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Unusual Photorearrangement of 1,7-Disubstituted 7-Azabenzonorbornadiene*

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Abstract—1-(11-Benzoyl-11-azatricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6,9-tetraen-1-yl)ethanone was synthesized by cycloaddition of 2-acetyl-*N*-benzoylpyrrole to benzyne. Direct photolysis of 1-(11-benzoyl-11-azatricyclo-[6.2.1.$0^{2,7}$]undeca-2,4,6,9-tetraen-1-yl)ethanone in benzene gave *N*-(4-acetylnaphthalen-1-yl)benzamide. The formation of this product is discussed in terms of radical-stabilizing and destabilizing effect of electron-withdrawing group in the formation of cyclopropane ring.

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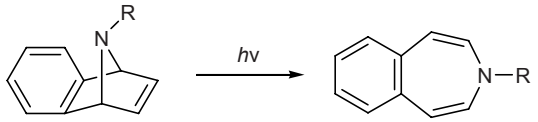
Fusion of benzene ring to cyclic hydrocarbons was widely reported in the literature [1–3]. The most general method for the preparation of such compounds involves cycloaddition of benzyne to appropriate conjugated dienes [4]. Benzyne is known to readily react with pyrrole derivatives to form 1,4-epimino-1,4-dihydronaphthalene (**I**, 7-azabenzonorbornadiene) [5, 6]. 1,4-Epimino-1,4-dihydronaphthalene (**I**) attracts much interest from the synthetic viewpoint due to its ability to be readily converted into other types of compounds. For example, Wolthuis et al. [6] studied reactions of 1,4-epimino-1,4-dihydronaphthalene with HCl in MeOH and showed formation of different naphthalene derivatives. It is also known that direct photolysis of 1,4-epimino-1,4-dihydronaphthalenes **I** produces 3-benzoazepines **II** [7–9] (Scheme 1). Benzoazepines and related compounds were found to exhibit important pharmacological properties [10].

Scheme 1.

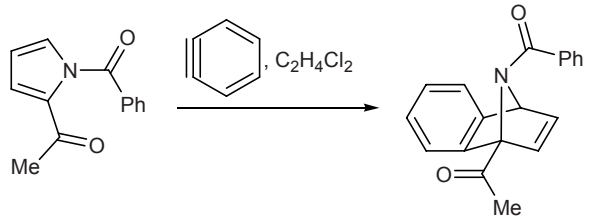


I **II**

Swenton et al. [9] reported the details of direct and photosensitized rearrangements of 7-azabenzonorbornadiene derivatives and proposed a mechanism for the formation of benzofulvene derivatives via sensitized irradiation of 7-azabenzonorbornadienes. Motyka [11] described the conversion of 1,4-epimino-1,4-dihydronaphthalene having electron-donating substituents on the nitrogen atom into indole derivatives by direct photolysis. The configuration of the nitrogen atom in 7-azabenzonorbornadiene derivatives can be determined by spectral methods [12, 13]. We previously studied photochemistry of bicyclic systems having heteroatoms and revealed very surprising results [14, 15]; it seemed interesting to examine photochemistry of aza bicyclic compounds bearing electron-withdrawing substituents.

In the present article we report on the photolysis of 7-azabenzonorbornadiene containing two electron-withdrawing groups, one on the nitrogen atom, and the other on the bridgehead carbon atom (C^1). The substrate structure differed from those reported in [7–9]. Our synthetic strategy was based on the Diels–Alder reaction of benzyne with 2-acetyl-*N*-benzoylpyrrole

Scheme 2.

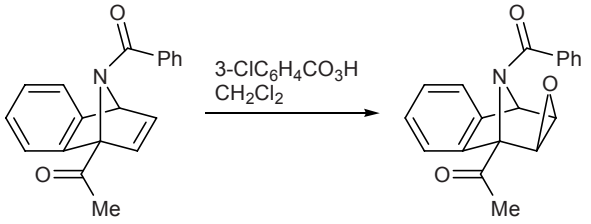


III **IV**

* The text was submitted by the authors in English.

(**III**) which was prepared according to the procedure reported previously for analogous compounds [16]. New 1,4-epiminonaphthalene derivative (**IV**) was thus obtained in 53% yield. Its NMR data indicated that it exists as a single isomer (Scheme 2). The configuration of **IV** was determined by further chemical reactions and X-ray analysis of epoxide **V**. The latter was synthesized by oxidation of 1-acetyl-*N*-benzoyl-1,4-epiminonaphthalene (**IV**) with *m*-chloroperoxybenzoic acid in methylene chloride; according to the X-ray diffraction data, compound **V** has *exo* orientation of the epoxy group [17] (Scheme 3).

