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Thermal and Photofragmentation of *N*-Benzoylhydrazone Derivatives

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Two selected benzoylhydrazones **I** and **II** were subjected to thermolysis by reflux at 200 °C. Benzil, benzoic acid, biphenyl, benzanilide together with the corresponding ketones, nitriles and imines were isolated. Similar treatment of the third hydrazone **III** at 250 °C afforded, in addition to the previous products, bibenzyl, stilbene, and 2-phenylindole. Photolysis of the same hydrazones **I-III** in acetonitrile gave the previously reported products but in different ratios along with azine derivatives and substituted methanes. A free radical mechanism involving homolysis of the N-N and C-N bonds is suggested, substantiated by trapping of phenyl radical with isoquinoline, to account for the formation of the identified products.

INTRODUCTION

Thermolysis of the phenylhydrazones of aldehydes and ketones has been a matter of controversy since Chattaway *et al.*[1] recorded the thermal breakdown of benzaldehyde phenylhydrazone into *N*-benzylidene aniline, stilbene, ammonia, benzene, and nitrogen. Also, thermolysis of phenyl hydrazone derivatives by reflux gave ammonia, benzonitrile, aniline, ketones, 7-methyl-3-phenylindole and 9-phenyl acridine.[2] Photochemistry of hydrazones has been extensively studied by Binkley *et al.*[3] Moreover, benzophenone hydrazone was photolyzed in the presence of air to yield diphenylmethane as the major photoproduct, together with benzophenone, benzophenone imine, and benzophenone azine as minor products.[4] Aldazines undergo N-N cleavage resulting in the formation of a nitrile and an imine.[5] Interestingly, Bhatnagar and George have reported that hydrazones of aldehydes and ketones are oxidized by manganese dioxide to give the corresponding ketones and biphenyl through a free radical mechanism.[6]

The biological activity of benzoylhydrazones[7,8] prompted us to clarify the behavior of these compounds when subjected to high temperature or light radiation, and reinvestigate such reactions in an effort to gain further information about more generalized photolytic and thermolytic mechanisms. Benzoylhydrazones selected in this study contain the biologically active moiety CO-NH-N=C<.[9]

RESULTS AND DISCUSSION

A number of preliminary experiments were carried out to determine the proper temperature for thermolysis. The decomposition of **I** and **II** starts only above 180 °C and above 230 °C for **III**. It was found that 200 °C is the lowest temperature at which the conversion of *N*-benzoyl hydrazones **I** and **II** (250 °C for **III**) was complete at the end of a 10 h thermolysis.

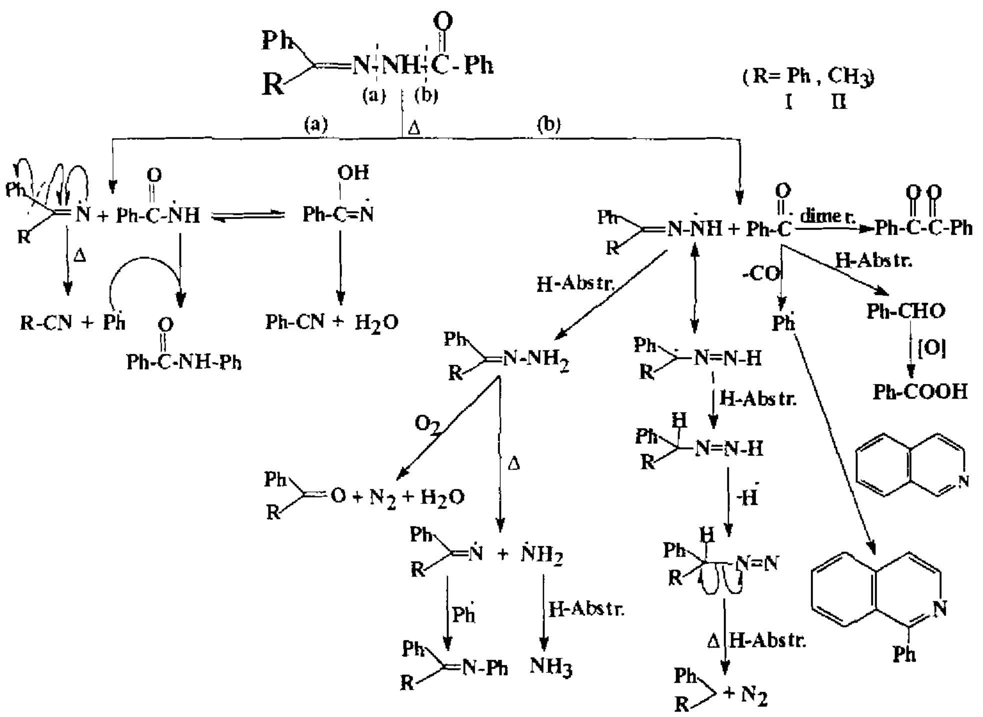
Thermolysis of *N*-benzoyl benzophenone hydrazone **I** at 200 °C for 10 hr gives benzonitrile, benzanilide, benzoic acid, benzophenone, benzil, and benzophenone *N*-phenylimine in addition to water, ammonia, and carbon monoxide as shown in Scheme I. Although some of the products are present in small amounts due to the variable rate of decay of the free radical intermediates, yet their presence is of great importance for mechanistic interpretation.

