Novel Aromatic Systems. Part IX.[1] Synthesis and Substitutions of Dibenzo[*b,f*]azepin-2-one [2]

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Dibenzo[*b,f*]azepin-2-one has been prepared and its reactions have been studied. Mononitro- and halogeno-derivatives were prepared by substitution reactions and their structures elucidated by n.m.r. spectroscopy, which showed that substitution had taken place in accordance with predictions made from calculations.

THE isolation of stable benzocycloheptenones [3] (I; R = OH and OMe), which we expected to have some aromatic properties,[4] encouraged us to seek heterocyclic analogues. However, we now [3b] have some reservations about the 'aromaticity' of these substances: for example, 3-methoxybenzocyclohepten-2-one (I; R = OMe) undergoes nucleophilic 1,6-addition [3a] as a quinone methide. Nevertheless, *N*-heterocyclic analogues [*e.g.* (II) and (III)] seemed of interest. Butenandt [5] and his co-workers have previously isolated members of this class of compound [*e.g.*, (III; $R^1 = R^2 = R^3 = OH$, $R^4 = Ac$)] from the alkaline oxidation of 2′-amino-3′-hydroxyacetophenone and also by treatment of insect pigments (the ommochromes) with alkali. Both the latter and the actinomycins [6] are derivatives of phenoxazinone (IV) which is a 10 π-electron system isosteric with the dibenzazepinones (III).

Our synthesis [2] of dibenz[*b,f*]azepin-2-one (III; $R^1 = R^2 = R^3 = R^4 = H$) is based on the known [7] oxidation of dihydrodibenzazepine (V; R = H) by Frémy's salt to the quinone imine (VI). Accordingly the dibenzazepine (VII; R = H) was treated with Frémy's salt at pH *ca.* 7·5 and the desired ketone (III; $R^1 = R^2 = R^3 = R^4 = H$) was obtained as a crystalline, deep red, monomeric solid, m.p. 135—136°, together with acridine-9-carbaldehyde. The yield of the former could be increased at the expense of the latter by raising the pH of the reaction above 8·0. We have previously [2] outlined the spectroscopic evidence for the structures of both of these substances (see also Experimental section). The structure of ketone (III; $R^1 = R^2 = R^3$ $R^4 = H$) was confirmed by catalytic hydrogenation to a phenol (V; R = OH), previously obtained by Schindler.[7a]

It is odd that the quinone imine (VI) could not be dehydrogenated; it was recovered unchanged after

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[3] (*a*) G. R. Proctor and A. H. Renfrew, *J. Chem. Soc.* (*C*), 1968, 1187; (*b*) D. J. Humphreys and G. R. Proctor, *J.C.S. Perkin I*, in the press.

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[5] A. Butenandt, E. Biekert, and G. Neubert, *Annalen*, 1957, **603**, 200.

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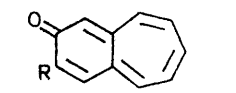
treatment with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), with manganese dioxide,[8] and with *N*-bromosuccinimide. Dibenzazepine reacted with iodine in dimethyl sulphoxide [9] but neither the dibenzazepinone nor an iodo-derivative were among the products.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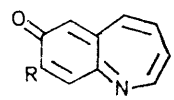
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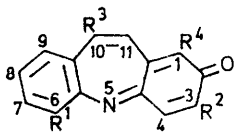
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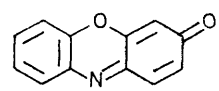
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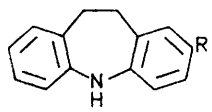
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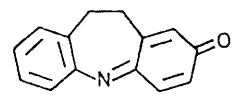
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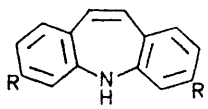
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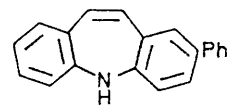
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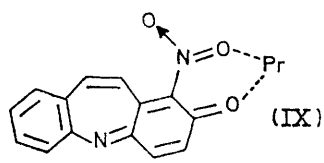
(IX)

