STUDIES IN THE FORMATION OF HETEROCYCLIC RINGS CONTAINING NITROGEN

Part XX. Products of Pyrolysis of 1, 3-Dibenzyl-2-Substituted-5-Chloro Benzimidazolines

By V. Veeranagaiah, C. V. Ratnam and N. V. Subba Rao

(*Department of Chemistry, Osmania University, Hyderabad-7*)

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Abstract

1, 3-Dibenzyl-2-substituted-5-chloro benzimidazolines have been prepared from N, N^2-dibenzyl-4-chloro-o-phenylenediamine and various aldehydes. Pyrolysis of these benzimidazolines yielded 1-benzyl-2-substituted-5-chloro-benzimidazoles, by preferential elimination of benzyl group from the N, meta to chloro group. Structure of the pyrolytic products has been confirmed by comparison with authentic 5-chloro and 6-chloro isomers.

In earlier communications[1, 2], we have discussed thermal decomposition of benzimidazolines obtained from simple and 4-methylN^1,N^2-dibenzyl-o-phenylenediamines and various aldehydes. Pyrolysis of these benzimidazolines involves the elimination of elements of toluene—a hydrogen from the carbon and a benzyl group from one of the nitrogens, to yield 1-benzyl-2-substituted benzimidazoles. A possible mechanism of the elimination reaction in the presence and absence of a base catalyst has also been presented[2]. The pyrolysis of 1,3-dibenzyl-2-substituted-5-methyl benzimidazolines yielded[2] 1-benzyl-2-substituted-6-methyl benzimidazoles exclusively by preferential elimination of benzyl group from N^1. In the present paper, the results of pyrolysis of 1,3-dibenzyl-2-substituted-5-chloro benzimidazolines are presented.

The required benzimidazolines (I, Chart I; Table I) have been synthesised from N^1,N^2-dibenzyl-4-chloro-o-phenylene diamine (II) and various aldehydes—aromatic, heterocyclic and aliphatic, following our earlier procedure[3].

1,3-dibenzyl-2-phenyl-5-chloro benzimidazoline (I, R = Ph), as a representative case, has been subjected to pyrolysis at 200° for about 2 hours when a crystalline solid, T.L.C. pure, was obtained in good yields which may be either 1-benzyl-2-phenyl-5-chloro benzimidazole (III, R = Ph) or

1-benzyl-2-phenyl-6-chloro benzimidazole (IV, R = Ph). On comparison with both the authentic compounds[4], the pyrolysis product has been found to be identical with 1-benzyl-2-phenyl-5-chloro benzimidazole, m.p. 172°, as their I.R. spectra are superimposable. It is different in m.p. and I.R. spectra with 6-chloro benzimidazole (m.p. 160°). Thus, during the pyrolysis preferential elimination of elements of toluene-benzyl group from N^3 and hydrogen from C^2—is taking place.

It may be expected that other benzimidazolines of this series also behave alike and yield the corresponding 5-chloro benzimidazoles on pyrolysis. This has indeed been found to be the case. All the benzimidazolines synthesised have been subjected to pyrolysis under similar conditions and the exact structure of the benzimidazole obtained in each case has been confirmed as 1-benzyl-2-substituted-5-chloro benzimidazole by comparison with authentic samples. Authentic 1-benzyl-2-substituted-5-chloro (III) and 1-benzyl-2-substituted-6-chloro (IV) benzimidazoles (Chart I; Table II) have been synthesised from N^1 benzyl-4-chloro-o-phenylenediamine (V) and N^2-benzyl-4-chloro-o-phenylenediamine (VI) respectively using the appropriate aldehyde by the oxidative cyclisation procedure[4] or using an acid in 4N hydrochloric acid[5]. The pyrolysis product has been found to be identical in m.p. and m.m.p. with the corresponding authentic 1-benzyl-2-substituted-5-chloro benzimidazole in each case and different from the corresponding 6-chloro isomer. It is interesting to note here that it is the same isomer that is formed exclusively in two other reactions, *i.e.*, condensation of 4-chloro-o-phenylenediamine (VII) and benzaldehyde[4] and in the benzylation[6] of 2-phenyl-5-(or 6)-chloro benzmidazole (VIII).

Thus, these results suggest that 5-chloro benzimidazoles are thermally more stable compared to their 6-chloro isomers. With a view to find out whether thermal isomerization of the 6-isomer to the 5-isomer is possible, 1-benzyl-2-phenyl-6-chloro benzimidazole has been heated at different temperatures in the range of 200–250° for periods ranging from 2 to 4 hours. In all these experiments, the 6-chloro benzimidazole has been recovered quantitatively, partly in the sublimed state. Thus, the possibility of any 6 chloro compound initially formed getting converted to the more stable 5-chloro isomer does not seem to be possible.