The nature of the identified products in the hydrazone pyrolyses (Table 1) points to a free radical mechanism. For example, the products formed during the thermolysis of hydrazone **I** can best be explained by a free radical mechanism involving the homolysis of the N-N bond (Scheme I, route a) forming benzophenoneiminyl and phenylamidyl radical pairs. The benzophenone iminyl radical undergoes further fragmentation into phenyl radicals and benzonitrile.[10] The phenylamidyl radical tautomerizes into the enolic form and finally produces benzonitrile and hydroxyl radical.[11] In addition, it may couple with phenyl radical, which is readily available in the reaction medium, to give benzanilide.

Moreover, homolysis of the C-N bond (Scheme I, route b) is less favorable than N-N bond as predicted from bond energy values 51 and 71.8 kcal mol^{-1}, respectively.[12] Homolysis of C-N bond produces benzophenone hydrazonyl and benzoyl free radicals. The benzoyl radical is the precursor of benzoic acid and benzil through the processes of oxidation and decarbonylation,[13,14] respectively.

On the other hand, the benzophenone hydrazonyl radicals may abstract hydrogen to form benzophenone hydrazone which decomposes[1] to diphenyliminyl radicals and

Scheme I



ammonia. The diphenyliminyl radical may couple with phenyl radical to form benzophenone *N*-phenylimine.[15] Furthermore, atmospheric oxidation of benzophenone hydrazone by trace of oxygen in the medium gives rise to benzophenone, nitrogen, and water as reported earlier.[3]

Table 1. Thermolysis Products of *N*-Benzoylhydrazones I-III in % Yield

Products* (%)	I (R=Ph)	II (R=CH3)	III[a] (R=H)	I[b]
Benzoic acid	12	11	14	10
Benzil	7	8	10	6
Bibenzyl	-	-	12	-
trans-Stilbene	-	-	8	-
Benzanilide	13	12	8	9
Nitriles	15	12	18	13
Imines	13	14	-	12
Ketones	11	13	-	10
1-Phenylisoquinoline	-	-	-	11
2-Phenylindole	-	-	12	-
Substituted methanes	10	12	8(23)[a]	8
Recovered hydrazones	6	5	2	4[c]
Unresolved residue (g)	(0.08)	(0.1)	(0.05)	(0.1)

* NH_3 and CO were detected by chemical means. H_2O formed in less than 1%.

[a] Heated in decaline as a solvent (23% yield of toluene).

[b] Heated in isoquinoline as a radical trap.

[c] Recovered isoquinoline was collected at bp 75-82 °C/5 torr; n_D^{20}: 1.6051; picrate derivative, mp and mmp 219-221 °C.

