Thermal Fragmentation and Rearrangement of 3-phenyl-4-aryl-5-phenylimino-1,2,4-oxadiazoline Derivatives

Abd El-Aal M. Gaber[a1*] and Nariman M. A. Nahas[b]

[a] **Department, Faculty of Applied Science, Umm Al-Qura University, Makkah 6503 (Al-Abedya), Saudi Arabia.** [b]**Chemistry Department, Faculty of Applied Science, Umm Al-Qura University, Makkah P.O. Box 16222, Saudia Arabia**

Fragmentación térmica y reordenamiento de derivados de 3-fenil-4-aril-5-fenilimino-1,2,4-oxadiazolina

Fragmentació tèrmica i reordenament de derivats de 3-fenil-4-aril-5-fenilimino-1,2,4-oxadiazolina

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RESUMEN

La fragmentación térmica de las 3-fenil-4-aril-5-fenilimino-1,2,4-oxadiazolinas **I** y **II** (Ar= Ph, *p*-tolil) en un tubo sellado bajo atmósfera de nitrógeno rinde derivados de benzonitrilo, arilamina, anilida, fenol, arilurea y benzimidazol. En presencia de naftaleno como disolvente, **I** da α- y β-naftoles junto a los productos previos. Además, la calefacción de **I** a reflujo en tetralina anhidra hirviendo conduce a la formación de 1-hidroxitetralina, α-tetralona y 1,1'-bitetralilo como productos mayoritarios. Los productos aislados se interpretan en términos de un mecanismo vía radicales libres que implica la homólisis del enlace N-O y/o del enlace C-N.

Palabras clave: Termólisis, 1,2,4-oxadiazolinas, benzimidazoles.

SUMMARY

Thermal fragmentation of 3-phenyl-4-aryl-5-phenylimino-1,2,4-oxadiazolines **I** and **II** (Ar= Ph, *p*-tolyl) in a sealed tube under nitrogen gives rise to benzonitrile, arylamines, anilides, phenols, arylureas, and benzimidazole derivatives. In the presence of naphthalene as solvent, **I** gave α- and β-naphthols beside the previous products. Also, heating of **I** under reflux in boiling anhydrous tetraline lead to the formation of 1-hydroxytetraline, α-tetralone and 1,1'-bitetralyl as the major products. The isolated products have been interpreted in term of a free radical mechanism involving the homolysis of N-O and/or C-N bond.

Key words: Thermolysis.1,2,4-Oxadiazolines. Benzimidazoles.

RESUM

La fragmentació tèrmica de les 3-fenil-4-aril-5-fenilimino-1,2,4-oxadiazolines **I** i **II** (Ar= Ph, *p*-tolil) en un tub segellat sota atmosfera de nitrogen dóna derivats de benzonitril, arilamina, anilida, fenol, arilurea i benzimidazole. En presència de naftalè com a dissolvent, **I** dóna α- i β-naftols junt als productes previs. A més, la calefacció d'**I** a reflux en tetralina anhidra bullent condueix a la formació d'1-hidroxitetralina, α-tetralona i 1,1'-bitetralil com a productes majoritaris. Els productes aïllats s'interpreten en termes d'un mecanisme via radicals lliures que implica l'homòlisi de l'enllaç N-O i/o de l'enllaç C-N.

Mots clau: Termòlisi, 1,2,4-oxadiazolines, benzimidazoles.

1*Corresponding Author: Permanent address: Chemistry Department, Faculty of Science, Assiut University, Assiut 71516, Egypt. gaber1371@hotmail.com

