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ORIGINAL PAPER

Thermolysis and photolysis of *N*-benzoylhydrazone derivatives

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Abstract Two selected *N*-benzoylhydrazones were subjected to thermolysis by refluxing at 200 °C. Benzil, benzoic acid, biphenyl, benzanilide together with the corresponding ketones, nitriles, substituted methanes, and imines were isolated. Similar treatment of a third hydrazone at 250 °C afforded, in addition to the previous products, toluene, bibenzyl, stilbene, and 2-phenylindole. Photolysis of the same hydrazones 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 the phenyl radical with isoquinoline, to account for the formation of the identified products.

Keywords Thermolysis · Photolysis · *N*-benzoylhydrazones · Free radicals · 2-Phenylindole

Introduction

Thermolysis of the phenylhydrazones of aldehydes and ketones has been a matter of controversy since Chattaway et al. [1] reported the thermal breakdown of benzaldehyde phenylhydrazone into *N*-benzylideneaniline, stilbene, ammonia, benzene, and nitrogen. Also, thermolysis of phenylhydrazone derivatives by refluxing gave ammonia, benzonitrile, aniline, ketones, 7-methyl-3-phenylindole, and 9-phenylacridine [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 [6] 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.

Furthermore, the hydrazone derivatives are widely applied in the treatment of diseases such as tuberculosis, leprosy, mental disorders, and are also used as herbicides, insecticides, and rodenticides; they can be used as plasticizers and antioxidants [7].

The biological activity of benzoylhydrazones [8, 9] 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 [10].

Results and discussion

A number of preliminary experiments were carried out to determine the proper temperature for thermolysis. The decomposition of **1a** and **1b** starts only above 180 °C and above 230 °C for **1c**. It was found that 200 °C is the lowest temperature at which the conversion of *N*-benzoylhydrazones **1a** and **1b** (250 °C for **1c**) was complete at the end of 10 h thermolysis.

Thermolysis of benzophenone *N*-benzoylhydrazone (**1a**) at 200 °C for 10 h gives benzonitrile (**2a**), benzanilide (**3**),

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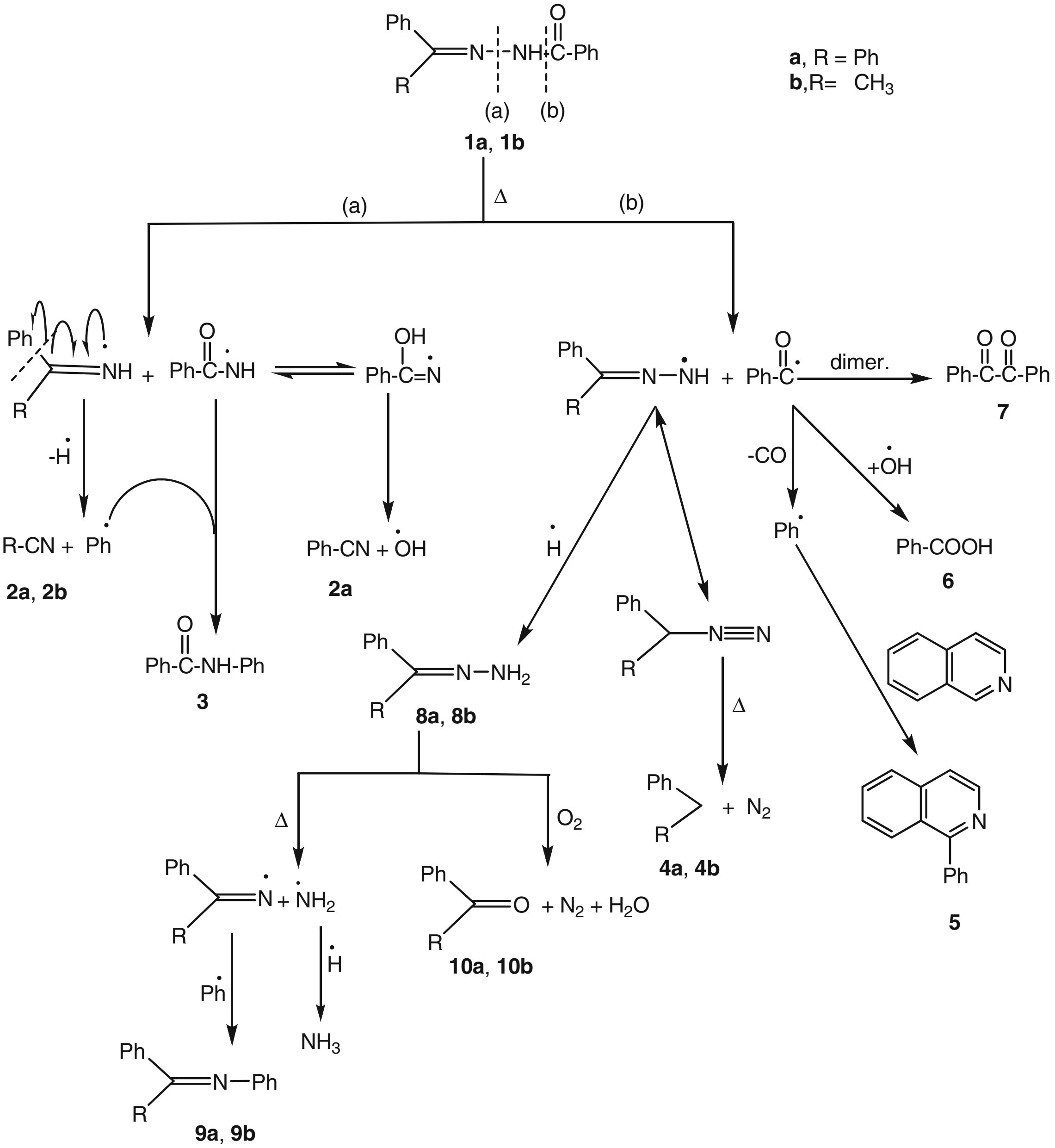
benzoic acid (**6**), benzophenone (**10a**), benzil (**7**), diphenylmethane (**4a**), and benzophenone *N*-phenylimine (**9a**) in addition to water, ammonia, and carbon monoxide as shown in Scheme 1.