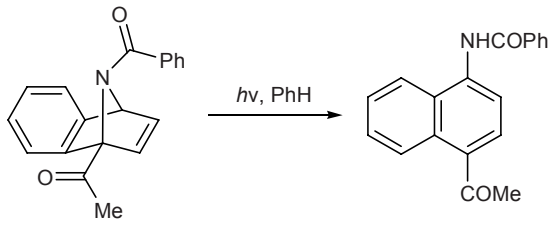
Scheme 3.



IV **V**

A solution of 1,4-epimino-1,4-dihydronaphthalene **IV** (0.5 g, 1.73 mmol) in benzene (100 ml) was irradiated under nitrogen for 30 h in a quartz tube using a mercury lamp (λ 240 nm). By thin-layer chromatography we isolated *N*-(4-acetylnaphthalen-1-yl)benzamide (**VI**) in 30% yield (0.15 g, 0.52 mmol), as well as 55% of unreacted starting compound (Scheme 4). The structure of **VI** was determined on the basis of the ^{1}H and ^{13}C NMR spectra. In the ^{1}H NMR spectrum of **VI**, methyl protons in the acetyl group resonated at δ 2.69 ppm, and aromatic proton signals appeared in the region δ 7.27–8.87 ppm. Double resonance experiments and ^{13}C NMR spectrum were also fully consistent with the assumed structure.

Scheme 4.



IV **VI**

1,4-Epimino-1,4-dihydronaphthalenes bearing electron-withdrawing substituents on the nitrogen atom were reported to undergo isomerization to benzoazepines upon direct irradiation. Expecting the formation of 3-benzoazepine **VIII**, direct photolysis of 1,4-epimino-1,4-dihydronaphthalene **IV** was performed at λ 254 nm. Repeated experiments surprisingly showed the formation of benzamide derivative **VI**. The product differed from those obtained by Prinzbach [8] and Swenton [9]. This can be attributed to the effect of electron-withdrawing acetyl group at the bridgehead carbon atom (C^1). In keeping with published data, electron-withdrawing groups destabilize formation of cyclopropane ring [18]. As shown in Scheme 5, the transformation of **IV** through di-π-methane rearrangement or intramolecular [2+2] cycloaddition would give product **VII**. Because of destabilizing effect of the acetyl group, cyclopropane ring is not formed, and the reaction does not follow path *b*. Instead, diradical **A** undergoes rearrangement into more stable diradical **B**. The subsequent hydrogen transfer to the nitrogen atom from the adjacent carbon atom leads to product **VI** through intermediate **C** (Scheme 5, path *a*).

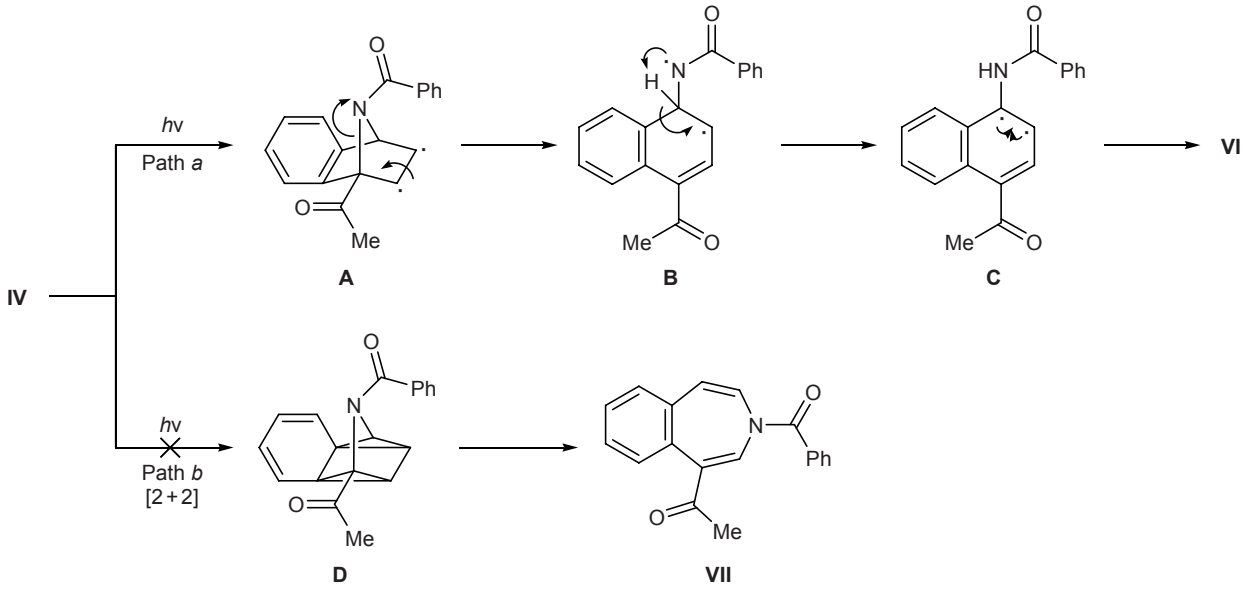
Thus we have demonstrated unusual rearrangement of 1,4-epimino-1,4-dihydronaphthalene **IV** to *N*-(4-acetylnaphthalen-1-yl)benzamide (**VI**) under conditions of direct photolysis. Benzamide derivatives exhibit various kinds of biological activity such as antihelminthic, antihistaminic, antifungal, and antibacterial properties [19]. We presume that this unexpected rearrangement takes place because of electron-withdrawing nature of the carbonyl group at the bridgehead position, which destabilizes cyclopropane ring. Our results showed that benzamide derivatives can be synthesized via photochemical transformations which tolerate several functional groups.