Our investigations of dibenz[*b*,*f*]azepin-2-one (III; $R^1 = R^2 = R^3 = R^4 = H$) have concentrated on its substitution reactions and on the n.m.r. spectra of derivatives. Although the azepinone appeared to be stable (*e.g.*, it was unaffected by irradiation in benzene for 12 h), we used only mild conditions for electrophilic substitution (*cf.* ref. 10). Repeated attempts to apply the Vilsmeier reaction at 0° and Friedel–Crafts acetylation ($SnCl_4$–Ac_2O) at 40° led to extensive decomposition. Attempted acetylation at 10° or below led to recovery of starting material, but nitration [10] [$Cu(NO_3)_2$–Ac_2O] at these temperatures was successful, and a mononitro-derivative was isolated. N.m.r. studies (see later) led us to conclude that this red product was the 1-nitro-isomer (III; $R^1 = R^2 = R^3 = H$, $R^4 = NO_2$). Treatment of dibenz[*b*,*f*]azepin-2-one with *N*-bromosuccinimide in the presence of benzoyl peroxide gave a red monobromo-substitution product which we believe to be the 1-isomer (III; $R^1 = R^2 = R^3 = H$, $R^4 = Br$). *N*-Chlorosuccinimide gave an analogous product (III; $R^1 = R^2 = R^3 = H$, $R^4 = Cl$), but the reaction was much slower. Thus both electrophilic and radical substitution take place at the 1-position, which is some indication that aromatic properties are exhibited by this molecule. It is clear that since the quinone imine (VI) did not react with *N*-bromosuccinimide; thus dibenz[*b*,*f*]azepin-2-one is demonstrably more easily substituted.

Calculation * of the π-electronic structure of dibenz[*b*,*f*]azepin-2-one by the Pariser–Parr–Pople method showed that the most nucleophilic centre is indeed at C-1. The 3-position is also likely to undergo electrophilic substitution; presumably this could be demonstrated for compounds with a 1-substituent. Analysis of the bond-order data indicates that the 1- and 9-positions have the same free valence and hence should be the most active positions towards attacking free radicals.

Dibenz[*b*,*f*]azepin-2-one also reacts with dibromocarbene (from CBr_3HgPh), with diazomethane, and with bromine in chloroform, but no products were isolated. Phenyl-lithium did not react at 20° in benzene; at 80° a reaction took place giving, in low yield, a substance, which we regard as the hitherto unknown 2-phenyldibenz[*b*,*f*]azepine (VIII). This formulation is based on the appearance of an N–H band in the i.r. spectrum, the general similarity of the n.m.r. spectrum to that of the dibenzazepine (VII; R = H), and consideration of its mode of formation, although the details of the latter are not clear.

Dibenz[*b*,*f*]azepin-2-one did not apparently undergo cycloadditions: after 2 days heating at 120° with either maleic anhydride or dimethyl acetylenedicarboxylate, it was largely unaffected: at higher temperatures, it decomposed.

It would be interesting to compare the α-hydroxyketones [*e.g.* (III; $R^1 = R^3 = H$, R^2 or $R^4 = OH$)] with tropolones, but attempted preparation by hydrolysis of the halogeno-derivatives (III; $R^1 = R^2 = R^3 = H$, $R^4 = Br$ or Cl) under mild conditions [11] caused decomposition. We now feel that synthesis of hydroxy-compounds will require the prior availability of hydroxy- or methoxy-dibenzazepines [*e.g.* (VII; R = OH or OMe)].

N.m.r. Studies.—The spectrum of dibenz[*b*,*f*]azepin-2-one (III; $R^1 = R^2 = R^3 = R^4 = H$) is complex, all resonances being found in the region τ 2—3·5. For elucidation of the spectrum, the shift reagent [12] tris(dipivalomethanato)praseodymium [13] was added. While the latter could form, in principle, a complex with the carbonyl group or the nitrogen atom, it appeared from

* We thank Professor P. G. Perkins for these data.

