Photochemical Induced Formation of α-Alkylamino or Alkylaminyl Radicals From Secondary Amines: Reaction with 4-Pyridinecarbonitrile

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Received November 4, 1991

The direct photolysis at 254 nm of 4-pyridinecarbonitrile in the presence of some aliphatic secondary amines brought to the substitution of the CN group and to the formation of 4-α-alkylaminopyridines, whereas the irradiation in the presence of benzophenone at 350 nm yields 4-alkylaminylpyridines and 4-diphenylketylpyridine. A mechanism is proposed to explain the different course of the reaction under the two different conditions.

J. Heterocyclic Chem., **29**, 975 (1992).

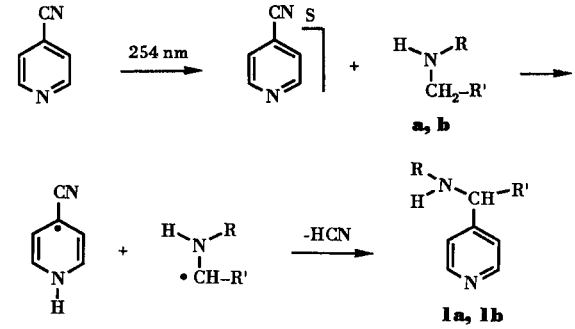
The reactivity of aliphatic amines toward excited or radical species has been extensively studied. The interest arises from the fact the primary and secondary amines react *via* hydrogen atom abstraction or electron transfer-proton transfer mechanism giving either alkylaminyl or α-aminoalkyl radicals. This ability is well documented in reaction with benzophenone triplet [1a-b], *tert*-butoxy radical [2a-b] and singlet excited arenecarbonitriles [3a-c]. This last case is very interesting because it was possible, carrying out the reaction in polar or non polar solvents, to isolate products derived from the attack of the alkylaminyl or α-aminoalkyl radicals to the arene ring.

The excited heteroaromatic bases give rise with some substrates to reactions (either hydrogen abstraction or electron transfer) which are in many cases similar to that of excited benzophenone and arenes [4]. Therefore it seems strange that few accounts have appeared on the photobehaviour of these compounds with amines [5a-b]. For some time we have studied the photochemical behaviour of pyridines substituted with electron withdrawing groups (CN, Cl) with substrates which are either a hydrogen atom or an electron donor [6a-b]; so it seemed interesting to us to determine whether or not the excited heteroaromatic bases were able to form with amines either α-aminoalkyl or alkylaminyl radicals or both.

Recently we reported that excited 2,4-pyridinedicarbonitrile reacts with primary and secondary amines to form 4-alkylaminyl-2-pyridinecarbonitriles [7]. We now report that the direct irradiation of 4-pyridinecarbonitrile in the presence of secondary amines at 254 nm yields 4-α-alkylaminopyridine, whereas the irradiation in the presence of benzophenone at 350 nm yields 4-alkylaminylpyridine and 4-diphenylketylpyridine.

In our opinions these results may be explained as follows. In our work concerning the photoreactivity of the heteroaromatic bases we put forth evidence that the dependence of the excited states implied two mechanisms may be involved [8]. The singlet state of these systems is able to abstract a hydrogen atom from a suitable donor, while the triplet state is able to give rise to an electron transfer reaction. As a result, the direct photolysis of 4-pyridinecarbonitrile in the presence of secondary amines (diethylamine, morpholine) give rise to direct hydrogen atom abstraction by singlet pyridine from the α-CH_2 of the amine; this process is followed by radical-coupling then HCN elimination to rearomatize and 4-α-alkylaminopyridine formation (Scheme 1).

