Preparation of new Benzimidazoles as Potential Therapeutic Agents - II.

MASHOODA HASAN, FARZANA LATIF AND MOHAMMAD AMJAD,

Department of Chemistry, Quid-i-Azam University, Islamabad, Pakistan.

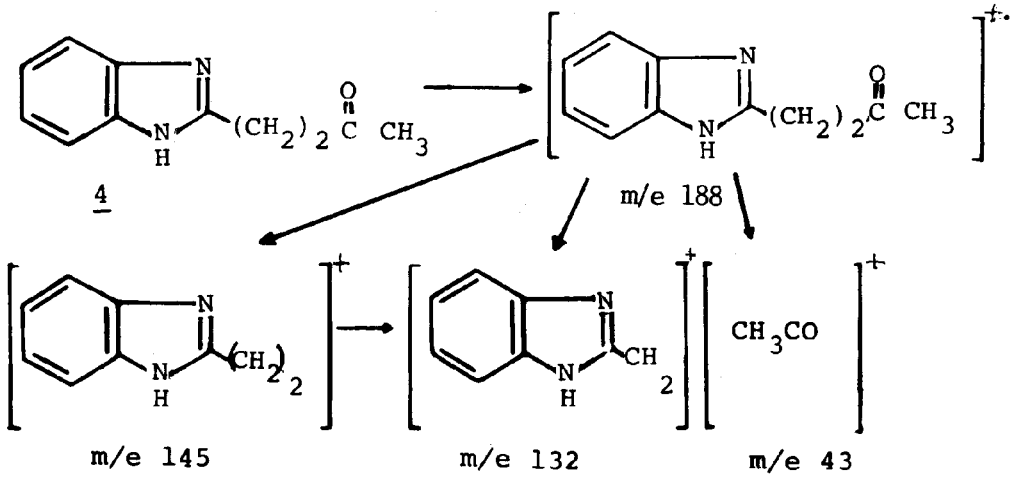
(Received 7th February, 1981)

Summary: Preparation, physical properties, infra-red and mass-spectra of two new benzimidazoles, namely (4) and (5) have been described. Since these new benzimidazoles have structure analogous with the three benzimidazoles described in the first paper of this series, and differe from them in the absene of *n*-hydroxyl group in their structure, determination of their pharmacological activities will help in establishing the structure-reactivity relationship.

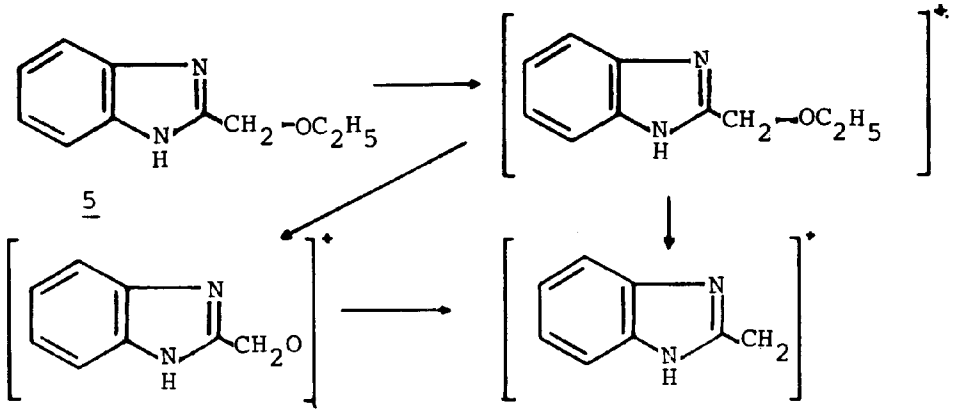
First paper of this series described[1] the preparation, physical properties and mass-spectral fragmentation pattern of three benzimidazoles, namely (2- Benzimidazolyl)-propan-1-ol (1), (2-Benzimidazolyl)-butan-2-ol (2), (2-Benzimidazolyl)-2, methyl butan-2-ol (3) Since these compounds have a *n*-hydroxyl group, the work was extended to the preparation of benzimidazoles which do not contain this function, but rather other oxygenated functional groups, in order to establish structure-reactivity relationships. As a result, two new benzimidazoles, (2-Benzimidazolyl)-butan-2-one (4) and Ethyl, 2-Benzimidazolyl-methyl ether (5) have been prepared by the reaction of levulinic acid and ethoxyacetic acid with o-phenylenediamine in 4n hydrochloric acid respectively. The pharmacological activity of these compounds will now be tested. The present paper describes the preparation, physical properties and their characterization through infra-red spectra and mass-spectral fragmentation pattern (Schemes 1 and 2). Physical properties and spectral data obtained are summarized in Table I. Preparation of more benzimidazoles having different functional groups is in progress.