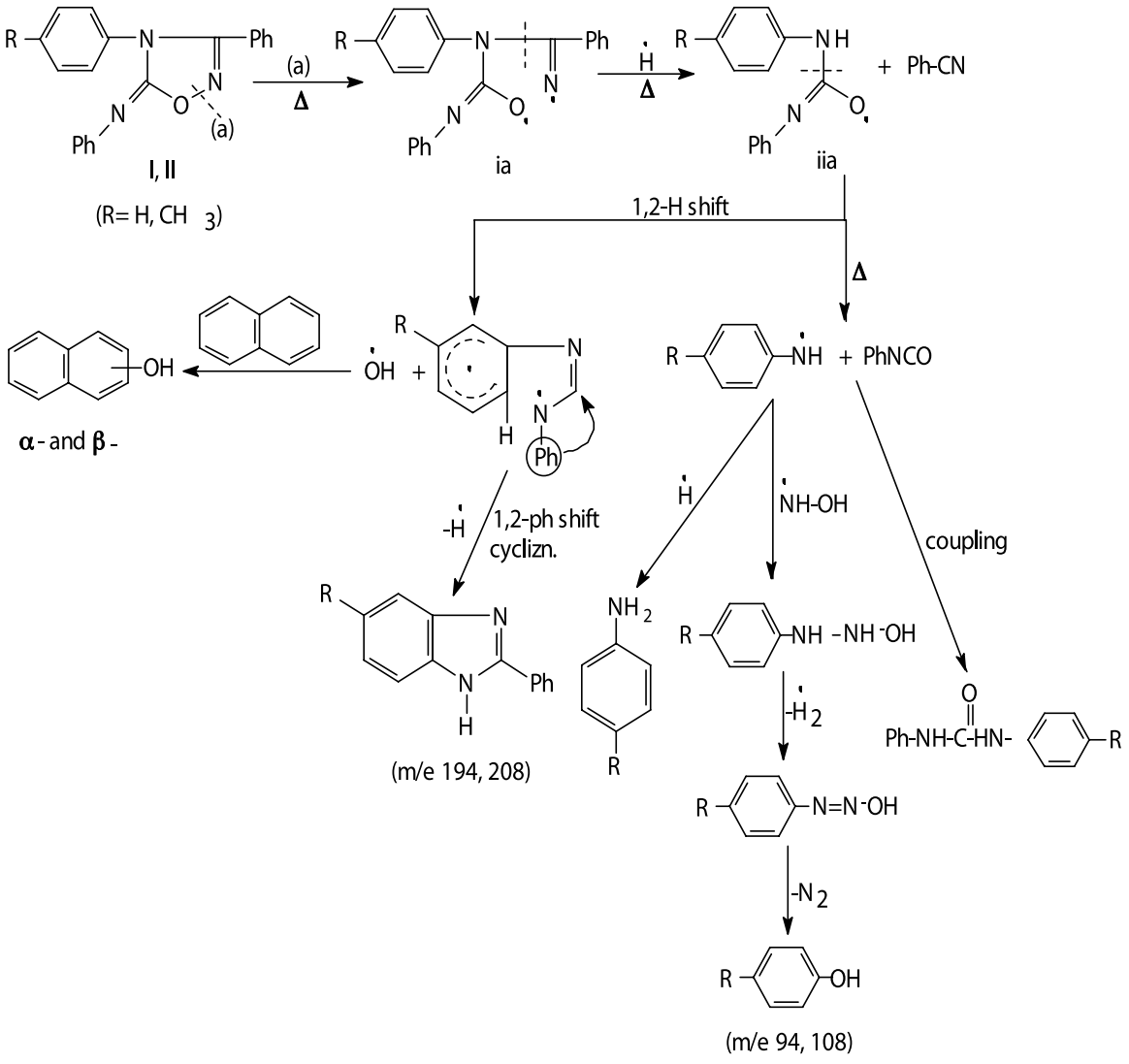
It has previously been reported [1] that thermal decomposition of the 1,2,4-oxadiazoline-3-carboxylic acids gives the corresponding benzamidines. Also, thermolysis and photolysis of 3,4-diphenyl-1,2,4-oxadiazoline-5-one gave 2-phenylbenzimidazole and diphenylcarbdiimide beside the removal CO_2.[2] Moreover, thermolysis of 5,5-dimethyl-2-diphenyl- methylenehydrazone-1,3,4-oxadiazoline in chlorobenzene led to the formation 1-diphenyl methyleneimino-4,4-dimethyl-3-oxo-1,2-diazetidinium hydroxide, inner salts.[3] Also, thermolytic fragmentation of 1,3,4-oxadiazolin-2-ones and 2-imino-1,2,4-oxadiazolines afforded five new bonds in the products via a multi-step mechanism [4] where Herges has analyzed these fragmentations within the framework of coarctate reactions.[5] On the other hand, triplet-sensitized photolysis of 2-methoxy-2,5,5-trimethyl-1,3,4-oxadiazoline led to the retro-cleavage diazoalkenes. [6] Also, photolysis of 2-pyrazolinyl-1,3,4-oxadiazoline led to the formation of gem-dimethylcyclopropane ketone. [7] Moreover, several papers have been published on the use of the oxadiazolines as antimicrobial activity [8] and antibacterial and antifungal activities.[9] The biological effects of 1,2,4-oxadiazoline derivatives have prompted us to investigate the thermolysis of these compounds in order to gain further insight into the scope and mechanism of these reactions. The present work throws light on the thermal fragmentation of 3-phenyl-4-aryl-5-phenylimino-1,2,4-oxadiazolines **I, II**.

