Photolysis of 1-*o*-Iodobenzoylbenzimidazoles

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Irradiations of 1-*o*-iodobenzoyl-2-methylbenzimidazole, 1-*o*-iodobenzoylbenzimidazole, and 1-*o*-iodobenzoyl-5,6-dimethylbenzimidazole in benzene gave compounds **1**, **2**, and **3**, respectively. The fragmentation patterns of these latter compounds upon electron impact are also reported with the aid of high resolution mass spectrometry.

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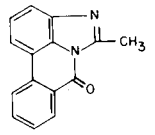
The photochemistry of iodoaromatic compounds and the free-radical nature of such processes were recognized early, but the synthetic utilities of these reactions were not fully demonstrated until recently (1). In connection with our studies (2) on the photochemistry of heterocyclic compounds, we have been interested in the intramolecular photocyclizations of iodohetero-aromatic compounds leading to new ring systems. Since similar work on iodobenzoylindoles has recently appeared in the literature (3), we report here the results obtained with benzimidazole derivatives.

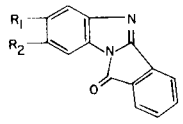
Irradiation of 1-*o*-iodobenzoyl-2-methylbenzimidazole in benzene yielded a product which was obtained as slightly pale yellowish crystals. The mass spectrum of this product gives a molecular ion peak at m/e 234, which corresponds to a cyclized structure. The nmr spectrum shows a singlet (3H) at δ 3.15 ppm due to the imidazole C-2 methyl group and a complex multiplet (7H) at δ 7.41-8.75 ppm characteristic of the aromatic protons. The uv spectrum [λ max (methanol): 214 infl, 226, 228, 248, 255, 275, 285, 325 infl. 340, and 355 nm (ε 16,455, 18,860, 18,101, 12,784, 12,784, 6,835, 8,227, 4,810, 6,329, and 5,569)] is somewhat similar to that of pyrrolo[3,2,1-*de*]phenanthridin-7-one (4). This compound was therefore assigned structure **1**.

Irradiation of 1-*o*-iodobenzoylbenzimidazole in benzene gave only a single product as yellow crystals. Its structure was determined on the basis of the following spectroscopic data. The molecular ion peak at m/e 220 in the mass spectrum corresponds to a cyclized structure. The uv spectrum shows [λ max (methanol): 212, 278 infl, 284 infl, 294, 334 infl, and 472 nm (ε 18,942, 5,800, 6,681, 6,975, 734 and 2,707)] (5), which is different from that of compound **1**. This indicated that a cyclization had occurred at C-2 but not at C-7, and thus structure **2** was assigned to this compound.

Photocycliztion of 1-*o*-iodobenzoyl-5,6-dimethylbenzimidazole under the same conditions as above also gave a single product as yellow crystals. The molecular ion peak at m/e 248 in the mass spectrum confirmed a cyclized structure. It shows the uv spectrum [λ max (methanol): 209, 285 infl, 294 infl, 305, 332 infl, and 472 nm (ε 18,362, 4,466, 4,962, 5,334, 2,853, and 3,722)] resembling closely that of compound **2**. Thus this compound was assigned structure **3**. It is interesting to note that in either of these cases no photo-Fries rearrangement product was formed, as had been observed in the photolysis of 1-*o*-benzoylindole.