EXPERIMENTAL

The melting points were determined on a Thomas Hoover capillary melting apparatus. The IR spectra were measured in KBr or from neat liquids on a Mattson 1000 FT-IR spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian spectrometer at 200 and 50 MHz, respectively. The mass spectra were obtained on a VG Zabspec GC–MS instrument. Column chromatography was performed on silica gel 60 (70–230 mesh ATSM). Silica gel 60 F_{254} on 0.2-mm analytical aluminum plates (Merck) was used for thin-layer chromatography.

1-(1-Benzoylpyrrol-2-yl)ethanone (III) [16]**.** A mixture of 1.74 g (22 mmol) of acetyl chloride and 2.1 g (22 mmol) of anhydrous aluminum chloride in 70 ml of 1,2-dichloroethane was stirred for 15 min at 30°C, a solution of 3.44 g (22 mmol) of 1-benzoyl-

Scheme 5.



pyrrole in 10 ml of dichloroethane was added, and the mixture was stirred for 5 h at 30°C. The mixture was cooled to 0°C, quenched with cold water, and extracted with methylene chloride. The organic layer was separated, washed with water (2×100 ml), and dried over Na_2SO_4. The solvent was removed, and the residue was purified by chromatography on silica gel using hexane–ethyl acetate (9:1) as eluent. The product was additionally recrystallized from diethyl ether–hexane. Yield 3.10 g (70%), colorless crystals, mp 65–66°C. IR spectrum (KBr), ν, cm^{-1}: 3113, 3080, 2936, 2953, 2876, 1727, 1676, 1600, 1548, 1446, 1421, 1344, 1319, 1268, 1217, 1191, 1089, 1038, 936. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 7.86 d.d (1H, 5-H, J = 2.0, 1.6 Hz), 7.77–7.60 m (5H, Ph), 7.27 d.d (1H, 3-H, J = 3.4, 1.6 Hz), 7.27 d.d (1H, 4-H, J = 3.4, 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 189.03, 171.31, 135.68 (2C), 135.56, 131.61, 130.81, 130.59, 123.03, 112.59, 28.34.

