Azabenzocycloheptenones. Part VIII.† Further Observations in the Dibenz[*b*,*d*]azepin-7-one Field

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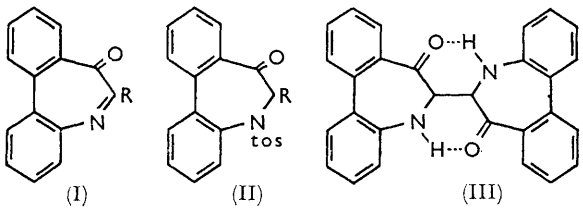
A compound formerly believed to be a monomeric dibenzazatropone is shown to be a dimer and to yield a bisazatropone on oxidation. The monomeric dibenzazatropone, 6-ethoxy-7-oxodibenz[*b*,*d*]azepine, has been prepared. Syntheses and reactions of further *N*-toluene-*p*-sulphonyl 6-substituted dibenz[*b*,*d*]azepinones with bases have been studied.

It was demonstrated in the preceding paper of this series † that a purple benzazatropone dimer arose in a base-catalysed elimination reaction in the benz[*b*]azepine series. This discovery cast doubt on structure (I; R = H) which we previously proposed [1,2] for a purple compound obtained by base reaction on the toluene-*p*-sulphonyl ketone (II; R = H). The original structure determination hinged on a mass spectrum which gave a molecular ion *m*/*e* 207; we now find that in a more refined spectrometer, ‡ a molecular ion *m*/*e* 414 is detected. Accordingly, it seems that this purple substance should be formulated as (III); this is to be expected from other work on toluene-*p*-sulphonyl eliminations [3] and evidence previously presented [1] is in accord with this assumption. One would expect that the hydrogen-bonded dimer (III) should be fairly easily oxidised to a bisazatropone (IV)

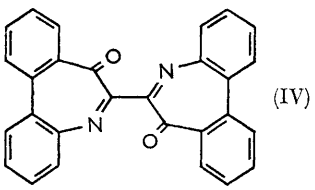
† Part VII, *J. Chem. Soc.* (*C*), 1968, 1280.
‡ AEI M.S.9.

[1] W. Paterson and G. R. Proctor, *J. Chem. Soc.*, 1962, 3468.
[2] G. R. Proctor, *Chem. and Ind.*, 1960, 408.
[3] T. Bryce, G. R. Proctor, and M. A. Rehman, *J. Chem. Soc.*, 1965, 7105.

and indeed, treatment of it with manganese dioxide [4] gave, in good yield, a yellow crystalline substance ($\nu_{max.}$ 1680 cm.$^{-1}$) which we believe to be (IV); this transformation is quantitatively reversed by catalytic



(I) (II) (III)

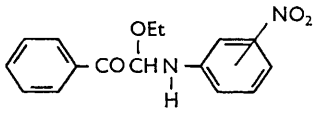


(IV)

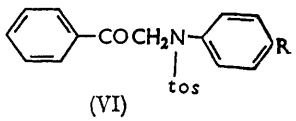
tos = $MeC_6H_4SO_2$

hydrogenation. It was inexpedient to attempt a synthesis of the six-membered ring alternative in this case (cf. Part VII) since failures to obtain ' phenanthridil ' have been reported.[5]

