Azabenzocycloheptenones. Part XVII.[1] Some Substitution Reactions in Tetrahydro-1-benzazepin-5-ones

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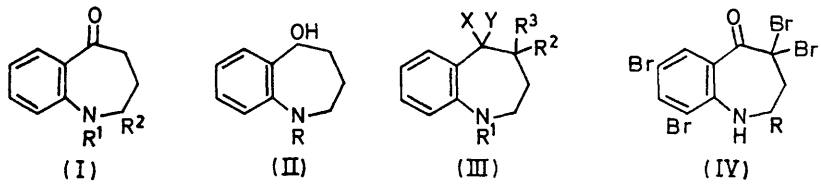
1,2,3,4-Tetrahydro-1-*p*-tolylsulphonyl-1-benzazepin-5-ones have been detosylated by two methods. *N*-Alkylation of 1,2,3,4-tetrahydro-1-benzazepin-5-one and 2,3-dihydro-1*H*-1-benzazepine with several reagents is reported. Substitution of the 4- and 5-positions of 1,2,3,4-tetrahydro-1-*p*-tolylsulphonyl-1-benzazepin-5-one has been studied and several transformation products are described. Dehydrogenation of 5,6-dihydrodibenz[*b,e*]-azepin-11-ones has been re-examined: the products are dibenz[*b,c*]azepin-11-ones.

PREVIOUSLY we have described syntheses [2,3] and dehydrogenation [4-6] of 1,2,3,4-tetrahydro-1-benzazepin-5-ones and we now report our studies into the reactivity of several centres in the seven-membered ring of this series.

Since the most productive synthesis of 1,2,3,4-tetrahydro-1-benzazepin-5-ones produces [2] the *N*-tosyl derivatives (I; R^1 = Ts), it is important to be able to remove the tosyl group. The method employing concentrated hydrochloric acid, acetic acid, and zinc chloride [7] has proved unreliable and we have developed two better methods. First, sulphuric acid in acetic acid [8] is convenient for the *N*-tosyl ketones (I; R^1 = Ts); the optimum time and temperature for each example has to be discovered by experimentation. Second, of wider applicability is sodium in liquid ammonia: thus, while the *N*-tosyl ketone (I; R^1 = Ts, R^2 = H) gives a mixture of the amino-ketone

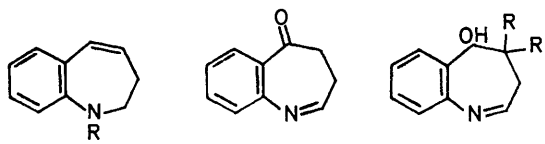


(I) (II) (III) (IV)

(I; $R^1 = R^2$ = H) and the amino-alcohol (II; R = H), the propylene acetal of (I; R^1 = Ts, R^2 = H) reacted with sodium in ammonia to give the acetal of the amino-ketone (I; $R^1 = R^2$ = H) in acceptable yield. The alcohol (II; R = Ts) was smoothly detosylated to (II; R = H) by sodium in ammonia; sulphuric acid in acetic acid was of no use in this case. On the other hand, the αα-dimethyl-ketone (III; R^1 = Ts, $R^2 = R^3$ = Me, X,Y = O) reacted with sodium in ammonia to give only the alcohol (III; R^1 = X = H, $R^2 = R^3$ = Me, Y = OH.

While treatment of the tosyl ketone (I; R^1 = Ts, R^2 = H) with an excess of bromine in chloroform gave a tetrabromoaminoketone [5] (IV; R = H) in good yield, the αα-dimethyl ketone (III; R^1 = Ts, $R^2 = R^3$ = Me, X,Y = O) reacted only sluggishly with bromine giving (presumably) the 7-bromo-tosyl ketone. Thus it seems that this useful detosylation reaction is inhibited when the carbonyl group cannot enolise to react rapidly with bromine: we associate rapid production of hydrogen bromide with successful [5,6] detosylations although the reaction is also inhibited [6] by a methyl group at C-2, *e.g.* in (I; R^1 = Ts, R^2 = Me). The amino-ketone (I; R^1 = H, R^2 = Me) obtained by the sulphuric acid in acetic acid method, did not react with an excess of bromine to give (IV; R = Me); thus the unexpectedly large effects of a methyl group at C-2 are continued [6,9] throughout this series.

Turning to *N*-alkylation, we find that rather forcing conditions are required: thus 2,3-dichloropropene and ethyl bromoacetate both failed to react with the amino-ketone (I; $R^1 = R^2$ = H) but 2-chloro-3-iodopropene reacted slowly when present in considerable excess to give (I; $R^1 = CH_2{:}CCl{\cdot}CH_2$, R^2 = H). Reduction of the latter to the corresponding alcohol (II; R = $CH_2{:}CCl{\cdot}CH_2$) proceeded uneventfully but the alcohol did not react with Lewis acids by ring closure onto the chloropropenyl group (*cf.* ref. 10), instead it underwent



(V) (VI) (VII)

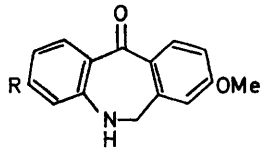
simple dehydration to (V; R = $CH_2{:}CCl{\cdot}CH_2$). 2-Dimethylaminoethyl chloride only reacted with the amino-ketone (I; $R^1 = R^2$ = H) in the presence of sodamide [giving (I; $R^1 = CH_2CH_2NMe_2$, R^2 = H)]

[1] Part XVI, A. McLean and G. R. Proctor, *J.C.S. Perkin I*, 1973, 1084.
[2] I. McCall, G. R. Proctor, and L. Purdie, *J. Chem. Soc.* (*C*), 1970, 1126.
[3] G. R. Proctor, W. I. Ross, and A. Tapia, *J.C.S. Perkin I*, 1972, 1803.
[4] G. R. Proctor, *J. Chem. Soc.*, 1961, 3989.
[5] E. D. Hannah, W. C. Peaston, and G. R. Proctor, *J. Chem. Soc.* (*C*), 1968, 1280.
[6] A. Cromarty, G. R. Proctor, and M. Shabbir, *J.C.S. Perkin I*, 1972, 2012.
[7] W. H. Bell, E. Hannah, and G. R. Proctor, *J. Chem. Soc.*, 1964, 4926.
[8] P. D. Carpenter and M. Lennon, *J.C.S. Chem. Comm.*, 1973, 664.
[9] A. Cromarty, K. E. Haque, and G. R. Proctor, *J. Chem. Soc.* (*C*), 1971, 3536.
[10] D. N. Gupta, I. McCall, A. McLean, and G. R. Proctor, *J. Chem. Soc.* (*C*), 1970, 2191.

