A novel photocycloaddition of substituted pyridines with benzofuran†

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Irradiation of a benzene solution containing 3-cyano-2-methoxypyridine (0.02 M) and benzofuran (0.5 M) resulted in the formation of stereo-isomeric 1:1 adducts, *endo* and *exo*-7-cyano-2-methoxy-4-methyl-9-oxa-3-aza-10,11-benzotricyclo[6.3.0.0^{4,7}]undeca-2,5-diene, accompanied by 5-cyano-2-methoxypyridine and a pyridine dimer; the structures of the adducts were established by X-ray structural analyses.

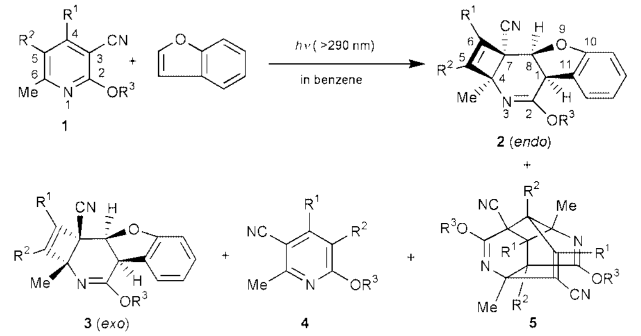
The photochemistry of heteroaromatics is an underdeveloped area compared with the carbon aromatics, such as benzene, naphthalene and anthracene derivatives, the photochemical behavior of which has been extensively studied from both mechanistic and synthetic perspectives.[1–7] In particular, the ring expansion or transformation of a pyridine ring with photochemical 4 + 4 or 2 + 2 cycloaddition is quite difficult.[8] We are interested in investigating the photochemical aspects of heteroaromatics and their utilization for the synthesis of new heterocycles. Recently, we reported that 2-alkoxy-3-cyanopyridines show comparatively high photochemical reactivity for promoting a variety of photochemical reactions, such as dimerization and 4 + 4 cycloaddition with furan.[9–11] The high reactivity of these pyridines compared with a simple pyridine is dependent on the polarization within the pyridine ring from the conjugate relationship of the cyano and alkoxy groups. We have identified a new photochemical 2 + 2 cycloaddition reaction between two heteroaromatics, pyridine and benzofuran.

When a benzene solution of 3-cyano-2-methoxy-6-methylpyridine **1a** (0.02 M) containing 0.05 M of benzofuran was irradiated with Pyrex filtered light, two types of 1 : 1 adducts of **1a** and benzofuran (**2a**, 32%; **3a**, 25%) were obtained, accompanied by **4a** and the pyridine dimer **5a**, in 7 and 33% yields, respectively, at 59% conversion (Table 1). The structures of the adducts, **2a** and **3a**, were determined on the basis of elemental analyses and the spectral data. Finally, the stereoisomeric structures were established by X-ray structural analyses (Fig. 1 and 2).‡ In the cases of the transpositional isomer **4a** and the dimer **5a**, we have already reported their formation by the direct irradiation of **1a**.[9] Irradiation of **1b** and **1c** also gave two stereoisomeric adducts as shown in Table 1, their structures were determined by comparison of the spectral data of **2a** and **3a**.

Usually, an electronically excited pyridine is not observed to undergo any radiative relaxation; however, this pyridine **1** shows strong emission of fluorescence at 310 nm. The emissive singlet excited state of pyridine reacts with the ground state of benzofuran, because the addition reaction was not quenched by triplet quenchers, such as 2,5-dimethylhexa-2,4-diene, penta-1,3-diene or stilbene, and also the sensitization by benzophenone or xanthone was quite inefficient. The formation of the adducts **2** and **3** is explainable in terms of the 2 + 2 cycloaddition taking place at the C-2 and C-3 positions of the singlet excited state of the pyridine ring with the C-3 and C-2 positions of benzofuran leading to **6** (Scheme 1). A subsequent ring-opening reaction gives cyclooctatriene **7**, which is followed by electrocyclization to the tricyclic adducts **2** and **3**.