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 **1a** involving the homolysis of the N–N bond (Scheme 1, route a) form benzophenone iminyl and phenylamidyl radical pairs. The benzophenone iminyl radical undergoes further fragmentation into phenyl radicals and benzonitrile (**2a**) [11]. The phenylamidyl radical tautomerizes into the enolic form and finally produces benzonitrile and hydroxyl radical [12, 13]. In addition, it may couple with a phenyl radical, which is readily available in the reaction medium, to give benzanilide (**3**). Moreover, homolysis of the C–N bond (Scheme 1, route b) is less favorable than the N–N bond as predicted from bond energy values 213.5 and 300.6 kJ mol^{-1}, respectively [14]. Homolysis of the C–N bond produces benzophenone hydrazonyl and benzoyl free radicals. The benzoyl radical is the precursor of benzoic acid (**6**) and benzil (**7**) through the processes of oxidation and dimerization [15, 16], respectively. Also, the mechanism of formation of



Scheme 1

Table 1 Thermolysis products of *N*-benzoylhydrazones **1a**–**1c** (% yield)

Products[a]	Reactant			
	1a (R = Ph)	**1b** (R = CH_3)	**1c** (R = H)	**1a**[c]
Benzoic acid (**6**)	12	11	14	10
Benzil (**7**)	7	8	10	6
Bibenzyl (**12**)	–	–	12	–
Stilbene (**13**)	–	–	8	–
Benzanilide (**3**)	13	12	8	9
Nitriles **2**	15	12	18	13
Imines **9**	13	14	–	12
Ketones **10**	11	13	–	10
1-Phenylisoquinoline (**5**)	–	–	–	11
2-Phenylindole (**11**)	–	–	12	–
Substituted methanes **4**	10	12	8 (23)[b]	8
Recovered hydrazones	6	5	2	4[d]
Unresolved residue/g	0.08	0.1	0.05	0.1

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

[b] Heated in decalin as a solvent (23% yield of toluene)

[c] Heated in isoquinoline as a radical trap

[d] Recovered isoquinoline was collected at b.p. 75–82 °C (7 mbar); $n_D^{20} = 1.6051$; picrate derivative, m.p. and mixed melting point (m.m.p.) 219–221 °C

diphenylmethane (**4a**) 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 [17] (Scheme 1). On the other hand, the benzophenone hydrazonyl radicals may abstract hydrogen to form benzophenone hydrazone (**8a**) which decomposes to diphenyliminyl radicals and ammonia [1]. The diphenyliminyl radical may couple with a phenyl radical to form benzophenone *N*-phenylimine (**9a**) [18]. Furthermore, oxidation of benzophenone hydrazone by traces of oxygen in the medium gives rise to benzophenone (**10a**), nitrogen, and water as reported earlier [3], as shown in Scheme 1.

