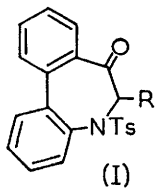
Azabenzocycloheptenones. Part X.† Brominated Dibenz[*b*,*d*]azepines

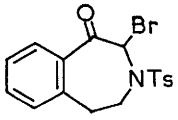
By **G. R. Proctor** * and **W. C. Peaston**, Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow C.1

Bromination of 5,6-dihydro-5-tolylsulphonyldibenz[*b*,*d*]azepin-7-one has been studied. 2-Bromo-5,6-dihydro-5-*p*-tolylsulphonyldibenz[*b*,*d*]azepin-7-one has been synthesised and has been converted into several derivatives.

We have been interested [1] in obtaining dibenz[*b*,*d*]-azepine derivatives suitable for *X*-ray study and have, therefore, investigated methods for the introduction of bromine into the ketone (I; R = H). Treatment of (I; R = H) with molar proportions of bromine in solvents or with *N*-bromosuccinimide in carbon tetra-



(I)



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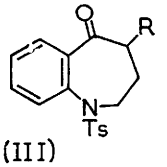

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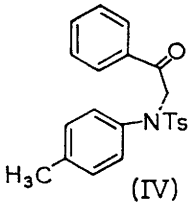
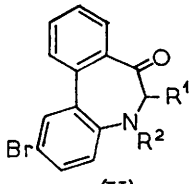


(IV)

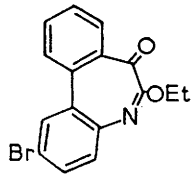
Ts = *p*-MeC$_6$H$_4$·SO$_2$

chloride gave mixtures of three main components in differing proportions. These were, the starting material (I; R = H), the alcohol (I; R = OH), and the hydrobromide of phenanthridine-6-carboxylic acid. It would appear that the desired bromo-compound (I; R = Br) is very reactive since, although some of the ethoxy-compound (I; R = OEt) could be obtained by quenching the reaction in ethanol, the yield was never more than 10%. When the ketone (I; R = H) was treated with an excess of bromine, the only product isolated was, what we believe to be, the hydrobromide of 2-bromophenanthridine-6-carboxylic acid. It is interesting that when the related benz[*d*]azepinone (II) is warmed in ethanol, the bromine atom is replaced [2] although the compound is unaffected by treatment with an excess of bromine; in contrast the benz[*b*]azepinone (III; R = H) gave both a monobromo- (III; R = Br) and a dibromo-ketone both of which crystallised unchanged from ethanol.[3] We find that an open-chain analogue of (I; R = H), *N*-*p*-tolysulphonyl-*N*-phenacyl-*p*-toluidine (IV) was also cleaved by bromination to give 2-bromo-*N*-*p*-tolylsulphonyl-*p*-toluidine: in this compound there is no driving force for reforming a carbon–nitrogen bond nor for cleavage of the N–S bond. Cleavage of C–N bonds during halogenation has been previously observed.[4]

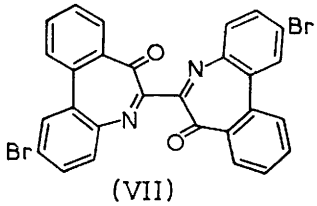
Since direct bromination of (I; R = H) was unsuccessful we synthesised the bromo-ketone (V; R^1 = H, R^2 = tosyl) (*cf.* ref. 5) from 5-*bromo*-2-(*N*-*p*-tolylsulphonylamino)biphenyl.[6] The ketone (V; R^1 = H, R^2 = tosyl) was converted into the amino-ketones (V; R^1 = OEt, R^2 = H) and (V; R^1 = OH, R^2 = H) as described for the parent system; [1] the bromodibenzazatropone (VI) and the dimeric bromoazatropone (VII) were also obtained. The *X*-ray data on these compounds will be published later.



(V)

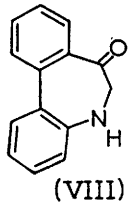


(VI)

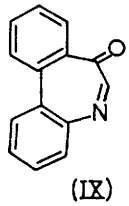


(VII)

Detosylation of the ketone (I; R = H) by sodium in liquid ammonia gave, unexpectedly, 6-methylphenanthridine; [7] it seems probable that cleavage of the N–C bond is followed by ring contraction to give a 6-substituted phenanthridine which is reduced by the medium.



(VIII)



(IX)

Since, as we described previously,[5] the N–S bond in (I; R = H) resists acid hydrolysis, we examined zinc chloride-catalysed hydrolysis; [8] the expected product (VIII) from this might have been expected to undergo bromination in the 6-position. In fact this reaction

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[8] D. Klamann and G. Hofbauer, *Annalen*, 1953, **581**, 182.

gave 6-formylphenanthridine [9] which we believe arises by oxidation of (VIII) to give the azatropone (IX) with subsequent hydrolysis of this (*cf.* ref. 10) to give the phenanthridine.