Experimental

Synthesis of 4: 6.0g of levulinic acid[2] and 5.5g o-phenylenediamine were reluxed for 10 hours in 100 ml. of 4n hydrochloric acid. The clear red solution was cooled in ice and then treated with excess of sodium carbonate. The pale yellow solution was extracted four



SCHEME I



5

m/e 147 SCHEME II m/e 132

Table 1. Yield, physical properties and spectral data of the synthesized benzimidazoles.

S.No.	Benzimidazole	m.p.	Colour	Yield	Molecular formula	Molecular weight	I.R. Spectral data	Mass spectral data	
								Strong peaks	Actual mass determination
1	4	138-40°C	Colourless thick needles.	10	$C_{11}H_{12}N_2O$	188	1650 cm^{-1} (>C=O) 2700-3300 cm^{-1} (–NH)	188 145 (base) 132 43	Not done
2	5	141-42°C	Colourless needles.	40	$C_{10}H_{12}N_2O$	176	2600-3100 cm^{-1} (–NH)	176 147 132 (base)	176.0942 = $C_{10}H_{12}N_2O$ 147.0556 = $C_8H_7N_2O$ 132.-689 = $C_8H_8N_2$

times with 75.0 ml. portions of chloroform. Chloroform extract was dried over anhydrous sodium sulphate and chloroform was removed from the solution. Small amount of brown sticky residue yielded colourless needles on crystallization from a mixture of ethyl acetate and pet-ether. Yield 10%. The dried crystals melted at 138-40°. Thin-layer chromatography in various solvents revealed the purity of the compound. R_f=0.91 in acetone: pet-ether (4:1) on silica gel G, type 60, (Merck,) plates. The infra-red and mass-spectra of the compound were then measured.

Synthesis of 5.

2,5g. of ethoxyacetic acid[4] and 2.7g. of o-phenylenediamine were refluxed for 8 hours in 150 ml. 4 n

hydrochloric acid. The clear brown solution was cooled in ice and then neutralized with excess of sodium carbonate. The light yellow precipitate so obtained was filtered, and dried over calcium chloride under vaccum. This solid was then recrystallized from water, to yield colourless crystals, melting at 141-42°, yield 40%. R_f = 0.90 on silica gel G, type 60, (Merck) plates in acetone: pet-ether (4:1). Infra-red and mass-spectra of the compound were then measured.

Infra-red spectra of the synthesized compounds were recorded on Pye-Unicam SP-1000 Spectrophotometer.

Acknowledgement

The authors thank H.E.J. Post-Graduate Institute of Chemistry, Karachi University and Dr. J. van Thuijl, Department of Chemistry, Gorleus Laboratories, State University, Leiden, The Netherlands, for the measurement of the mass-spectra of 4 and 5 respectively. Financial assistance from the Quaid-i-Azam University Research Funds is also gratefully acknowledged.

References

1. Preparation of new Benzimidazoles as potential therapeutic Agents-I, Mashooda Hasan, M. Uppal Zubair and Farzana Latif, (in press).
2. Dr Elamin I. Elonia, Microbiology Section, Department of Pharmaceutics, Riyadh University, Riyadh, Saudi Arabia. Personal communication. (Details will be published elsewhere).
3. Peter P.T. Sah and Shao – Yuan Ma., J. Amer. Chem. Soc. 52, 4881 (1930).
4. Org. Synth., Coll-Vol. II, p. 260.