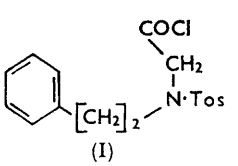
681. *Azabenzocycloheptenones. Part IV.* An Azadibenzotropone.*

By W. Paterson and G. R. Proctor.

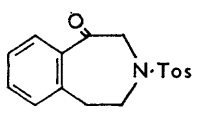
The synthesis of the first of a new class of heterocyclic compound, azadibenzotropones, is described. It appears to be more polar than was expected.

Previous work [1] has shown that the Friedel–Crafts cyclisation reaction did not give cyclic 7-membered amino-ketones when applied to arylamino-acids except in the case of the acid chloride (I) which gave a mixture of an isoquinoline derivative [2] and the ketone (II), the former predominating. A study of the conditions which favoured decarbonylation in this and other examples [3] suggested that it could be minimised by working at low temperatures and that a ketone might be produced as the major product in a sterically more favourable example (*e.g.*, III).



(I)

(Tos = p-$C_6H_4Me{\cdot}SO_2$)



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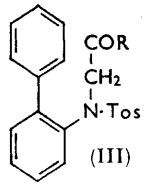
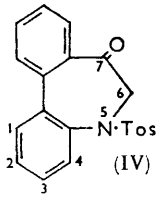


(III)



(IV)

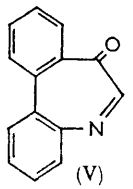
In agreement with these predictions the acid chloride (III; R = Cl) gave the ketone (IV) in almost quantitative yield [4] when treated with anhydrous aluminium chloride in chloroform at −70°; other variants employing stannic chloride, polyphosphoric acid, or aluminium chloride at higher temperatures gave derivatives of phenanthridine.

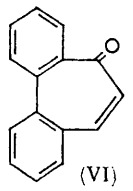
Although mineral acids had little effect on compound (IV), it was converted into the azatropone (V) in 60% yield by sodium alkoxide in toluene at room temperature. The by-products were phenanthridone and a substance $C_{14}H_{11}NO_2$ of m. p. 230° which was also obtained from the product (V) on treatment with zinc dust and dilute acetic acid. We previously [4] suggested structure (VII) for this by-product but we now prefer (VIIa) for the following reasons. The substance did not react with acetic anhydride, sodium borohydride, or toluene-*p*-sulphonyl chloride, but gave phenanthridone when heated with palladised

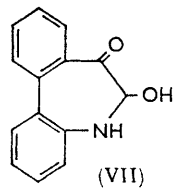
* Part III, *J.*, 1961, 3989.

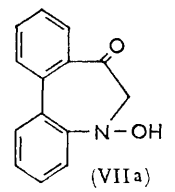
[1] Part I, *J.*, 1957, 2302.
[2] von Braun, Blessing, and Cahn, *Ber.*, 1924, **57**, 910.
[3] Rothstein and Saville, *J.*, 1949, 1946 *et seq.*
[4] Proctor, *Chem. and Ind.*, 1960, 408.

charcoal in boiling trichlorobenzene.[5] The infrared spectrum was consistent with structure (VIIa); although little information is available on the absorption spectra of substituted hydroxylamines, the peaks at 3220, 1484, and 1136 cm.$^{-1}$ correspond with those reported for an isopropylhydroxylamine.[6] Moreover, a positive ferrous hydroxide colour test [7] for hydroxylamines was obtained; and the nuclear magnetic resonance spectrum showed eight


(V)


(VI)


(VII)


(VIIa)

aromatic protons (τ 2·17—3·08), one hydroxyl proton (τ 5·35), and two methylene protons (τ 6·99).

Although the ketone (IV) was reduced to the corresponding alcohol by lithium aluminium hydride, the azatropone (V) was remarkably resistant to reduction: it was unaffected by hydrogen on a platinum or palladium catalyst in dioxan at atmospheric pressure and by lithium in diethylamine; [8] with lithium aluminium hydride in tetrahydrofuran it gave phenanthridone as the only product isolated. The latter was also obtained by heating the compound alone. It was not possible to demonstrate that this interesting reaction was monomolecular and involved the extrusion of a single carbon atom: since the yield was always about 50%, a disproportionation is not excluded.