EXPERIMENTAL

Reaction of 5,6-*Dihydro*-5-p-*tolylsulphonyldibenz*[b,d]*azepin*-7-*one* (I; R = H] *with Bromine*.—The azepinone (2·85 g.), bromine (0·4 ml.), and dry methylene dichloride were stirred together for 2 hr.; the solvent was removed and the residue was left in sodium-dried benzene. After 2 months the hydrobromide phenanthridine-6-carboxylic acid (250 mg.) was obtained as a yellow *powder*, m.p. 178° (decomp.) (Found: C, 55·7; H, 3·4; N, 4·15; Br, 25·9. $C_{14}H_{10}BrNO_2$ requires C, 55·3; H, 3·3; N, 4·6; Br, 26·3%]. This was identical to compound obtained by passing hydrogen bromide into phenanthridine-6-carboxylic acid [11] in dry benzene. A quantity of the latter compound (220 mg.) was obtained by extracting the benzene liquors from the former experiment with ammonium hydroxide solution. It crystallised from benzene as a buff powder, m.p. 158° (efferv.) [11] (Found: C, 75·45; H, 4·1; N, 6·3. Calc. for $C_{14}H_9NO_2$: C, 75·4; H, 4·05; N, 6·3%). The benzene solution after chromatography upon silica gave the starting azepinone (900 mg.; m.p. and mixed m.p. 136°) and 5,6-*dihydro*-6-*hydroxy*-5-*tolyl*-*p*-*sulphonyldibenz*[b,d]*azepin*-7-*one* (I; R = OH) (200 mg.) as cubes, m.p. 207° (from benzene (Found: C, 66·25; H, 4·45; N, 3·4. $C_{21}H_{17}NSO_4$ requires C, 66·55; H, 4·5; N, 3·7%), τ 2·15—3·2 (m, 12H, aryl), τ 4·99 (d, 1H, 6-H), τ 6·26 (d, 1H, OH), and 7·74 (s, 3H, Me): the signal at τ 4·99 collapsed to a singlet on addition of D_2O and the signal at τ 6·26 disappeared.

Essentially the same results were obtained when *N*-bromosuccinimide in dry carbon tetrachloride at room temperature or using phenyltrimethylammonium tribromide [12] in tetrahydrofuran were used for the bromination. When ethanol was used in place of benzene in the above procedure, the product which crystallised was 5,6-*dihydro*-6-*ethoxy*-5-p-*tolyldibenz*[b,d]*azepin*-7-*one* (I; R = OEt), m.p. 103° (Found: C, 68·05; H, 5·3; N, 3·35. $C_{23}H_{20}NO_4S$ requires C, 67·85; H, 5·2; N, 3·45%), $\nu_{max.}$ (Nujol) 1706 cm.$^{-1}$ (C=O), τ 2·3—3·4 (m, 12H), 3·87 (s, 1H), 6·0 (m, 2H), 7·75 (s, 3H), and 8·72 (t, 3H).

5,6-*Dihydro*-6-*methoxy*-5-p-*tolylsulphonyldibenz*[b,d]-*azepin*-7-*one* (I; R = OMe) was obtained from methanol and had m.p. 117° (Found: C, 67·25; H, 5·05; N, 3·5. $C_{22}H_{18}NO_4S$ requires C, 67·25; H, 4·85; N, 3·55%).

6-*Methoxydibenz*[b,d]*azepin*-7-*one*.—The ketone (I; R = OMe) (400 mg.), sodium hydride (25 mg.), and dry tetrahydrofuran were stirred together 3 hr. After filtration through neutral alumina, the product was obtained by chromatography in benzene on silica gel (MFC); it crystallised from methanol as *needles*, m.p. 112° (Found: C, 76·45; H, 4·85. $C_{15}H_{11}NO_2$ requires C, 76·0; H, 4·7%), τ 2·1—2·7 (m, 8H) and 6·05 (s, 3H), $\nu_{max.}$ (Nujol) 1684 (C=O) and 1661 (C=N–) cm.$^{-1}$.

2-*Bromophenanthridine*-6-*carboxylic Acid*.—5,6-Dihydro-5-*p*-tolylsulphonyldibenz[*b*,*d*]azepin-7-one (I; R = H) (1 g.), dry methylene dichloride (50 ml.), and bromine (1 ml.), were set aside overnight. The orange precipitate (800 mg.), washed with methylene dichloride, crystallised from benzene–methanol as *needles*, m.p. 178—180° (efferv.) (185 mg.); the compound was the hydrate of the hydrobromide (Found: C, 42·0; H, 3·1; Br, 39·25; N, 3·3. $C_{14}H_9NO_2$-Br_2,H_2O requires C, 41·95; H, 2·8; Br, 39·85, N, 3·5%]. Neutralisation of the compound yielded the *acid* as prisms, m.p. 172° (efferv.) (from benzene) (Found: C, 55·25; H, 1·9; Br, 26·4; N, 4·5. $C_{14}H_8BrNO_2$ requires C, 55·65; H, 2·6; Br, 26·5; N, 4·65%).