EXPERIMENTAL

1. *Synthesis of* 1,3-*dibenzyl-2-substituted-5-chloro benzimidazolines*

To a solution of N^1, N^2-dibenzyl-4-chloro-o-phenylenediamine[3] in ethyl alcohol the appropriate aldehyde, dissolved in the same solvent, was

TABLE I. *1, 3-Dibenzyl-2-substituted-5-chloro benzimidazolines and their pyrolysis products*

R =	1, 3-Dibenzyl-2-substituted-5-chloro benzimidazoline				Pyrolysis product	
	m.p. °C	Mol. formula	% Nitrogen		m.p. °C	Yield (%)
			Calc.	Found		
1	2	3	4	5	6	7
1. Phenyl[a] ..	125[3]	$C_{27}H_{23}ClN_2$	6·8	6·9	172	80
2. *p*-Methyl phenyl[b] ..	124	$C_{28}H_{21}ClN_2$	6·6	6·8	141	75
3. *p*-Hydroxy phenyl[a] ..	140	$C_{27}H_{23}ClN_2O$	6·6	6·6	230	75
4. 3-Methoxy-4-hydroxy phenyl[b] ..	78	$C_{28}H_{25}ClN_2O_2$	6·1	6·2	116	70
5. *p*-Methoxyphenyl[a] ..	130	$C_{28}H_{25}ClN_2O$	6·4	6·6	147	72
6. 3, 4-Dimethoxyphenyl[b] ..	127	$C_{29}H_{27}ClN_2O_2$	6·0	6·2	118	70
7 3, 4-Methylenedioxyphenyl[a] ..	156	$C_{28}H_{23}ClN_2O_2$	6·2	6·3	154	69
8. *p*-Chlorophenyl[a] ..	118	$C_{27}H_{22}Cl_2N_2$	6·3	6·5	186	73
9. *m*-Nitrophenyl[b] ..	105	$C_{27}H_{22}ClN_3O_2$	9·2	9·0	130	72
10. *p*-Nitrophenyl[a] ..	150	$C_{27}H_{22}ClN_3O_2$	9·2	9·1	197	70
11. *p*-Dimethylaminophenyl[a] ..	154	$C_{29}H_{28}ClN_3$	9·3	9·4	195	65
12. Cinnamyl[a] ..	115	$C_{29}H_{25}ClN_2$	6·4	6·5	182	62
13. Furyl[c] ..	103	$C_{25}H_{21}ClN_2O$	7·0	7·2	150	50
14. 4-Pyridyl[b] ..	135	$C_{26}H_{22}ClN_3$	10·2	10·3	140	67
15. Methyl[c] ..	65	$C_{22}H_{21}ClN_2$	8·0	8·2	120	52
16. Ethyl[b] ..	96	$C_{23}H_{23}ClN_2$	7·7	7·9	132	59

Recrystallised from: (*a*) Ethyl alcohol-acetone; (*b*) Methyl alcohol-acetone; (*c*) Methyl alcohol.

TABLE II. *Synthetic 1-benzyl-5-chloro (III) and 1-benzyl-6-chloro (IV)-2-substituted benzimidazoles*

R =	m.p. °C		Mol. formula	% Nitrogen		
	III	IV		Calc.	Found	
					III	IV
1	2		3	4	5	
1. Phenyl[4] ..	172[a]	160[b]	..	..	..	..
2. *p*-Methylphenyl ..	141[b]	130[a]	$C_{21}H_{17}ClN_2$	8·4	8·4	8·5
3. *p*-Hydroxyphenyl ..	231[e]	240[b]	$C_{20}H_{15}ClN_2O$	8·4	8·2	8·4
4. 3-Methoxy-4-hydroxyphenyl ..	116[d]	178[a]	$C_{21}H_{17}ClN_2O_2$	7·7	7·7	7·8
5. *p*-Methoxyphenyl ..	148[b]	122[a]	$C_{21}H_{17}ClN_2O$	8·0	7·8	8·1
6. 3, 4-Dimethoxyphenyl ..	120[e]	130[f]	$C_{22}H_{19}ClN_2O_2$	7·4	7·6	7·6
7. 3, 4-Methylenedioxyphenyl ..	155[a]	153[a]	$C_{21}H_{15}ClN_2O_2$	7·7	7·7	7·8
8. *p*-Chlorophenyl ..	188[e]	140[a]	$C_{20}H_{14}Cl_2N_2$	7·9	7·7	7·8
9. *m*-Nitrophenyl ..	130[g]	115[a]	$C_{20}H_{14}ClN_3O_2$	11·6	11·8	11·7
10. *p*-Nitrophenyl ..	198[d]	163[f]	$C_{20}H_{14}ClN_3O_2$	11·6	11·7	11·8
11. *p*-Dimethylaminophenyl ..	197[b]	150[f]	$C_{22}H_{20}ClN_3$	11·6	11·4	11·5
12. Cinnamyl ..	183[a]	196[f]	$C_{22}H_{17}ClN_2$	8·1	8·3	8·0
13. Furyl ..	153[a]	140[e]	$C_{18}H_{13}ClN_2O$	9·1	9·2	9·3
14. 4-Pyridyl ..	140[a]	163[a]	$C_{19}H_{14}ClN_3$	13·2	13·3	13·4
15. Methyl[7] ..	121[a]	124[a]	..	..	..	..
16. Ethyl ..	133[a]	115[e]	$C_{16}H_{15}ClN_2$	10·4	10·5	10·3

