SHORT COMMUNICATIONS

LARVAECIDAL ACTIVITY OF SOME REDUCED CARBAZOLES AND COMPOUNDS CONTAINING METHYLENE-DIOXY-PHENYL RING

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CARBAZOLE derivatives are biologically active, displaying antibacterial, antifungal, inseticical and anticancer activity[1,5]. Of the carbazole alkaloids, Girinimbine, Mahanimbine and Murrayanine have antifungal activities[1,2]. Studies on the insecticidal and antimicrobial properties of carbazole derivatives in our laboratory reveal that tetrahydrocarbazole derivatives are more active than the corresponding carbazole derivatives on disease spreading common household pests like house-flies, human and plant pathogenic microbes (fungii and bacteria)[3,4]. Tetrahydrocarbazoles have also hypoglycemic activity[6]. Comparitive studies of the activity of tetrahydrocarbazole, carbazole, glycozoline and glycozolidine (carbazole alkaloids from the root bark of *Glycosmis pentaphylla*) on mosquito larvae (*Culex* sp.) also revealed that tetrahydrocarbazoles are active on mosquito larvae (*Culex* sp.), but the naturally occurring carbazoles, *viz.*, glycozoline, glycozolidine and carbazole cannot destroy the mosquito-larvae at all[3]. Such high activity of tetrahydrocarbazoles as compared to the corresponding carbazoles is due to the presence of partially reduced carbazole moiety[3,4].

Harvill, Hartzell and Arther reported that piperine, the principal alkaloid of black pepper (*Piper nigrum* Linn.), is more toxic to houseflies than pyrethrin, although, the knock-down effect is less than that of pyrethrins[7]. Moreover, compounds containing methylene-dioxy-phenyl group have been reported to have synergistic effect[7-9].

A comparative study of the activity of some tetrahydrocarbazole derivatives along with piperine and piperic acid on mosquito larvae (*Culex* sp.) has been reported in this paper. As piperine and piperic acid contain methylene-dioxy-phenyl ring the synergistic effect of these two compounds with the active tetrahydrocarbazole derivatives has also been studied.

The following compounds were used for bio-assay: (1) 1,2,3,4-tetrahydrocarbazole[10] (I); (2) 1-oxo-1,2,3,4-tetrahydrocarbazole[11] (IV); (3) 1,2,3,4,4a,9a-hexahydracarbazole (*cis*)[12] (V); (4) N-acetyl 1,2,3,4-tetrahydrocarbazole[13] (II); (5) *bis*-(9-(1,2,3,4-tetrahydrocarbazolyl)) methane[14] (III); (6) piperine[15] (VI) and (7) piperic acid[16] (VII). The compounds, presented below, were prepared in this laboratory.

Of the reduced carbazole compounds mentioned above, (I), (IV) and (V) contain free NH group, and II and III are N-substituted compounds, Moreover (V) is a further reduced form of (I). Our aim of bio-assay was to determine the relative toxicity of I, IV and V (containing free NH group) and II and III (N-substituted compounds). As VI and VII contain methylene-dioxy-phenyl ring we were interested to determine the toxicity of these compounds and synergistic effect with active reduced carbazoles. For this purpose following procedure was adopted for toxicity tests on mosquito larvae.

Toxicity tests on mosquito larvae (*Culex* sp.) were carried out with ethanolic solution of all the compounds except *bis*-9-tetrahydrocarbazolyl methane

TABLE 1

Percentage of mortality of mosquito larve (Culex sp.) after 24 hr interval.