Properties of compounds (VI) and (V).

Compound (VI) *	Compound (V)
M. p. 84°.	M. p. 265°.
Very pale yellow.	Deep red. Hydrochloride, violet.
Soluble in organic solvents.	Poorly soluble in organic solvents.
$\nu_{max.}$ 1645 cm.$^{-1}$ (in KBr).	$\nu_{max.}$ 1590, 1620 cm.$^{-1}$ (in KCl).†
2,4-Dinitrophenylhydrazone,‡ m. p. 231—232°.	No 2,4-dinitrophenylhydrazone.

* We thank Professor Heilbronner for a gift of this material (cf. Naville, Strauss, and Heilbronner, *Helv. Chim. Acta*, 1960, **43**, 1221.

† It is not certain whether the infrared carbonyl stretching frequency should be allocated to the peak at 1620 cm.$^{-1}$ or to that at 1590 cm.$^{-1}$.

‡ Cook, Dickson, and London, *J.*, 1947, 749.

A comparison (see Table) indicates that the azatropone (V) is more polar than the dibenzotropone (VI) and this should stimulate interest in the simple heterocyclic analogues.

Experimental

2-Aminobiphenyl.—When the technical product was unobtainable the amine was prepared by the reduction of 2-nitrobiphenyl,[9] itself obtained by direct nitration of biphenyl [10] or from *o*-nitroaniline by the Gomberg reaction.[11]

*2-Toluene-*p*-sulphonamidobiphenyl.*—When 2-aminobiphenyl (16 g.), toluene-*p*-sulphonyl chloride (22·5 g.), and dry pyridine (100 ml.) were heated together for 5 min., then set aside for 2 hr., and the mixture was worked up in the usual way, the *amide* was obtained; it crystallised from methanol in prisms, m. p. 99·5° (82%) (Found: C, 70·3; H, 5·2; N, 4·5; S, 9·85. $C_{19}H_{17}NO_2S$ requires C, 70·7; H, 5·3; N, 4·35; S, 9·9%).

[5] Cook, Gibb, Raphael, and Somerville, *J.*, 1952, 603.
[6] Gilsdorf and Nord, *J. Amer. Chem. Soc.*, 1952, **74**, 1840.
[7] Feigl, " Spot Tests in Inorganic Analyses," Elsevier, Amsterdam, 1958, p. 246.
[8] Birch and Smith, *Quart. Rev.*, 1958, **12**, 21.
[9] Scarborough and Waters, *J.*, 1927, 91.
[10] Bell, Kenyon, and Robinson, *J.*, 1926, 1242; Dewar, Mole, Urch, and Warford, *J.*, 1956, 3572.
[11] Elks, Haworth, and Hey, *J.*, 1940, 1285.

N-2-*Biphenylyl*-N-*toluene*-p-*sulphonylglycine* (III; R = OH).—The above sulphonamide (73 g.), ethyl bromoacetate (41 g.), and anhydrous sodium carbonate (70 g.) were refluxed together in dry toluene (300 ml.) for 48 hr. The mixture was filtered and the residue was washed with chloroform. Evaporation of the combined solvents left an oil (95 g.) which yielded the *ethyl ester* (63 g.), prisms (from ethanol), m. p. 119° (Found: C, 67·7; H, 5·6; N, 3·45. $C_{23}H_{23}NO_4S$ requires C, 67·45; H, 5·65; N, 3·4%). (Direct hydrolysis of the mother-liquors gave a further 19 g. of the acid, bringing the overall yield to 91%.) Hydrolysis with aqueous-methanolic sodium hydroxide for 3 hr. at 30° yielded quantitatively the *acid* which, crystallised from benzene, had m. p. 199° (Found: C, 66·4; H, 5·3; N, 3·6; S, 8·5. $C_{21}H_{19}NO_4S$ requires C, 66·1; H, 5·0; N, 3·7; S, 8·4%), $\nu_{max.}$ (in Nujol) 3150, 1750, and 1760 cm.$^{-1}$. The *methyl ester* was obtained from methanol in prisms, m. p. 117° (Found: C, 66·7; H, 5·1; N, 3·5. $C_{22}H_{21}NO_4S$ requires 66·8; H, 5·3; N, 3·5%).