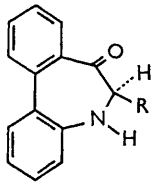
In recent work [6] on the toluene-*p*-sulphonyl elimination, we suspected that in some cases ethoxide ions had intervened to attack the nucleophilic carbon atom (adjacent to nitrogen) of activated anils; we isolated such products [*e.g.* (V)] in reactions of nitroanilines with phenylglyoxal hydrate in ethanol.[7] It was, therefore, appropriate to re-examine some cases of the toluene-*p*-sulphonyl elimination using ethanolic sodium ethoxide The bromo-compound (VI; R = Br) gave the same dimer [3] as it had done in aprotic conditions but the methyl compound (VI; R = Me) yielded what we consider to be the *p*-toluidide of benzoylformic acid; the toluene-*p*-sulphonyl ketone (II; R = H) also gave a monomeric product (VII; R = OEt) which was identified by the usual methods (see Experimental section). In the n.m.r. spectrum of the ketone (VII; R = OEt), the signal due to methylene protons of the ethyl group appear as a blurred quintuplet as has been observed [7] for disastereotopic nuclei; this signal is a sharp quartet in the product, $C_{16}H_{13}NO_2$, obtained from (VII; R = OEt) by manganese dioxide treatment. This compound is the azatropone (I; R = OEt), a colourless substance having an i.r. carbonyl absorption at 1697 cm.$^{-1}$ in hexane, shifting to 1682 cm.$^{-1}$ in chloroform (cf. ref. 8). The dipole moment of this azatropone is 4·8 ± 0·4 D* in benzene; it is thus not particularly polar. Significantly, and predictably, the dibenzazatropone (I; R = OEt) is converted by mineral acid to the isomeric ethyl ester of phenanthridine-6-carboxylic acid, dilute aqueous alkali converted it to the hydroxy-ketone (VIII; R ‖ OH). We were unable to obtain seven-membered ring derivatives of the azatropone (I; R = OEt), and reaction with methyl iodide, 2,4-dinitrophenylhydrazine, or with dry hydrogen bromide gave the ethyl ester of phenanthridine-6-carboxylic acid.



(V)



(VI)



(VII)

Treatment of the ketone (VII; R = OEt) with mineral acids gave a substance (m.p. 238°) which we previously [1,2] isolated during the aprotic elimination reaction on (II; R = H). The most reasonable structure for this is (VII; R = OH) which was our original [2] deduction; we later altered this on considering its colour reaction and an n.m.r. spectrum.[1] We regret that due to a misunderstanding, we were studying the wrong spectrum and now report that the signals obtained from a fresh sample [Experimental section) are quite in accord with structure (VII; R = OH).

The ketone (II; R = CH_2Ph) (cf. ref. 9) reacted with sodium hydride to give a complex mixture containing benzaldehyde and a substance, $C_{21}H_{15}NO$, in such poor yield that a full structure determination was impracticable; however, the mass spectrum contains a base peak at *m/e* 178 (dehydrophenanthridinium) which categorises it with all the seven-membered ring compounds in this series (10 in number). Some of these also contain a strong peak at *m/e* 179 (phenanthridinium) which is the base peak in the phenanthridines that we have examined (five in number): none of the latter showed the *m/e* 178 peak. Accordingly, we believe that the substance from (II; R = CH_2Ph) is an azatropone, (6-benzyl-7-oxodibenzyl[*b*,*d*]azepine), rather than the alternative 6-phenacylphenanthridine.

When the ketone (II; R = Me) was treated with sodium hydride, the compound (VII; R = Me) was obtained; apparently the azatropone (I; R = Me) had been reduced by hydride ions. Interestingly, the ketone (VII; R = Me) reacted with manganese dioxide to give only phenanthridone; we conclude, therefore, that the azatropone (I; R = Me) is quite reactive. This is supported by the observation that reaction of the ketone (II; R = Me) with sodium methoxide in toluene gave

* We cordially thank Professor A. M. North for this measurement.

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[5] ' Heterocyclic Compounds,' ed. R. C. Elderfield, J. Wiley, New York, vol. 4, p. 590.

[6] E. D. Hannah, G. R. Proctor, and M. A. Rehman, *J. Chem. Soc.* (*C*), 1967, 256.

[7] G. R. Proctor and M. A. Rehman, *J. Chem. Soc.* (*C*), 1967, 2696; M. van Gorkom and G. E. Hall, *Quart. Rev.* 1968, **22**, 14.

[8] G. Naville, H. Strauss, and E. Heilbronner, *Helv. chim. Acta*, 1960, **43**, 1221.

[9] G. Hazebroucq, Ph.D. Thesis, Paris, 1966.

(after chromatography) a substance, $C_{15}H_{11}NO$, which we believe is the hitherto unknown 6-acetylphenanthridine (base peak *m/e* 179 only). We were, however, unable to synthesise the latter for comparison.

We have previously noted (Part VII) a similar example where a ring-contracted isomer of an azatropone was obtained. Future work will be directed to the synthesis of azatropones in which the carbonyl group is more distant from the group C=N–, hopefully to avoid this ring-contraction.