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[13] J. Briggs, G. H. Frost, F. A. Hart, G. P. Moss, and M. L. Staniforth, *Chem. Comm.*, 1970, 749.

the resulting spectra that there was only contact with the carbonyl group. Thus (see Table) the 1-, 3-, 4-, 9-, and 10-proton signals could be assigned; signals of the remaining protons remained unidentified. It is obvious from the Table that in the case of the nitro-derivative, the 1-proton is missing. In the halogeno-derivatives, addition of the shift reagent precipitated a complex, which frustrated observation of $\Delta\tau$ values: in these cases assignment of signals depended only on comparison with the uncomplexed parent molecule and the mono-nitro-derivative. Thus it is possible that the assign-

N.m.r. spectra of dibenz[*b*,*f*]azepin-2-one and derivatives [a]

Parent compound			Nitro-derivative			Bromo-derivative		Chloro-derivative	
Proton position	Resonance [b] position	$\Delta\tau$ [c]	Proton position	Resonance [b] position	$\Delta\tau$ [c]	Proton position	Resonance [b] position	Proton position	Resonance [b] position
1	3·53	12·0							
	3·57								
3	3·03	12·0	3	2·84	11·8	3	2·79	3	2·81
	3·07			2·94			2·89		2·91
	3·19								
	3·24								
4	2·45	3·0	4	2·20	3·2	4	2·30	4	2·32
	2·61			2·30			2·40		2·40
10	3·04	1·0	10	2·59	2·2	10	2·32	10	2·39
	3·24			2·71			2·44		2·51
11	3·31	2·0	11	3·12	3·8	11	2·71	11	2·75
	3·51			3·24			2·83		2·87
$J_{1.3}$ [d] 2·8									
$J_{3.4}$ 10·0			$J_{3.4}$ 10·0			$J_{3.4}$ 10·0		$J_{3.4}$ 10·0	
$J_{10.11}$ 12·0			$J_{10.11}$ 12·0			$J_{10.11}$ 12·0		$J_{10.11}$ 12·0	

[a] Spectra were recorded with Perkin-Elmer R10 (60 MHz) and R14 (100 MHz) instruments. [b] Chemical shifts are given on the τ scale with reference to internal tetramethylsilane. [c] $\Delta\tau$ is defined as the shift for the appropriate resonance in p.p.m. per mol of shift reagent per mol of substrate.[14] [d] J Values in Hz.

ments for 9- and 10-H should be reversed for the halogeno-derivatives, but those for 3- and 4-H are beyond doubt. The slight differences in $\Delta\tau$ values for the 1-nitro-isomer compared with dibenz[*b*,*f*]azepin-2-one itself may be due to the slight tendency of the former to act as a bidentate ligand with the shift reagent, giving the complex (IX).

EXPERIMENTAL

Dibenz[b,f]*azepin-2-one* (III; $R^1 = R^2 = R^3 = R^4 = H$). —A solution of Frémy's salt [15] (25 g) and disodium hydrogen phosphate (18 g) in water (950 ml) was added in portions to dibenz[*b*,*f*]azepine [16] (donated by J. R. Geigy and Co., Basle) (5·5 g) in acetone (600 ml) with shaking. After 10 min, the mixture was filtered and left in the refrigerator overnight. After concentration in a stream of nitrogen at $\gtrsim$20°, the product was obtained by extraction with ether and chromatography on neutral alumina (benzene elution). The first fraction (0·31 g) was the starting material. The second fraction (1·7 g) was acridine-9-carbaldehyde, yellow needles, m.p. 141—142° (from ether) (lit.,[16] 139—140°) (Found: C, 80·75; H, 4·4; N, 6·85%; M^+, 207·06842. Calc. for $C_{14}H_9NO$: C, 81·25; H, 4·4; N, 6·75%; M^+, 207·06841), $\nu_{max.}$ (CCl_4) 1700 cm^{-1}, τ −1·4 (1H, s, CHO) and 1·2—2·8 (8H, m, aryl); 2,4-dinitrophenyl hydrazone, m.p. 232—235° (lit.,[17] 235°).

The third fraction (3·5 g) was the desired *ketone*, a deep red microcrystalline powder, m.p. 135—136° (from ether) (Found: C, 80·9; H, 4·55; N, 6·6%; M^+, 207·06877. $C_{14}H_9NO$ requires C, 81·25; H, 4·4; N, 6·75%; M, 207·06842), $\nu_{max.}$ (Nujol) 1640, 1590, and 1550 cm^{-1}, $\lambda_{max.}$ (EtOH) 255, 293, and 476 nm (ε 20,420, 28,460, and 4310).