Compounds	Concentration g/50 ml	% of mortality
1,2,3,4-tetrahydrocarbazole	0.0025	100.0 (90)*
1-oxo-tetrahydrocarbazole	0.0025	58.3 (49.78)
N-acetyl tetrahydrocarbazole	0.0025	25.7 (30.46)
bis-9(1,2,3,4-tetrahydrocarbazolyl) methane	0.0025	—
1,2,3,4,4a,9a-hexahydrocarbazole	0.0025	—
Piperine	0.0025	100.0 (90)
Piperic acid	0.0025	—
Alcohol/Acetone		—
F-value	51.11	(Significant at 1% level)
Degree of freedom (3,12)		
CD at 1%	17.14	
at 5%	12.22	

* Figures in the brackets represent angular transformation;— Represents no mortality.

which was only slightly soluble in ethanol and therefore, its acetone solution was used. A definite concentration of the solution of the compounds in 1 ml of solvent was added in a thin stream with stirring to mosquito larvae in water and the ultimate volume made 50 ml. Control was run in the similar way with solvent. Five replications were made for each compound at 32 ± 1° C. About 30–40 larvae were used for each replication. Results are presented in table 1. With the help of analysis of variance it has been shown that all the treatments are not equivalent. Moreover the order of toxicity has been determined by critical difference.

It is evident from table 1. that 1,2,3,4-tetrahydrocarbazole, 1-oxo-1,2,3,4-tetrahydrocarbazole and piperine were toxic to mosquito larve (*Culex* sp.). Though N-acetyl tetrahydrocarbazole has some toxicity, *bis* 9-(1,2,3,4-tetrahydrocarbazolyl) methane and piperic acid were not at all toxic. Highest toxicity was noticed in the case of tetrahydrocarbazole and piperine. So it appears that introduction of oxo-group in 1-position or replacement NH proton in tetrahydrcarbazole had a diminishing effect on the toxicity whereas its further reduction to hexahydrocarbazole completely eliminated its toxicity.

100% mortality in tetrahydrocarbazole and piperine was noticed at 6×10^{-4}g/50 ml and 25×10^{-4}g/ 50 ml respectively, but in the case of 1-oxo-tetrahydrocarbazole 100% mortality was not noticed even upto 50×10^{-4}g/50 ml LC_{60} of tetrahydrocarbazole, piperine and 1-oxo-tetrahydrocarbazole were 2.5×10^{-4}, 9.5×10^{-4} and 21×10^{-4}g/ 50 ml respectively.

Synergistic effect of piperine and piperic acid was observed with 1-oxo-tetrahydrocarbazole but not with tetrahydrocarbazole.

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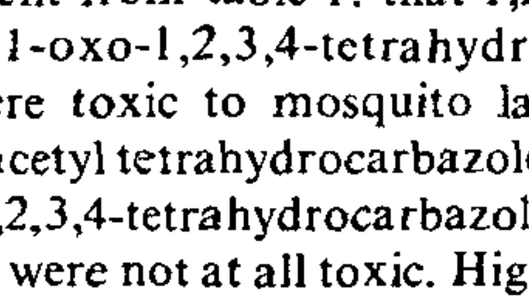
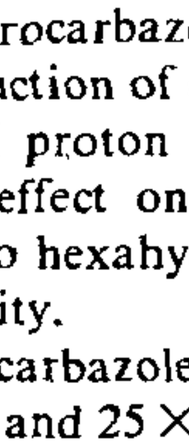
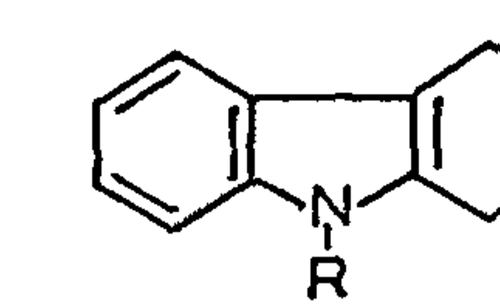
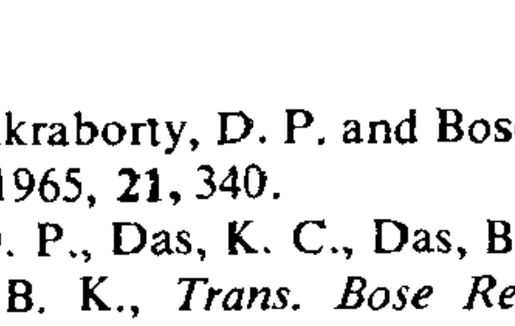