EXPERIMENTAL

6,6′-Bis-7-oxodibenz[b,d]*azepine* (IV).—The purple dimer [1] (III) (155 mg.) was stirred with methylene dichloride (60 ml.) and active manganese dioxide (1 g.) for 18 hr. After filtration and evaporation of the solvent, the *product* remained (141 mg.); it crystallised from methylene dichloride–light petroleum (b.p. 60—80°) as orange–yellow crystals, m.p. 244° [Found: C, 81·25; H, 4·3; N, 6·7%; *M*(mass spectroscopy), 412·1225. $C_{28}H_{16}N_2O_2$ requires C, 81·55; H, 3·9; N, 6·8%; *M*, 412·1212], $\nu_{max.}$ (Nujol) 1680 cm.$^{-1}$ (CO). Treatment with ethanol yielded a *monoethanolate* (sesquiacetal ?), m.p. 203° [Found: C, 78·9; H, 5·4; N, 6·35%; *M*(mass spectrum), 458·16299. $C_{30}H_{22}N_2O_3$ requires C, 78·7; H, 5·84; N, 6·1%; *M*, 458·16303]. The i.r. spectrum contained no peaks attributable to carbonyl groups.

Hydrogenation of 6,6′-*Bis*-7-*oxodibenz*[b,d]*azepine*.—The azepine (200 mg.) in benzene (100 ml.) and glacial acetic acid (25 ml.) was hydrogenated at atmospheric pressure over 10% palladised charcoal. After gas uptake had ceased the product was isolated and crystallised from methylene dichloride as purple prisms (189 mg.), m.p. 265° identical to material previously obtained.[1]

Treatment of p-*Bromo*-N-*phenacyl*-N-*toluene*-p-*sulphonylaniline with Sodium Ethoxide*.—The sulphonamide [3] (3·17 g.) in benzene (50 ml.) was added to sodium ethoxide [from sodium (2·2 g.)] in ethanol (100 ml.) and left for 16 hr. On working up, the only detectable product was the dimer, m.p. 227° (decomp.), identical to that obtained previously [3] in an aprotic experiment.

Treatment of N-*Phenacyl*-N-*toluene*-p-*sulphonyl*-p-*toluidine with Sodium Ethoxide*.—The sulphonamide [3] (3·2 g.) in benzene (30 ml.) was added to sodium ethoxide [from sodium (2·2 g.)] in ethanol (200 ml.). On pouring onto ice after 16 hr., the smell of isocyanide was evident: separation, washing, drying and evaporation of the organic phase gave a yellow solid (1·25 g.), the p-*toluidide of benzoyl formic acid*, [purified by recrystallisation from light petroleum (b.p. 60—80°)], m.p. 112° (lit.,[10] m.p. 112—113°) (Found: C, 75·2; H, 5·65; N, 5·75%; *M*(mass spectrum), 239·09507. $C_{15}H_{13}NO_2$ requires C, 75·4; H, 5·5; N, 5·85%; *M*, 239·09462], $\nu_{max.}$ (Nujol) 3330 (N–H), 1680, and 1668 (C=O) cm.$^{-1}$. The n.m.r. spectrum consisted of a broad singlet at τ 1·05 (1 amino H, disappears on deuteriation), several multiplets between τ 1·4 and 3·0 (9ArH), a singlet at τ 7·68 (3, methyl).

5,6-Dihydro-6-ethoxy-7-oxodibenz[b,d]*azepine*.— 5,6-Dihydro-7-oxo-5-toluene-*p*-sulphonyldibenz[*b,d*]azepine (2·0 g.) in benzene (50 ml.) was added with mechanical stirring to sodium ethoxide [from sodium (2·5 g.)] in ethanol (100 ml.) After 16 hr., the reaction mixture was treated with water and allowed to separate; the organic layer was washed with water, dried, and evaporated to leave the *product* (1·5 g.) which recrystallised from light petroleum (b.p. 60—80°) as prisms, m.p. 134° [Found: C, 76·0; H, 5·8; N, 5·8%; *M* (mass spectrum), 253·10971. $C_{16}H_{15}NO_2$ requires C, 75·95; H, 6·0; N, 5·55%; *M*, 253·11027], $\nu_{max.}$ (Nujol), 3170 (N–H), 1638 (C=O), and 1595; 1572 cm.$^{-1}$ (aryl C=C). The n.m.r. spectrum (in $CDCl_3$) consisted of a multiplet between τ 2·1 and 3·0 (8 aryl H), a doublet centred at τ 5·2 (1 tertiary H), a multiplet centred at τ 5·75 (2 methene H), a doublet centred at τ 6·42 (1 amino H) and a triplet centred at τ 8·75 (3H methyl). Deuteriation removed the signal at τ 6·42 and the τ 5·2 signal collapsed to a singlet.