Analogous results were also obtained in the thermolysis of acetophenone *N*-benzoylhydrazone (**1b**) under similar conditions: acetonitrile (**2b**), benzanilide, benzoic acid, acetophenone (**10b**), benzil, ethylbenzene (**4b**), and acetophenone *N*-phenylimine (**9b**) in addition to water, ammonia, and carbon monoxide were formed. The formation of these products is also consistent with the mechanism suggested in Scheme 1.

Thermolysis of benzophenone *N*-benzoylhydrazone (**1a**) by refluxing at 200 °C in the presence of isoquinoline as a radical scavenger afforded the same products mentioned above, in addition to 1-phenylisoquinoline (**5**, 11% yield). This confirms the formation of phenyl radicals during the reaction and is consistent with the proposed free radical mechanism [19] (Scheme 1).

Similarly, thermolysis of benzaldehyde *N*-benzoylhydrazone (**1c**) at 250 °C for 10 h leads to the formation of toluene (**4c**), benzanilide, benzoic acid, benzil, bibenzyl (**12**), stilbene (**13**), and 2-phenylindole (**11**) together with benzonitrile (**2a**) as major products in addition to water, ammonia, and carbon monoxide as shown in Scheme 2 and Table 1.

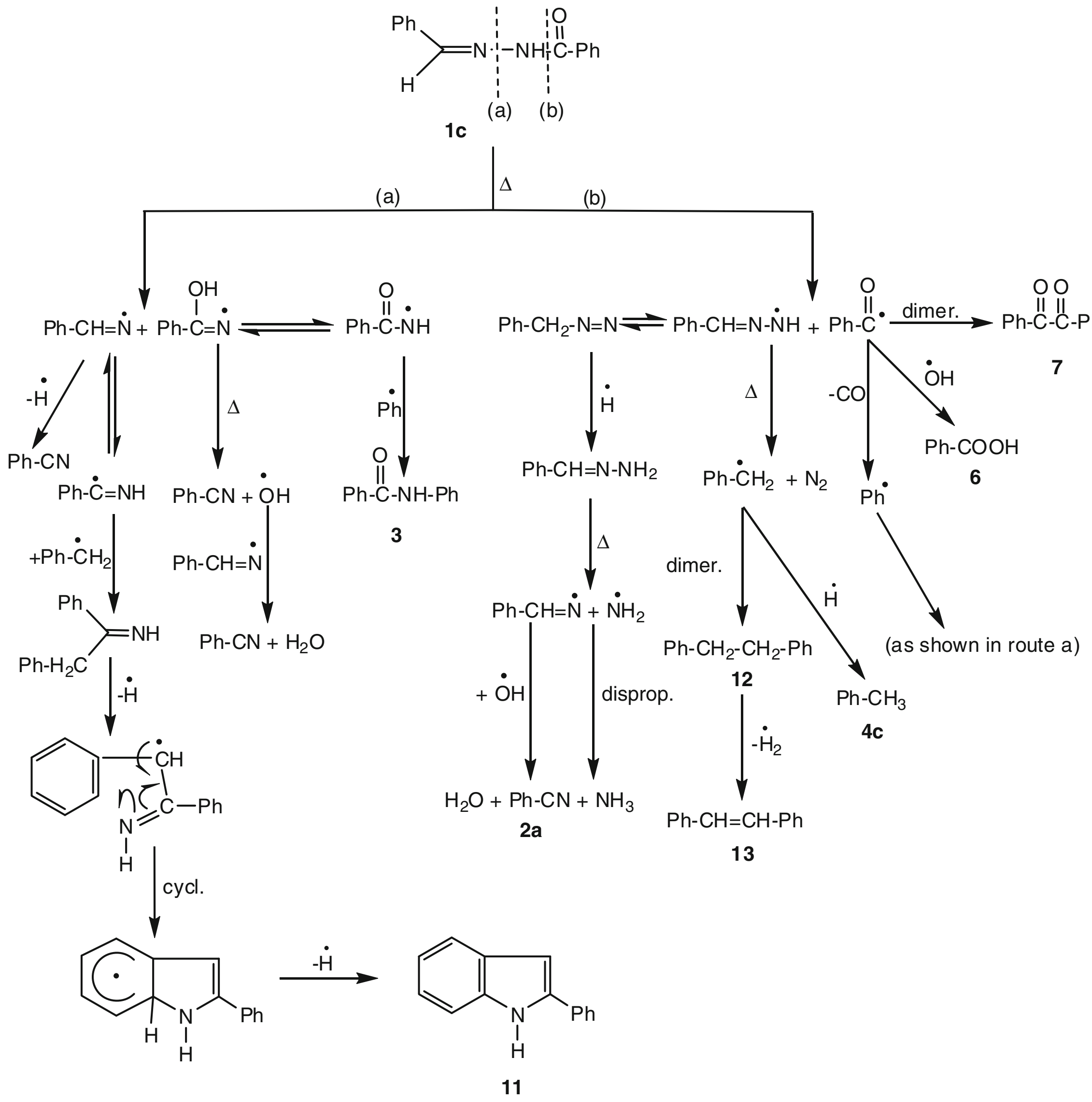
Another competing pathway for the thermolysis of benzaldehyde *N*-benzoylhydrazone (**1c**) is the homolysis of the C–N bond (Scheme 2, route b) furnishing benzalhydrazonyl and benzoyl free radicals. The benzalhydrazonyl radical may undergo isomerization to the corresponding benzylazoalkane, as observed by other workers, initiated by free radicals present in the reaction medium [20]. The isomerized benzylazoalkane undergoes α-scission to form N_2 and the benzyl radical, which can form toluene (**4c**) and bibenzyl (**12**) through H-abstraction and dimerization as shown in Scheme 2. Stilbene (**13**) can be formed by free radical dehydrogenation [21, 22] of bibenzyl, whereas the benzoyl radicals produce benzoic acid and benzil through the same mechanism suggested in Scheme 1.