Also, the mechanism of diphenylmethane formation may be described as a Wolff-Kishner reduction involving an initial hydrogen migration to form the azo compound followed by loss of nitrogen and radical recombination.[16]

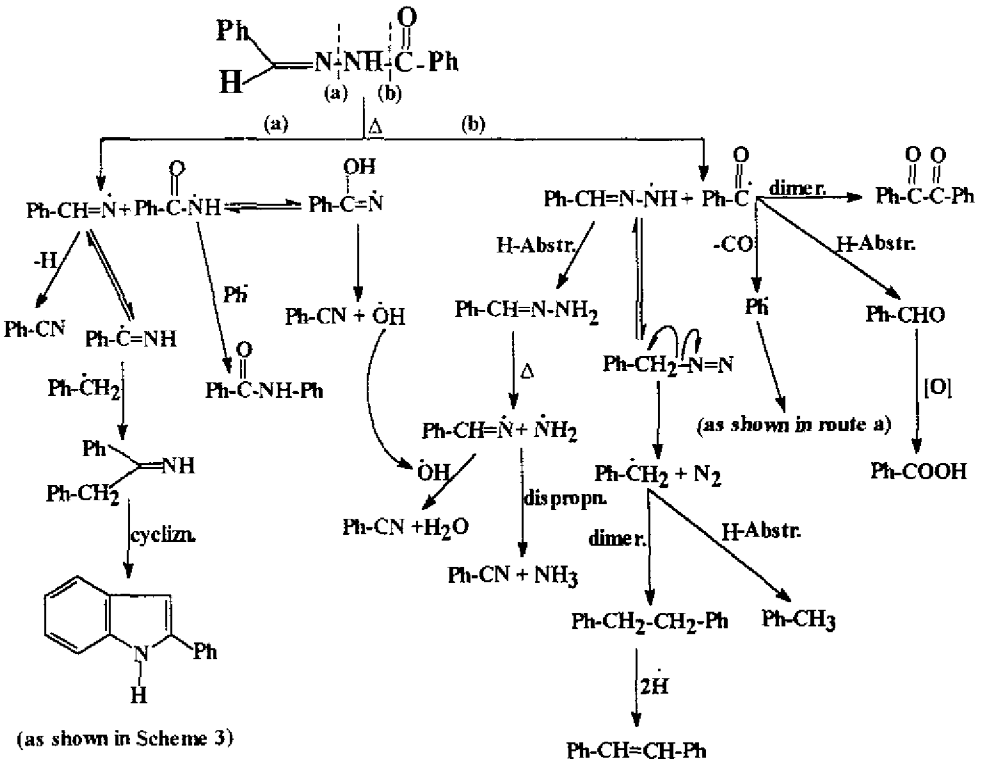
Analogous results were also obtained in the thermolysis of *N*-benzoyl acetophenone hydrazone **II** under similar conditions, where acetonitrile, benzanilide, benzoic acid, acetophenone, benzil, and acetophenone *N*-phenylimine, in addition to water, ammonia, and carbon monoxide were formed. The formation of these products is also consistent with the mechanism suggested in Scheme I.

Thermolysis of *N*-benzoyl benzophenone hydrazone **I** by reflux at 200 °C in the presence of isoquinoline as a radical scavenger afforded the same products mentioned above, in addition to 1-phenylisoquinoline (11% yield). This confirms the formation of phenyl radicals during the reaction and is consistent with the free radical mechanism in Scheme I.

Similarly, thermolysis of *N*-benzoyl benzaldehyde hydrazone **III** at 250 °C for 10 h led to the formation of toluene, benzanilide, benzoic acid, benzil, bibenzyl, stilbene, and 2-phenylindole together with benzonitrile as major products in addition to water, ammonia, and carbon monoxide as shown in Scheme II and Table 1.

Scheme II includes the homolysis of N-N bond (route a) to give benzaliminyl and phenylamidyl radical pairs. The phenylamidyl gave benzanilide and benzonitrile through the

Scheme II



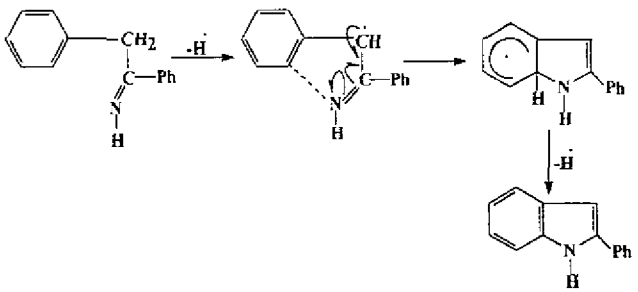
same mechanism suggested in Scheme I.

