Photochemistry of heteroaromatics–a novel photocycloaddition of 2-alkoxy-3-cyanopyridines with methacrylonitrile

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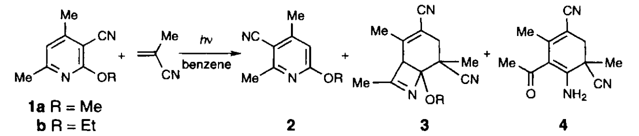
The photochemical cycloaddition of 2-alkoxy-3-cyano-4,6-dimethylpyridine with methacrylonitrile gives a bicyclic azetine, 6-alkoxy-3,5-dicyano-2,5,8-trimethyl-7-azabicyclo[4.2.0]octa-2,7-diene (45–55% yield) and 3-acetyl-4-amino-1,5-dicyano-2,5-dimethylcyclohexa-1,3-diene (15–17% yield).

The photochemical cycloaddition of aromatic compounds has received much attention from both mechanistic and synthetic perspectives.[1,2] In particular, the photochemical [2 + 2] and [3 + 2] addition of benzene and its derivatives to various kinds of alkenes has been investigated extensively.[3,4] Relatively little is known about the photochemical reaction of heteroaromatics in the presence of alkenes.[5,6] Here we report that the photolysis of 2-alkoxy-3-cyano-4,6-dimethylpyridine in the presence of methacrylonitrile promotes [2 + 2] cycloaddition from the singlet excited state.

We previously reported that the photolysis of a benzene solution containing 3-cyano-2-methoxy-4,6-dimethylpyridine **1a** resulted in a 92% yield of the transpositional isomer **2a** (Table 1, entry 1).[7,8] However, irradiation in the presence of alkenes resulted in considerably different photochemical behaviour. When an argon-purged benzene solution of **1a** and methacrylonitrile (1.0 mol dm^{-3}) in a Pyrex vessel was irradiated using a high pressure mercury lamp and the photolysate was subjected to chromatography in silica gel, a bicyclic azetine, 3,5-dicyano-6-methoxy-2,5,8-trimethyl-7-azabicyclo[4.2.0]octa-2,7-diene **3a** (45% yield) and 3-acetyl-4-amino-1,5-dicyano-2,5-dimethylcyclohexa-1,3-diene **4a** (17% yield) were obtained and the yield of **2a** decreased (Table 1, entry 2).

The chemical structure of **3a** was determined by spectroscopy. The mass spectrum (FAB) showed a molecular ion peak at 230 (MH$^+$ calculated for $C_{13}H_{16}N_3O$), indicating that **3a** is a 1 : 1 adduct of **1a** with methacrylonitrile. The ^{1}H NMR displayed methylene protons at δ 2.22 and 2.64 (ABq, *J* 15.8 Hz, 2 H, 4-CH$_2$) and a methine proton at δ 3.88 (s, 1 H, 1-CH) in addition to four singlet peaks derived from methyl protons at δ 1.57 (s, 3 H, 5-Me), 2.10 (s, 3 H, 8-Me), 2.19 (s, 3 H, 2-Me) and 3.43 (s, 3 H, OMe). The ^{13}C NMR exhibited sp^2 carbon peaks at δ 188.0 (s, 8-C=N), 149.0 (s, 2-C) and 106.9 (s, 3-C) in addition to the peaks derived from methylene carbon at δ 35.2 (4-C), the methine group at δ 53.7 (d, 1-C), and singlet peaks at δ 120.5 (s, 3-CN), 116.9 (s, 5-CN), 91.9 (s, 6-C) and 39.7 (s, 5-C).

Table 1 Photolysis of 2-alkoxy-3-cyano-4,6-dimethylpyridine **1** in the presence of methacrylonitrile



Entry	Pyridine **1**[a]	Conc. of Alkene	Conv. (%)[b]	Yield (%)[c]		
				2	**3**	**4**
1	**a**	0	54	92	—	—
2	**a**	1.0	72	8	45	17
3	**b**	0	58	90	—	—
4	**b**	1.0	80	6	55	15

[a] Concentration of pyridines was 0.02 mol dm^{-3}. [b] All samples were irradiated using a 1 kW high-pressure mercury lamp in an argon atmosphere through a Pyrex filter for 1.5 h. [c] Yields were determined based on consumed pyridines **1**.