1-(11-Benzoyl-11-azatricyclo[6.2.1.0^{2,7}]undeca-2,4,6,9-tetraen-1-yl)ethanone (IV) was prepared by reaction of benzyne [20] with pyrrole **III**. 2-Carboxybenzenediazonium hydrochloride, 2.60 g (17 mmol), and 2-methyloxirane, 1.7 g (40 mmol), were added under stirring to a solution of 3.10 g (15.00 mmol) of compound **III** in 70 ml of dichloroethane. The mixture was heated for 3.5 h under reflux, cooled to room temperature, and evaporated. The residue was treated with 100 ml of diethyl ether, and the extract was washed with 10% aqueous $NaHCO_3$ (2×100 ml) and water (100 ml) and dried over Na_2SO_4. After removal of the solvent, the residue was subjected to chromatography on silica gel using hexane–ethyl acetate (9:1) as eluent. The product was additionally recrystallized from diethyl ether–hexane. Yield 2.30 g (53%), colorless crystals, mp 135–136°C. IR spectrum (KBr), ν, cm^{-1}: 3438, 3310, 3106, 3080, 3029, 2927, 1727, 1676, 1600, 1472, 1370, 1344, 1268, 1242, 1140, 1114, 1063, 961. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 7.66–7.26 m (8H, H_{arom}), 7.09–7.04 quasi d.d (2H, 10-H, H_{arom}, J = 5.5, 1.2 Hz), 6.25 d.d (1H, 9-H, J = 5.5, 2.2 Hz), 5.66 d (1H, 8-H, J = 2.2 Hz), 2.41 s (3H, CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 201.32, 172.76, 148.04, 147.17, 144.58, 142.22, 133.67, 132.28, 128.93, 128.72, 126.00, 125.97, 121.07, 120.82, 82.91 (C^1), 70.65 (C^8), 29.99. High-resolution mass spectrum: m/z 289.1111 $[M]^+$. Calculated: M 289.1102.

Epoxidation of 1-(11-benzoyl-11-azatricyclo-[6.2.1.0^{2,7}]undeca-2,4,6,9-tetraen-1-yl)ethanone (IV) [17]**.** A solution of 0.5 g (1.74 mmol) of compound **IV** and 0.36 g (2.09 mmol) of *m*-chloroperoxybenzoic acid in 30 ml of methylene chloride was stirred for 20 h at room temperature in the presence of 1 g of solid $NaHCO_3$. The mixture was then filtered and washed with 10% aqueous $NaHCO_3$ (2×20 ml). The organic layer was dried over sodium sulfate and evaporated under reduced pressure, and the residue was recrystallized from methylene chloride–hexane to obtain 0.48 g (78%) of 1-(11-benzoyl-9,10-epoxy-11-azatricyclo[6.2.1.0^{2,7}]undeca-2,4,6-trien-1-yl)ethanone (**V**) as colorless crystals with mp 208–209°C. IR spectrum (KBr), ν, cm^{-1}: 3027, 2931, 2858, 1708, 1631, 1581, 1457, 1427, 1373, 1276, 1130, 1064, 1025, 944, 887, 848, 755,698. ^1H NMR spectrum ($CDCl_3$), δ,

ppm: 7.68–7.12 m (9H, H_{arom}), 5.09 s (1H, 8-H), 3.97 d and 3.39 d (1H each, 9-H, 10-H, J = 3.5 Hz), 2.42 s (3H, CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 201.20, 175.78, 145.79, 145.33, 136.07, 132.97, 130.47, 130.16, 129.64, 129.57, 123.49, 123.02, 82.11 (C^1), 67.91 (C^8), 58.54, 54.52, 29.77.

***N*-(4-Acetylnaphthalen-1-yl)benzamide (VI).** A solution of 0.50 g (1.73 mmol) of compound **IV** in 100 ml of benzene was placed into a quartz tube, flushed with nitrogen under stirring with a magnetic stirrer, and irradiated at λ 254 nm for 30 h. The solvent was removed under reduced pressure, and the residue was purified by thin-layer chromatography on silica gel using hexane–ethyl acetate (4:1) as eluent. The product was recrystallized from methylene chloride–hexane. Yield 0.15 g (30%), yellow crystals, mp 156–158°C. IR spectrum (KBr), ν, cm^{-1}: 3285, 3080, 3004, 2927, 2851, 1702, 1651, 1600, 1523, 1497, 1446, 1370, 1293, 1242, 1191, 1114, 1012, 910. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 8.87 br.d (1H, 5-H, J = 8.1 Hz), 8.61 br.s (1H, NH), 8.10 (1H, 3-H) and 7.85 (1H, 2-H) (*AB* system, J = 8.1 Hz), 7.97 d (2H, *o*-H, J = 7.4 Hz), 7.84 d (1H, 8-H, J = 8.6 Hz), 7.58-7.27 m (5H, 6-H, 7-H, *m*-H, *p*-H), 2.69 s (3H, CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 201.77, 167.39, 138.56, 136.67, 133.99, 133.77, 133.26, 131.55, 130.78, 129.82, 129.4, 129.28, 128.49, 121.93, 119.72, 31.52. High-resolution mass spectrum: m/z 289.1098 $[M]^+$. Calculated: M 289.1102.

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