Another competing pathway for the thermolysis of *N*-benzoyl benzaldehyde hydrazone **III** is the homolysis of C-N bond (route b, Scheme II) furnishing benzalhydrazonyl and benzoyl free radicals. The benzalhydrazonyl radical may undergo isomerization to the corresponding benzylazoalkane, as observed by other workers, initiated by free radicals present in the reaction medium.[17] The isomerized benzylazoalkane undergoes β-scission to form N_2 and the benzyl radical, which can form toluene and bibenzyl through H-abstraction and dimerization as shown in Scheme II. Stilbene can be formed by free-radical dehydrogenation[18] of bibenzyl whereas the benzoyl radicals produced benzoic acid and benzil through the same mechanism suggested in Scheme I.

The formation of benzonitrile (route b, Scheme II) can account for the decomposition of benzaldehyde hydrazone[19] to give benzaliminyl and ammonia. The benzaliminyl radical is considered to be the precursor of benzonitrile and water via reaction with the hydroxyl radical, which is readily available in the reaction medium. However, substituted indoles in case of compounds **I** and **II** (R=CH_3, Ph) are not formed. This result reflects the difference in behavior as a factor of substituents in the hydrazone series, i.e. absence of benzyl radical, which is responsible for the indole formation.

A possible pathway for the formation of 2-phenylindole is the isomerization of benzaliminyl radical followed by coupling with benzyl radical (C-C rather than C-N) to form benzyl phenylketimine. Hydrogen abstraction at benzylic position followed by intramolecular cyclization and hydrogen abstraction produces 2-phenylindole[20] as shown in Scheme III.

Scheme III



Thermolysis of *N*-benzoyl benzaldehyde hydrazone **III** in the presence of decalin as a hydrogen donor solvent under the conditions used afforded a great increase in the yield of toluene (formed by H-abstraction; 23% yield) in addition to a small amount of benzoic acid, benzil, benzonitrile, and benzanilide. No bibenzyl, stilbene or 2-phenylindole were formed, further evidence of the free radical nature of the reactions. However, the formation of benzonitrile from both routes (a and b) correlates for its high yield among the identified products.

Photolysis of *N*-benzoylhydrazones **I-III** in acetonitrile at ambient temperature for 24 h gave benzonitrile, benzoic acid, and benzil, in addition to the corresponding azines, ketones, and substituted methanes as shown in Scheme IV and Table 2.

The formation of azines only upon photolysis of the investigated hydrazones **I-III** indicates the homolysis of N-N bond in the excited state forming iminyl free radical (route a, Scheme IV) followed by dimerization within the solvent cage.

Also, bibenzyl, stilbene, benzanilide, and imines were formed only in the thermolysis reactions as a result of multistage bond fission induced by further heating of the primary radicals. Benzil, benzoic acid, benzonitrile, and substituted methanes are formed in all cases.

The formation of benzoic acid and benzophenone can be explained on the basis of hydrolysis by water present in the reaction medium (Scheme IV).

The percentage of benzoic acid in photolysis is almost twofold that in thermolysis. This may be due to long period of photolysis (24 h) compared with thermolysis (10 h).