The formation of benzonitrile (**2a**) (Scheme 2, route b) can account for the decomposition of benzaldehyde hydrazone [23] 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 are not formed in the case of compounds **1a** and **1b** (R = Ph, CH_3). This result reflects the difference in behavior as a factor of substituents in the hydrazone series, i.e., absence of a benzyl radical, which is responsible for the indole formation.

A possible pathway for the formation of 2-phenylindole (**11**) 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 the benzylic position followed by intramolecular cyclization and hydrogen abstraction produces 2-phenylindole [24] as shown in Scheme 2.

Thermolysis of benzaldehyde *N*-benzoylhydrazone (**1c**) in the presence of decalin as a hydrogen donor solvent under the conditions used afforded a great increase in the yield of toluene (**4c**, formed by H-abstraction, 23% yield) in addition to other minor products. However, the formation of benzonitrile from both routes a and b correlates with its high yield among the identified products.

Photolysis of *N*-benzoylhydrazones **1a**–**1c** in acetonitrile at ambient temperature for 24 h gave benzonitrile, benzoic acid, and benzil, in addition to the corresponding azines **14a**–**14c**, ketones **10a**–**10c**, and substituted methanes **4a**–**4c** as shown in Scheme 3 and Table 2. The formation



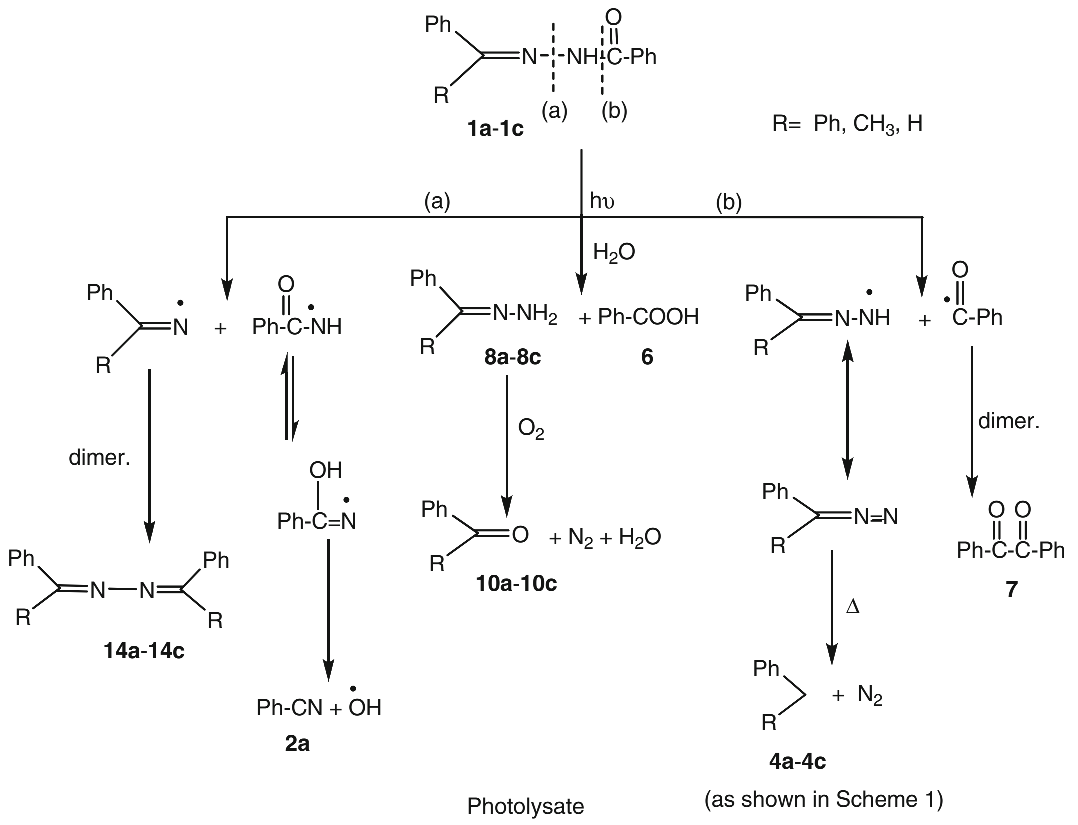
Scheme 2

of azines **14a**–**14c** only upon photolysis of the investigated hydrazones **1a**–**1c** indicates the homolysis of the N–N bond in the excited state forming an iminyl free radical (Scheme 3, route a) 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 (**6**) and benzophenone (**10a**) can be explained on the basis of hydrolysis by water present in the reaction medium (Scheme 3). The yield of benzoic acid in photolysis is almost twice that obtained in thermolysis. This may be due to the long period of photolysis (24 h) compared with thermolysis (10 h).

Conclusions