Treatment of the acid with an excess of thionyl chloride gave the *acid chloride* which crystallised from light petroleum (b. p. 100—120°) in needles, m. p. 132—133° (Found: C, 63·7; H, 4·6; Cl, 8·1. $C_{21}H_{18}ClNO_3S$ requires C, 63·1; H, 4·55; Cl, 8·8%).

The *anilide* crystallised from acetic acid and had m. p. 245° (decomp.) (Found: C, 71·05; H, 5·35. $C_{27}H_{24}N_2O_3S$ requires C, 71·05; H, 5·3%).

Treatment of the Acid (III; R = OH) *with Polyphosphoric Acid.*—The acid described above (2 g.) was treated with polyphosphoric acid (20 g.) for 40 hr. at 60°; the mixture was then diluted with water, extracted with chloroform, basified with 10% aqueous sodium carbonate, and extracted with chloroform. The latter was dried and evaporated, leaving the product which crystallised from aqueous methanol in needles, m. p. 105—106° undepressed by genuine phenanthridine. This base formed a picrate, obtained from methanol as a yellow powder, m. p. 247° (230—240° on a Kofler block; lit., 220°) (Found: C, 55·6; H, 3·4. Calc. for $C_{19}H_{12}N_4O_7$; C, 55·9; H, 3·0%).

Treatment of the Acid Chloride (III; R = Cl) *with Stannic Chloride.*—The acid chloride described above (2·0 g.) was dissolved in dry benzene (20 ml.), cooled to 5°, and treated with anhydrous stannic chloride (2·5 g.) in benzene (20 ml.) with stirring. After 1 hr. at 5°, the mixture was kept at room temperature for 17 hr. and then worked up. An acidic fraction (0·5 g.) was obtained from which the starting acid (III; R = OH) was isolated. The neutral fraction yielded 9,10-*dihydro*-N-*toluene*-p-*sulphonylphenanthidine* from methanol as a solid, m. p. 102° (Found: C, 71·4; H, 5·2; N, 4·2. $C_{20}H_{17}NO_2S$ requires C, 71·6; H, 5·1; N, 4·2%).

5,6-*Dihydro*-7-*oxo*-5-*toluene*-p-*sulphonyldibenz*[b,d]*azepine* (IV).—The acid (III; R = OH) (28 g.) was refluxed with thionyl chloride (80 ml.) for 1 hr. and the excess of reagent was removed *in vacuo*. The crude acid chloride was dissolved in dry chloroform (100 ml.) and cooled with stirring to −70°; freshly powdered anhydrous aluminium chloride (38 g.) was added at once and stirring continued while the mixture was allowed to reach room temperature in 4—5 hr. After treatment with ice, the chloroform was separated, washed successively with dilute hydrochloric acid, cold dilute sodium hydroxide solution, dilute hydrochloric acid, and water, dried, and evaporated, to yield the *product*. This was chromatographed on alumina and crystallised from methanol, giving colourless material, m. p. 137° (90%) (Found: C, 69·1; H, 4·9; N, 3·9. $C_{21}H_{17}NO_3S$ requires C, 69·4; H, 4·7; N, 3·8%), $\nu_{max.}$ (in Nujol) 1685 cm.$^{-1}$. Use of carbon disulphide in this reaction gave less successful results.

The 2,4-*dinitrophenylhydrazone* was orange and had m. p. 212° (Found: C, 59·3; H, 4·1; N, 12·9. $C_{27}H_{21}N_5O_6S$ requires C, 59·65; H, 3·9; N, 12·9%. The ketone could be regenerated from this in 60% yield by using *m*-nitrobenzaldehyde in butan-1-ol.[12]

The ketone was recovered after treatment for 5 days with hydrogen bromide and phenol in glacial acetic acid [13] at room temperature. Refluxing the ketone with an excess of concentrated hydrochloric acid in acetic acid led to an 82% recovery of the starting material and a small (~1%) yield of an oil which, with Brady's reagent, gave a precipitate. The latter was presumed to be the 2,4-*dinitrophenylhydrazone* of 5,6-dihydro-7-oxo-dibenz[*b,d*]azepine and was obtained from nitrobenzene as a yellow solid, m. p. 301° (Found: C, 61·85; H, 3·6; N, 17·8. $C_{20}H_{15}N_5O_4$ requires C, 61·7; H, 3·9; N, 18·0%).