(I) R = H
(II) R = $COCH_3$
(III) R = CH_2-

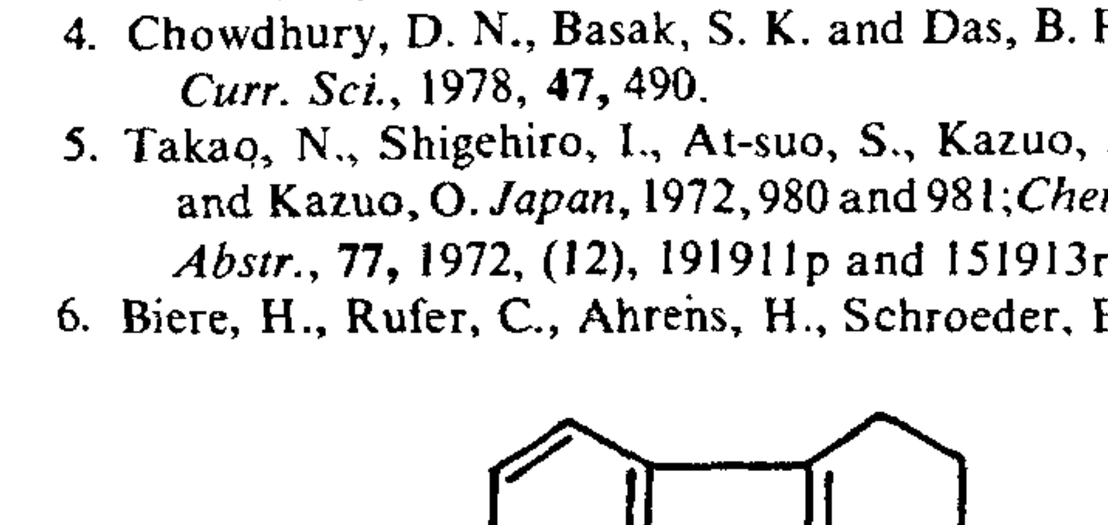




(V)



(IV)



(VI) R_1 = N
(VII) R_1 = OH

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THE MASS SPECTRA OF 4-(BENZALAMINO) ANTIPYRINES

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THE mass spectral fragmentation of several pyrazoles[1] and pyrazolones[2-4] have been studied. It has been found that the heterocyclic ring system undergoes extensive rearrangement and ring opening during the mass spectral fragmentation of pyrazolone derivatives. Also, the position and general type of substitution have been observed to have a pronounced effect on the fragmentation of pyrazolones[1].

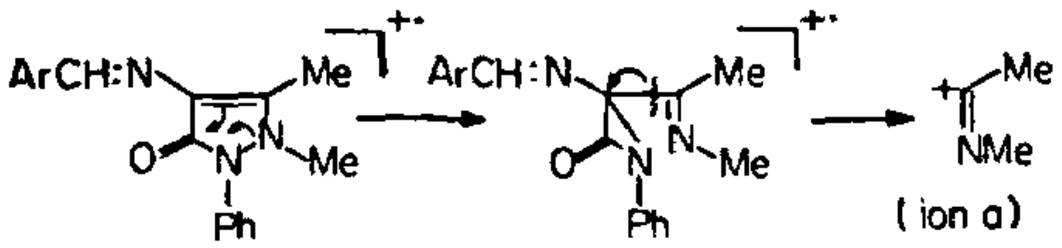
The present investigation was undertaken with a view to studying the effects of a 4-benzalamino substituent on the pyrazolone ring fragmentation. The compounds studied are 4-benzalamino and 4-(2-fluro, 2-chloro, 2-bromo, 2-hydroxy, 4-hydroxy and 4-methoxybenzal amino) antipyrines (1a-g) which are useful chelating agents for various transition metal ions[5]. The general trends observed are discussed and tentative assignment of the structure to the ions made.

The main fragments can be classified into two groups. Those which retain the aryl group of the arylidine part and those which arise from the pyrazolone part. Generally the M^+ peaks are strong, reflecting the stability of the system. The base peaks of all the compounds occur at m/e 56. This fragment should be the result of the cleavage of the pyrazolone ring system. It is noteworthy that aminoantipyrine also shows this fragment along with one at m/e 57. This fragment is thought to arise directly from the molecular ion (Scheme I).