The thermolysis and photolysis of *N*-benzoylhydrazones **1a**–**1c** are a complex process in the condensed phase. At least three independent primary thermolysis processes have been observed, viz. (a) homolysis of the C–N bond to provide radicals which gave benzonitrile, benzil, benzanilide, imines, and ketones; (b) homolysis of the N–N bond to give radicals which cyclize to 2-phenylindole; (c) homolysis of the N–CO bond to form benzoic acid, bibenzyl, and stilbene. The complexities are compounded by intermolecular secondary processes which lead to the observed products. In addition, a free radical mechanism is suggested, substantiated by trapping of the phenyl radical with isoquinoline, to account for the formation of the identified products.



Scheme 3

Table 2 Photolysis products of hydrazone derivatives **1a**–**1c** (% yield)

Products	Reactant		
	1a	**1b**	**1c**
Benzoic acid (**6**)	21	23	27
Benzil (**7**)	12	10	11
Ketones **10**	10	12	10
Benzonitrile (**2**)	20	18	15
Methanes **4**	13	14	16
Azine derivatives **14**	18	16	17
Residue/g	0.02	0.03	0.01

Experimental

General procedures

All melting points were determined on a Gallenkamp apparatus. The IR spectra were recorded on a Pye-Unicam spectrometer model SP 3-100 G. ^{1}H NMR spectra for some reaction products were obtained using an EM-390 200 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: petroleum ether (40–60 °C), petroleum ether (60–80 °C), and mixtures thereof (1:1 and 1:2 v/v); petroleum ether (60–80 °C)/benzene (1:2 and 2:3 v/v), benzene/ether (2:1 v/v), and finally methanol. Gas–liquid chromatography (GLC) 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% (phenylmethyl)polysiloxane using a 30-m DB-1 capillary column. Products were identified by co-injection with authentic materials and/or by comparison with known GC/MS library fragmentation patterns.

Irradiations

Solvents were Merck Uvasol grade and used as received.

The irradiation apparatus comprised an immersion well reactor (50 cm^3, solidex glass) allowing evacuation, with a central 125-W high pressure mercury lamp (Philips HPK 125), magnetic stirring, nitrogen atmosphere after degassing the reactant solution, tap water as coolant, and ambient temperature. This apparatus provides a line spectrum with a range of light greater than 300 nm in the irradiated solution.