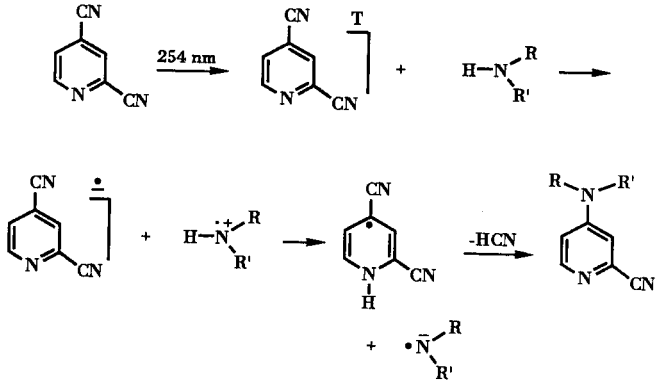
Scheme 1



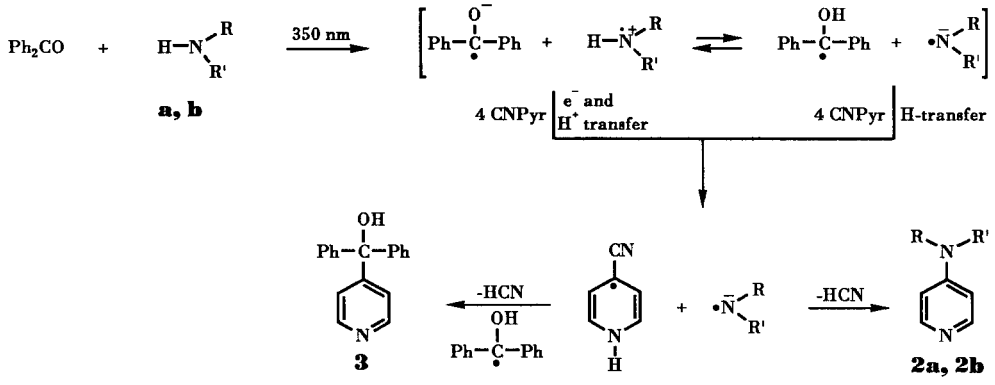
a = diethylamine
b = morpholine

In contrast the triplet 2,4-pyridinedicarbonitrile gives rise to an electron transfer from the amine followed by proton transfer from $H-\dot{N}^{+}<$: the coupling of radicals and rearomatization yields the 4-alkylaminyl-2-pyridinecarbonitrile (Scheme 2).

Scheme 2



Scheme 3



a = diethylamine
b = morpholine

The fact that we are not able to obtain aminylalkyl substitution in the case of the 4-pyridinecarbonitrile brings us to the conclusion that the quenching of the singlet state by the amine is very effective and hence it is not possible for the photoinduced electron transfer to occur.

With the objective to obtain cyano substitution with an

With the objective to obtain cyano substitution with an aminylalkyl group, we chose to sensitize the heterocyclic base chemically with excited benzophenone; as reported above, the results are positive and we obtained the product that is formally the same as if an electron transfer took place. This photochemical method was applied by us to other reactions of pyridinecarbonitrile in which we obtained functionalization of the heterocyclic ring even if at the wavelength used (350 nm), only benzophenone absorbs the incident light with the knowledge that the triplet state of pyridine is higher in energy then that of benzophenone. The mechanism we propose is depicted in Scheme 3.

It was reported that triplet benzophenone reacts with aliphatic amines to form a ^{3}CTC* complex; an internal proton transfer gives diphenylketyl and aminylalkyl radicals. Principally we can deal with a diphenylketyl radical or its radical anion; in the presence of 4-pyridinecarbonitrile these species may transfer to the base a hydrogen atom in the first case or an electron followed by proton transfer in the second case: cross coupling of 4-pyridinyl with aminylalkyl or diphenylketyl radicals followed by decyanation to rearomatize brings to final products.

