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BENZIMIDAZOLES TO QUINOXALINES- A NOVEL THERMAL REARRANGEMENT

G. Mahesh Reddy, P.L. Prasunamba and P.S.N. Reddy.*

Department of Chemistry, Osmania University, Hyderabad 500 007 India.

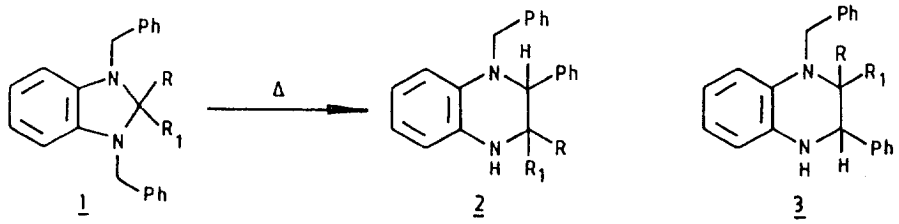
Abstract: On heating at 200°C, 2,2-dialkyl-1,3-dibenzyl-2,3- dihydrobenzimidazoles rearranged to the isomeric 1-benzyl-3,3-dialkyl-2-phenyl-1,2,3,4-tetrahydroquinoxalines.

Recently, imidazole and benzimidazole radicals received considerable attention for study, following the reported intermediacy of imidazol-1-yl radicals in the key process of oxidative phosphorylation[1-3]. N,N-Linked biazoles were considered as good precursors for N-azolyls[4], and the generation of benzimidazolyl radicals from 1,1-bisbenzimidazoles was explored[5]. During our efforts to develop a convenient synthesis for 1,1-bisbenzimidazoles from 2,2-dialkyl-1,3-dibenzyl-2,3-dihydrobenzimidazoles, we discovered a novel benzimidazole-quinoxaline rearrangement under thermal conditions. To our knowledge, it is the first example of its kind known under laboratory conditions, though such a transformation was proposed to occur under electron impact in the mass spectra of 2-alkyl benzimidazoles[6].

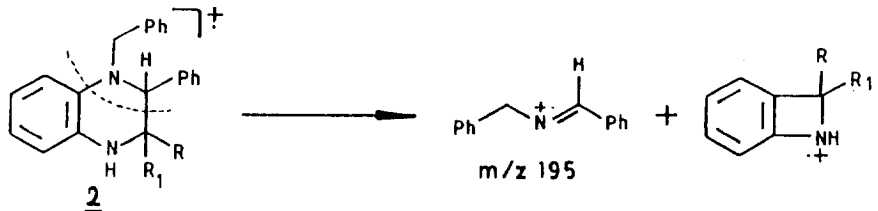
2,2-Dialkyl-1,3-dibenzyl-2,3-dihydrobenzimidazoles required for this study were prepared by reacting 1,2-dibenzylaminobenzene with ketones in methanol containing catalytic amounts of acetic acid[7]. 1,3-Dibenzyl-2,2-dimethyl benzimidazole, **1a**, m.p 135°C, on melt pyrolysis in a sealed tube at 200°C yielded benzaldehyde and an isomeric product, **2a**, m.p 195°C, in 11% yield, isolated from the pyrolysate by column chromatography using petroleum ether (60-80) as eluent. 1-Benzyl-3,3-dimethyl-2-phenyl-1,2,3,4-tetrahydroquinoxaline structure was assigned to **2a** based on spectral data. [IR(KBr)γ_{max} 3350cm^{-1} (NH); MS m/z 328(M^+); ^{1}H-NMR($CDCl_3$) δ(ppm) 1.1(3H,s), 1.15(3H,s), 3.9(1H,s), 4.24(1H,s), 4.4(2H,s), 6.6(4H,m), 7.25(10H,m)]. Pyrolysis of **1b-e** under similar conditions yielded the corresponding quinoxaline derivatives **2b-e**[8]. The C_2-H in **2** appeared as a sharp singlet around δ 4.2 in the ^{1}H-NMR and remained unchanged on adding D_2O. It indicates that NH and CH are not vicinal, and rules out the alternate structure **3**. The mass spectral fragmentation of **2** is also

in support of this observation. The appearance of peaks corresponding to benzylidene benzylamine (Ph-CH_2-N=CH-Ph, m/z 195) and 2,2-disubstituted benzazetidine moiety characterise the spectra (Chart 1).

CHART 1



	a	b	c	d	e
R	CH_3	CH_3	CH_3	$-(CH_2)_5-$	$-(CH_2)_4-$
R_1	CH_3	C_2H_5	n-C_3H_7		
M^+	328	342	356	368	354
RI(%)	52	20	88	89	68