but the amine (V; R = H) proved just as unreactive to this reagent [giving (V; R = $CH_2CH_2NMe_2$)] so the lack of reactivity might not be wholly due to the electron-attracting effect of the carbonyl group being transmitted to the nitrogen atom *via* the benzene ring. Contrastingly, however, the amine (V; R = H) could be methylated easily [giving (V; R = Me)]. The amino-ketone (I; $R^1 = R^2 = H$) reacted with dimethyl acetylenedicarboxylate to give the *N*-substituted adduct [I; $R^1 = C(CO_2Me){:}CHCO_2Me$, $R^2 = H$] but the amino-ketone (I; $R^1 = H$, $R^2 = Me$) failed to react.

3,4-Dihydro-1-benzazepin-5-ones (VI) have never been isolated. We find that amino-ketones (I; R^1 = H) cannot be directly dehydrogenated by, for example, manganese dioxide, palladised charcoal, or mercuric acetate.[11] This is in contrast to amino-alcohols (II; R = H) and (III; $R^1 = X = H$, $R^2 = R^3 = Me$, Y = OH) which react with manganese dioxide to give the imino-alcohols (VII; R = H and Me respectively). Repeated attempts to oxidise the alcohol (VII; R = H) led only to decomposition so we conclude that (VI) is reactive.

This was further suggested by the reaction of diethyl azodicarboxylate [12] with the amino-ketone (I; R^1 = H) in chloroform from which only the corresponding hydrazine could be isolated.



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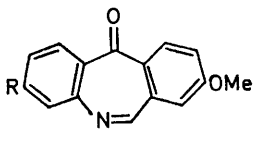
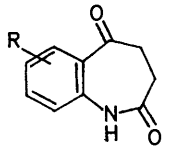


(IX)



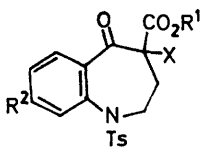
(X)

It is interesting that manganese dioxide is efficaceous in dehydrogenating amino-ketones (VIII; R = H and Cl) to imino-ketones (IX; R = H and Cl) in which C-2 of the seven-membered ring is benzylic. Doubts [13] have been expressed about the veracity of our claim [14] to have synthesised the imino-ketone (IX; R = H) but we have repeated this work and append further details (see Experimental section) along with the preparation of the chloro-compound (IX; R = Cl). It is advantageous to use manganese dioxide prepared by ozonising manganous nitrate.[15] We conclude that substitution of C-2 of the tetrahydro-1-benzazepine system can best be attained [16] *via* the 2-oxo-derivatives (X) for which an excellent general synthesis has recently been published.[17]

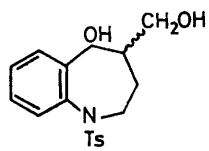
Substitution of the 4-position in tetrahydro-1-benzazepines is straightforward since the β-keto-esters (XI; X = H) are readily available.[2,*] In this way the substituted products (XI; R^1 = Me or Et, R^2 = H, X = $CH_2CCl{:}CH_2$, CH_2CO_2Et, or Me) were made in good yield with 2,3-dichloropropene, ethyl bromoacetate, or methyl iodide respectively. Ester interchange took place on prolonged refluxing in alcohols.

It should be noted, however, that alkaline hydrolysis of the diesters (XI; R^1 = Et and Me, R^2 = H, X = CH_2CO_2Et) yielded the corresponding diacid (XI; $R^1 = R^2$ = H, X = CH_2CO_2H) rather than the expected decarboxylated product. These keto-esters (XI; X = H) exist largely as enols which may explain why they fail to undergo some typical reactions of β-keto-esters, *e.g.* with guanidine and acetamidine; [18] but it is not clear why the keto-ester (XI; R^1 = Et, $R^2 = X = H$) is attacked by sodium borohydride yielding a diol (XII). Acid treatment of the latter in aromatic solvents caused reaction with the solvent, presumably *via* an allylic carbonium ion formed from a dehydrated intermediate.

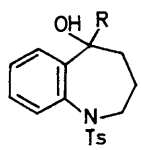
An interesting exception to the general C-4 alkylation behaviour was encountered using dimethyl acetylenedicarboxylate. In this case the product still contained the enolisable β-keto-ester chromophore although the molecular formula was that expected from a 1 : 1 adduct with (XI; R^1 = Et, $R^2 = X = H$). This result can only be explained [19] by assuming that a polar addition reaction took place leading to eventual ring-expansion to (XIV) *via* the cyclobutene (XV). Precedents exist for such reactions with enamines. We are looking into the generality of this reaction.[20]



(XI)



(XII)



(XIII)

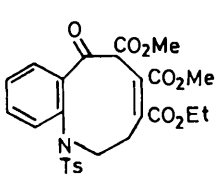
Alkylation of C-4 in ketones [*e.g.* (I; R^1 = Ts, R^2 = H)] is unpredictable. Thus while methylation with methyl iodide and potassium t-butoxide proceeded normally [giving (III; R^1 = Ts, $R^2 = R^3$ = Me; X, Y = O)] and reaction with ethyl formate proceeded [4]

* Unless the crude cyclisation product (XI; $X = R^2 = H$) was exhaustively refluxed with ethanol, some batches contained mixtures of the methyl and ethyl esters (XI; $X = R^2 = H$, R^1 = Me and Et).