2-*Bromo*-N-p-*tolylsulphonyl*-p-*toluidine*.[13]—*N*-Phenacyl-*N*-*p*-tolylsulphonyl-*p*-toluidine (IV) (5 g.) in chloroform (100 ml.) was treated with bromine (1·4 ml.). After 24 hr. the solvent was removed and the product (2·5 g.) was crystallised from ethanol. It had m.p. 117° and was identical with a genuine sample.[14]

Ethyl N-(5-*Bromobiphenyl*-2-*yl*)-N-p-*tolylsulphonylglycinate*.—5-Bromo-2-(*N*-*p*-tolylsulphonylamino)biphenyl [6] (22 g.), ethyl bromoacetate (10 g.), anhydrous sodium carbonate (50 g.), and dry toluene (250 ml.) were stirred and heated under reflux for 48 hr. After filtration and evaporation of solvent and washings, the product (20 g.) was crystallised from ethanol; it formed flakes, m.p. 120° (Found: C, 56·75; H, 4·7; N, 2·75. $C_{23}H_{22}BrNO_4S$ requires C, 56·6; H, 4·55; N, 2·85%), $\nu_{max.}$ (Nujol) 1754 cm.$^{-1}$ (ester).

N-(5-*Bromobiphenyl*-2-*yl*)-N-p-*tolylsulphonylglycine*.—The above ester (15 g.), aqueous sodium hydroxide (15 ml., 15%), and ethanol (5 ml.) were stirred 1 hr. at 55°. Work up gave the product (12 g., 84%) from ethanol as an ethanol *adduct*, m.p. 166° (Found: C, 54·5; H, 4·8; N, 2·9. $C_{21}H_{16}$-$BrNO_4S$,C_2H_5OH requires C, 54·6; H, 4·8; N, 2·75%), $\nu_{max.}$ (Nujol) 3460 (OH) and 1718 (C=O) cm.$^{-1}$. Crystallisation from toluene–light petroleum (b.p. 60—80°) yielded a solvent-free product, m.p. 160° (Found: C, 54·65; H, 3·9. $C_{21}H_{16}BrNO_4S$ requires C, 55·05; H, 3·5%).

2-*Bromo*-5,6-*dihydro*-5-p-*tolylsulphonyldibenz*[b,d]*azepin*-7-*one* (V; R^1 = H, R^2 = tosyl).—The above acid (10 g.) was converted into the corresponding acid chloride with thionyl chloride. The acid chloride in methylene dichloride (60 ml.) was then cooled and stirred at −30° whilst anhydrous aluminium chloride (8·7 g., finely powdered) was added. After 2 hr. at −20°, the reaction mixture was poured onto ice. The neutral product crystallised from ethanol as needles (6·6 g.), m.p. 145° (Found: C, 56·9; H, 3·65; N, 3·15. $C_{21}H_{16}BrNO_3S$ requires C, 57·05; H, 3·65; N, 3·15%), $\nu_{max.}$ (Nujol) 1689 cm.$^{-1}$ (C=O), τ 2·53—3·3 (m, 11H), 5·2 (q, 2H), and 7·78 (s, 3H).

2-*Bromo*-5,6-*dihydro*-6-*ethoxydibenz*[b,d]*azepin*-7-*ene* (V; R^1 = OEt, R^2 = H).—The above ketone (1 g.) in dry benzene (50 ml.) was added to a solution of sodium ethoxide [from sodium (1 g.) in absolute ethanol (80 ml.)] and the mixture was stirred 20 hr.; it was then poured into water and extracted with benzene. The extract was dried, the solvent was removed; the product (700 mg., 93%) crystallised from ethanol as prisms, m.p. 151° (Found: C, 58·05; H, 4·25; N, 4·45. $C_{16}H_{14}BrNO_2$ requires C, 57·9; H, 4·25; N, 4·2%), $\nu_{max.}$ (Nujol) 3333 (N–H) and 1645 cm.$^{-1}$ (C=O).