Reduction of Dibenz[b,f]*azepin-2-one.*—Dibenz[*b*,*f*]azepin-2-one (0·3 g) in methanol (85 ml) was hydrogenated over palladised charcoal (0·1 g; 10%). The product (0·275 g) was repeatedly crystallised from chloroform, chromatographed on silica gel, and then recrystallised from ether to give a grey solid, m.p. 155° (decomp.) (lit.,[7a] 169—171°). This product was identical with that obtained by catalytic reduction of 10,11-dihydrodibenz[*b*,*f*]azepin-2-one (VI) and was regarded as 10,11-dihydro-2-hydroxydibenzo[*b*,*f*]azepine (V; R = OH) although the discrepancy in the reported [7a] m.p. of this substance remains unexplained.

1-*Nitrodibenz*[b,f]*azepin-2-one* (III; $R^1 = R^2 = R^3 = H$, $R^4 = NO_3$).—To dibenzo[*b*,*f*]azepine-2-one (0·3 g) in acetic anhydride (40 ml) was added copper(II) nitrate (0·3 g) in portions, with stirring during 15 min at 20°. After being stirred a further 30 min, the mixture was poured into water and extracted with benzene. After evaporation of the benzene, the *product* (160 mg) was purified by chromatography on silica gel (elution with benzene–methanol, 99 : 1 v/v) and crystallisation from benzene to give deep red flakes, m.p. 200—201° (decomp.) (Found: C, 66·8; H, 3·1; N, 10·8%; M^+, 252·05510. $C_{14}H_8N_2O_3$ requires C, 66·7; H, 3·2; N, 11·1%; M, 252·05349).

1-*Bromodibenz*[b,f]*azepin-2-one* (III; $R^1 = R^2 = R^3 =$ H, R^4 = Br).—Dibenz[*b*,*f*]azepin-2-one (0·15 g), *N*-bromosuccinimide (0·14 g), and benzoyl peroxide (10 mg) were heated together under reflux in dry carbon tetrachloride (75 ml) while being irradiated with a lamp (150 W) for 90 min. After filtration and removal of solvent, the mixture was chromatographed on silica gel; benzene eluted the *product* (135 mg), which crystallised from chloroform–methanol as deep red needles, m.p. 170—172° (Found: C, 58·8; H, 2·65; N, 4·75%; M^+, 286·978264, 284·979354. $C_{14}H_8BrNO$ requires C, 58·75; H, 2·8; N, 4·9%; M, 286·977005, 284·978975).

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1-*Chlorodibenz*[b,f]*azepin*-2-*one* (III; $R^1 = R^2 = R^3 = H$, $R^4 = Cl$).—Dibenz[*b,f*]azepin-2-one (0·3 g), *N*-chlorosuccinimide (0·3 g), and benzoyl peroxide (10 mg) were heated together under reflux in dry carbon tetrachloride (75 ml) while being irradiated with a lamp (150 W) for 30 h. T.l.c. of the mixture showed only a small conversion into the desired material. *N*-Chlorosuccinimide (1·5 g) and benzoyl peroxide (600 mg) was added and the mixture heated under reflux for a further 36 h. Work-up as before gave the *product* (300 mg) which crystallised from benzene–methanol as deep red needles, m.p. 175—177° (Found: C, 69·1; H, 3·3; N, 14·95. $C_{14}H_8ClNO$ requires C, 69·6; H, 3·3; N, 14·7%).

Reaction of Dibenz[b,f]*azepin*-2-*one with Phenyl-lithium.*—The title ketone (0·2 g) in dry benzene (100 ml) was treated dropwise with phenyl-lithium (1 ml; 2·14M in benzene–ether, 7 : 3 v/v) at 5° and then was stirred for 4 h at 20°. T.l.c. of the mixture showed that no reaction had taken place; it was then heated under reflux for 1 h. After cooling and addition of water, the organic layer was washed and evaporated to yield 2-phenyldibenzo[*b,f*]azepine (VIII) (30 mg), which was crystallised from dichloromethane as a straw-coloured solid, m.p. 198—200° (decomp.) (Found: M^+, 269·1197. $C_{20}H_{15}N$ requires *M*, 269·1204), $\nu_{max.}$ (Nujol) 3365 cm^{-1} (NH), τ 2·5—3·85 (14H, m) and 5·1br (1H, exchangeable).

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