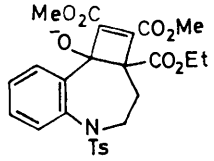
[11] M. F. Grundon and B. E. Reynolds, *J. Chem. Soc.*, 1964, 2445.
[12] F. Yoneda, K. Suzuki, and Y. Nitta, *J. Amer. Chem. Soc.*, 1966, **88**, 2328; but *cf.* G. W. Kenner and R. J. Stedman, *J. Chem. Soc.*, 1952, 2089; R. Huisgen and F. Jakob, *Annalen*, 1954, **590**, 37.
[13] R. G. Cooke and I. M. Russell, *Austral. J. Chem.*, 1972, **25**, 2421.
[14] I. McDonald and G. R. Proctor, *J. Chem. Soc.* (*C*), 1969, 1321.
[15] J. S. Belew and C. Tek-ling, *Chem. and Ind.*, 1967, 1958.
[16] A. H. Rees and K. Simon, *Canad. J. Chem.*, 1969, **47**, 1227.
[17] J. Witte and V. Boekelheide, *J. Org. Chem.*, 1972, **37**, 2849.
[18] B. Smith, unpublished results.
[19] I. W. Sinclair, personal communication.
[20] C. D. Gutsche and D. Redmore, 'Carbocyclic Ring Expansion Reactions,' Academic Press, New York, 1968, p. 173 *et seq.*

at 0°, ethyl bromoacetate failed to react even under forcing conditions.

As expected, substitution at C-5 can be brought about by reaction of ketones (I; R^1 = Ts) with Grignard



(XIV)



(XV)

reagents, although in the two cases we studied, the reaction was sluggish [yielding (XIII; R = $PhCH_2$ and *m*-$MeOC_6H_4CH_2$); however, the Wittig reaction failed even when the phosphonate carbanion from $(EtO)_2P(O)CH_2CO_2Et$ [21] was employed.

EXPERIMENTAL

2,3,4,5-*Tetrahydro*-1H-1-*benzazepin*-5-*ol* (II; R = H).—To 2,3,4,5-tetrahydro-1-*p*-tolylsulphonyl-1*H*-1-benzazepine-5-ol [5] (II; R = Ts) (30·4 g, 96·5 mmol) in ammonia (1200 ml) was added sodium (7·75 g, 0·34 g atom) over 30 min, causing the colour to remain blue finally. After 3 min ammonium chloride (in excess) was added and the ammonia allowed to evaporate. Working up the basic fraction gave the crude product (13·5 g, 85%) which crystallised from methylene dichloride–light petroleum (b.p. 40—60°) as *material* (11·4 g, 73%), m.p. 88—90° (Found: C, 73·6; H, 8·0; N, 8·9. $C_{10}H_{11}NO$ requires C, 73·6; H, 8·05; N, 8·55%), $\nu_{max.}$ (Nujol) 3300 cm^{-1} (NH and OH), τ 2·7—3·4 (4H, m, Ar), 5·2br (1H, m, 5-H), 6·7 (2H, s, exch., NH and OH), 7·0 (2H, m, 2-H), and 8·1 (4H, m, 3- and 4-H).

Reaction of 1,2,3,4-*Tetrahydro*-1-p-*tolylsulphonyl*-1-*benzazepin*-5-*one* (I; R^1 = Ts, R^2 = H) *with Sodium in Ammonia*.—To the tosyl ketone (31·75 g, 0·11 mol) in dry tetrahydrofuran (THF) and ammonia (700 ml) was added sodium (5·2 g) over 30 min and then ammonium chloride (excess) as before. The basic fraction was chromatographed on alumina; elution with benzene gave 1,2,3,4-tetrahydro-1-benzazepin-5-one [7] (I; R^1 = R^2 = H) (8 g). Ether eluted 2,3,4,5-tetrahydro-1*H*-1-benzazepin-5-ol (3·6 g) (II; R = H), m.p. 88—90°, as above.

Reaction of the Tosyl Ketone (I; R^1 = Ts, R^2 = H) *with Sulphuric and Acetic Acid*.—The tosyl ketone (44 g), concentrated sulphuric acid (150 ml), and acetic acid (450 ml) were stirred together at 70—75° for 22 h. Working up the basic fraction gave 1,2,3,4-tetrahydro-1-benzazepin-5-one [7] (I; R^1 = R^2 = H) (15 g, 70%), m.p. 68—70°.

1,2,3,4-*Tetrahydro*-2-*methyl*-1-*benzazepin*-5-*one* (I; R^1 = H, R^2 = Me).—1,2,3,4-Tetrahydro-2-methyl-1-*p*-tolylsulphonyl-1-benzazepin-5-one [6] (I; R^1 = Ts, R^2 = Me) (2 g), concentrated sulphuric acid (10 ml), and acetic acid (15 ml) were stirred together for 8 h at 70°. Working up as previously gave the *product* (550 mg) from light petroleum (b.p. 60—80°) as blades, m.p. 75° (Found: C, 75·9; H, 7·65; N, 8·25. $C_{11}H_{13}NO$ requires C, 75·5; H, 7·5; N, 8·0%), $\nu_{max.}$ 3300 (NH) and 1650 (C=O) cm^{-1}, τ 2·2—2·35 (1H, m, Ar), 2·7—2·9 (1H, m, Ar), 3·15 (2H, m, Ar), 5·78br (1H, s, exch.), 6·7—7·1 (2H, m, 4-H), 7·3—7·6 (1H, dq, *J* 8 and 2 Hz, 2-H), 7·7—8·2 (2H, m, 3-H), 8·7 (3H, d, *J* 8 Hz, Me).

1,2,3,4-*Tetrahydro*-4,4-*dimethyl*-1-p-*tolylsulphonyl*-1-*benzazepin*-5-*one* (III; R^1 = Ts, R^2 = R^3 = Me, X,Y = O).—The tosyl ketone (I; R^1 = Ts, R^2 = H) (20 g), potassium t-butoxide [from potassium (6·5 g)], methyl iodide (25 g), and t-butyl alcohol (200 ml) were refluxed and stirred together for 24 h. After acidification, addition of water, and extraction, the *product* (23 g) was obtained from ethanol in needles, m.p. 164° (Found: C, 66·55; H, 6·55; N, 4·2. $C_{19}H_{21}NO_3S$ requires C, 66·55; H, 6·15; N, 4·1%).