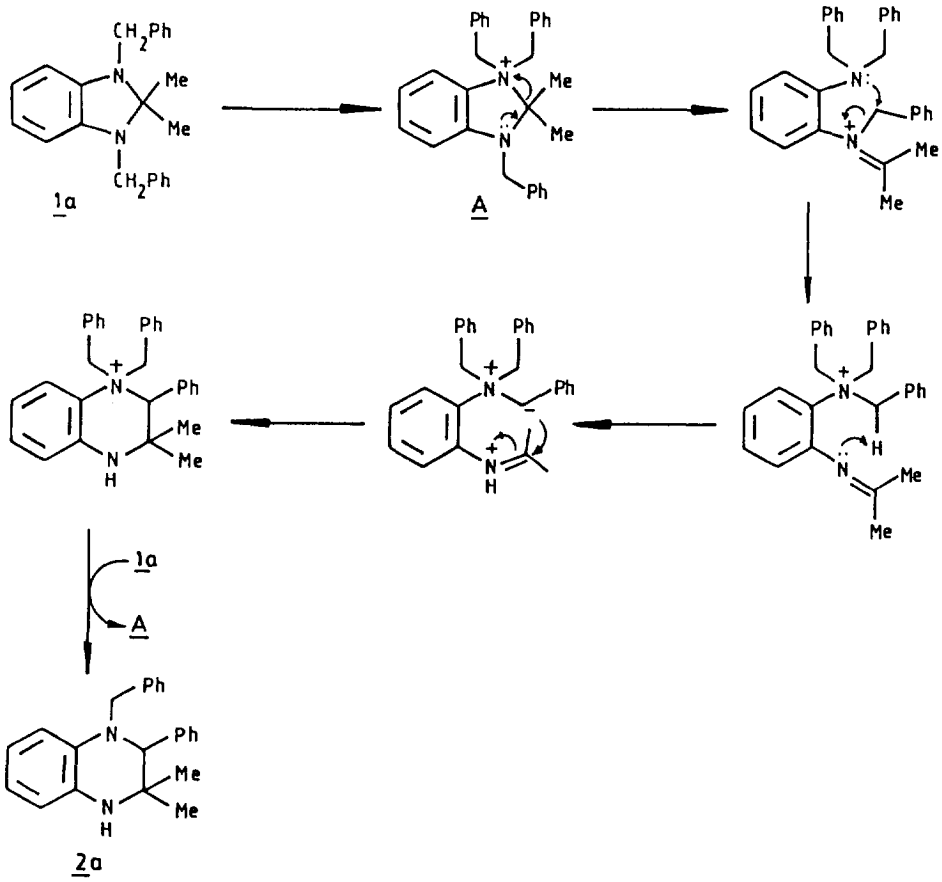


Relative intensity (%)

	2a	2b	2c	2d	2e
m/z 195	14	10	29	18	18
Benzazetidine (m/z)	(133) 100	(147) 92	(161) 74	(173) 10	(159) 15

The reaction may proceed in discrete steps by radical or ionic mechanism, and one of the more attractive is indicated in the chart 2[9]. The formation of a benzimidazolium ion could be the first step. It cleaves to 2-tribenzylamino alkylideneaniline which then undergoes a Michael type ring closure.

CHART 2



Work is in progress to determine the scope of this rearrangement in other heterocyclic systems.

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7. **Characterisation data of 1 a-e:**

1a R=R_1=CH_3; MP 135°c; Yield 76%; ^{1}H-NMR δ(ppm) 1.4(6H,s), 4.2(4H,s), 5.9(2H,m), 6.3(2H,m), 7.3(10H,m); MS m/z 328 (M^+), 313, 221, 208, 91.

1b R=CH_3, R_1=C_2H_5; MP 140°c; Yield 71%; ^{1}H-NMR δ(ppm) 1.1(3H,t), 1.5(3H,s), 1.8(2H,q), 4.3(4H,s), 5.9(2H,m), 6.4(2H,m), 7.3(10H,m); MS m/z 342 (M^+), 327, 314, 313, 222, 91.

1c R=CH_3, R_1=n-C_3H_7; MP 115°c; Yield 70%; ^{1}H-NMR δ(ppm) 1.1(3H,t), 1.7(3H,s), 1.9(2H,m), 2(2H,t), 4.5(10H,s), 6.2(2H,m), 6.6(2H,m), 7.5(10H,m); MS m/z 356 (M^+), 341, 314, 313, 91.

1d R,R_1=-$(CH_2)_5$; MP 167°c; Yield 75%; ^{1}H-NMR δ(ppm) 1.7(10H,s), 4.2(4H,s), 5.9(2H,m), 6.4(2H,m), 7.2(10H,m); MS m/z 368 (M^+), 326, 325, 312, 221, 91.

1e R,R_1=-$(CH2)_4$; MP 154°c; Yield 78%; ^{1}H-NMR δ(ppm) 1.7(8H,s), 4.2(4H,s), 5.9(2H,m), 6.4(2H,m), 7.2(10H,m), MS m/z 354 (M^+), 312, 311, 235, 221, 91.

8. **Characterisation data of 2b-e :**

2b R=CH_3, R_1=C_2H_5; MP 148°c; Yield 13%; IR (KBr) 3370cm^{-1}; ^{1}H-NMR δ(ppm) 1.0(3H,s), 1.25(3H,t), 4.4(3H,br), 6.4(4H,m), 7.1(10H,m); MS m/z 342 (M^+), 313, 285, 251, 195, 147, 91.

2c R=CH_3, R_1=n-C_3H_7; MP 134°c; Yield 10%; IR (KBr) 3380cm^{-1}; ^{1}H-NMR δ(ppm) 0.84(3H,t), 1.03(3H,s), 1.5(4H,m), 4.2(2H,s), 4.03(1H,s), 4.18(1H,s), 6.26(4H,m), 7.1(10H,m); MS m/z 356 (M^+), 313, 285, 265, 195, 161, 133, 91.

2d R,R_1=-$(CH_2)_5$; MP 167°c; Yield 16%; IR (KBr) 3380cm^{-1}; ^{1}H-NMR δ(ppm) 1.60(10H,m), 4.04(1H,s), 4.2(2H,s), 4.6(1H,s), 6.60(4H,m), 7.10(10H,m); MS m/z 368 (M^+), 341, 285, 278, 195, 173, 133, 91.

2e R,R_1=-$(CH_2)_4$; MP 154°c; Yield 14%; IR (KBr) 3370cm^{-1}; ^{1}H-NMR δ(ppm) 1.50(8H,m), 4.08(1H,s), 4.15(2H,s), 4.18(1H,s), 6.50(4H,m), 7.15(10H,m); MS m/z 354 (M^+), 312, 264, 263, 195, 159, 133, 91.

9 The ionic mechanism is suggested by the referee, and is gratefully acknowledged.

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