The structure of cyclohexadiene derivative **4a** was unequivocally established by X-ray crystallography (Fig. 1).† In

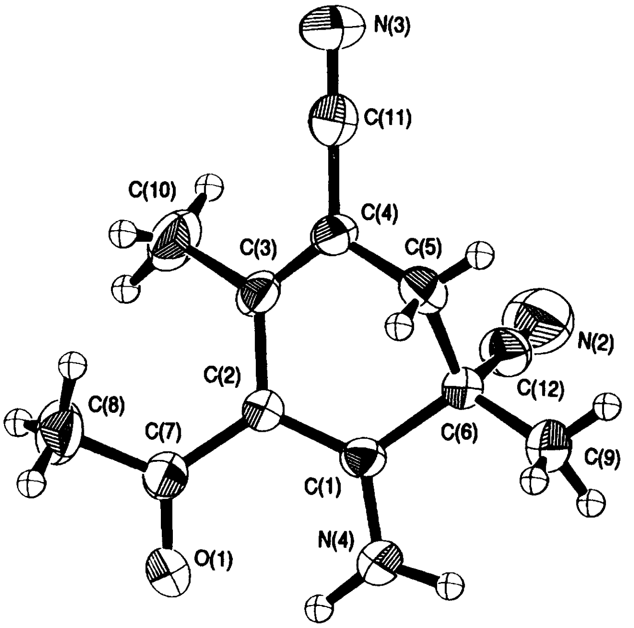


Fig. 1 ORTEP drawing of **4a**. Selected bond lengths (Å) and angles (°); O(1)–C(7) 1.237 (7), N(2)–C(12) 1.120(8), N(3)–C(11) 1.148(9), N(4)–C(1) 1.334(8), C(1)–C(2) 1.386(8), C(1)–C(6) 1.537(8), C(2)–C(3) 1.463(9), C(2)–C(7) 1.457(8), C(3)–C(4) 1.337(9), C(3)–C(10) 1.52(1), C(4)–C(5) 1.490(9), C(4)–C(11) 1.431(9), C(5)–C(6) 1.537(9), C(6)–C(9) 1.503(9), C(6)–C(12) 1.461(9), C(7)–C(8) 1.499(10); N(4)–C(1)–C(2) 123.8(6), N(4)–C(1)–C(6) 116.5(6), C(2)–C(1)–C(6) 116.5(6), C(2)–C(1)–C(6) 119.7(6), C(1)–C(2)–C(3) 118.4(6), C(1)–C(2)–C(7) 120.0(6), C(3)–C(2)–C(7) 121.5(6), C(2)–C(3)–C(4) 119.5(6), C(2)–C(3)–C(10) 119.4(7), C(4)–C(3)–C(10) 120.7(7), C(3)–C(4)–C(5) 119.3(6), C(3)–C(4)–C(11) 121.6(7), C(5)–C(4)–C(11) 119.1(7), C(4)–C(5)–C(6) 110.8(6), C(1)–C(6)–C(5) 107.3(5), C(1)–C(6)–C(9) 113.4(6), C(1)–C(6)–C(12) 106.8(6), C(5)–C(6)–C(9) 110.5(6), C(5)–C(6)–C(12) 108.9(6), C(9)–C(6)–C(12) 109.8(6), O(1)–C(7)–C(2) 121.8(6), O(1)–C(7)–C(8) 117.2(7), C(2)–C(7)–C(8) 120.6(7), N(3)–C(11)–C(4) 178.1(10), N(2)–C(12)–C(6) 177.8(8).

addition, the hypothetical structure was supported by the fact that **3a** was easily hydrolysed to **4a**.

Table 2 shows the quantum yields for the cycloaddition of **1a** in the presence of methacrylonitrile under various conditions. Cycloaddition was not observed at methacrylonitrile concentrations lower than 0.1 mol dm^{-3} (Table 2, entry 1), and the quantum efficiency increased with increasing alkene concentration (Table 2, entries 1–3). The quantum yield was found to be independent of the solvent polarity (Table 2, entries 3–6), and quenching by 2,5-dimethylhexa-2,4-diene **7** was found to be inefficient (Table 2, entry 7). The addition of alkenes did not affect the absorption spectrum, which showed no interaction between pyridine and alkenes in the ground state. The fluorescence spectrum exhibited emission at 322 nm in cyclohexane. The intensity of this fluorescence decreased after the addition of alkenes; however, new fluorescence emission due to the formation of pyridine–alkene exciplex was not observed. These results indicate that photocycloaddition proceeded from the pyridine singlet excited state.