2,3,4,5-*Tetrahydro*-4,4-*dimethyl*-1H-1-*benzazepin*-5-*ol* (III; R^1 = X = H, R^2 = R^3 = Me, Y = OH).—To the previous ketone (5 g, 14·6 mmol), THF (25 ml), and ammonia (150 ml) was added sodium (1·58 g, 0·069 g atom) slowly with stirring. After evaporation of ammonia, working up of the basic fraction and chromatography on silica gel [elution with ether–light petroleum (b.p. 40—60°)] gave the *product* (1 g, 36%), m.p. 101—102° (from ethanol) (Found: C, 75·15; H, 8·7; N, 7·35. $C_{12}H_{17}NO$ requires C, 75·3; H, 8·95; N, 7·3%), $\nu_{max.}$ (Nujol) 3200—3300 cm^{-1} (NH,OH), τ 2·6—3·2 (4H, m, Ar), 5·85 (1H, s, 5-H), 6·32 (2H, s, exch., NH, OH), 6·9 (2H, m, 2-H), 7·9 (1H, m, 3-H), 8·7 (1H, m, 3-H), 8·9 (3H, s, Me), and 9·2 (3H, s, Me).

4,5-*Dihydro*-4,4-*dimethyl*-3H-1-*benzazepin*-5-*ol* (VII; R = Me).—The previous amino-alcohol (0·48 g), active manganese dioxide [15] (1 g), and dry benzene (60 ml) were stirred together and refluxed 30 min. Filtration and evaporation left the *product* (0·43 g, 90%) which sublimed at 80° at 0·1 mmHg and had m.p. 90—91° (Found: C, 76·65; H, 7·85; N, 7·4%; M^+, 189·11669. $C_{12}H_{15}NO$ requires C, 76·15; H, 8·0; N, 7·4%, *M*, 189·11536), $\nu_{max.}$ (Nujol) 3340 and 3290 (OH) cm^{-1}, τ 2·8—3·4 (4H, m, Ar), 4·8 (1H, d, *J* 7 Hz, 2-H), 5·7 (1H, s, 5-H), 6·0 (1H, s, exch., OH), 8·0 (1H, dd, *J* 7 and 13 Hz, 3a-H), 8·35 (1H, d, *J* 13 Hz, 3b-H), 8·8 (3H, s, Me), and 9·1 (3H, s, Me).

4,5-*Dihydro*-3H-1-*benzazepin*-5-*ol* (VII; R = H).—2,3,4,5-Tetrahydro-1*H*-1-benzazepin-5-ol (II; R = H) (4·3 g), active manganese dioxide [15] (10 g), and dry benzene (150 ml) were stirred and refluxed together for 3 h. The *product* (3·7 g) was distilled (b.p. 105—110° at 0·1 mmHg) and crystallised from methylene dichloride–light petroleum (b.p. 40—60°) to yield plates, m.p. 88—89° (Found: C, 74·3; H, 6·9; N, 8·7. $C_{10}H_{11}NO$ requires C, 74·5; H, 6·85; N, 8·7%), $\nu_{max.}$ (Nujol) 3290 cm^{-1} (OH), τ 2·8—3·5 (4H, m, Ar), 4·7 (1H, d, *J* 6 Hz, 2-H), 5·0 (1H, m, 5-H), 5·7 (1H, s, exch., OH), and 7·7—8·1 (4H, m, 3- and 4-H).

7-*Bromo*-1,2,3,4-*tetrahydro*-4,4-*dimethyl*-1-p-*tolylsulphonyl*-1-*benzazepin*-5-*one*.—1,2,3,4-Tetrahydro-4,4-dimethyl-1-*p*-tolylsulphonyl-1-benzazepin-5-one (2 g, 5·8 mmol), bromine (6·2 g, 38·8 mmol), and chloroform (30 ml) were stirred for 24 h at 20°. After being washed with aqueous sodium hydrogen carbonate the organic layer was washed and evaporated to yield a brown solid (2·4 g). Crystallisation from ethanol gave *needles* (0·9 g, 37%), m.p. 169—170° (Found: C, 54·1; H, 4·95; N, 3·35. $C_{19}H_{20}BrNO_3S$ requires C, 54·1; H, 4·75; N, 3·3%), $\nu_{max.}$ (Nujol) 1700 (C=O) cm^{-1}, τ 2·3—2·8 (7H, m, Ar), 6·2 (2H, m, 2-H), 7·6 (3H, s, Me of tosyl), 8·3 (2H, m, 3-H), and 9·0 (6H, s, 4-Me).

Trimethylene Acetal of the Tosyl Ketone (I; R^1 = Ts, R^2 = H).—The tosyl ketone (20 g), toluene (900 ml), propane-1,3-diol (5 g), and toluene-*p*-sulphonic acid (1 g)

[21] W. S. Wadsorth, jun., and W. D. Emmons, *J. Amer. Chem. Soc.*, 1961, **83**, 1733.

were refluxed with a Dean–Stark trap, and three further quantities of propane-1,3-diol (5 g) were added every 12 h. After 48 h the reaction was cooled and evaporated. Crystallisation of the residue (26 g) from ethanol gave *prisms* (15 g, 63%), m.p. 130—131° (Found: C, 64·35; H, 6·4; N, 3·95. $C_{20}H_{23}NO_4S$ requires C, 64·35; H, 6·2; N, 3·75%). The i.r. spectrum contained no carbonyl absorption.

Reaction of the Acetal of 1,2,3,4-*Tetrahydro*-1-p-*tolylsulphonyl*-1-*benzazepin*-5-*one with Sodium in Ammonia.*—To the foregoing acetal (10 g, 26·8 mmol), THF (200 ml), and ammonia (1100 ml) was added sodium (1·02 g, 0·043 g atom) over 30 min with stirring. After addition of ammonium chloride (excess) ammonium was allowed to evaporate, water was added, and the product extracted with chloroform.* After treatment with aqueous ethanol containing toluene-*p*-sulphonic acid (0·5 g) for 24 h at 20°, chromatography gave 1,2,3,4-tetrahydro-1-benzazepin-5-one [7] (I; $R^1 = R^2 = H$) (2·1 g, 48%) as before, τ 2·1—3·3 (4H, m, Ar), 5·3 (1H, s, exch., NH), 6·6—6·9 (2H, m, 4-H), 7·0—7·3 (2H, m, 2-H), and 7·7—8·0 (2H, m, 3-H).