Starting materials

Benzophenone *N*-benzoylhydrazone (**1a**) [25], crystallized from ethanol, m.p. 116–117 °C (Ref. [25] 118 °C). Acetophenone *N*-benzoylhydrazone (**1b**) [26], crystallized from ethanol, m.p. 153–155 °C (Ref. [26] 155 °C). Benzaldehyde *N*-benzoylhydrazone (**1c**) [27], crystallized from ethanol, m.p. 204–206 °C (Ref. [25] 205 °C).

*General method for the thermal decomposition of hydrazones **1a**–**1c***

The appropriate hydrazone **1a** or **1b** (0.046 mol) was heated under reflux either alone or in 5 cm^3 isoquinoline at 200 °C, while hydrazone **1c** 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 [26], respectively. The pyrolysate was separated via fractional distillation up to 180 °C whereby water, toluene, ethylbenzene (**4b**), and acetonitrile (**2b**) were isolated, followed by distillation under reduced pressure to afford the following compounds.

Toluene (**4c**), b.p. 60–65 °C (4 mbar); its GLC revealed a single peak at 1.0 min comparable with an authentic sample using an 8 × 1/20-inch SE 30 column at 90 °C. Acetophenone (**10b**), b.p. 82–85 °C (4 mbar); $n_D^{20} = 1.5325$; 2,4-dinitrophenylhydrazone (2,4-DNP derivative), m.p. and m.m.p. 250 °C. Diphenylmethane (**4a**) [28], b.p. 95–100 °C (4 mbar); $n_D^{20} = 1.5788$; on oxidation with $K_2Cr_2O_7/H_2SO_4$ gave benzophenone; 2,4-DNP derivative, m.p. 238 °C. Acetophenone *N*-phenylimine (**9b**) [29], b.p. 180–185 °C (4 mbar); m.p. 41–42 °C. Benzonitrile (**2a**), b.p. 41–45 °C (4 mbar); $n_D^{20} = 1.527$; on hydrolysis gave benzoic acid, m.p. and m.m.p. 121 °C.

The remaining residue was separated by column chromatography on alumina using a gradient elution technique as follows.

Benzoic acid (**6**), m.p. 120 °C; identified by preparative TLC using petroleum ether (60–80 °C)/acetone (5:1 v/v) as eluent, $R_f = 0.65$. Benzil (**7**), eluted from column chromatography using petroleum ether (60–80 °C)/benzene (1:2 v/v); m.p. and m.m.p. 96 °C. Bibenzyl (**12**) [30], eluted from column chromatography using petroleum ether (40–60 °C)/petroleum ether (60–80 °C) (1:2 v/v); m.p. 52 °C; its GLC on a 8 × 1/20-inch column packed with SE 30 over chromosorb at 140 °C showed a peak at 3.3 min; 4,4′-dinitrobibenzyl, m.p. and m.m.p. 179–180 °C. Stilbene (**13**) [31], eluted with petroleum ether (60–80 °C); m.p. and m.m.p. 125 °C. Benzanilide (**3**), eluted from column chromatography using petroleum ether (60–80 °C)/benzene (5:1 v/v); m.p. and m.m.p. 162 °C. Benzophenone *N*-phenylimine (**9a**) [32], eluted with benzene; m.p. 110–114 °C. Benzophenone (**10a**), eluted from column chromatography using petroleum ether (60–80 °C)/benzene (1:2 v/v); m.p. 49–50 °C; 2,4-DNP derivative, m.p. and m.m.p. 238 °C. 1-Phenylisoquinoline (**5**) [33], eluted from column chromatography using petroleum ether (60–80 °C)/benzene (2:3 v/v); m.p. and m.m.p. 95 °C; picrate derivative, m.p. 164 °C. 2-Phenylindole (**11**) [34], eluted with successive portions of petroleum ether (60–80 °C)/benzene (1:2 v/v); m.p. 188–190 °C; picrate derivative, m.p. and m.m.p. 127 °C. Benzophenone azine (**14a**) [35], m.p. 163–164 °C; identified by ^{1}H NMR and m.m.p. as compared with an authentic sample. Acetophenone azine (**14b**) [36], crystallized on standing and recrystallized from ethanol; m.p. 122–124 °C. Benzalazine (**14c**) [37], m.p. 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 **1a**–**1c***

A solution of *N*-benzoylhydrazone derivatives **1a**–**1c** (0.004 mol) in 100 cm^3 acetonitrile was irradiated at ambient temperature in a Pyrex apparatus under nitrogen until **1a**–**1c** 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 [38]. Samples were analyzed by GLC, and products were identified by comparison with authentic samples and quantified using nitrobenzene as an internal standard. The results are summarized in Table 2.

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