RESULTS AND DISCUSSION

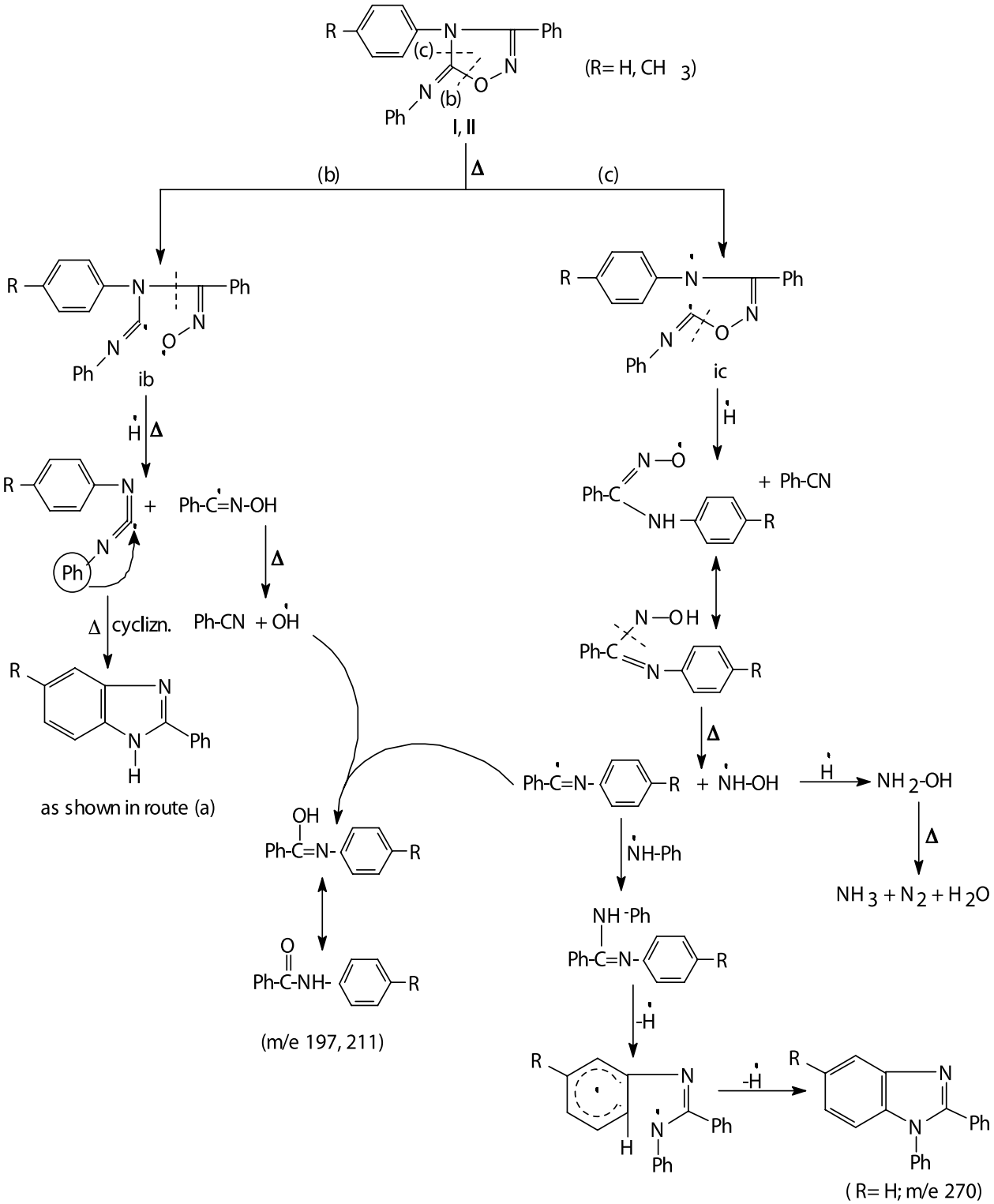
3,4-Diphenyl-5-phenylimino-1,2,4-oxadiazoline **I** on thermolysis at 180-200°C under nitrogen atmosphere gives rise to benzonitrile, aniline, phenol, carbanilide, 2-phenylbenzimidazole, benzanilide and 1,2-diphenylbenzimidazole (Schemes 1 and 2). Although some of the products are present in small amounts due to the variable rates of decay of the free radical intermediates, yet their presence is of great importance for mechanistic interpretation.