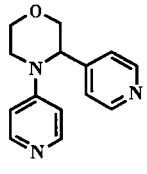


Figure 1

We would like to put in evidence on another aspect of this reaction. The fact that from this reaction we are able to obtain only the nitrogen substituted pyridine provides evidence, in our opinion, that once the amino radical cation is formed, the subsequent reaction that occurs is deprotonation forming an aminylalkyl radical and, at least under our experimental conditions, there is no loss of proton from the α-CH_2 and/or abstraction by the amine radical of a hydrogen carried on a carbon in another molecule, otherwise we should obtain both products: the nitrogen substitution and the carbon substitution and this is not true. Finally we need to mention that when the reaction was carried out in usual way but with morpholine in a molar ratio of 1 to 1 with 4-pyridinecarbonitrile and when irradiation lasted 4 hours, we were able to obtain the double substitution product **4** (Figure 1). This product arises from **2b**. This was indeed the only product formed if the reaction was carried out for a shorter time. Considering the rather good yield and considering the fact that if an amine is attached to the pyridinic ring its ionization potential increases, we think that the second substitution occurs *via* hydrogen abstraction by the excited benzophenone, chemical sensitization on 4-pyridinecarbonitrile, cross coupling and then HCN elimination to rearomatize.

EXPERIMENTAL

Photochemical irradiations were carried out using a Rayonet RPR-100 photochemical reactor equipped with 16 lamps with a maximum emission at 254 nm or at 350 nm. Melting points are uncorrected. The proton nmr spectra were recorded on a Varian EM 390 90 MHz spectrometer using deuteriochloroform as the solvent. All chemical shifts are reported in parts per million (ppm) from tetramethylsilane as the internal standard. Mass spectra were recorded with a Hitachi-Perkin-Elmer RMV 6 D single focusing spectrometer.

Materials.

4-Pyridinecarbonitrile and benzophenone were available in a reasonably pure state and were used without further purification. Diethylamine and morpholine were used after distillation. All solvents used were of an analytical grade.

Photolysis of 4-Pyridinecarbonitrile with Diethylamine at 250 nm. Ethyl-(1-pyridin-4-yl-1-ethyl)amine (**1a**).

A degassed solution (100 ml) of 4-pyridinecarbonitrile (0.1*M*) and diethylamine (0.5*M*) in acetonitrile was irradiated in a quartz tube for 2.5 hours. The solvent was evaporated and the residue was chromatographed using different ratios of hexane-ethyl acetate mixtures. Unreacted 4-pyridinecarbonitrile and product **1a** (yield 10%) with identical nmr, ir and ms data to that reported [5a] were isolated.

Photolysis of 4-Pyridinecarbonitrile and Diethylamine in the Presence of Benzophenone at 350 nm. Diethylpyridin-4-ylamine (**2a**) and Diphenyl(4-pyridyl)carbinol (**3**).

A degassed solution (100 ml) of 4-pyridinecarbonitrile (0.1*M*), benzophenone (0.1*M*) and diethylamine (0.5*M*) in acetonitrile was irradiated at 350 nm in a pyrex tube for 2.5 hours. After that period of time a white solid (1.2 g) crystallized and after separation from the solution, it was identified as diphenyl(4-pyridyl)carbinol (**3**) by comparison with an authentic sample. Then the solvent was evaporated and the residue was chromatographed on a silica gel column using different ratios of hexane-ethyl acetate mixtures as the eluent; unreacted benzophenone, 0.100 g of 4-pyridinecarbonitrile, 0.300 g of **3** (total yield 57%), and 0.44 g of 4-diethylaminopyridine (**2a**) (yield 30%) as solid with a very low mp were separated. The nmr, ir and ms data of **2a** are identical to those reported [10].

Photolysis of 4-Pyridinecarbonitrile with Morpholine at 250 nm. 3-(Pyridin-4-yl)morpholine (**1b**).

A degassed solution (100 ml) of 4-pyridinecarbonitrile (0.1*M*), and morpholine (0.5*M*) in acetonitrile was irradiated at 250 nm in a quartz tube for 2.5 hours. The solvent was evacuated and the residue was chromatographed on silica gel column using ethyl acetate-methanol (9:1) and 1% of aqueous ammonia; 0.500 g of unreacted 4-pyridinecarbonitrile was recovered and 0.20 g (yield 15%) of **1b** as oil separated; ^{1}H nmr (deuteriochloroform): 8.50 (2 H, dd, H_A and H_D), 7.3 (2 H, dd, H_B and H_C), 4.0-3.0 (ms, 7 H, morpholine), 2.33 (1 H, s, N-H, removed with deuterium oxide); ms: 164, 163, 133, 119, 105, 86, 78.

