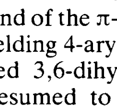
Photoaddition Reaction of 1,2-Dialkyl-indoles and -pyrroles to 1-Methyl-2-pyridone *via* Proton Transfer from the 2-Methylene Group of the Indole or Pyrrole

Nobuhiro Sakurai and Shigeru Ohmiya*

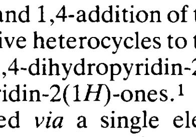
Faculty of Pharmaceutical Sciences, Hoshi University, Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan

On irradiation, 1,2-dialkyl-indoles and -pyrroles undergo 1,2- and 1,4-addition to 1-methyl-2-pyridone in a reaction involving single electron transfer followed by proton transfer from the 2-alkyl group of the indole or pyrrole; bonding takes place between C-3 of the indole, or C-1 of the 2-alkyl group of the indole or pyrrole and C-4 or C-6 of the pyridone, respectively.

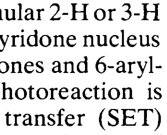
Recently we have reported that irradiation of 1-methyl-2-pyridone **1** in the presence of indoles and pyrroles primarily gives rise to the 1,2- and 1,4-addition of the annular 2-H or 3-H bond of the π-excessive heterocycles to the 2-pyridone nucleus yielding 4-arylated 3,4-dihydropyridin-2(1*H*)-ones and 6-arylated 3,6-dihydropyridin-2(1*H*)-ones.[1] The photoreaction is presumed to proceed *via* a single electron transfer (SET) process, followed by proton transfer and then combination of the resulting radicals. The presence of a pyrrolyl or an indolyl NH group is essential to the photoaddition reaction because it acts as a proton source in the proton transfer process, which is similar to the photoaddition reaction of pyrrole to benzene[2] and naphthalene.[3] We report here the photoaddition reaction of 1,2-dialkyl-indole **2**–**5** and -pyrrole derivatives **6**, **7** to 1-methyl-2-pyridone **1**, in which the methylene (or methyl) group at the 2-position of the indole and the pyrrole ring acts as a proton source instead of the NH group.



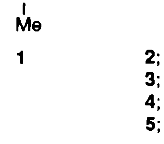
1



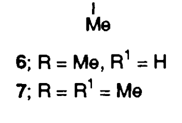
2; X = R = H
3; X = H, R = Me
4; X = CO_2Et, R = H
5; X = CN, R = H



6; R = Me, R^1 = H
7; R = R^1 = Me

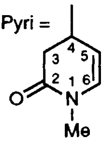


8; X = R^1 = H, R = 4-Pyri
9; X = R^1 = H, R = 6-Pyri
10; X = R = H, R^1 = 4-Pyri
11; X = H, R = Me, R^1 = 6-Pyri
12; X = CO_2Et, R = 6-Pyri, R^1 =H
13; X = CO_2Et, R = H, R^1 = 4-Pyri
14; X = CN, R = 6-Pyri, R^1 = H
15; X = CN, R = H, R^1 = 4-Pyri
16; X = CN, R = H, R^1 = 6-Pyri

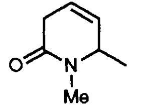


17; R = Me, R^1 = H, R^2 = 4-Pyri
18; R = Me, R^1 = H, R^2 = 6-Pyri
19; R = R^1 = Me, R^2 = 4-Pyri
20; R = R^1 = Me, R^2 = 6-Pyri

4-Pyri =



6-Pyri =

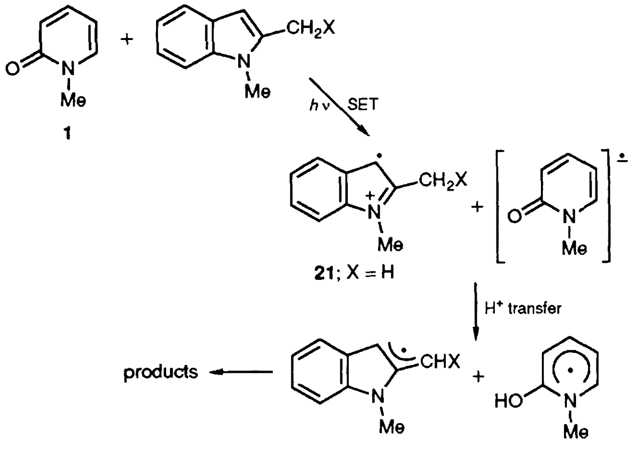


The photoreactions were performed on degassed dioxane or acetonitrile solutions of the π-excessive heterocycles (1.0 mol dm^{-3}) and **1** (0.05 mol dm^{-3}) by external irradiation with a 400 W high-pressure mercury lamp through a Pyrex filter for 15 h at ambient temperature. Table 1 records product distribution and yields.