2-*Bromo*-6-*ethoxydibenz*[b,d]*azepin*-7-*one* (VI).—The above ethoxyazepine (50 mg.) was stirred 24 hr. at 20° with

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[12] A. Marquet and J. Jacques, *Bull. Soc. chim. France*, 1962, 90.
[13] T. Bryce, G. R. Proctor, and M. A. Rehman, *J. Chem. Soc.*, 1965, 7105.
[14] F. Bell, *J. Chem. Soc.*, 1955, 2376.

active manganese dioxide[15] (excess) in methylene dichloride (50 ml.). After filtration and removal of solvent at $<30°$, the *product* was crystallised from ethanol as needles, m.p. 103° (45 mg., 90%) (Found: C, 58·3; H, 3·95; N, 4·1; *M* (mass spectrum), 329·00501. $C_{16}H_{12}BrNO_2$ requires C, 58·25; H, 3·65; N, 4·25%, *M*, 329·00524), $\nu_{max.}$ (Nujol) 1695 (C=O), 1653 (C=N), and 1600 cm.$^{-1}$ (C=C).

6,6′-*Bi*-(2-*bromo*-5,6-*dihydro*-7-*oxodibenz*[b,d]*azepinylidene*).—A nitrogen-saturated solution of 2-bromo-5,6-dihydro-5-*p*-tolylsulphonyldibenz[*b*,*d*]azepin-7-one (2·75 g.) in dry toluene (50 ml.) was added to a nitrogen-saturated suspension of sodium methoxide (500 mg.) in dry toluene (150 ml.). After being stirred 17 hr., the reaction mixture was poured onto ice and left 24 hr. The product (950 mg.) was filtered off and crystallised from chloroform; it gave dark red microcrystals, m.p. 325° [Found: C, 58·45; H, 3·0; N, 4·75; *M* (mass spectrum), 573·95478. $C_{28}H_{16}{}^{81}Br_2N_2O_2$ requires C, 58·75; H, 2·8; N, 4·9%; *M*, 573·95385]. The toluene filtrate was washed with water and evaporated to give 2-*bromo*-5,6-*dihydro*-6-*hydroxydibenz*[b,d]*azepinone* (V; R^1 = OH, R^2 = H) as a creamy solid (500 mg.), m.p. 257° (from methanol) (Found: C, 55·2; H, 3·4; N, 4·6. $C_{14}H_{10}BrNO_2$ requires C, 55·3; H, 3·3; N, 4·45%).

6,6′-*Bi*-(2-*bromo*-7-*oxodibenz*[b,d]*azepinyl*).— Treatment of the above benzazepinylidene with active manganese dioxide in methylene dichloride at 20° gave 6,6′-*bi*-(2-*bromo*-7-*oxodibenz*[b,d]*azepinyl*) (VII) from chloroform as a yellow powder, m.p. 335° (decomp.) (Found: C, 59·1; H, 2·8; N, 4·8. $C_{28}H_{14}Br_2N_2O_2$ requires C, 58·8; H, 2·5; N, 4·9%), $\nu_{max.}$ (Nujol) 1665 cm.$^{-1}$ (C=O).

6-*Formylphenanthridine*.— 5,6-Dihydro-5-*p*-tolylsulphonyldibenz[*b*,*d*]azepin-7-one (5 g.), glacial acetic acid (100 ml.), concentrated hydrochloric acid (100 ml.), and fused zinc chloride[8] (500 mg.) were heated under reflux 72 hr. and diluted with water. Unchanged starting material (2·9 g.) was extracted with chloroform: the aqueous layer was basified with ammonium hydroxide and extracted with chloroform. The crude, basic material (1·08 g.) was chromatographed on silica gel (MFC) to give the product (VII) (630 mg.) as yellow rosettes, m.p. 136—137° [from light petroleum (b.p. 60—80°] (lit.,[9] 139°) (Found: C, 80·8; H, 4·35; N, 7·0. Calc. for $C_{14}H_9NO$: C, 81·2; H, 4·4; N, 6·75%), $\nu_{max.}$ (Nujol) 1692 cm.$^{-1}$ (C=O), τ −0·4 (1H, s), 0·4—0·65 (1H, m), and τ 1·2—2·7 (7H, m): addition of D_2O had no effect.

6-*Methylphenanthridine*.[7]— 5,6-Dihydro-5-*p*-tolylsulphonyldibenz[*b*,*d*]azepine (5 g.) in liquid ammonia (75 ml.) was treated with sodium until the blue colour persisted. Ammonium chloride was added to the solution until the blue colour was discharged and the ammonia was then allowed to evaporate. The product (650 mg.) was chromatographed on silica gel (MFC), and distilled (135°/0·05 mm.); it crystallised from light petroleum (b.p. 60—80°) as a waxy solid, m.p. 83—84° (lit., 84°) [Found: C, 87·15; H, 5·85; N, 6·95%; *M* (mass spectrum), 193·089008. Calc. for $C_{14}H_{11}N$ C, 87·1; H, 5·75; N, 7·25%; *M*, 193·089145]; τ 1·5—2·85 (8H, m) and 7·1 (3H, s).

Phenanthridone (350 mg.), m.p. and mixed m.p. 286°, was isolated during the chromatography.

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