1



2 , $R_1 = R_2 = H$

3 , $R_1 = R_2 = CH_3$

Since the mass spectra of compounds **1**, **2**, and **3** have not been reported thus far (6), we have studied them in some detail with the aid of high resolution mass spectrometry. Upon electron impact, **1**, **2**, and **3** all give very intense molecular ions (100) (7), but some characteristic differences are noted between the mass spectrum of **1** and those of **2** and **3** (see Schemes 1-4). The main fragmentation mode of **1** is the elimination of CO, ($\dot{H}$ + CO), (CO + CH_3CN), and ($\dot{H}$ + CO + CH_3CN) from the molecular ion to give the ions **a**, **b**, **c**, and **c** - H, respectively. These processes have been confirmed by observing metastable ion peaks. Expulsion of CH_3CN from the ion **a** would also lead to the ion **c**. The ion **b** would further lose a molecule of hydrogen to give the m/e 203 ion. Some ions (M + H at m/e 235 and **c** + H at m/e 166) also occur in protonated form. Elimination of HCN from the ions **c**, **c** - H, and **c** + H would then yield the ions at m/e 138, 137, and 139, respectively. The ion **c** + H would also lose CH≡CH to give the m/e 140 ion from which the m/e 113 ion would be formed by loss of HCN. Loss of (CO +  , (CO + ), and ($\dot{C}H_3$ + $\dot{N}$=C=O) from the molecular ion would lead to the ions at m/e 151, 152, and **d**, respectively. The ion **d** would further degrade to the ions at m/e 103 and 76.

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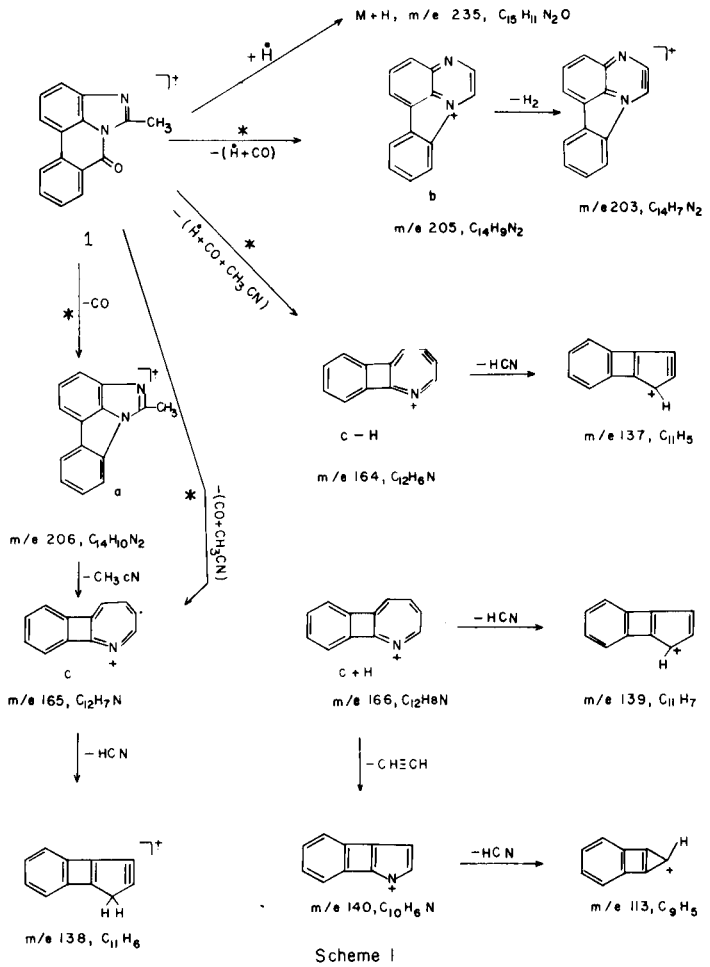
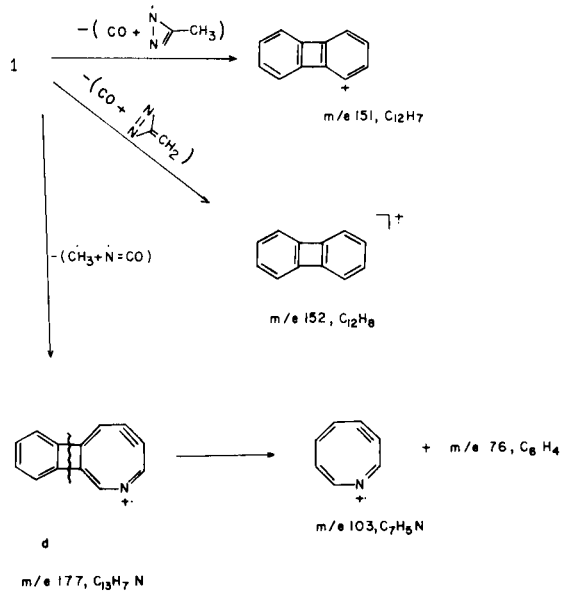
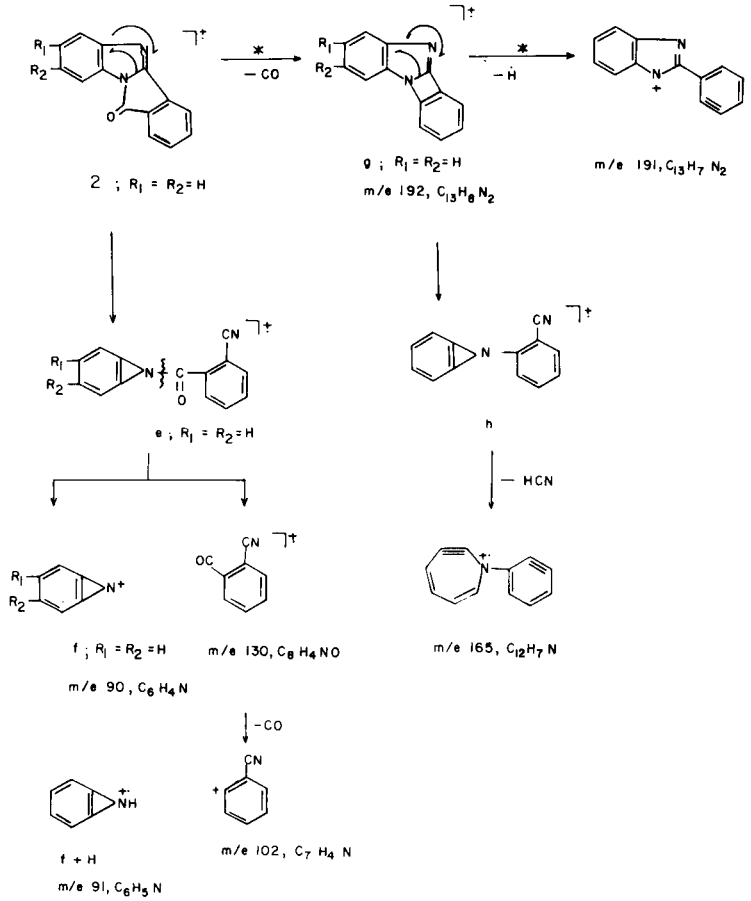