5,6-Dihydro-6-hydroxy-7-oxodibenz[b,d]*azepine*.[1,2]— The previous ethoxy-azepine (200 mg.) was left 2 hr. at 30° with ethanol (50 ml.) containing concentrated hydrochloric acid (0·5 ml.) and then treated with water (excess). The product (110 mg.) was obtained by extraction with chloroform and crystallised from ethanol as needles, m.p. 239—240° (lit.,[1,2] m.p. 238°) undepressed by the material obtained previously [1,2] [Found: C, 74·6; H, 5·1%; *M*(osmometer) 223, (mass spectrum) 225·07868. Calc. for $C_{14}H_{11}NO_2$: C, 74·65; H, 4·9%; *M*, 225·07897]. The n.m.r. spectrum (in C_5D_5N) consisted of a multiplet between τ 1·5 and 2·9 (8 aryl protons) and three singlets (each area 1) at τ −1·8 (OH), 1·3 (amino) and 4·7 (tertiary). The *monoacetate* had m.p. 267° [Found: C, 71·5; H, 5·1; N, 5·3; *M*(mass spectrum), 267·0904. $C_{16}H_{13}NO_3$ requires C, 71·9; H, 4·85; N, 5·25%; *M*, 267·0895].

6-Ethoxy-7-oxodibenz[b,d]*azepine*.— 5,6-Dihydro-6-ethoxy-7-oxodibenz[*b,d*]azepine (1 g.) was heated under reflux (Dean and Stark) in dry benzene (500 ml.) containing active manganese dioxide [4] (1 g.) for 18 hr. After filtration through Kieselguhr, the solvent was removed leaving the *product* (0·95 g.) which crystallised as needles (ethanol), m.p. 118° [Found: C, 76·15; H, 5·2; N, 5·6%; *M* (mass spectrum), 251·09307. $C_{16}H_{13}NO_2$ requires C, 76·5; H, 5·15; N, 5·55%; *M*, 251·09462]. Carbonyl $\nu_{max.}$ 1697 (hexane), 1691 (benzene), 1682 (chloroform) cm.$^{-1}$ C=N– $\nu_{max.}$ 1645 ± 2 cm.$^{-1}$ in all solvents (P.E. 125 instrument). The n.m.r. spectrum ($CDCl_3$) showed a multiplet between τ 2·0 and τ 2·9 (8ArH), a quartet centred at τ 5·6 (2H CH_2) and a triplet centred at τ 8·62 (3H CH_3).

Phenanthridine-6-carboxylic Acid.—This product, m.p. 154° was obtained by a literature method,[11] its identity was checked by mass spectroscopy which gave a molecular ion *m/e* 223·06335 (Calc. for $C_{14}H_9NO_2$: 223·06332). It was converted to the ethyl ester (m.p. 54°)[12] which had a molecular ion *m/e* 251·09437 (Calc. for $C_{16}H_{13}NO_2$: 251·09462).

N-2-*Biphenylyl*-N-*toluene*-p-*sulphonyl*-α-*alanine*.— 2-Toluene-*p*-sulphonamidobiphenyl (32 g.), ethyl α-bromopropionate (18·1 g.), anhydrous potassium carbonate (12 g.), and dry acetone (500 ml.) were heated under reflux for 40 hr. The mixture was filtered and the residue was washed with chloroform. Evaporation of the combined solvents left the *ethyl ester* (40 g.) which crystallised from ethanol as needles, m.p. 123° [Found: C, 68·3; H, 6·05; N, 3·3. $C_{24}H_{25}NO_4S$ requires C, 68·1; H, 5·95; N, 3·3%], $\nu_{max.}$ (Nujol) 1724 cm.$^{-1}$ (ester). Sodium hydroxide (4·5 g.) in water (50 ml.) was added during 2 hr. to the ethyl ester (39·5 g.) in ethanol (600 ml.) and water (50 ml.) at 65° with stirring. After 15 hr. at 20° the *acid* was isolated and