Anal. Calcd. for $C_9H_{12}N_2O$: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.73; H, 7.25; N, 16.80.

Photolysis of 4-Pyridinecarbonitrile with Morpholine (molar ratio 1:5) in the Presence of Benzophenone at 350 nm. 4-(Pyridin-4-yl)-morpholine (**2b**) and Diphenyl(4-pyridyl)carbinol (**3**).

A degassed solution (100 ml) of 4-pyridinecarbonitrile (0.1*M*), benzophenone (0.1*M*) and morpholine (0.5*M*) was irradiated at 350 nm in a pyrex tube for 4 hours. After that time compound **3** crystallized and was separated from the solution (0.75 g). Then the solvent was evaporated and the residue was chromatographed on a silica gel column using different ratios of hexane-ethyl acetate mixtures as the eluent. Unreacted benzophenone, 0.3 g of 4-pyridinecarbonitrile, 0.28 g of **3** (total yield 40%) were separated. Then eluting the column with ethyl acetate-methanol (9:1) and 1% of aqueous ammonia, 0.35 g of the compound **2b** (yield 20%) was separated.

Compound **2b** had ^{1}H nmr (deuteriochloroform): 8.50 (2 H, dd, H_A and H_D, J_{AB} and J_{DC} = 5 Hz, J_{AD} and J_{BC} = 1 Hz), 6.60 (2 H, dd, H_B and H_C, J_{BA} and J_{CD} = 5 Hz, J_{BC} and J_{AD} = 1 Hz), 3.80 (4 H, m, $-CH_2O-CH_2-$), 3.30 (4 H, m, $-CH_2NCH_2-$); ms: 164, 163, 133, 119, 105, 86, 78.

Anal. Calcd. for $C_9H_{12}N_2O$: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.68; H, 7.30; N, 16.85.

Photolysis of 4-Pyridinecarbonitrile with Morpholine (molar ratio 1:1) in the Presence of Benzophenone at 350 nm. Compound **3**, **2b** and 3,4-Di(pyridin-4-yl)morpholine (**4**).

A degassed solution (100 ml) of 4-pyridinecarbonitrile (0.1*M*), benzophenone (0.1*M*) and morpholine (0.5*M*) in acetonitrile was irradiated at 350 nm in a pyrex tube for 2.5 hours. After that time compound **3** crystallized and was separated from the solution (0.8 g). The solvent was evaporated and the residue was chromatographed on a silica gel column using different ratio of hexane-ethyl acetate mixtures as the eluent. Unreacted benzophenone, 0.150 g of 4-pyridinecarbonitrile and 0.35 g of **3** (total yield 42%) were separated. Then eluting the column with ethyl acetate-methanol (9:1) and 1% of aqueous ammonia, 0.580 g of **2b** (yield 35%) and 0.100 g of **4** (yield 4%) as white solid (mp 117°) were separated.

Compound **4** had ^{1}H nmr (deuteriochloroform): 8.50 and 7.18 (N morpholine-pyridine: 2 H, dd, H_A and H_D; 2 H, dd, H_B and H_C), 8.25 and 6.60 (C morpholine-pyridine: 2 H, dd, H_A and H_D; 2 H, dd, H_B and H_C), 4.75 (1 H, m, Py-CH-N-), 4.30-3.20 (6H, ms, morpholine); ms: 241, 210, 183, 163, 105, 78.

Anal. Calcd. for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.27; N, 17.41. Found: C, 69.52; H, 6.20; N, 17.25.

The coupling constants (J) are in Hz. H_A, H_B, H_C and H_D refer respectively to the protons in position 2, 3, 5, and 6 of the pyridine ring; J_{AB}, J_{DC}, J_{AD}, and J_{BC} values are reported only for product **2b**; for products **1b** and **3** the values are the same.

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