1,2,3,4-*Tetrahydro*-1-(2-*chloroprop*-2-*enyl*)-1-*benzazepin*-5-*one* (I; $R^1 = CH_2CCl{:}CH_2$, $R^2 = H$).—1,2,3,4-Tetrahydro-1-benzazepin-5-one (2 g) in 2-chloro-3-iodopropene [2] (40 g) was held at 60° in a pressure bottle for 48 h. Chromatography on silica gel (elution with 5% ether–benzene) gave the *product* (1·6 g), m.p. 81—82° [from benzene–light petroleum (b.p. 60—80°)] (Found: C, 66·2; H, 6·1; N, 6·05. $C_{13}H_{14}ClNO$ requires C, 66·15; H, 6·0; N, 5·9%), $\nu_{max.}$ (Nujol) 1672 (C=O) cm^{-1}, τ 2·25 (1H, dd, *J* 12 and 2 Hz, 6-H), 2·55—3·45 (3H, m, Ar), 4·55—4·8 (2H, m, $=CH_2$), 5·8 (2H, s, $-CH_2-$), 6·63 (2H, t, 4-H), 7·18 (2H, t, 2-H), and 7·5—8·0 (2H, m, 3-H).

2,3-*Dihydro*-1-(2-*chloroprop*-2-*enyl*)-1H-1-*benzazepine* (V; $R = CH_2CCl{:}CH_2$).—The foregoing ketone (1·3 g), lithium aluminium hydride (130 mg), and dry ether (80 ml) were stirred at 20° for 24 h. The intermediate obtained in the usual way was an oil (1·2 g), $\nu_{max.}$ 3450 cm^{-1} (OH), which was stirred with polyphosphoric acid (15 g) at 75° for 1 h. The product was chromatographed on silica gel; elution with benzene–light petroleum (b.p. 60—80°) (50%) gave the *product* (550 mg), m.p. 55° (Found: C, 70·8; H, 6·5; N, 6·75; Cl, 16·1. $C_{13}H_{15}ClN$ requires C, 70·95; H, 6·4; N, 6·4; Cl, 15·9%), τ 2·7—3·35 (4H, m, Ar), 2·6—2·75 (1H, m, 5-H), 3·85—4·2 (1H, m, 4-H), 4·5—4·7 (2H, m, $=CH_2$), 6·0 (2H, s, $-CH_2-$), 6·77 (2H, t, 2-H), and 7·4—7·65 (2H, m, 3-H). Treatment of this material with polyphosphoric acid at up to 120° or with 90% sulphuric acid at 0° caused only slight decomposition, and no new products could be detected.

Reaction of 1,2,3,4-*Tetrahydro*-1-*benzazepin*-5-*one with Dimethyl Acetylenedicarboxylate.*—The amino-ketone (I; $R^1 = R^2 = H$) (4·5 g), dimethyl acetylenedicarboxylate (4·95 g), and anhydrous methanol (55 ml) were refluxed together for 48 h. Evaporation of solvent left 1-(1,2-*bis*-*methoxycarbonylvinyl*)-1,2,3,4-*tetrahydro*-1-*benzazepin*-5-*one* which crystallised from ether in cubes (4·88 g, 57%), m.p. 143—144° (Found: C, 63·4; H, 5·7; N, 4·6. $C_{16}H_{17}NO_5$ requires C, 63·4; H, 5·65; N, 4·6%), $\nu_{max.}$ (Nujol) 1725 (ester) and 1665 (ArCO) cm^{-1}, τ 1·9—2·7 (4H, m, Ar), 4·9 (1H, s, $=CH$), 6·2 (3H, s, OMe), 6·4 (3H, s, OMe), 6·3—6·45 (2H, m, 4-H), 7·2 (2H, m, 2-H), and 7·8 (2H, m, 3-H).

Hydrobromide of 2,3-*Dihydro*-1-*methyl*-1H-1-*benzazepine* (V; R = Me).—2,3-Dihydro-1H-1-benzazepine [7] (V; R = H) (2 g), anhydrous methanol (25 ml), anhydrous potassium carbonate (4 g), and methyl iodide (4·8 g) were stirred and refluxed together for 18 h. Filtration and evaporation gave an oil (2 g) which was chromatographed (silica gel, benzene) to give a pale yellow oil (1·43 g, 65%) which darkened on standing. Treatment of a chloroform solution with hydrogen bromide precipitated the *product* which crystallised from acetone in prisms, m.p. 176—177° (Found: C, 55·5; H, 6·2; N, 5·6. $C_{10}H_{14}BrN$ requires C, 55·05; H, 5·9; N, 5·8%), $\nu_{max.}$ (Nujol) 2450 ($\overset{+}{N}H$) cm^{-1}, τ −3·5br (1H, s, exch., $\overset{+}{N}H$) 1·5—2·6 (4H, m, Ar), 3·35 (1H, d, *J* 10 Hz, 5-H), 3·8 (1H, m, 4-H), 5·9 (1H, m, 2-H), 6·4 (1H, m, 2H), 6·9 (3H, d, *J* 2 Hz, NMe), and 7·0 (2H, m, 3-H).

1-(2-*Dimethylaminoethyl*)-1,2,3,4-*tetrahydro*-1-*benzazepin*-5-*one* (I; $R^1 = Me_2NCH_2CH_2$, $R^2 = H$).—1,2,3,4-Tetrahydro-1-benzazepin-5-one (I; $R^1 = R^2 = H$) (2 g) in dry toluene (25 ml) was added with stirring to freshly prepared sodamide [from sodium (2 g)] in ammonia (400 ml), followed by 2-dimethylaminoethyl chloride [from its hydrochloride (10 g)] in toluene (25 ml). After the ammonia had evaporated off the product was obtained by chromatography on alumina. Elution with ether gave an oil (810 mg), b.p. 140° at 0·1 mmHg (Found: C, 71·95; H, 8·65; N, 11·5%; M^+, 232·1573. $C_{14}H_{20}N_2O$ requires C, 72·45; H, 8·7; N, 12·05%; *M*, 232·1576), τ 2·3 (1H, dd, *J* 8 and 1·5 Hz, 6-H), 2·65—2·85 (1H, m, Ar), 3·09—3·37 (2H, m, Ar), 6·42 (2H, t, $-CH_2-$), 6·72 (2H, t, $-CH_2-$), 7·25 (2H, t, $-CH_2-$), 7·44 (2H, t, $-CH_2-$), 7·5—7·9 (2H, m, 3-H), and 7·7 (6H, s, NMe).