Scheme 1



Scheme 2

The fragmentation patterns of **2** and **3** upon electron impact show a significant similarity. One of the common features in fragmentation is the formation of the ion **f** (and **f** + H) and the ion at m/e 130 from the molecular ions. These ions may be formed *via* an intermediate **e**. The other common behavior is the loss of CO from the molecular ions to form the ion **g**. The ion **f** ($R_1 = R_2 = CH_3$) would further eject $\dot{H}$ successively to form the m/e 117 and 116 ions. The m/e 130 ion would lose CO to form the m/e 102 ion. The m/e 191 ion would be formed by loss of $\dot{H}$ from the ion **g** ($R_1 = R_2 = H$). Loss of HCN from the ion **g** to the m/e 165 ion may occur *via* an intermediate **h**. In the case of **3**, besides the fragmentations mentioned above, the molecular ion would expel either $\dot{C}H_3$ or $\dot{H}$ to form the m/e 233 ion or the ion **i**. The ion **i** would further lose $\dot{H}$, $\dot{C}H_3$, or $\dot{C}O$ to give the m/e 246, 232, or 219 ion. Loss of CO from the m/e 246 ion and that of $\dot{H}$ from the m/e 219 ion would yield the same m/e 218 ion which would subsequently eliminate HCN perhaps *via* an intermediate **j** to form the m/e 190 ion. The m/e 232 ion would also lose CO to give the m/e 204 ion.



