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2,3-DIHYDRO-2-PHENYL-1,4-BENZOXAZEPIN-5(4H)-ONE FROM THE REACTION OF THE FLAVANONE WITH HYDRAZOIC ACID. A REAPPRAISAL

D. Misiti and V. Rimatori

Laboratori Chimica Terapeutica - Istituto Superiore di Sanità - Rome - Italy

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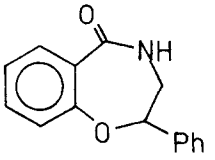
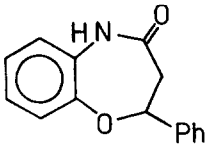
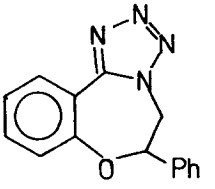
From the reaction of the flavanone with sodium azide in acetic and sulphuric acid at 40-50°, Krapcho et al.(1) obtained a product, m.p. 124-5°, which they suggested to be 2,3-dihydro-2-phenyl-1,5-benzoxazepin-4(5H)-one (II). From this reaction, with the same reagents and at the same temperature, we isolated benzoxazepines (I) 83%, (II) 3% and (III) 5%, whose structures follow from the chemical and spectroscopic evidence.



I



II



III

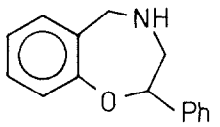
Of our compounds, the major product (I) from the reaction agrees in m.p. and infrared absorption maxima with the corresponding sole reaction product obtained by Krapcho et al.. Accordingly, the structure (II) proposed by these workers is incorrect, as well as the ones of the corresponding pharmacologically active N-derivatives (1-3). The true structure (I), and its relative yield are consistent with the view that in the Schmidt reaction on benzocycloalkenyl-ketones with an ether linkage ortho or para to the carbonyl group, the alkyl migration is concurrent with the aryl migration (4). Further, only alkyl migration was observed during the Schmidt reaction on unsubstituted chromanones at the 5-position (5).

Comparison of the I.R. carbonyl absorption of the two lactams shows a small but significant difference (ca.15cm^{-1}) between the benzamide (I) which has the lower frequency and the anilide (II).

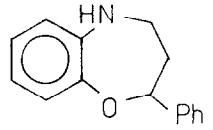
N.M.R. data also support the structures assigned to the products. The difference between chemical shifts of the methylene group of (I) (δ 3.48) and (II) (δ 3.05) is in agreement with the view that a methylene next to the NH-

function in a lactam group absorbs at lower field (ca. δ 3.4) when compared to a similar methylene group next to the carbonyl function of the lactam group (ca. δ 2.8)(5b,6,7). An additional way of distinguishing between the isomeric lactams is the presence in the N.M.R. spectrum of (I) of a single proton absorption at low field (δ 7.77dd), assigned to the deshielded C-6 aromatic proton (5a,8,9).

The ultraviolet absorption spectra of the reduction products of the lactams with $LiAlH_4$ confirmed the assigned structures of the lactams. Whereas the ultraviolet spectra of the amine (IV) derived from the lactam (I) remained essentially unaltered in both acid and alkaline media, that of the reduction product (V) of the lactam (II) showed an hypsochromic shift on acidification of its alcoholic solution, indicating that the nitrogen atom is linked to the benzene ring.



IV



V

The patterns of fragmentation by electron impact of the two isomeric benzoxazepines are very different. The above mentioned structures can also be assigned on the basis of the interpretation of some of the most significant peaks in the mass spectra of (I):m/e 121 $(o\text{-}HO\text{-}C_6H_4\text{-}CO)^+$, m/e 120()$^+$, m/e 119 $(Ph\text{-}C_2H_4N)^+$ and (II): m/e 131 $(Ph\text{-}CH{=}CH\text{-}CO)^+$.

Final evidence came from the chemical degradation, which defined unequivocally the structure of the benzoxazepinone (I). This compound dissolves in conc. HCl and upon refluxing is hydrolysed to salycilic acid and phenyl-acetaldehyde, probably formed from the intermediate 2-amino-1-phenyl-ethanol(*).

The structure of tetrazole (III) was elucidated by $LiAlH_4$ reduction of the tetrazole ring (10) to give the benzoxazepine (IV).

A paper, supplying more details, is in preparation.

(*) Hydrolysis of 2-amino-1-phenyl-ethanol in the same conditions gave, with high yield, phenyl-acetaldehyde.

	Formula[a]	m.p.	I.R. cm^{-1}	U.V. λ_{max}^{EtOH}, nm(log ε)	N.M.R., δ ($CDCl_3$)			
					NH[b]	aromatic(9H)	-CH-Ph	$-CH_2-$
I	$C_{15}H_{13}NO_2$	125-6°	$CHCl_3$: ν_{NH} 3344,3125 ν_{CO} 1651	284(3.26)	8.25	7.90-6.90m	5.35q	3.48m
II	"	141-2°	$CHCl_3$: ν_{NH} 3300,3125 ν_{CO} 1666	245(3.95),275^{sh}(3.43)	8.55	7.40-7.05m	5.62q	3.05m
III	$C_{15}H_{12}N_4O$	137-8°	$CHCl_3$: $\nu_{C=N}$ 1650	250(4.12),260(3.99)	-	8.60-7.05m	5.30-4.65 m	
IV	$C_{15}H_{15}NO$	79-80°	film : ν_{NH} 3225	258(2.86),264(2.91) 266(2.90),273(2.84)	1.47	7.43,7.18s	4.63q	3.98m 3.13m
IV.HCl	" .HCl	231-3°d.	nujol: ν_{N^+-H} 2700ca.	258(2.84),264(2.93) 267(2.94),272(2.88)				
V	"	43-4°[c]	film : ν_{NH} 3280	237(3.68),283(3.27)	3.40	7.58-6.56m	4.91q	3.33m 2.19m
V.HCl	" .HCl	177-9°[c]	nujol: ν_{N^+-H} 2700ca.	252(2.87),258(2.96) 263(3.02),269(2.98)				

[a] Analytical data of all compounds are in agreement with their formulations. [b] With a trace of D_2O the signal disappears. [c] 2-Phenyl-2,3,4,5-tetrahydro-1,5-benzoxazepine from $LiAlH_4$-reduction of flavanone oxime was reported to have m.p. 42.5-3.5° (hydrochloride m.p. 171-2.5° d.)(11).

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