2,3-*Dihydro*-1-(2-*dimethylaminoethyl*)-1H-1-*benzazepine* (V; $R = CH_2CH_2NMe_2$).—2,3-Dihydro-1H-1-benzazepine (V; R = H) (2 g) was submitted to the same treatment as in the previous experiment. The *product* (510 mg) had b.p. 125—130 at 0·1 mmHg (Found: C, 77·75; H, 8·8. $C_{14}H_{20}N_2$ requires C, 77·85; H, 9·3%), τ 2·8—3·8 (5H, m, 4 Ar and 4-H), 4·0—4·25 (1H, m, 5-H), 6·6 (2H, t, $-CH_2-$), 6·83 (2H, t, $-CH_2-$), 7·4—7·6 (4H, m, 2- and 3-H), and 7·74 (6H, s, NMe).

8-*Methoxydibenz*[b,e]*azepin*-11-*one* [14] (IX; R = H).—5,6-Dihydro-8-methoxydibenz[*b*,*e*]azepin-11-one [14] (VIII; R = H) (1 g), dry benzene (200 ml), and manganese dioxide [15] (2 g; previously dried by refluxing in benzene) were refluxed for 30 h (Dean–Stark). After filtration and evaporation of solvent the product (980 mg) was recrystallised from toluene in yellow needles, m.p. 142—145° (decomp.) (Found: C, 76·2; H, 4·55; N, 6·05. Calc. for $C_{15}H_{11}NO_2$: C, 76·0; H, 4·7; N, 5·9%), $\nu_{max.}$ (Nujol) 1640 (C=O) and 1620 (C=N) cm^{-1}, τ 1·3 (1H, s, 6-H), 1·75—2·85 (7H, m, Ar), and 6·08 (3H, s, OMe), $\lambda_{max.}$ 211, 244, and 364 nm (ε 12,095, 21,502, and 3808).

4-*Chloro*-N-m-*methoxybenzyl*-N-p-*tolylsulphonylanthranilic Acid.*—Methyl 4-chloro-*N*-*p*-tolylsulphonylanthranilate [6] (71·2 g), *m*-methoxybenzyl bromide [22] (61 g), and freshly roasted potassium carbonate (70 g) were stirred together at 140° for 24 h. After cooling, leaching with methylene dichloride, filtration, and evaporation of the filtrate, the

* Preparative t.l.c. of a sample (390 mg) on silica gel eluting with ether–benzene (1 : 10) gave 1,2,3,4-tetrahydro-1-benzazapin-5-one (40 mg) and its *trimethyl acetal* (140 mg) as an oil, b.p. 135° at 0·1 mm Hg (Found: M^+, 219·124921. $C_{13}H_{17}NO_2$ requires *M*, 219·125053), $\nu_{max.}$ (Nujol) 3340 cm^{-1}, τ 2·2—3·6 (4H, m, Ar), 5·9—6·3 (4H, m, CH_2O), 6·6—7·0 (3H, m, 2-H and NH, exch.), and 7·6—8·4 (6H, m, 3- and 4-H and CH_2 of acetal ring).

[22] W. Q. Beard, D. N. van Eenam, and C. R. Hauser, *J. Org. Chem.*, 1961, **26**, 2310.

methyl ester (93·5 g), m.p. 85° (from ethanol), was obtained. The latter (65 g) was hydrolysed as in a previous case [14] to give the *product* (46 g), m.p. 182° (from toluene) (Found: C, 59·7; H, 4·7; N, 3·45. $C_{22}H_{20}ClNO_5S$ requires C, 59·3; H, 4·55; N, 3·15%).

3-*Chloro*-5,6-*dihydro*-8-*methoxy*-N-p-*tolylsulphonyldibenz*[b,e]*azepin*-11-*one*.—The foregoing acid (47·3 g) was cyclised as previously described for the parent system [14] and gave the *product* (42 g), purified by chromatography on alumina (benzene elution) and by crystallisation from ethanol, m.p. 238° (Found: Cl, 8·3; N, 3·3%; M^+, 429·0603, 427·0578. $C_{22}H_{16}ClNO_4S$ requires Cl, 8·05; N, 3·5%; *M*, 429·0616, 427·0645). Consistently low carbon analyses were obtained.

3-*Chloro*-5,6-*dihydro*-8-*methoxydibenz*[b,e]*azepin*-11-*one* (VIII; R = Cl).—The previous *N*-tosyl ketone (5 g) and polyphosphoric acid (62 g) were stirred at 110° for 5 h. The basic fraction (2 g) was purified by chromatography on silica gel (benzene elution) and by crystallisation from benzene–light petroleum (b.p. 60—80°) (1 : 1), m.p. 148° (Found: C, 66·35; H, 4·4; N, 5·05. $C_{15}H_{12}ClNO_2$ requires C, 65·9; H, 4·45; N, 5·15%), $\nu_{max.}$ (Nujol) 3290 (NH) and 1700 (C=O) cm^{-1}.

3-*Chloro*-8-*methoxydibenz*[b,e]*azepin*-11-*one* (IX; R = Cl).—The above amino-ketone (230 mg) and active manganese dioxide (370 mg) were treated as for the parent substance. The *product* (160 mg) crystallised from toluene in needles, m.p. 163° (Found: C, 66·25; H, 4·05; N, 5·15%; *M*, 273·0381, 271·0395. $C_{15}H_{10}ClNO_2$ requires C, 66·5; H, 3·75; N, 5·1%; *M*, 273·0371, 271·0400), $\nu_{max.}$ (Nujol) 1640 cm^{-1} (C=O), $\lambda_{max.}$ 210, 246, and 364 nm (ε 15,634, 28,352, and 5367).