Formation of the various products can be assumed to follow the series of reactions shown in Scheme 1, which involves preliminary homolysis of the N-O bond [10] to form the biradical (ia) through route (a). The site of bond rupture of the resulting radicals.

As shown in Scheme 1, the biradical (ia) may fragment into benzonitrile and biradical (iia). The latter may abstract hydrogen atom from a suitable source followed by fragmentation to give anilino radical and phenyl isocyanate which



Scheme 1


(R= H, CH 3)
I, II
(b)
(c)
ib
ic
+ Ph-CN
Ph-C=N-OH
Ph-CN + OH
cyclizn.
as shown in route (a)
(m/e 197, 211)
+ NH-OH
NH 2-OH
NH 3 + N 2 + H 2O
(R= H; m/e 270)

Scheme 2

may couple together to yield carbanilide [11] whereas the anilino radical may abstract hydrogen to form aniline, or may couple with the hydroxylaminyl radical which is readily available in the reaction medium followed by dehydrogenation and extrusion of nitrogen to produce phenol (m/e 94) [12] Scheme 1.

A possible pathway for the formation of 2-phenylbenzimidazole (m/e 194) can be assumed to take place through intramolecular cyclization of the biradical (iia) followed by 1,2-phenyl shift [13] and loss hydroxyl radical. The hydroxyl radical attacks the naphthalene nucleus in the α- or β-position through the formation of the benzocyclo- hexadienyl free radical intermediate (i) which subsequently dehydrogenates to give α- and β-naphthols [14] (estimated by glc 15% yield in the ratio 1:6 respectively), as shown in Scheme 1.

Another competing pathway for the thermal fragmentation of 3,4-Diphenyl-5-phenyl imino-1,2,4-oxadiazoline **I** is the homolysis of the C-N bond by route (b) leading to the formation of biradicals (ib) which ultimately fragment into carbodiimide and benzi- minoxy radical. The latter undergoes fragmentation to form benzonitrile and the hydroxyl radical [13]; Scheme 2.

The formation of benzimidazole derivatives may be rationalized through heating carbodiimide, possibly with an initial phenyl shift occurring, with a subsequent intramolecular cyclization as suggested previously [15] (Scheme 2).

The formation of 2-phenylbenzimidazole by routes (a) and (b) may be correlated with high yield among the observed products.