5,6-*Dihydro*-7-*hydroxy*-5-*toluene*-p-*sulphonyldibenz*[b,d]*azepine*. — 5,6-Dihydro-7-oxo-5-toluene-*p*-sulphonyldibenz[*b,d*]azepine (1·9 g.), lithium aluminium hydride (excess), and tetrahydrofuran (250 ml.) were refluxed for 17 hr. After addition of ice and hydrochloric acid, the

[12] Proctor and Thomson, *J.*, 1957, 2314; Rupe and Gassman, *Helv. Chim. Acta*, 1936, **19**, 569.
[13] Weisblat, Magerlein, and Myers, *J. Amer. Chem. Soc.*, 1953, **75**, 3630.

mixture was extracted with chloroform, from which a neutral product was obtained. This *alcohol* crystallised from methanol in prisms, m. p. 140° (70%) (Found: C, 68·8; H, 5·3; N, 3·9. $C_{21}H_{19}NO_3S$ requires C, 69·0; H, 5·2; N, 3·9%), $\nu_{max.}$ (in Nujol) 3390 cm.$^{-1}$.

7-*Oxodibenz*[b,d]*azepine* (V).—A nitrogen-saturated suspension of 5,6-dihydro-7-oxo-5-toluene-*p*-sulphonyldibenz[*b*,*d*]azepine (1·9 g.) in dry toluene (80 ml.) was added at once to a nitrogen-saturated suspension of sodium methoxide (2 g.) in dry toluene (150 ml.). The mixture was left at 20° for 12 hr., poured into water (300 ml.), and filtered. The residual *ketone* (610 mg.) crystallised from tetralin in purple needles, m. p. 267° [Found: C, 81·0; H, 4·3; H, 7·0%; *M* (by mass spectroscopy), 207. $C_{14}H_9NO$ requires C, 81·1; H, 4·3; N, 6·8%; *M*, 207], $\nu_{max.}$ (in KCl) 1620, 1590, 1575 cm.$^{-1}$, $\lambda_{max.}$ (in $CHCl_3$) 247, 290 infl., 495 mμ (ε 21,600, 6030, 4630). From the aqueous alkaline layer phenanthridone (13%) was obtained.

Phenanthridone.[14]—Sodium methoxide (4·5 g.), 5,6-dihydro-7-oxo-5-toluene-*p*-sulphonyldibenz[*b*,*d*]azepine (1·9 g.), and dry toluene (250 ml.) were saturated with oxygen and left at 20° for 2½ hr. After addition of water, the aqueous layer was acidified and extracted with chloroform which was dried and evaporated, to leave phenanthridone, which crystallised from methanol in needles, m. p. 285° (sublimed) (35%) (Found: C, 80·1; H, 4·3; N, 7·4. Calc. for $C_{13}H_9NO$: C, 80·0; H, 4·6; N, 7·2%), $\lambda_{max.}$ (in EtOH) 242, 250, 260, 310, 322 (ε 23,300, 17,650, 19,700, 8310, and 10,800). This material was distilled with zinc dust and yielded phenanthridine.

5,6-*Dihydro*-5-*hydroxy*-7-*oxodibenz*[b,d]*azepine* (VIIa).—The toluene solution from the previous experiment was washed with dilute hydrochloric acid, dried, and evaporated, leaving an oil which crystallised from methanol in needles, m. p. 230° (42%) [Found: C, 74·6; H, 5·0; N, 6·3%; *M* (cryoscopically), 233, $C_{14}H_{11}NO_2$ requires C, 74·65; H, 4·9; N, 6·2%; *M*, 225], $\nu_{max.}$ (in Nujol) 3225, 1680 cm.$^{-1}$, $\lambda_{max.}$ (in EtOH) 209, 232, 250 infl. (ε 27,600, 42,700, 12,000). A positive reaction was obtained with ferrous hydroxide,[7] whereas a negative result was found for phenanthridone and the ketone (IV).