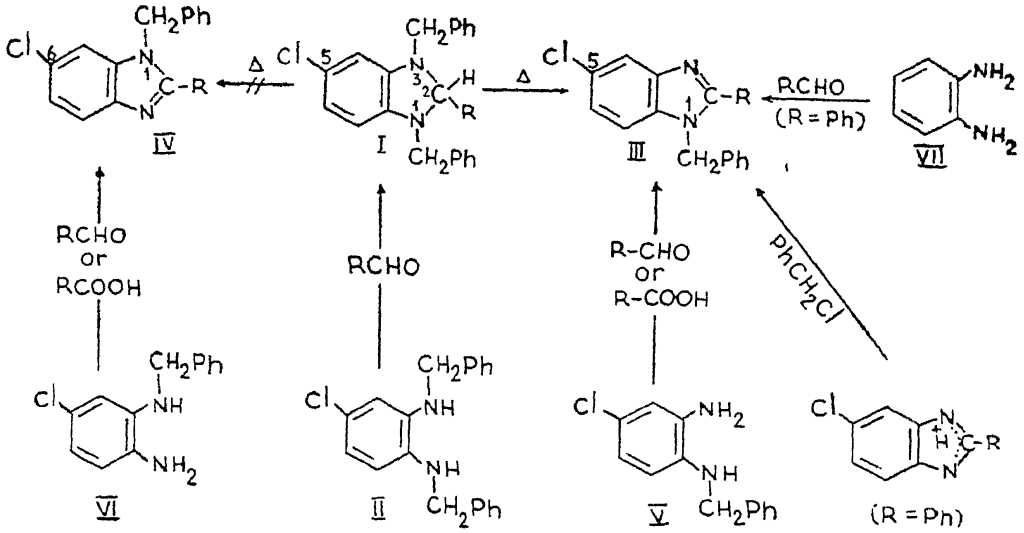
Recrystallised from: (*a*) Methyl alcohol; (*b*) Ethyl alcohol; (*c*) Pet-ether-benzene; (*d*) Benzene; (*e*) *n*-Hexane-benzene; (*f*) Methyl alcohol-benzene; (*g*) Ethyl alcohol-benzene.

added with thorough shaking. The solid that separated from the reaction mixture during a period of 10–30 minutes was filtered, washed with cold ethyl alcohol and recrystallised from appropriate solvent (Table I).

2. *Pyrolysis of 1,3-dibenzyl-2-substituted-5-chloro benzimidazolines*

The pyrolysis of 1,3-dibenzyl-2-substituted-5-chloro benzimidazolines (1 g) was carried out at a suitable temperature (200–230°) for two hours. The resinous residue obtained in each case was triturated with an appropriate solvent to yield a granular solid. The products thus obtained were recrystallised and characterised as 1-benzyl-2-substituted-5-chloro benzimidazoles (Table I) by comparison with authentic compounds.

CHART–I



3. *Synthesis of 1-benzyl-2-substituted-5-chloro benzimidazoles*

(*a*) *2-Aryl and 2-heterocyclic benzimidazoles.*—A mixture of N^1-benzyl-4-chloro-o-phenylenediamine (0·01 mole), the appropriate aldehyde (0·01 mole) and nitrobenzene (10 ml) in methyl alcohol (30 ml) was refluxed for one hour. The solution remaining after the distillation of methyl alcohol was steam-distilled to remove nitrobenzene. The crude benzimidazole was purified using a suitable solvent (Table II).

(*b*) *2-Alkyl benzimidazoles.*—N^1-Benzyl - 4-chloro - o-phenylenediamine (0·01 mole) was dissolved in 4N hydrochloric acid and the required aliphatic acid (0·01 mole) was added to it. The reaction mixture was refluxed for one hour. The resulting solution was cooled, diluted and made ammoniacal.

The crude 2-alkyl benzimidazole was recrystallised from a suitable solvent (Table II).

4. *Synthesis of 1-benzyl-2-substituted-6-chloro benzimidazoles*

2-Aryl and 2-heterocyclic benzimidazoles making use of the corresponding aldehyde and 2-alkyl benzimidazoles using the appropriate acids were synthesised from N^2-benzyl-4-chloro-o-phenylenediamine following the procedures given under 3 (*a*) and 3 (*b*) respectively (Table II).

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