The mechanism is also supported by Frontier-MO calculations using the PM3 Hamiltonian.[12] The orbital energies and coefficients of the singlet excited state for **1a** (HSOMO and LSOMO) and those of the ground state of benzofuran (LUMO and HOMO) were obtained (Fig 3). The energy gap (ΔE) between the LSOMO and HOMO is smaller than that between the HSOMO and LUMO, and this frontier orbital interaction is most important in this photocycloaddition. The coefficients at

Table 1 Photoreaction of the pyridine–benzofuran system



Pyridine	R¹	R²	R³	conv.(%)	Yield (%)[a] 2	3	4	5
1a	H	H	Me	59	32	25	7	33
1b	H	H	Et	64	34	27	3	34
1c	Me	H	Me	46	31	11	56	0

[a] Isolated yield. A benzene solution 0.02 M in pyridine **1** and 0.05 M in benzofuran was irradiated with a high-pressure mercury lamp.

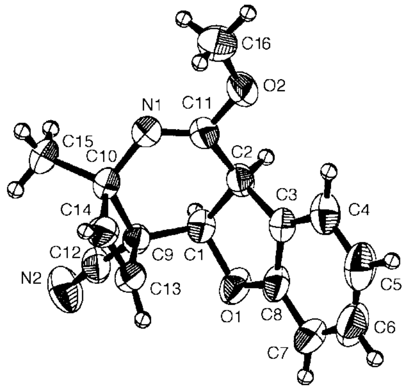


Fig. 1 ORTEP drawing of pyridine–benzofuran adduct **2a**. Selected bond lengths (Å) and angles (°); N(1)–C(10) 1.442(6), C(1)–C(9) 1.663(7), C(9)–C(10) 1.698(7), C(9)–C(13) 1.618(7), C(10)–C(14) 1.617(7), C(13)–C(14) 1.322(7), C(10)–C(9)–C(13) 84.3(4), C(9)–C(10)–C(14) 85.1(4), C(9)–C(13)–C(14) 95.6(4), C(10)–C(14)–C(13) 94.8(4), O(1)–C(1)–C(9)–C(13) 47.1(6), N(1)–C(10)–C(9)–C(13) 107.6(6), N(1)–C(10)–C(14)–C(13) −115.0(6), C(1)–C(9)–C(10)–C(14) 124.1(5), C(1)–C(9)–C(13)–C(14) 120.1(5), C(2)–C(1)–C(9)–C(13) −70.3(6).

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† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b0/b002396p/

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the 3-position in the LSOMO of the singlet excited state of the pyridine ring and those at the 2-position of the HOMO in the ground state of furan are larger than those at any other positions. It is concluded that the initial bond formation occurs between the C2–C3 positions of pyridine and the C3–C2 positions of benzofuran, leading to **6**.

Gilbert and Heath reported the photochemical addition of 2-cyanoanisole to vinyl ether leading to a 2 + 2 adduct, and subsequently followed by ring-opening to a cylcooctatriene.[13]

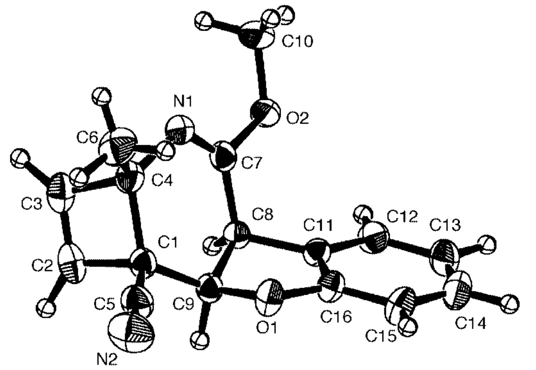
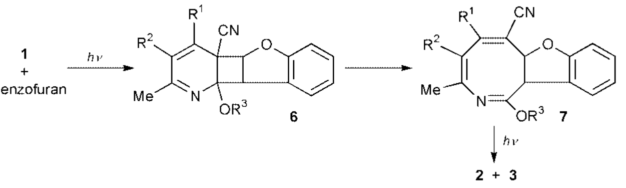


