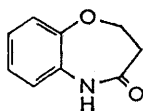
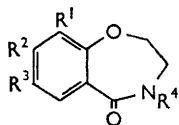


The Synthesis and Proton Magnetic Resonance Spectra of 2,3-dihydro-1,4-benzoxazepin-5(4*H*)-ones

By G. S. Sidhu, G. Thyagarajan, and U. T. Bhalarao

Eight 2,3-dihydro-1,4-benzoxazepin-5(4*H*)-ones carrying substituents in the aromatic ring have been synthesised. The parent compound has also been prepared in considerably better yields than reported by earlier workers. P.m.r. spectra have been used to distinguish between the isomeric 1,4- and 1,5-benzoxazepin-ones.

HUCKLE, LOCKHART, and WRIGHT¹ have reported the preparation of 2,3-dihydro-1,4-benzoxazepin-5(4*H*)-one (I) in 56% yield by the Schmidt reaction on chromanone.



(II)

	R ¹	R ²	R ³	R ⁴
(I)	H	H	H	H
(Ia)	Me	H	H	H
(Ib)	Cl	H	H	H
(Ic)	Cl	H	H	Me
(Id)	H	OMe	H	H
(Ie)	H	H	Me	H
(If)	H	H	OMe	H
(Ig)	H	H	Cl	H
(Ih)	H	H	Br	H



This prompts us to report the results of similar work that has been in progress in our laboratory. The same reaction in our hands gave compound (I) in 78% yield. Analogues (Ia—h) (Table 1) carrying substituents in the aromatic ring have also been prepared by us; p.m.r. (Table 2) and infrared data (see Experimental section) support the structures assigned to the products.

In the infrared region, the lactam carbonyl absorption

is at 1650—1655 and the ether (C—O—C) at 1200 cm.⁻¹. The p.m.r. spectrum of compound (I) shows a quadruplet at τ 6.57 assigned to the methylene adjacent to the >NH group and a triplet at τ 5.65 ($J = 5$ c./sec.) assigned to the methylene adjacent to the oxygen. The quadruplet at τ 6.57 can best be explained by the participation of the >NH proton in spin-spin coupling, as it collapses to a triplet on exchange by addition of a deuterioethanol-deuterioacetone mixture. Further, the signal of the corresponding methylene group in (Ic), in which the nitrogen carries a methyl group instead of a hydrogen atom, is a clean triplet centered at τ 6.55 ($J = 5$ c./sec.). That the >NH proton can take part in spin-spin coupling is also borne out by the p.m.r. spectrum of *N*-methylacetamide (III) in which the *N*-methyl signal is a doublet centred at τ 7.15 ($J = 5$ c./sec.).

These assignments are further supported by the p.m.r. spectrum of the isomeric 1,5-benzoxazepin-4-one (II), which also shows triplets at τ 5.55 ($J = 6$ c./sec.) (—O—CH₂—) and 7.15 ($J = 6$ c./sec.) (—NH—CO—CH₂—). It is known that a methylene next to the carbonyl function in a lactam group absorbs at higher field (*ca.* τ 7.2) when compared to a similar methylene group next to the >NH function of the lactam group (*ca.*

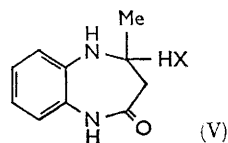
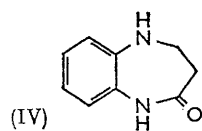
¹ D. Huckle, I. M. Lockhart, and M. Wright, *J. Chem. Soc.*, 1965, 1137.

TABLE 1
Substituted 2,3-dihydro-1,4-benzoxazepin-5(4*H*)-ones

Compound	M. p.	Yield (%)	Found (%)				Formula	Required (%)			
			C	H	N	Cl		C	H	N	Cl
(I)	114°	78	66.1	5.6	8.1	—	C ₉ H ₇ NO ₂	66.2	5.6	8.6	—
(Ia)	87	70	67.3	6.4	7.5	—	C ₁₀ H ₁₁ NO ₂	67.8	6.3	7.9	—
(Ib)	111	75	54.6	3.9	6.7	17.8	C ₆ H ₅ ClNO ₂	54.7	4.1	7.1	18.0
(Ic) *	B. p. 175°/ 2.5 mm.	51	56.4	4.7	6.3	16.5	C ₁₀ H ₁₀ ClNO ₂	56.7	4.7	6.6	16.8
(Id)	62	50	61.8	5.9	6.8	—	C ₁₀ H ₁₁ NO ₃	62.2	5.7	7.3	—
(Ie)	107	79	67.4	6.3	7.5	—	C ₁₀ H ₁₁ NO ₂	67.8	6.3	7.9	—
(If)	78	52	61.8	5.8	6.9	—	C ₁₀ H ₁₁ NO ₃	62.2	5.7	7.3	—
(Ig)	109	65	54.4	3.8	6.8	17.7	C ₆ H ₅ ClNO ₂	54.7	4.1	7.1	18.0
(Ih)	155	70	44.2	3.3	5.5	—	C ₉ H ₅ BrNO ₂	44.6	3.3	5.8	—

* Prepared from compound (Ib) by using sodamide and methyl iodide.

τ 6.6).^{2,3} This is further borne out by the p.m.r. spectra of compounds (IV) and (V) (Table 2). The methylene signal at τ 7.15 in (II) is only a triplet and thus lends



further support to the participation of the $>\text{NH}$ proton of (I) in spin-spin coupling. The observed clear-cut distinction in the p.m.r. patterns of the isomeric 1,4- and 1,5-benzoxazepinones might thus prove useful in the assignment of structure to unknown products of Schmidt rearrangement.