Scheme 3

EXPERIMENTAL

Melting points were recorded on a Kofler hot-stage apparatus and are uncorrected. Nmr spectra were obtained on a Varian A-60 instrument and chemical shifts are reported in parts per million downfield from internal TMS (δ scale); abbreviations: s = singlet, d = doublet, and m = multiplet. Uv spectra were measured with a Hitachi S_{12}-B instrument and ir with a Perkin-Elmer 337 Infracord. Low resolution mass spectra and metastable ion peaks were measured with a Hitachi-Perkin Elmer RMU 6H spectrometer at 70 eV using a direct inlet system. High resolution mass spectra and the relative abundances of each ion were determined with a Varian MAT-711 mass spectrometer with a resolution of 10,000 at 70 eV.

2-Methylbenzimidazole, benzimidazole, and 5,6-dimethylbenzimidazole were purchased from Aldrich Chemical Company. All irradiations were carried out in a vessel into which a quartz immersion well containing a Pyrex filter sleeve and a Hanovia 450W medium pressure mercury lamp was fitted. The double-walled immersion well containing the light sources was cooled with water and the solution irradiated while nitrogen was bubbled through the solution before and during the irradiation. The formation of the product was monitored by thin layer chromatography (Merck Aluminum oxide 150 F254 or Kieselgel 60). For column chromatography, Merck Kieselgel 60 (35-70 mesh) was used. Microanalysis were carried out by A. Bernhardt Microanalytical Laboratory, 5521, Elbach über Engelskirchen, West Germany.

1-*o*-Iodobenzoyl-2-methylbenzimidazole.

A solution of *o*-iodobenzoyl chloride [from *o*-iodobenzoic acid (16 g.) and thionyl chloride (20 ml.)] in tetrahydrofuran (20 ml.) was added dropwise at room temperature during 1 hour to a vigorously stirred solution of 2-methylbenzimidazole (5 g.) and triethylamine (12.6 g.) in tetrahydrofuran (40 ml.). The mixture was stirred at room temperature for 1 hour and then filtered on silica gel. The filtrate was evaporated *in vacuo* and the crude product was chromatographed over silica gel. Elution with benzene yielded a product which after recrystallization from chloroform-ether showed m.p. 138-140° (yield, 4 g.); nmr (deuteriochloroform): 2.53 (3H, CH_3 at C-2) and 6.3-7.9 (8H, m, aromatic H); ir (potassium bromide): 1700 cm^{-1} (amide CO); uv (methanol): 208, 235, 265 inf. 269 infl, 274, and 280 nm (ε 18,467, 5,582, 1,810, 2,414, 3,258, and 3,771); ms: m/e 362 (M^+).

Anal. Calcd. for $C_{15}H_{11}IN_2O$: C, 49.74; H, 3.06; N, 7.74. Found: C, 49.56; H, 2.89; N, 7.54.

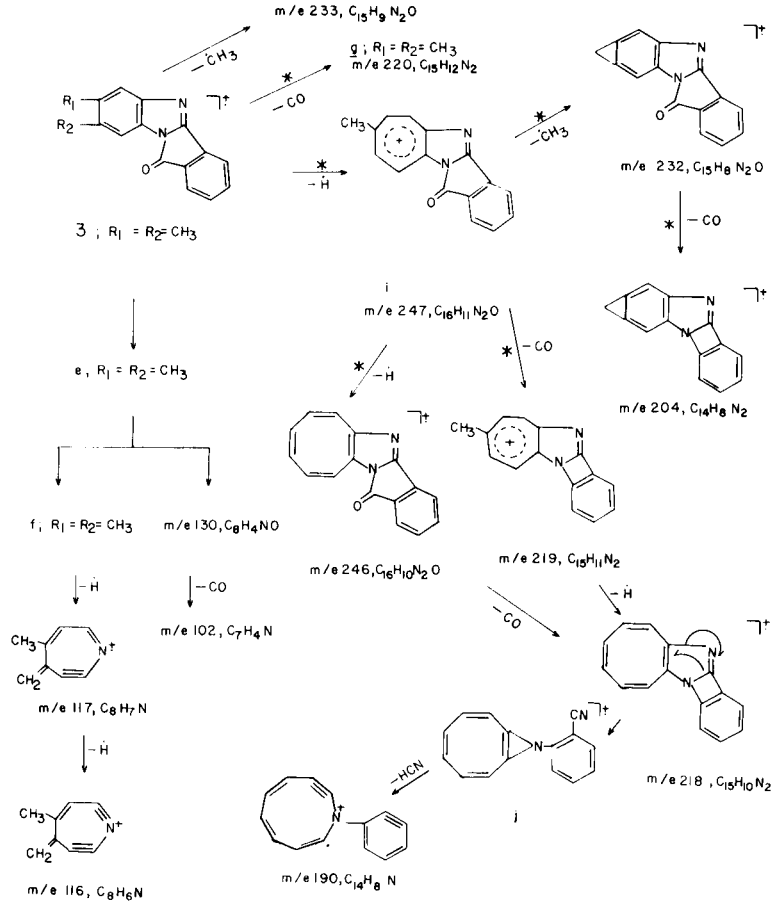
1-*o*-Iodobenzoyl benzimidazole.