The same product was obtained (7%) in similar fashion during the preparation of 7-oxodibenz[*b*,*d*]azepine.

Reactions of 5,6-*Dihydro*-5-*hydroxy*-7-*oxodibenz*[b,d]*azepine*.—(*a*) The azepine (130 mg.), 20% palladised charcoal (542 mg.), and trichlorobenzene were refluxed together for 5 hr., cooled, and filtered. The organic layer was washed successively with dilute alkali, acid, and water; after drying and evaporation of the solvent, a colourless solid (70 mg.) indistinguishable from phenanthridone was obtained.

(*b*) The azepine was recovered quantitatively after treatment with an excess of acetic anhydride in dry pyridine at room temperature for 48 hr.

(*c*) The azepine was recovered in 80% yield after boiling for 1 hr. in acetic acid–concentrated hydrochloric acid (1 : 1) at the b. p. and after 2 hr. in polyphosphoric acid at 100°.

(*d*) The azepine (30 mg.) in an excess of dry pyridine was treated with toluene-*p*-sulphonyl chloride (25 mg.) at room temperature overnight, but the starting material (24 mg.) was recovered.

Reactions of 7-*Oxodibenz*[b,d]*azepine*.—(*a*) The azepine (77 mg.) was heated for 60 hr. in a sealed tube at 190°. White crystals sublimed into the cold part of the tube and crystallised from methanol in needles, m. p. 293° (43%). The m. p. was undepressed on admixture with phenanthridone.

(*b*) The azepine (1·2 g.), dry tetrahydrofuran (250 ml.), and lithium aluminium hydride (excess) were refluxed together for 40 hr. and worked up as described previously. This gave 30% of phenanthridone.

(*c*) The azepine (58 mg.), " AnalaR " glacial acetic acid (25 ml.), and zinc dust (2 g.) were left at 20° for 48 hr. before filtration. Removal of the solvent, chromatography on alumina, and elution with 99 : 1 chloroform–methanol gave phenanthridone (12 mg.).

(*d*) The azepine was recovered unchanged after being shaken for 24 hr. at 1 atm. with hydrogen and the following catalysts: palladium–carbon, palladium–calcium carbonate, reduced platinum oxide–carbon. Both dioxan and ethanol were used as solvents.

(*e*) The azepine was recovered after treatment in tetrahydrofuran for 24 hr. with an excess of lithium in diethylamine [8] at 20°.

(*f*) When experiment (*c*) was repeated with the addition of water, the product was 5,6-dihydro-5-hydroxy-7-oxodibenz[*b*,*d*]azepine, m. p. and mixed m. p. 230°.

[14] Oyster and Adkins, *J. Amer. Chem. Soc.*, 1921, **43**, 210; Walls, *J.*, 1935, 1405.

7-*Oxodibenz*[b,d]*azepine Hydrochloride*.—(*a*) When 7-oxodibenz[*b*,*d*]azepine (108 mg.) in dioxan was saturated with dry hydrogen chloride, a violet *hydrochloride* (100 mg.) separated. This crystallised from ether in needles, m. p. 249° (Found: C, 68·5; H, 4·5; Cl, 14·7. $C_{14}H_{10}ClNO$ requires C, 69·0; H, 4·1; Cl, 14·6%), $\lambda_{max.}$ (in EtOH) 202, 211, 238, 530 mμ (ε 22,100, 20,000, 17,250, 2625).

(*b*) 70% Perchloric acid (1 ml.) was added to 7-oxodibenz[*b*,*d*]azepine (188 mg.) in dioxan (100 ml.). The solution was extracted with chloroform which was washed with water, dried, and evaporated, leaving a purple solid (260 mg.), m. p. 135—140°. Crystallisation from ether yielded the hydrochloride (180 mg.), m. p. 249°.

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