[10] P. A. Petyunin, *Zhur. obsch. Khim.*, 1960, **30**, 4042.
[11] G. Wittig, M. A. Jesaitis, and M. Glos, *Annalen*, 1952, **577**, 1.
[12] L. P. Walls, *J. Chem. Soc.*, 1934, 104.

crystallised from benzene as needles (12 g.), m.p. 159—160° [Found: C, 68·6; H, 5·7; N, 3·5. $C_{22}H_{22}NO_4S$ requires C, 68·8; H, 5·4; N, 3·55%], $\nu_{max.}$ (Nujol) 1718 cm.$^{-1}$ $\left(-C\begin{matrix}O\\OH\end{matrix}\right)$.

5,6-Dihydro-6-methyl-7-oxo-5-toluene-p-*sulphonyldibenz*[b,d]*azepine*.—The previous acid (12 g.) was converted (thionyl chloride) to the acid chloride and cyclised at from −70° to 20° as previously described for the parent compound [1] excepting that the solvent was methylene dichloride. The chromatographed *product* (8·2 g.) crystallised from methanol as needles, m.p. 131—132° [Found: C, 70·4; H, 5·2; N, 3·65. $C_{22}H_{19}NO_3S$ requires C, 70·0; H, 5·1; N, 3·7%], $\nu_{max.}$ (Nujol) 1669 cm.$^{-1}$ (C=O). The n.m.r. spectrum showed a multiplet from τ 2·3 to 3·3 (12 ArH), a quartet at τ 4·6 (1 tertiary H on C-6), a singlet at τ 7·7 (3 methyl H, *p*-tolyl) and a doublet at τ 8·57 (3 methyl H on C-6). The 2,4-*dinitrophenylhydrazone* crystallised from ethanol as yellow needles, m.p. 192—195° [Found: N, 12·5. $C_{28}H_{23}N_5O_6S$ requires N, 12·55%].

The first eluates from the column yielded *6-methyl-N-toluene*-p-*sulphonyl-5,6-dihydrophenanthridine*, m.p. 167° from benzene–light petroleum (b.p. 60—80°) [1·64 g.] [Found: C, 72·1; H, 5·8; N, 4·2. $C_{21}H_{19}NO_2S$ requires C, 72·2; H, 6·05; N, 4·0%]. The i.r. spectrum contained no peaks attributable to carbonyl, hydroxy- or amino-groups. The n.m.r. spectrum consisted of the following signals: τ 2·0 to 3·5 (m, 12 Ar), τ 4·56 (quartet 1 tertiary H), τ 7·9 (s 3H; methyl) and τ 8·78 (d, 3H, methyl).

6-Acetylphenanthridine.— 5,6-Dihydro-6-methyl-7-oxo-5-toluene-*p*-sulphonyldibenz[*b,d*]azepine (1·1 g.) in dry toluene (15 ml.) was added under nitrogen to a suspension of sodium methoxide (150 mg.) in dry toluene (30 ml.). After 24 hr. at 0°, the mixture was poured into ice-cold water (10 ml.) and allowed to separate. The toluene solution was poured onto a column (1·5 in. × 1·5 in.) of neutralised, deactivated alumina and eluted with benzene; evaporation of the eluate gave a crude product (350 mg.) from which starting material (75 mg.) was first crystallised (m.p. and mixed m.p. 131—132°) using benzene. The liquor was diluted with light petroleum (b.p. 60—80°) and kept 24 hr. at 0°: *6-acetylphenanthridine* (165 mg.) was obtained as yellow needles, m.p. 89—90° [Found: C, 81·3; H, 5·2; N, 6·2%; *M* (mass spectrum), 221·08364. $C_{15}H_{11}NO$ requires C, 81·4; H, 5·05; N, 6·3%; *M*, 221·08406], $\nu_{max.}$ (Nujol) 1692 cm.$^{-1}$ (C=O). The n.m.r. spectrum showed a multiplet from τ 1·0 to 2·7 (8 ArH) and at τ 7·1 (s, 3H, CH_3). The 2,4-*dinitrophenylhydrazone* crystallised from ethanol as needles, m.p. 283—285° [Found: N, 17·6. $C_{21}H_{15}N_5O_4$ requires N, 17·45%].