The *N*-benzoylation was effected in the same manner as above. From benzimidazole (5 g.) the iodobenzoyl derivative (3 g.) was obtained, m.p. 121-124° (from chloroform-ether); nmr (deuteriochloroform): 7.0-8.3 (9H, m, aromatic and 2-H); ir (potassium bromide): 1700 cm^{-1} (amide CO); uv (methanol): 268, 236 infl, 266, 274, and 280 nm (ε 12,500, 5,122, 2,151, and 2,786); ms: m/e 348 (M^+).

Anal. Calcd. for $C_{14}H_9IN_2O$: C, 48.30; H, 2.61; N, 8.05. Found: C, 48.15; H, 2.44; N, 7.75.

1-*o*-Iodobenzoyl-5,6-dimethylbenzimidazole.

This compound was also prepared in the same manner as above. The iodobenzoyl derivative (4 g.) was obtained from 5,6-dimethylbenzimidazole (5 g.), m.p. 100-105° (from chloroform-ether); nmr (deuteriochloroform): 2.63 (6H, s, $2CH_3$ at C-5 and 6) and 6.4-7.9 (7H, m, aromatic and 2-H); ir (potassium bromide): 1700 cm^{-1} (amide CO); uv (methanol): 214, 235 infl, 274 infl, 278, 282, and 288 nm (ε 17,345, 7,399, 3,153, 4,730, 4,852, and 5,458); ms: m/e 376 (M^+).



Scheme 4

Anal. Calcd for $C_{16}H_{13}IN_2O$ C, 51.08; H, 3.48; N, 7.45. Found: C, 50.89; H, 3.26; N, 7.19.

Photolysis of 1-*o*-Iodobenzoyl-2-methylbenzimidazole.

The compound (1.06 g.) in benzene (100 ml.) was irradiated for 48 hours. The solution was washed with aqueous 5% aqueous sodium thiosulfate, dried over anhydrous magnesium sulfate, and evaporated *in vacuo*. The residue was crystallized from ether to give compound **1** (200 mg.) as pale yellowish crystals, m.p. 155-157°. Preparative layer chromatography over silica gel (Merck Kieselgel 60 F254, eluant benzene-ether, 1:1) yielded nearly colorless crystals, m.p. 159-163°; ir (potassium bromide): 1685 cm^{-1} (amide CO); ms: m/e (relative intensity): 235 (16), 234 (100), 220 (1), 206 (2), 205 (9), 203 (2), 179 (2), 177 (1), 167 (1), 166 (7), 165 (7), 164 (10), 152 (1), 151 (2), 140 (2), 139 (6), 138 (4), 137 (2), 113 (1), 103 (8), 83 (1), 76 (1), and 63 (2).

Anal. Calcd. for $C_{15}H_{10}N_2O$: C, 76.91; H, 4.30; N, 11.96. Found: C, 76.65; H, 4.15; N, 11.67.

Photolysis of 1-*o*-Iodobenzoylbenzimidazole.