TABLE 2

Proton magnetic resonance spectral data (τ values)

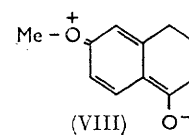
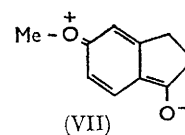
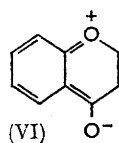
Compd.	NH	Aromatic	OCH ₂	NH·CH ₂	CO·CH ₂	CH ₃
(I)	1.5b	2.0—3.0m	5.65t	6.57q		
(Ia) ...	1.55b	2.1—3.1m	5.65t	6.55q		7.65s
(Ib) ...	1.5b	2.1—3.1m	5.55t	6.57q		
(Ic) ...		2.3—3.1m	5.55t	6.55t		6.82s
				(NMe·CH ₂)		(N·CH ₃)
(II) ...	0.6b	3.0s	5.55t		7.15t	
(III) ...	2.8b				7.15d	7.95s
					(NH·CH ₂)	
(IV) ...	1.1b, 5.1b	3.0—3.2		6.38t	7.3t	
(V)	1.5b, 6.28b	3.0—3.2	5.98q (HX)		7.45t	8.65d

s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad.

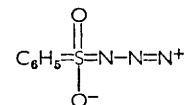
The formation of 1,4-benzoxazepin-5-ones as the major product in this reaction might be ascribed to the extension of conjugation arising out of the lone pair of electrons on oxygen participating in mesomeric structures of type (VI).⁴ This would make it more difficult for the aryl group to migrate.

Similarly, Uyeo's observation⁵ that the Schmidt re-

action on hydrindones and tetralones with a methoxyl group *ortho* or *para* to the carbonyl group gives the corresponding dihydroisocarbostyryl or dihydrohomoisocarbostyryl as the major product, can also be explained by the same postulate involving mesomeric structures of type (VII) and (VIII).



Huckle and co-authors¹ could not isolate the isomeric 1,5-benzoxazepin-4-one (II) in the reaction product and ascribed this to its ready susceptibility to hydrolysis under acidic conditions. We were also unable to isolate (II) but on working up the acidic layer during the preparation of (Ib), we isolated a small quantity of a liquid product which, rather surprisingly, turned out to be aniline. This could have originated only by the action of hydrazoic acid on benzene which we had used as a solvent in the Schmidt reaction. The amination of benzene may have been effected by the $\cdot\text{NH}$ radical⁶ or the $^+\text{NH}_2$ cation.⁷ It is also possible that the aminating agent may be benzenesulphonylazide as an electrophile:⁸



We shall report in detail on the mechanism of formation of aniline in a subsequent communication.

EXPERIMENTAL

Only a typical experiment is reported here; all rearrangements were carried out using essentially this procedure. All m. p. were determined by the capillary method and are

² P. T. Lansbury, J. G. Colson, and N. R. Muncuso, *J. Amer. Chem. Soc.*, 1964, **86**, 5225.

³ See spectra Nos. 68, 116, and 265, "Varian Spectra Catalog," Varian Associates, Palo Alto, California, 1962.

⁴ C. B. Hurd and S. Hanyao, *J. Amer. Chem. Soc.*, 1954, **76**, 5065.

⁵ S. Uyeo, *Pure Appl. Chem.*, 1963, **7**, 269.

⁶ Cf. K. F. Schmidt, *Ber.*, 1924, **57**, 704.

⁷ Cf. R. N. Keller and P. A. S. Smith, *J. Amer. Chem. Soc.*, 1944, **66**, 1122, and references contained therein.

⁸ Cf. W. von E. Doering and C. H. DePuy, *J. Amer. Chem. Soc.*, 1953, **75**, 5955.

⁹ (a) W. H. Perkin, jun., J. H. Ray, and R. Robinson, *J. Chem. Soc.*, 1962, 941; (b) S. G. Powell, *J. Amer. Chem. Soc.*, 1923, **45**, 2708; (c) D. Chakravarti and J. Dutta, *J. Indian Chem. Soc.*, 1939, **16**, 639.

uncorrected. Infrared spectra were recorded on a Perkin-Elmer model 221 and p.m.r. spectra on a Varian A-60 instrument, in deuteriochloroform solutions, with tetramethylsilane as internal standard.

Chromanones used in the reaction were prepared as reported in the literature.^{9a-c}

2,3-Dihydro-1,4-benzoxazepin-5(4H)-one (I).—Freshly distilled chromanone (5 g.) was dissolved in benzene (150 ml.) in a three-necked flask fitted with a stirrer, dropping funnel, and a condenser, and sodium azide (5.6 g.) was added in one lot. Keeping the temperature well below 5°, concentrated sulphuric acid (14 ml.) was added drop-wise over 1.5 hr. The reaction mixture was then allowed to come to room temperature (25°) when the evolution of nitrogen started. After keeping overnight, it was decomposed by water and

extracted with chloroform (50 ml.) to give the amide (4.3 g.), m. p. 114° after recrystallisation from chloroform–light petroleum (b. p. 60–80°) (2:3) (Found: C, 66.1; H, 5.6; N, 8.1. Calc. for C₉H₉NO₂: C, 66.2; H, 5.6; N, 8.6%), ν_{\max} . (Nujol) 3290, 3185, 3060, 1650, 1600, 1550, 1450, 1390, 1360, 1340, 1300, 1260, 1240, 1200, 1160, 1110, 1080, 1070, 1030, 985, 970, 950, 800, 770, 740, and 665 cm.⁻¹.

In a similar reaction on 8-chlorochromanone the acid layer after extraction with chloroform was diluted with water, basified, and extracted with ether. Removal of ether left a liquid which after distillation was identified as aniline by the preparation of acetanilide, benzanilide, and 2,4,6-tribromoaniline.

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INDIA. [5/1122 Received, October 18th, 1965]