborane reduction of **15a** was carried out according to the method of Witkop.[20] From **15a** (295 mg, 1·42 mmol) there was obtained 7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* (200 mg; 72·5%) as an oil which showed NMR τ 3·47 (s, 2, aromatic protons), 4·13 (s, 2, —OCH_2O—), 6·05 (s, 1, NH, exchanged with D_2O), 7·17 (br s, 8, —CH_2—) and which was used without further purification in the next reaction. To a soln of the above compound (235 mg; 1·22 mmol) in benzene (25 ml) was added freshly distilled ethyl chloroformate (162 mg; 1·5 mmol) while the temp was held below 10°. After 30 min the mixture was diluted with water and extracted with benzene. The benzene extract was washed successively with 5% $NaHCO_3$ aq. and water and then dried (Na_2SO_4). The benzene soln was taken to dryness *in vacuo* to yield 246 mg (77%) of crystalline **16a**. Sublimation (0·01 mm, 145°) gave an analytical sample, mp 96–97°; IR 1690 (C=O) cm^{-1}. (Found: C, 63·94; H, 6·42; N, 5·28. Calcd for $C_{14}H_{17}NO_4$: C, 63·87; H, 6·51; N, 5·32%).

2-*Methyl*-3-*ethoxycarbonyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazapine* (**16b**)

Compound **15b** was reduced with diborane in the manner described above to give 2-*methyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* as a homogeneous oil in 74% yield. This material (IR 3600, 3400 cm^{-1}; NMR τ 3·53 (s, 2, aromatic protons), 4·20 (s, 2, —OCH_2O—), 6·48 (t, 1, J = 6 Hz, —$CH(N)CH_3$), 6·80–7·60 (m, 6, —CH_2—), 8·03 (br s, 1, NH, exchanged with D_2O), 8·92 (d, 3, J = 6 Hz, CH_3) was used without purification for the next reaction. Treatment of this material with ethyl chloroformate as described for the preparation of **16a** gave **16b** in 74% yield as an oil, bp 135–140° (0·15 mm); IR 1680 (C=O) cm^{-1}. (Found: C, 64·97; H, 6·94; N, 5·09. Calcd for $C_{15}H_{19}NO_4$: C, 64·97; H, 6·91; N, 5·05%).

3-*Methyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* (**13a**)

Compound **16a** (177 mg, 0·67 mmol) was reduced with LAH in THF at reflux for 18 hr to give **13a** (116 mg; 84%) as a homogeneous colorless oil. The methiodide salt was recrystallized from EtOH to give an analytical sample, mp 258–260°. (Found: C, 44·96; H, 5·14; I, 36·39; N, 4·00. Calcd for $C_{13}H_{18}INO_2$: C, 44·97; H, 5·22; I, 36·55; N, 4·04%).

2,3-*Dimethyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* (**13b**)

LAH reduction of **16b** according to the above method gave **13b** in 74% yield as an oil, bp 110° (0·01 mm). The methiodide salt was recrystallized from EtOH and showed mp 268–269·5°. (Found: C, 46·60; H, 5·50; I, 35·19; N, 3·75. Calcd for $C_{14}H_{20}INO_2$: C, 46·55; H, 5·58; I, 35·13; N, 3·88%).

Aqueous treatment of the aziridinium perchlorate mixture (**8** + **9**)

1-*Hydroxy*-3-*methyl*-7,8-*methylenedioxy*-1,2,4,5-*tetrahydro*-3H-3-*benzazepine* (**10b**) *and* 3-*methyl*-5-*hydroxy*-8,9-*methylenedioxy*-1,2,4,5,6-*pentahydro*-3H-3-*benzazocine* (**11b**). A soln of the mixture **8** and **9** (400 mg; *ca* 1·3 mmol) in distilled water (10 ml) was heated on a steam bath for 1 hr. The dark red soln was made basic with 2N NaOH and extracted with CH_2Cl_2 to afford 265 mg of a red oil which was subjected to a thick-layer chromatographic separation.

Fraction 1 yielded 65 mg (22%) of **10b** as a homogeneous oil. The methiodide derivative was recrystallized from EtOH and showed mp 242–245°. (Found: C, 43·21; H, 5·03; I, 34·98; N, 4·01. Calcd for $C_{13}H_{18}INO_3$: C, 42·99; H, 4·99; I, 34·94; N, 3·86%).

Fraction 2 gave 43 mg (15%) of **11b** as an oil which yielded a crystalline methiodide derivative, mp 236–238° (acetone–benzene). (Found: C, 44·46; H, 5·38; I, 33·36; N, 3·70. Calcd for $C_{14}H_{20}INO_3$: C, 44·56; H, 5·34; I, 33·64; N, 3·71%).

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