The compound (1.00 g.) in benzene (100 ml.) was irradiated for 48 hours. The solution was washed with 5% aqueous sodium thiosulfate, dried over anhydrous magnesium sulfate, and evaporated *in vacuo*. The crude product was chromatographed over Merck standardized alumina, activity II-III. Elution with hexane-benzene (1:1) yielded compound **2** (200 mg.) as yellow crystals, m.p. 225-227° (from ether); ms: m/e (relative intensity) 222 (1), 220 (100), 192 (9), 191 (7), 165 (5), 164 (6), 138 (3), 130 (1), 102 (6), 91 (1), 90 (2), 88 (7), 76 (2), 75 (3), 64 (1), 63 (3), 62 (2), 51 (3), and 50 (1).

Anal. Calcd. for $C_{14}H_8N_2O$: C, 76.36; H, 3.66; N, 12.72. Found: C, 76.21; H, 3.46; N, 12.38.

Photolysis of 1-*o*-Iodobenzoyl-5,6-dimethylbenzimidazole.

The compound (1.05 g.) in benzene (100 ml.) was irradiated for 48 hours. The solution was discolored with sodium thiosulfate as above and then evaporated *in vacuo*. The residue was crystallized from chloroform-ether to give compound **3** (200 mg.) as yellow crystals, m.p. 230-237°. Preparative layer chromatography over silica gel (Merck Kieselgel 60 F254, eluant benzene-chloroform, 1:1) yielded the pure compound, m.p. 237-240° (from ether); ir (potassium bromide): 1750 cm^{-1} (amide CO); ms: m/e (relative intensity) 250 (2), 248 (100), 247 (36), 246 (2), 233 (36), 220 (3), 220 (1), 219 (2), 218 (3), 217 (1), 205 (3), 204 (1), 203 (1), 192 (2), 190 (1), 177 (1), 151 (1), 130 (2), 129 (1), 117 (1), 116 (2), 110 (4), 103 (1), 102 (4), 91 (3), 89 (4), 83 (2), 77 (3), 76 (1), 75 (1), 65 (4), 63 (1), and 51 (2).

Anal. Calcd. for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28. Found: C, 77.21; H, 4.69; N, 11.01.

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REFERENCES AND NOTES

(1) R. K. Sharma and N. Kharash, *Angew. Chem., Int. Ed. Engl.*, 7, 36 (1968) and references cited therein.

(2) T. Nakano, C. Rivas, C. Pérez and K. Tori, *J. Chem. Soc., Perkin*

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(3) W. Carruthers and N. Evans, *J. Chem. Soc., Perkin Trans. I*, 1523 (1974).

(4) See reference 3. The outstanding feature of the uv spectra of five-membered heterocycles fused to benzene rings is their general resemblance to the spectra of the corresponding fused-ring hydrocarbons with the same number and disposition of rings, all six-membered and aromatic. Comparison of the heterocyclic compounds must be made with the corresponding system in which all rings are aromatic, the heteroatom being equivalent to a $-CH=CH-$ ring (see H. H. Jaffé and M. Orchin, "Theory and Application of Ultraviolet Spectroscopy", John Wiley and Sons, Inc., New York, N. Y., 1964, p. 353.

(5) Note that this uv spectrum is very similar to that of compound **3**. The carbonyl absorption of compound **2** in the ir spectrum (potassium bromide): appears as two separated bands at 1762 and 1742 cm^{-1}. Although Carruthers, *et al.* (3), did not report the ir spectrum of isoindolo[2,1-*a*]indol-6-one from the photolysis of 1-*o*-iodobenzoylindole, we confirmed that it does also exhibit two bands at 1765 and 1740 cm^{-1} in the carbonyl region.

(6) For the mass spectra of heterocyclic compounds, see Q. N. Porter and J. Baldas, "Mass Spectrometry of Heterocyclic Compounds," Wiley-Interscience, John Wiley and Sons, Inc., New York, N. Y., 1971.

(7) The relative intensities of the ions are indicated as a percentage of the base peak. Those ions which are given the molecular compositions have had them determined by exact mass measurements and the presence of a metastable ion for a particular process is depicted by an asterisk. Only relevant ions greater than 1% are formulated in Schemes 1-4.