When methyl-lithium was treated under nitrogen in tetrahydrofuran with phenanthridine-6-carboxylic acid, several products were identified but none was identical with the one described above.

5,6-Dihydro-6-methyl-7-oxodibenzyl[b,d]*azepine*.— 5,6-Dihydro-6-methyl-7-oxo-5-toluene-*p*-sulphonyldibenz[*b,d*]-azepine (250 mg.) in dry tetrahydrofuran (50 ml.) was treated with sodium hydride (50% dispersion, 100 mg.) under nitrogen. After 2 hr. at 20°, the reaction mixture was poured onto a small pad of neutral deactivated alumina and eluted with benzene. Evaporation yielded the *product* (140 mg.), m.p. 182° (from chloroform) [Found: C, 80·3; H, 6·1; N, 6·2%; *M* (mass spectrum), 223·09967. $C_{15}H_{13}NO$ requires C, 80·8; H, 5·9; N, 6·3%; *M*, 223·09971], $\nu_{max.}$ (Nujol) 1635 cm.$^{-1}$ (C=O) [P.E. 125].

When the above substance was stirred with manganese dioxide in dry methylene dichloride, phenanthridone, m.p. and mixed m.p. 285—287°, was obtained.

6-Benzylidine-5,6-dihydro-7-oxo-5-toluene-p-*sulphonyldibenz*[b,d]*azepine*.— 5,6-Dihydro-7-oxo-5-toluene-*p*-sulphonyl dibenz[*b,d*]azepine (6 g.), benzaldehyde (2·5 ml. freshly distilled), ethanol (100 ml.), benzene (25 ml.), and piperidine (0·8 ml.) were left together 4 days and the product (5 g.) was filtered off. It crystallised from benzene–light petroleum (b.p. 60—80°) as prisms, m.p. 200° [Found: N, 2·9; O, 11·1. $C_{28}H_{21}NO_3S$ requires N, 3·1; O, 10·6%], $\nu_{max.}$ (Nujol) 1690 (C=C) and 1668 (C=O) cm.$^{-1}$. In similar fashion was obtained *5,6-dihydro-6-p-nitrobenzylidine-7-oxo-5-toluene*-p-*sulphonyldibenz*[b,d]*azepine* from toluene as a pale yellow solid, m.p. 250° (Found: C, 67·65; H, 4·15; N, 5·45; O, 15·8. $C_{23}H_{20}N_2O_5S$ requires C, 67·8; H, 4·05; N, 5·65; O, 16·1%).

5,6-Dihydro-6-benzyl-7-oxo-5-toluene-p-*sulphonyldibenz*[b,d]*azepine*.—The corresponding 6-benzylidine compound from above (1 g.) was hydrogenated in acetic acid over 10% palladised charcoal (uptake 56 c.c.). The *product* (0·6 g.) was obtained in the usual way from ethanol and had m.p. 147° (Found: C, 73·55; H, 5·2; N, 3·1. $C_{28}H_{23}NO_3S$ requires C, 73·4; H, 5·1; N, 3·1%), $\nu_{max.}$ (Nujol) 1667 cm.$^{-1}$ (C=O).

When the above benzylazepinone (500 mg.) was allowed to react with sodium hydride (50% dispersion, 100 mg.) in dry tetrahydrofuan (100 ml.) under nitrogen for 3 hr. at 20°, the product was obtained as a gum in the previously described manner. This was chromatographed on a short, silica-gel column; only one fraction gave crystalline *6-benzyl-7-oxodibenz*[b,d]*azepine* (15 mg.), m.p. 105° (from ethanol) [Found: C, 84·7; H, 5·3%; *M* (mass spectrum), 297·11458. $C_{21}H_{15}NO$ requires C, 84·9; H, 5·1%; *M*, 297·11539], $\nu_{max.}$ (Nujol) 1695 cm.$^{-1}$ (C=O). All other fractions from the above chromatography contained benzaldehyde.

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