Reaction of 4-*Ethoxycarbonyl*-1,2,3,4-*tetrahydro*-1-p-*tolylsulphonyl*-1-*benzazepin*-5-*one with Dimethyl Acetylenedicarboxylate*.—The keto-ester (XI; R^1 = Et; R^2 = X = H)[2] (7·75 g), sodium methoxide [from sodium (0·5 g)], and methanol were stirred together for 0·5 h: the solvent was then evaporated and the residual sodium salt stirred with toluene (150 ml) and dimethyl acetylenedicarboxylate (3 g) for 2 h. After being washed with dilute hydrochloric acid and water, the solution was dried and evaporated. The tarry product (9 g) crystallised from ethanol giving 4-*ethoxycarbonyl*-1,2,3,6-*tetrahydro*-5,6-*bismethoxycarbonyl*-1-p-*tolylsulphonyl*-1-*benzazonin*-7-*one* (XIV) (7·2 g), m.p. 141—144° (Found: C, 59·1; H, 5·0; N, 2·83%; *M*, 529·1419. $C_{26}H_{27}NO_9S$ requires C, 59·05; H, 5·15; N, 2·65%; *M*, 529·1406), $\nu_{max.}$ (Nujol) 1710—1740br (ester) and 1650 (H-bonded ester) cm^{-1}, τ −3·2 (1H, s, exch.), 2·2—2·75 (8H, m, Ar), 5·9 (2H, q, OCH_2CH_3), 6·12 (3H, s, CO_2Me), 6·35 (3H, s, CO_2Me), 6·0—6·3 (1H, m, 2-H), 6·7—7·4 (3H, m, 2- and 3-H), 7·52 (3H, s, Ar*Me*), and 8·9 (3H, t, CH_3CH_2O).

4-(2-*Chloroprop*-2-*enyl*)-4-*ethoxycarbonyl*-1,2,3,4-*tetrahydro*-1-p-*tolylsulphonyl*-1-*benzazepin*-5-*one* (XI; R^1 = Et, R^2 = H, X = CH_2·CCl:CH_2).—The mixed keto-esters (XI; R^1 = Me and Et, R^2 = X = H)[2] (1·24 g), 2,3-dichloropropene (0·4 g), sodium hydride (0·3 g; 50%), and dry dimethylformamide (25 ml) were stirred under nitrogen at 85° for 3·5 h. The product was obtained in the usual way and purified by chromatography on silica gel (2% ether–benzene) to give needles (900 mg), m.p. 129—130° (from ethanol) (Found: C, 59·8; H, 5·35; N, 3·05. $C_{23}H_{24}ClNO_5S$ requires C, 59·8; H, 5·25; N, 3·05%), $\nu_{max.}$ (Nujol) 1745 (ester) and 1690 (C=O) cm^{-1}, τ 2·4—2·8 (8H, m, Ar), 4·8 (2H, d, :CH), 5·8—6·2 (4H, m, :CH_2 and OCH_2CH_3), 6·9—7·2 (2H, m, 2-H), 7·6 (3H, s, Ar*Me*), 7·95—8·25 (2H, m, 3-H), and 7·9 (3H, t, CH_3CH_2O).

4-*Hydroxymethyl*-2,3,4,5-*tetrahydro*-1-p-*tolylsulphonyl*-1H-1-*benzazepin*-5-*ol* (XII).—The keto-ester (XI; R^1 = Et, R^2 = X = H)[2] (10·25 g), absolute ethanol (200 ml), and sodium borohydride (2·15 g) were stirred together for 48 h. The usual work-up gave a *solid* (7·1 g), m.p. 106—108° (from benzene–ethanol) (Found: C, 61·85; H, 5·95; N, 4·25. $C_{18}H_{21}NO_4S$ requires C, 62·2; H, 6·1; N, 4·05%), $\nu_{max.}$ (Nujol) 3300br (OH) cm^{-1}.

When this compound (3·5 g) was refluxed for 48 h in benzene with toluene-*p*-sulphonic acid (0·5 g), the product (2·3 g) was purified by chromatography on alumina and crystallisation from light petroleum (b.p. 40—60°) to give prisms, m.p. 79—80°, of 4-*benzyl*-2,3-*dihydro*-1-p-*tolylsulphonyl*-1H-1-*benzazepine* (Found: C, 74·0; H, 6·05; N, 3·6. $C_{24}H_{23}NO_2S$ requires C, 74·0; H, 5·95; N, 3·6%), τ 2·4—3·1 (8H, m, Ar), 4·08 (1H, s, 5-H), 6·25 (2H, t, 2-H), 6·8 (2H, s, CH_2Ph), 7·6 (2H, t, 3-H), and 7·66 (3H, s, Me). Refluxing in toluene gave a similar product as a waxy solid having an almost identical n.m.r. spectrum with an additional signal, τ 7·72 (3H, s, Me).

2,3,4,5-*Tetrahydro*-5-m-*methoxybenzyl*-1-p-*tolylsulphonyl*-1H-1-*benzazepine* (XIII; R = *m*-$MeOC_6H_4CH_2$).—The tosyl ketone (I; R^1 = Ts, R^2 = H) (19·3 g) in dry THF (100 ml) was added to the Grignard reagent prepared from magnesium (1·8 g) and *m*-methoxybenzyl bromide (15·8 g) in dry ether (100 ml). After being refluxed for 3 h with stirring, the mixture was worked up to yield the *product* (19·7 g), m.p. 116—118° (from ethanol) (Found: C, 68·6; H, 6·2; N, 3·2. $C_{25}H_{27}NO_4S$ requires C, 68·7; H, 6·15; N, 3·45%), $\nu_{max.}$ (Nujol) 3505 (OH) cm^{-1}. A similar reaction using benzylmagnesium bromide and the tosyl ketone (29 g) gave 5-*benzyl*-2,3,4,5-*tetrahydro*-1-p-*tolylsulphonyl*-1H-1-*benzazepin*-5-*ol* (XIII; R = $PhCH_2$) (18·9 g), m.p. 122·5—124° (Found: C, 70·4; H, 5·85; N, 3·4. $C_{24}H_{25}NO_3S$ requires C, 70·75; H, 6·2; N, 3·45%). Significantly lower yields were obtained using shorter reaction times.