Scheme 2 also includes the homolysis of the C-N bond (route c) to give biradical (ic) which abstract hydrogen atom from a suitable source forming benzonitrile and phenylbenzoamidoximyl radical. The latter undergoes tautomerism to form N-phenyl- benzoamidoxime as reported by Tiemann [16] which ultimately fragmentation via the homolysis of the C-N bond leading to the formation of benziminyl and hydroxyaminyl radical pairs. The hydroxyl radical may abstract hydrogen atom from a suitable source to afford hydroxylamine which subsequently decomposes into ammonia and water [17] as show in Scheme 2. Moreover, the benziminyl radicals may abstract a hydroxyl radical which is readily available in the reaction medium to form benzanilide.

The formation 1,2-diphenylbenzimidazole (m/e 270) can be assumed to take place through coupling of anilino radical with benziminyl radical to form anilinobenzylide- amine which ultimately undergoes intramolecular cyclization [15,18] as shown in Scheme 2.

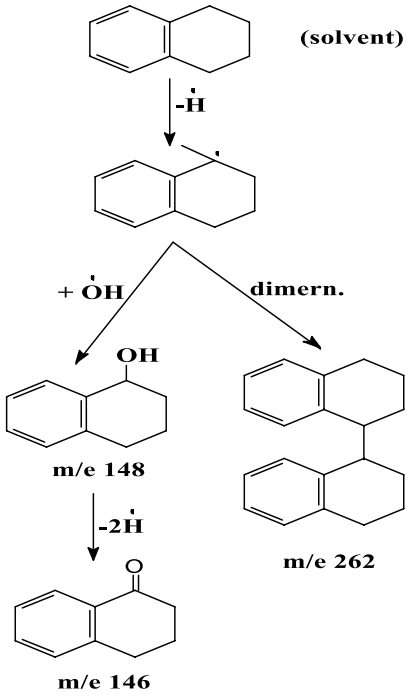
Analogous results were also obtained in the thermal fragmentation of 3-phenyl-4-p-tolyl-5-phenylimino-1,2,4-oxadiazoline **II** under the same condition which gave p-toluidine, p-cresol, benzonitrile, p-toluanilide and 5-methyl-2-phenylbenzimidazole. Such products can be interpreted with the same mechanism suggested previously as shown in Schemes 1 and 2.

Attention has been given to thermal fragmentation of **I** under reflux in boiling anhydrous tetraline (210°C) formed 1-hydroxytetraline, α-tetralone and 1,1'-bitetralyl as the major products beside the same products as mentioned before as shown in Schemes 1, 2 and 3.

The formation of these products can be explained similar suggested mechanism as mentioned previously in Schemes 1 and 2.

A possible pathway for the formation 1-hydroxytetraline (m/e 148), α-tetralone (m/e 146) and 1,1'-bitetralyl (m/e 262) through a process of initial hydrogen abstraction [19] from the solvent nuclei (tetraline) to form 1-tetralyl radical that interaction with hydroxyl radical which is readily available in the reaction medium followed by oxidative dehydrogenation or the 1-tetralyl radical may undergoes dimerization,[12] respectively as shown in Scheme 3.

It is noticed that phenol was absent from the pyrolysate as demonstrated by GC/MS and in Table 1. This is because the hydroxyl radical prefers to couple with 1-tetralyl radical to form 1-hydroxytetraline, hence consumption of hydroxyl radical due to the presence of other competing pathway such as H-abstraction (Scheme 3).



Scheme 3

EXPERIMENTAL

All Melting points are uncorrected. The IR spectroscopic analyses were carried out on a Pye-Unicam spectrophotometer Model SP-3-100 using the KBr wafer technique. ^{1}H NMR spectra were recorded on a Varian EM-390 90 MHz spectrometer in suitable deuterated solvents using TMS as internal standard. Thin-layer chromatography (TLC) was carried out on glass plates (10x3 cm) coated with silica gel (25-40 mesh) eluted with ether-pentane (1:4 v/v). GC/MS analyses were carried out using a Finnigan MAT SSQ 7000 spectrophotometer with 5% (phenylmethylpolysiloxane) using a 30m DB-1 capillary column. Products were identified either by co-injection with authentic samples and/ or by comparison with known GC/MS library fragmentation pattern. Gas-liquid chromatography (GLC) was carried out using a Perkin-Elmer model Sigma 3B apparatus, using a column 4ft x 4 mm packed with SE 30 over Chromosorb W (35-80 mesh) or 10% SE on Celite (60-80 mesh) at 200°C, using nitrogen as a carrier gas. Microanalyses were per-