EXPERIMENTAL SECTION

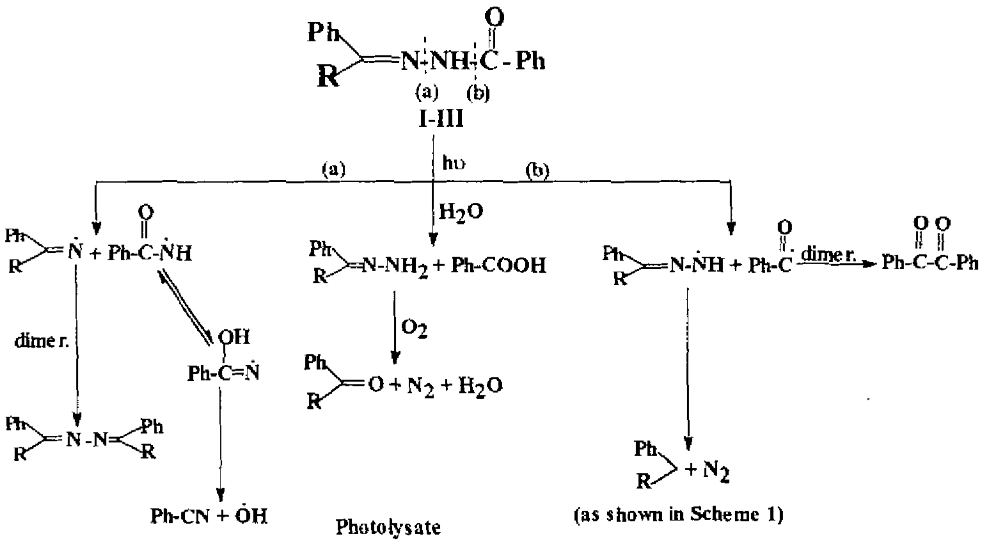
General

All melting points were determined on a Gallenkamp apparatus and are uncorrected. The IR spectra analyses were recorded on a Pye-Unicam spectrophotometer model SP 3-100 G. ^{1}H NMR spectra for some reaction products were obtained using an EM 390 90 MHz NMR spectrometer. Thin-layer chromatography was carried out using glass plates (10 × 3 cm) coated with silica gel (25-40 mesh) eluted with ether-pentane (1:4 v/v). Preparative column chromatographic separations were performed using a 120 × 2.5 cm glass column packed with alumina and using the following solvents successively: pet. ether (40-60 °C), pet. ether (60-80 °C) and mixtures (1:1 v/v) and (1:2 v/v); pet. ether (60-80 °C)-benzene mixtures (1:2 v/v) and (2:3 v/v); benzene-ether mixtures (2:1 v/v); ether; ether-methanol mixtures (1:2 v/v), and finally methanol. Gas-liquid chromatography was carried out using a Perkin-Elmer model Sigma 3B apparatus, 8 × 1/20 inch column, packed with 30% SE 30 on a Chromosorb W (35-80 mesh) thermal conductivity detector, using nitrogen as a carrier gas. GC/MS analyses were carried out using a Finnigan MAT SSQ 7000 spectrophotometer with 5% (phenylmethylpolysiloxane) using a 30 m DB-1

Table 2. Photolysis Products of Hydrazone Derivatives I-III in % Yield

	Reactants		
Products (%)	I	II	III
Benzoic acid	21	23	27
Benzil	12	10	11
Ketones	10	12	10
Benzonitrile	20	18	15
Substituted methanes	13	14	16
Azine derivatives	18	16	17
Residue (g)	(0.02)	(0.03)	(0.01)

Scheme IV



capillary column. Products were identified either by co-injection with authentic materials and/or by comparison with known gc/ms library fragmentation patterns. Ultraviolet irradiations were carried out using a high pressure Philips 125W HPK mercury lamp. Acetonitrile was used as received for HPLC analysis using a Merck & Hitachi L-6000 UV-Vis-Detector with solvent MeOH-H_2O (80:20).

Starting Materials

N-benzoyl benzophenone hydrazone **I**, crystallized from ethanol, mp 116-117 °C (lit.,[21] mp 118 °C). *N*-Benzoyl acetophenone hydrazone **II**, crystallized from ethanol, mp 153-155 °C (lit.,[22] mp 155 °C). *N*-Benzoyl benzaldehyde hydrazone **III**, crystallized from ethanol, mp 204-206 °C (lit.,[21] mp 205 °C).