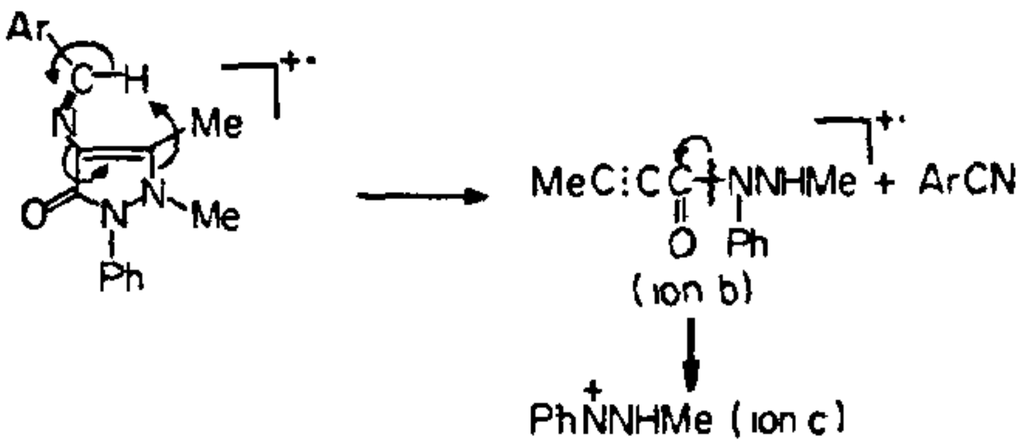
Two other important fragments which are common to all compounds studied and which have comparatively large abundance are the ions at m/e 188 and m/e 121. The former is assigned the structure (M-ArCN). The loss of ArCN (Scheme II) could lead to the ion of parent antipyrine. However, the ion (M-ArCN) is not assigned such a structure, since the ion is thought to decompose further into the ion at m/e 121. The mass spectra of antipyrine[2] does not show the presence of the ion at the m/e value 121. The pathway suggested for the fragmentation of the above two ions is shown in Scheme II.

The ion next in importance belongs to the set of ions having the aryl ring of the arylidine part and is thought to be formed by the loss of the 92 mass units corresponding to (PhNH) from the M^+ ion. It is to be noted that those pyrazolones without a 2-Me substituent do not give this fragmentation[2,4]. Therefore, it is assumed that the hydrogen lost in the neutral radical arises from the N-Me group as shown in Scheme III.

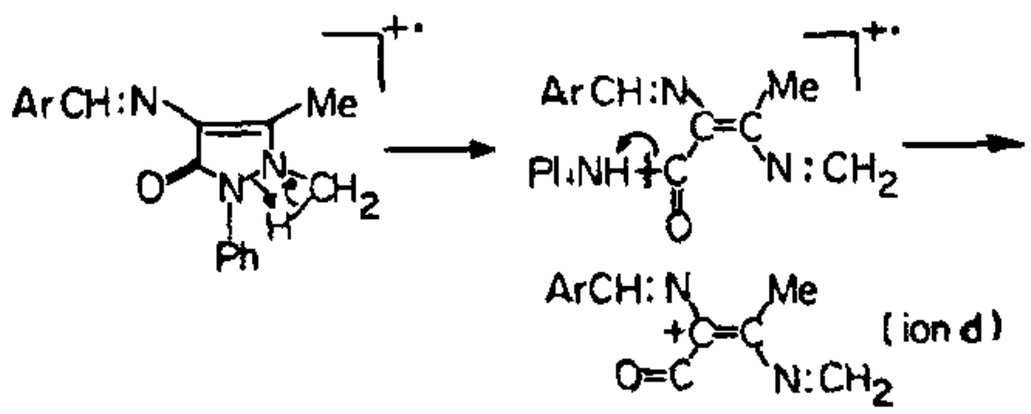
Another ion also incorporating the aryl moiety of the aryl aldehyde is (M-109) ion and which may have the composition (ArCHNHPh) ion. It is very difficult



Scheme - I



Scheme - II



Scheme - III