formed using a Perkin-Elmer 240 C microanalyser. Separation on column chromato- graphy packed with kieselgel 60 (0.040-0.063 mm) using successive solvents: pet.ether (40-60ºC), pet.ether (60-80ºC), benzene, ether-pentane as mixtures.

3,4-Diphenyl-5-phenylimino-1,2,4-oxadiazolines I, crystallized from ethanol, m.p. 158-160ºC, (lit.,[18] m.p. 159-160ºC); found: C, 76.9; H, 4.7; N, 13.4 %. $C_{20}H_{15}ON_3$ requires C, 76.7; H, 4.8; N, 13.4 %); m/e 313.

3-Phenyl-4-p-tolyl-5-phenylimino-1,2,4-oxadiazolines II, crystallized from ethanol, m.p. 165-7ºC, (lit.,[18] m.p. 166-8ºC); found: C, 77.00; H, 5.76; N, 12.34 %. $C_{21}H_{17}ON_3$ requires C, 77.06; H, 5.20; N, 12.84 %); m/e 327.

A number of preliminary experiments were carried out to determine the proper temperature for thermolysis. The results showed the decomposition of **I** and **II** starts at 180ºC. Also, it was found that this temperature was the lowest at which the conversion of the oxadiazolines was complete within a reasonable time.

General method for thermal fragmentation of 1,2,4-oxadiazolines I and II

The oxadiazolines **I, II** (1g) was placed in 50 ml round flask fitted with an efficient reflux condenser, gas inlet and heated, using a temperature controlled heating mantle adjusted to the desired temperature (ca. 200ºC) for 2 hours either alone or in naphthalene (0.5 g) as a solvent, while **I** was heated in anhydrous tetraline (distillation over lithium aluminum hydride under nitrogen) as a solvent. The temperature was measured using a thermometer immersed in the reaction flask. The top of the condenser was attached to a gas trap and driven off by a stream of dry nitrogen which passed through the gas inlet into the reaction vessel. The gas evolved was detected by standard chemical means (NH_3 was detected by Nessler's reagent). After decomposition was completed as judged by tlc monitoring, the pyrolysate was distilled using a microdistillation system at reduced pressure for separation of low boiling points products such as water, aniline, p-toluidine, benzonitrile, phenol, p-cresol, α- and β-naphthols and unreacted naphthalene whereby the following compounds were collected: Phenol was collected at 70-5ºC/5 Torr; picrate derivatives, m.p. and mm.p. 83ºC; m/e 94; further identified by chemical test.[20] p-Cresol was collected at b.p. 60-5ºC/ 6 Torr; benzoyl derivative, m.p. and mm.p. 71-2ºC; m/e 108. Aniline at 80-5ºC/ 6 Torr; acetyl derivative, mp and mmp 113-4ºC. p-Toluidine collected at 70-5ºC/3 Torr; mp and mmp 45-6ºC; benzoyl derivative mp and mmp 144-5ºC. Benzonitrile at bp 41-5ºC/3 Torr; on hydrolysis gave benzoic acid, mp and mmp 121ºC. α-Naphthol, collected at b.p. 120-130ºC/8 Torr; m.p. 96ºC and β-naphthol, collected at b.p. 150-8ºC/10 Torr; estimated by glc in the ratio 1:6 respectively. The remaining (non-distillable) residue was dissolved in ether and shaken several times with ethanolic potassium hydroxide solution (Claisen's solution) to dissolve the resulting phenols. The Claisen extract was acidified with 2N HCl and the liberated phenols were extracted with ether. Phenols (in part) were separated and identified either by vacuum distillation or by chemical tests as mentioned before. The neutral fraction was extracted with ether. Ether was evaporated in vacuo. The remaining residue was separated by column chromatography on Kieselgel 60 (0.040-0.063 mm) using a gradient elution technique as follows: Benzanilide was eluted from column chromatography using pet.ether (60-80ºC)-benzene (2:1v/v), m.p. and mm.p. 164; m/e 197. p-Toluanilide [21] was eluted from column chromatography using benzene, m.p. and mm.p. 145-6ºC; IR (KBr) 3330 (NH) and 1645 (C=O) cm^{-1}; found: C, 79.77; H, 6.19; N, 6.71%. $C_{14}H_{13}NO$ requires C, 79.62; H, 6.16; N, 6.64%; m/e 211. 2-Phenylbenzimidazole [18] was eluted from column chromatography using pet.ether (60-80ºC)–benzene (1:1 v/v) as eluent, m.p. and mm.p. 293-5 ºC; ^{1}HNMR (DMSO-D_6) δ 7.1-7.2 (m, 2H, Ar), 7.3-7.4 (m, 2H, Ar), 7.6 (m, 5H, Ar), 8.6 (s, 1H, NH); m/e 194. 5-Methyl-2-phenylbenzimidazole [22] was eluted from column chromatography using pet.ether (60-80ºC)–benzene (1:1 v/v) as eluent, m.p. and mm.p. 242-4ºC, ^{1}HNMR ($CDCl_3$) δ 6.8-7.2 (m, 2H, Ar), 7.3-7.4 (m, 2H, Ar), 7.5 (m, 5H, Ar), 2.1 (s, 3H, CH_3); m/e 208. 1,2-Diphenylbenzimidazole [23] was eluted from column chromatography using a mixture 1% ether-pentane, m.p and mm.p.112-3ºC; ^{1}HNMR (DMSO-D_6) δ 7.1-7.2 (m, 2H, Ar), 7.3 (m, 2H, Ar), 7.4-7.5 (m, 5H, Ar), 7.6 (m, 5H, Ar); m/e 270. Carbanilide [24] eluted by using a mixture 2% ether-pentane, m.p. and mmp.241-2 ºC; m/e 212. The products are summarized in Table 1.