General Method for the Thermal Decomposition of Hydrazones I-III

The appropriate hydrazone **I** or **II** (0.046 mol) was heated under reflux either alone or in isoquinoline (5 mL) at 200 °C, while hydrazone **III** was heated either alone or in decalin as a solvent at 250 °C for 10 h. The products NH_3 and CO were detected by Nessler's reagent and palladium chloride,[23] respectively. The pyrolysate was separated via fractional distillation up to 180 °C whereby water, toluene, ethylbenzene, and acetonitrile were isolated followed by distillation under reduced pressure where the following compounds were collected: Toluene (in part) at bp 60-65 °C/3 torr; its glc revealed a single peak at 1.0 min comparable with an authentic sample using (8 × 1/20 inch) SE 30 column at 90 °C. Acetophenone at bp 82-85 °C/3 torr; n_D^{20}: 1.5325; 2,4-dinitrophenylhydrazone (2,4-DNP) derivative, mp and mmp 250 °C, diphenylmethane[24] at bp 95-100 °C/3 torr; n_D^{20}: 1.5788; on oxidation with $K_2Cr_2O_7/H_2SO_4$ gave benzophenone; 2,4-DNP derivative, mp 238 °C, acetophenone *N*-phenylimine[25] at bp 180-185 °C/3 torr, mp 41-42 °C and benzonitrile at bp 41-45 °C/3 torr; n_D^{20}: 1.527; on hydrolysis gave benzoic acid, mp and mmp 121 °C. The remaining residue was separated by column chromatography on alumina using a gradient elution technique as follows: Benzoic acid, mp 120 °C; identified by preparative tlc using pet. ether (60-80 °C)-acetone (5:1 v/v) as eluent, R_f = 0.65. Benzil was eluted from column chromatography using pet. ether (60-80 °C)-benzene (1:2 v/v), mp and mmp 96 °C. Bibenzyl[26] was eluted from column chromatography using pet. ether (40-60 °C)-pet. ether (60-80 °C) (1:2 v/v) mixture, mp 52 °C; its glc on a column (8 × 1/20 inch) packed with SE 30 over Chromosorb at 140 °C, showed a peak at 3.3 min; 4,4′-dinitrobibenzyl, mp and mmp 179-80 °C. Stilbene[27] was eluted with pet. ether (60-80 °C), mp and mmp 125 °C. Benzanilide was eluted from column chromatography using pet. ether (60-80 °C)-benzene (2:3 v/v) mixture, mp and mmp 162 °C. Benzophenone *N*-phenylimine[28] was eluted with benzene, mp 110-114 °C. Calcd. N, 5.54; found: N, 5.65%. Benzophenone was eluted from column chromatography using pet. ether (60-80 °C)-benzene (1:2 v/v) mixture, mp 49-50 °C; 2,4-DNP derivative, mp and mmp 238 °C. 1-Phenylisoquinoline[29] was eluted from column chromatography using pet. ether (60-80 °C)-benzene (2:3 v/v) mixture, mp and mmp 95 °C; picrate derivative, mp 164 °C. 2-Phenylindole[30] was eluted with successive portions of pet. ether (60-80 °C)-benzene (1:2 v/v) mixture mp 188-190 °C; picrate derivative, mp and mmp 127 °C. Calcd. N, 7.25; found: N, 7.20%; *m/z* 193. Benzophenone azine,[31] mp 163-164 °C; identified by nmr and mmp as compared with an authentic sample. Calcd for ($C_{26}H_{20}N_2$): C, 86.66; H, 5.56; N, 7.78. Found: C, 86.93; H, 5.48; N, 7.59%; *m/z* 360. Acetophenone azine,[32] mp 122-124 °C, which crystallized on standing and was recrystallized from ethanol. Calcd. for ($C_{16}H_{16}N_2$): C, 81.36; H, 6.78; N, 11.86. Found: C, 81.95; H, 6.82; N, 11.23%; *m/z* 236. Benzalazine,[33] mp 92-93 °C; a spot with the same R_f value (0.8) as compared with an authentic sample was visualized by tlc.

General Method for the Photolysis of *N*-Benzoylhydrazone Derivatives I-III

A solution of *N*-benzoylhydrazone derivatives **I-III** (0.004 mol) in acetonitrile (100 mL) was irradiated at ambient temperature in Pyrex apparatus under nitrogen until **I-III** completely disappeared (24 h according to tlc monitoring). The photolysate was separated into amine and neutral products by extracting with hydrochloric acid (0.1 M) as previously described.[34] Samples were analyzed by glc, and products were identified by comparison with authentic samples and quantitated using nitrobenzene as an internal standard. The results are summarized in Table 2.

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Key Words

Thermolysis; Photolysis; *N*-Benzoylhydrazones; Free radicals.

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