Irradiation of **1** with 1,2-dimethylindole **2** gave three 1 : 1 adducts **8**, **9** and **10**† in 8.5, 10 and 4% yields, respectively, based on consumed **1**. The former two, **8** and **9**, were attributable to the 1,2- and 1,4-addition of the nuclear 3-H bond of **2** to **1**, in analogy with the photoreaction between

---

† All new compounds were characterized by ^{1}H NMR, IR and mass spectra. *Selected spectroscopic data*: for **8**: ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3H, 2′-Me), 2.62 (ddd, 1H, *J* 16.5, 6.7 and 1.2 Hz, 3-H), 2.90 (dd, 1H, *J* 16.5 and 14.7 Hz, 3-H′), 3.15 (s, 3H, 1-Me), 3.66 (s, 3H, 1′-Me), 4.12 (dddd, 1H, *J* 14.7, 6.7, 3.7 and 3.1 Hz, 4-H), 5.32 (ddd, 1H, *J* 7.3, 3.7 and 1.2 Hz, 5-H), 6.16 (dd, 1H, *J* 7.3 and 3.1, 6-H), 7.04 (dd, 1H, *J* 7.9 and 7.9 Hz, 5′-H), 7.16 (dd, 1H, *J* 7.9 and 7.9 Hz, 6′-H), 7.27 (d, 1H, *J* 7.9 Hz, 7′-H), 7.60 (d, 1H, *J* 7.9 Hz, 4′-H); IR ($CHCl_3$): 1650 cm^{-1} (C=O). For **10**: ^{1}H NMR ($CDCl_3$) δ 2.25 (s, 3H, 2′-Me), 2.67–2.88 (m, 2H, 3-H_2), 2.93 (dd, 1H, *J* 14.5 and 8.5 Hz, one of CH_2), 3.07 (s, 3H, 1-Me), 3.24 (dd, 1H, *J* 14.4 and 4.8 Hz, one of CH_2), 3.66 (s, 3H, 1′-Me), 4.07 (m, 1H, 6-H), 5.69 (ddd, 1H, *J* 7.3, 4.3 and 2.4 Hz, 5-H), 5.76 (ddd, 1H, *J* 10.4, 4.3 and 2.4 Hz, 4-H), 7.10 (dd, 1H, *J* 7.9 and 7.9 Hz, 5′-H), 7.20 (dd, 1H, *J* 7.9 and 7.9 Hz, 6′-H), 7.26 (d, 1H, *J* 7.9, 7′-H), 7.51 (d, 1H, *J* 7.9, 4′-H); IR ($CHCl_3$): 1620 cm^{-1} (C=O).



Scheme 1

Table 1 Photoaddition products from irradiation of 1-methyl-2-pyridone **1** with indoles **2–5** and pyrroles **6** and **7**

Indole or Pyrrole	Solvent[a]	Products and yields (%)[b]			
		Annular		Lateral	
2	D	**8**(8.5)	**9**(10)	**10**(4)	
	A	**8**(8.5)	**9**(9.5)	**10**(2)	
3	D			**11**(24)	
4	D	**12**(14)		**13**(22.5)	
5	A	**14**(22)		**15**(20)	**16**(4)
6	D			**17**(20)	**18**(27)
7	D			**19**(44)	**20**(39)

[a] D, dioxane; A, acetonitrile. [b] Isolated yields based on consumed **1**.

indoles and **1**.[1] The last product **10** came from the 1,2-addition of the C–H bond of the 2-methyl group of **2** to **1**. This was a new type of addition product in the photoreaction between π-excessive heterocycles and aromatic compounds. Similarly, indoles **4** and **5** gave the products attributable to both annular (**12**, **14**) and lateral (**13**, **15**, **16**) addition. On the other hand, the introduction of a methyl group in the 3-position of the indole ring showed significant regiocontrol for the lateral addition. Indole **3** afforded only the side-chain addition product **11**. In addition, the photoreaction of pyrroles **6** and **7** also occurred exclusively by the lateral addition to give adducts **17** and **18**, and **19** and **20**, respectively.

Holze and Hamann[4] have reported that the electron distribution of the 1,2-dimethylindole radical cation is as shown in the resonance structure **21**. This indicates the extreme probability for proton release from the 2-methyl group on the side chain. Therefore, the photoaddition reaction was presumed to proceed by way of proton transfer from the 2-methyl (or methylene) group of the pyrrole or indole to the ketyl radical of **1**, following an SET process, as shown in Scheme 1. The present reaction provides the first example of the formation of the side-chain addition products in photoaddition reactions of π-excessive heterocycles to aromatic compounds.

Received, 13th October 1992; Com. 2/05474D

References

1 S. Ohmiya, M. Noguchi, S. Ina, H. Kubo and H. Otomasu, *Chem. Pharm. Bull.*, 1992, **40**, 854.
2 D. Bryce-Smith, M. T. Clarke, A. Gilbert, G. Klunklin and C. Manning, *Chem. Commun.*, 1971, 916.
3 J. J. McCullough, C. W. Huang and W. S. Wu, *Chem. Commun.*, 1970, 1368; J. J. McCullough, W. S. Wu and C. W. Huang, *J. Chem. Soc., Perkin. Trans. 2*, 1972, 370.
4 R. Holze and C. H. Hamann, *Tetrahedron*, 1991, **47**, 737.