TABLE 1
Thermolysis products of 1,2,4-oxadiazolines I and II in yield %

Products[a]	I (Ar =Ph)	II (Ar = p-Tolyl)	I[b]
Arylamines	13[c]	11[d]	8[c]
Phenols	10[e]	8[f]	-
Benzonitrile	17.6	15.5	8.5
Anilide derivatives	11[g]	9[h]	6[g]
Urea derivatives	15[i]	13[j]	9[i]
Benzimidazole derivatives	16.5[k]	18.8[l]	12.5[k]
1,2-Diphenyl benzimidazole	12	15	10
α-Tetralone[m]	-	-	12
1-Hydroxytetraline[n]	-	-	14
1,1'-Bitetralyl[o]	-	-	16
Other products	p)	-	-
Unresolved residue(g)	(0.02)	(0.05)	(0.02)

a) NH_3 was detected by chemical means; H_2O as a trace amount.

b) Heating of **I** in anhydrous boiling tetraline as aromatic solvent.

c) Aniline d) p-Toluidine e) Phenol f) p-Cresol

g) Benzanilide h) p-toluanilide i) Carbanilide

k) 2-Phenylbenzimidazole l) 5-Methyl-2-phenylbenzimidazole

m) Collected at b.p. 113-6ºC/6 Torr; n^{20}_D: 1.5679; m/e 146.

n) Collected at b.p. 102-5ºC/2 Torr as pale yellow oil; n^{20}_D: 1.5638; phenyl urethane derivative (ligroin), m.p. and mm.p. 120-2ºC; m/e 148.

o) Eluted from column chromatography using 2% mixture of ether-pentane, m.p. and mm.p.113ºC; on heating with elemental sulfur give bis-naphthylene;[25] m/e 262.

p) α- and β-Naphthols; estimated by glc in the ratio 1:6 respectively.

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