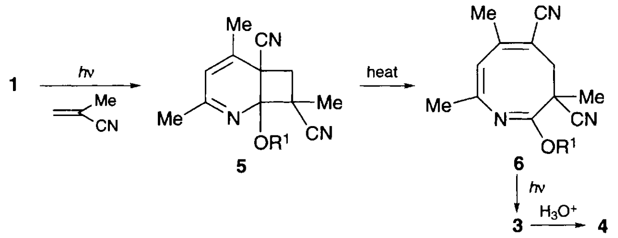
A mechanism has been postulated for the formation of adducts **3** and **4** that involves [2 + 2] photocycloaddition between the C(2)–C(3) of pyridine ring and the alkenyl double bonds leading to cyclobutane **5**, which easily transforms to azacyclooctatriene **6** (Scheme 1).[9] Upon excitation with a quantum of light, the azacyclooctatriene ring cyclizes into 8-azabicyclo[4.2.0]octa-4,7-diene **3**, which further hydrolyses into cyclohexadiene **4** during the isolation procedure.

Frontier-MO calculations by the AM1 method available in the MOPAC program help to explain the highly regioselective cycloaddition.‡ Using this method, the orbital energies and coefficients of the singlet excited state of **1a** (LSOMO: orbital energy, −6.56318 eV; coefficients, N-1, 0.04716; C-2, 0.37764; C-3, 0.57750; C-4, 0.00499; C-5, −0.45440; C-6, −0.37039, and HSOMO: orbital energy, −3.55472; coefficients, N-1, 0.14025; C-2, 0.43035; C-3, −0.50828; C-4, 0.28715; C-5, 0.20226; C-6, −0.54475) and those of the ground state of methacrylonitrile (HOMO: orbital energy, −10.43767 eV; coefficients C-1, 0.58375; C-2, 0.64865, and LUMO: orbital energy, −0.09739 eV; coefficients, C-1, 0.55119; C-2, −0.67893) were obtained. The energy gap (ΔE) between HSOMO and LUMO is smaller than that between LSOMO and HOMO, and the frontier orbital interaction is the most important factor in this reaction. The largest coefficient is observed at the 6-position in the HSOMO of the excited state. However, the predicted $\Delta\Delta E$ value supports the hypothesis that initial bond formation occurs between the C(2)–C(3) bond of the pyridine ring and the alkenyl double bond, leading to the experimentally obtained yield.§

Table 2 Quantum yield of photochemical reaction of **1a**

Entry	Solvent[a]	Conc. of alkene/ mol dm^{-3}	$10^{-2}\ \Phi_{add}$[b]
1	C_6H_6	0.1	0 (1.1)[c]
2	C_6H_6	0.2	0.6
3	C_6H_6	1.0	2.7
4	Et_2O	1.0	1.9
5	MeCN	1.0	2.6
6	MeOH	1.0	2.7
7	C_6H_6	1.0 + **7**[d]	2.6

[a] Concentration of pyridine **1a** was 0.02 mol dm^{-3}. [b] A varelophenone actinometer was used in reference to the 313 nm line. [c] Photoaddition was not observed. Value in parentheses shows quantum yield for the *trans*-isomerization from **1a** to **2a**. [d] 2,5-Dimethylhexa-2,4-diene **7** (0.05 mol dm^{-3}) was added.



Scheme 1

Footnotes

† *Crystal data* for **4a**: $C_{12}H_{13}N_3O$, M_W 215, colourless prismatic crystal, monoclinic space group $P2_1/c$, a = 9.368(3), b = 12.566(2), c = 10.203(2) Å, β = 97.13(2)°, V = 1191.7(5) Å^3, Z = 4, ρ = 1.20 g cm^{-3}, μ(Cu-Kα) = 6.42 cm^{-1}. Final R and R_w were 0.075 and 0.081 for 1294 reflections. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/80.

‡ These results are calculated by 'PASOCON MOPA C/386', which is based on the MOPAC (V6.0 QCPE No. 455), of Toray System Center.

§ The HSOMO coefficient on C-6 position is larger than the coefficient on C-3 position (−0.54475 *vs* −0.50828). For a more accurate approach, the predicted $\Delta\Delta E$ of the reaction was calculated using the Salem–Klopman equation (see for example I. Fleming, *Frontier Orbital and Organic Chemical Reactions*, Wiley-Interscience New York, 1976). The $\Delta\Delta E$ is proportional to $(ca1cb1)^2 + (ca2cb2)^2$ where cX is the orbital coefficient in the reactive site for the addition reaction of the a1–a2 and the b1–b2 bonds. The value of $(cC3cC2')^2 + (cC2cC1')^2$ is 1.7535×10^{-1} and 1.4922×10^{-1} respectively to that of $(cC6cC2')^2 + (cC5cC1')^2$ for the alternative pathway. These results support that the initial bond formation occurs between C(2)–C(3) bond of **1** and C(1′)–C(2′) bond of methacrylonitrile leading to the experimentally observed product.

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