Reaction of 4-*Ethoxy*(*and* 4-*methoxy*-)*carbonyl*-1,2,3,4-*tetrahydro*-1-p-*tolylsulphonyl*-1-*benzazepin*-5-*one* [2] (XI; R^1 = Me *and* Et, R^2 = X = H) *with Ethyl Bromoacetate*.—The mixture of esters [2] (12·1 g), sodium hydride (1·35 g; 60%), and 1,2-dimethoxyethane (50 ml) were stirred together and refluxed for 2 h. To the cooled suspension was added ethyl bromoacetate (6 g) in 1,2-dimethoxyethane (75 ml). After being stirred overnight, the mixture was refluxed for 3 h, cooled, and poured into an excess of water. Extraction with chloroform gave the product, which was rapidly chromatographed on alumina (800 g; 24 h deactivation). Elution with 25% ether–benzene gave an oil (14·4 g) which decomposed on attempted distillation. It appeared to be a mixture of methyl ethyl and diethyl esters (XI; R^1 = Me and Et, R^2 = H, X = CH_2CO_2Et) (Found: M^+, 473·1467 and 459·1379. Calc. for $C_{24}H_{27}NO_7S$: *M*, 473·1508; Calc. for $C_{23}H_{25}NO_7S$: *M*, 459·1352), $\nu_{max.}$ (film) 1730 (ester) and 1690 (ArCO) cm^{-1}. The mass spectrum and the n.m.r. spectrum indicated that the mixture contained *ca.* 50% of each product.

4-*Carboxymethyl*-2,3,4,5-*tetrahydro*-5-*oxo*-1-p-*tolylsulphonyl*-1H-1-*benzazepine*-4-*carboxylic acid* (XI; R^1 = R^2 = H, X = CH_2CO_2H).—The previous diesters (9 g), ethanol (75 ml), and aqueous sodium hydroxide (10% excess) were refluxed for 1 h and left for 18 h at 20°; dilution with water, extraction with benzene, and acidification

of the aqueous layer gave the *hydrated product* (6·65 g), m.p. 161—162° (from ether) (Found: C, 55·35; H, 4·85; N, 3·6; S, 7·25. $C_{20}H_{19}NO_7S,H_2O$ requires C, 55·2; H, 4·85; N, 3·2; S, 7·35%), $\nu_{max.}$ 2640br (OH) and 1700br (CO_2H) cm^{-1}, τ (CD_3CN) 2·05—3·2 (8H, m, Ar), 2·7—3·1br (2H, OH), 6·2—6·6br (2H, s, H_2O), 7·0—7·3 (2H, m, 4-CH_2), 7·47—7·66 (2H, m, 2-H), 7·6 (3H, s, Me), and 8·1—8·45 (2H, m, 3-H).

Acid Hydrolysis of the Diesters (XI; R^1 = Me *and* Et, R^2 = H, X = CH_2CO_2Et).—The diesters (1·72 g), glacial acetic acid (24 g), ethanol (8 ml), concentrated hydrochloric acid (4 ml), and water (4 ml) were refluxed for 20 h. Working up the acidic fraction gave *4-ethoxycarbonyl-2,3,4,5-tetrahydro-5-oxo-1-p-tolylsulphonyl-1H-1-benzazepine-4-acetic acid* (XI; R^1 = Et, R^2 = H, X = CH_2CO_2H), b.p. 160° at 0·15 mmHg (Found: C, 59·9; H, 5·7; N, 3·45%; M^+, 445·1190. $C_{22}H_{23}NO_7S$ requires C, 59·4; H, 5·2; N, 3·15%; *M*, 445·1195), $\nu_{max.}$ (Nujol) 2650—2750br (OH), 1735 (ester), 1720 (CO_2H), and 1690 (ArC=O) cm^{-1}, τ 2·3—3·05 (8H, m, Ar), 5·9—6·2 (2H, q, OCH_2CH_3), 6·4 (2H, s, $-CH_2CO_2H$), 6·8 (1H, s, exch., CO_2H), 7·2—7·3 (2H, m, 2-H), 7·6 (3H, s, Ar*Me*), 7·55—7·75 (2H, m, 3-H), and 8·9 (3H, t, CH_3CH_2O).

4-Methoxycarbonyl-4-methyl-1,2,3,4-tetrahydro-1-p-tolylsulphonyl-1-benzazepin-5-one (XI; R^1 = X = Me, R^2 = H).—The keto-esters (XI; R′ = Me and Et, R^2 = X = H) (7·5 g), dimethylformamide (75 ml), and sodium hydride (1·5 g; 80%) were stirred and heated for 1 h at 60—70° before addition of methyl iodide (4 ml), and for 1 h afterwards. After dilution with water, acidification (pH 4), and extraction with chloroform, the *product* (10 g) was crystallised from methanol in prisms, m.p. 118° (Found: C, 62·25; H, 5·55; N, 3·6. $C_{20}H_{21}NO_5S$ requires C, 62·05; H, 5·45; N, 3·6%), $\nu_{max.}$ (Nujol) 1750 (ester) and 1690 (ArC=O) cm^{-1}, τ 2·4—2·85 (8H, m, Ar), 5·9—6·3 (2H, m, 2-H), 6·41 (3H, s, CO_2Me), 7·6 (3H, s, Ar*Me*), 8·05—8·35 (2H, m, 3-H), and 8·7 (3H, s, 4-Me). Refluxing for 2 h with ethanolic aqueous sodium hydroxide converted the ester into *1,2,3,4-tetrahydro-4-methyl-1-p-tolylsulphenyl-1-benzazepin-5-one* (III; R^1 = Ts, R^2 = H, R^3 = Me, X,Y = O), which crystallised from ethanol in prisms, m.p. 126° (Found: C, 65·3; H, 5·75; N, 4·4. $C_{19}H_{19}NO_3S$ requires C, 65·7; H, 5·8; N, 4·25%), $\nu_{max.}$ (Nujol) 1675 cm^{-1} (ArC=O), τ 2·2—2·8 (8H, m, Ar), 5·65—5·9 (1H, m, 4-H), 6·4—6·7 (1H, m, 2-H), 7·2—7·45 (1H, m, 2-H), 7·6 (3H, s, Ar*Me*), 7·6—7·9 (1H, m, 3-H), 8·2—8·6 (1H, m, 3-H), and 8·92 (3H. d, 4-Me).

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