Fig. 2 ORTEP drawing of pyridine–benzofuran adduct **3a**. Selected bond lengths (Å) and angles (°); O(1)–C(9) 1.459(4), N(1)–C(4) 1.453(4), C(1)–C(2) 1.526(4), C(1)–C(4) 1.610(4), 1.521(4), C(2)–C(3) 1.317(6), C(3)–C(4) 1.526(4), C(2)–C(1)–C(4) 84.4(2), C(1)–C(2)–C(3) 95.6(3), C(2)–C(3)–C(4) 95.4(3), C(1)–C(4)–C(3) 84.6(2), O(1)–C(9)–C(1)–C(2) 170.3(3), O(1)–C(9)–C(1)–C(4) 93.0(3), O(1)–C(9)–C(1)–C(6) −40.4(3), N(1)–C(4)–C(1)–C(2) −111.6(3), N(1)–C(4)–C(1)–C(5) 136.2(3), N(1)–C(4)–C(3)–C(2) 117.1(3), C(1)–C(4)–C(3)–C(2) −0.3(3), C(2)–C(1)–C(4)–C(3) 0.2(2), C(3)–C(2)–C(1)–C(4) −0.3(3).



Scheme 1

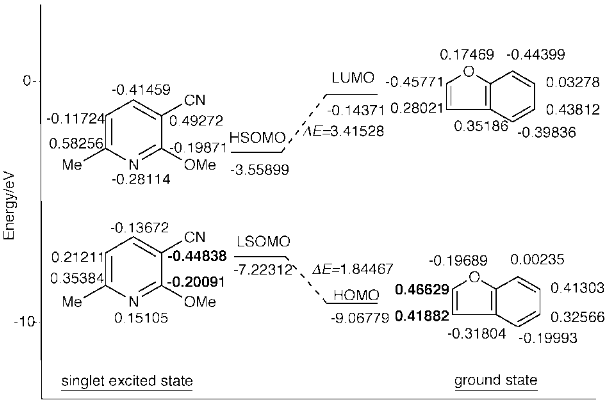


Fig. 3 Estimated energies and coefficients of 3-cyano-2-methoxy-6-methylpyridine **1a** and benzofuran obtained from the PM3 Hamiltonian contained within the MOPAC program.

The cyclooctatriene cyclizes to a secondary photoproduct, a bicyclo[4.2.0]octa-2,7-diene structure, upon irradiation. The reversibility of the photochemical reaction and the thermal conversion between the cyclooctatriene and the bicyclo[4.2.0]octa-2,7-diene were confirmed. In our present reaction, the thermal and photochemical reactions of **2** and **3** were carried out to obtain further supporting information on the reaction. However, the pyrolysis and the photolysis at 254 nm of the photoadducts gave polymerized materials, furthermore, when the addition reaction was followed by ^{1}H NMR spectroscopy, primary cyclobutane **6** or cyclooctatriene **7** could not be detected on irradiation in an NMR tube. The high reactivity of **6** may be due to steric crowding or the bond-weakening character of the cyano and methoxy groups facilitates the ring opening to the cyclooctatriene, subsequently leading to **7**.[14]

In conclusion, we have detailed the first example of a photochemical reaction between two heteroaromatic compounds, a pyridine and benzofuran system, leading to 1:1 cycloadducts. Attempts at photoaddition with benzothiophene, indole or *N*-methylindole instead of benzofuran proved unsuccessful. We are continuing to explore the details and the scope of the photochemical reactions of heteroaromatics.

Notes and references

‡ *Crystal data*: for **2a**; colorless prismatic crystal, $C_{16}H_{14}N_2O_2$, orthorhombic space group $Fdd2$, a = 17.024(6), b = 29.192(7), c = 11.183(4) Å, V = 5557(3) Å^3, Z = 16, D_c = 1.273 g cm^{-3}, μ(Cu-Kα) = 6.93 cm^{-1}. The structure was solved by the direct method and refined by full-matrix least squares, where the final R and R_w were 0.057 and 0.065 for 1410 reflections.

For **3a**; colorless prismatic crystal, $C_{16}H_{14}N_2O_2$, triclinic space group $P\bar{1}$, a = 9.903(2), b = 10.132(2), c = 7.430(1) Å, α = 91.75(1), β = 105.73(2), γ = 108.74(1)°, V = 673.8(2) Å^3, Z = 2, D_c = 1.312 g cm^{-3}, μ(Cu-Kα) = 7.14 cm^{-1}. The structure was solved by the direct method and refined by full-matrix least squares, where the final R and R_w were 0.055 and 0.066 for 2777 reflections.

CCDC 182/1655. See http://www.rsc.org/suppdata/cc/b0/b002396p/ for crystallographic files in .cif format.

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