SELECTIVE PHOTO-REDUCTION OF 1-ALKYLISATINS IN DEGASSED ALCOHOLIC SOLUTIONS

Jiro Tatsugi, * Kenji Ikuma, and Yasuji Izawa*

Department of Applied Chemistry, Aichi Institute of Technology,
Yakusa, Toyota 470-03, Japan

Abstract —— Irradiation of 1-alkylisatins (**1**) in degassed alcohols afforded 1-alkyl-3-hydroxyoxindoles (**2**) and 1-alkyloxindoles (**3**) as chemoselective photoproducts.

The photochemical behavior of carbonyl groups of cyclic vicinal polyketones has received considerable attention in the last few years.[1] On the other hand, the photochemical reactions of heterocyclic vicinal diketones have also attracted interest from synthetic viewpoints.[2] Recently, it has been reported that photochemical reaction of *isatin, which has been used as* valuable synthetic intermediates in both the pharmaceutical and dye industries,[3] with cyclohexane-1,3-dione and with pyrazolone gave the corresponding spiro compounds[4] and the ring expanded heterocyclic compound[5] derived from fission of the amide bond of isatin, respectively. In these cases, particularly interesting is the photochemical reaction of the amide moiety to give phenylpyrazolebenzazepine. In order to clarify the photochemically intrinsic behavior of heterocyclic vicinal diketones, we have examined the photochemical reactions of isatins in alcohols. Herein, we wish to report the chemoselective photoreduction of 1-alkylisatins in degassed alcohols.

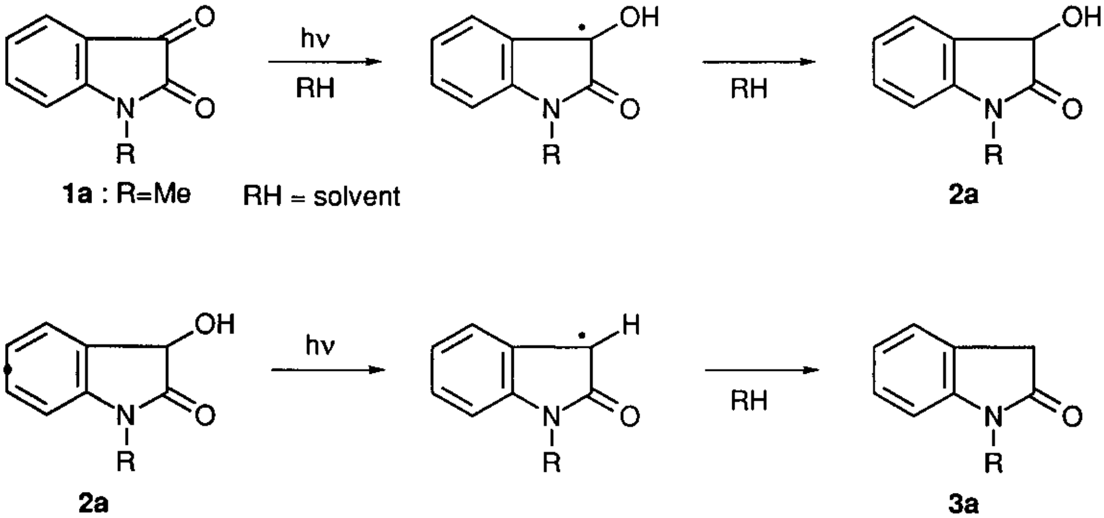
1-Alkylisatins (**1a-d**) were prepared from the reaction of isatin sodium salt with the appropriate alkyl halides in DMF.[6] Before irradiation, the 1-alkylisatins in alcoholic solutions in Pyrex tubes were degassed by an ultrasonic generator under purging argon and cooled with ice-water for 15 minutes.[7] Irradiation of **1a-d** in degassed alcoholic solutions at 15 °C with a 300 W high-pressure mercury lamp gave a mixture of products which were analyzed by GC and GC-ms. The photoproducts were also separated by column chromatography and characterized by ir, ^{1}H-nmr, and ms spectroscopies.[8] The results of the photochemical reactions of 1-methylisatin (**1a**) in alcoholic solutions are summarized in **Table 1**. When **1** was irradiated in 2-propanol, the formation of acetone was also detected by GC.

Table 1. Photochemical Reactions of 1-Methylisatin (**1a**) in Alcohols

			Products/%^{a}	
Solvent	Irr.time/h	Conv./%	**2a**	**3a**
2-propanol	4	2	90	trace
	8	34	29	68
	10	76	0	98
2-butanol	0.5	12	99	0
	1	40	72	26
	2	98	10	85

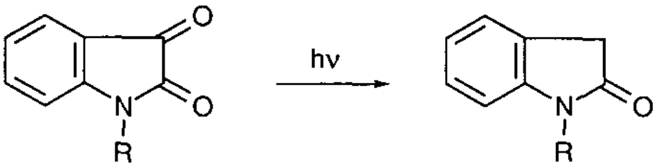
a) Determined by GC analysis.

As can be see from **Table 1**, the photochemical reactions of **1a** in degassed alcoholic solutions underwent a chemoselective reaction to afford 3-hydroxy-1-methyloxindole (**2a**)[9] as a primary photoproduct and 1-methyloxindole (**3a**)[10] derived from **2a**.



Scheme 1

The formation of **3a** *via* **2a** can be explained in terms of the possible reaction pathway outlined in **Scheme 1**. The primary step in the photochemical processes of **1a** in degassed alcohols is abstraction of hydrogen atom from the solvent exclusively by the excited carbonyl group of benzoyl moiety of **1a** to genarate a semidione radical which subsequently undergoes a disproportionation or additional abstraction of hydrogen atom to give **2a**. The excited **2a** suffers cleavage of the C-OH bond to give an α-carbonylbenzyl radical followed by a hydrogen abstraction from the solvent to afford **3a**. To confirm the reaction pathway to **3a** *via* **2a**, we carried out the irradiation of **2a** in 2-propanol. Irradiation of **2a** in 2-propanol under similar conditions gave **3a** in 61% yield along with a small amount of 1-methyl-4-hydroxyoxindole.[11]



1b : R=Et
c : R=Pr
d : R=Bu

3b : R=Et
c : R=Pr
d : R=Bu

Similar products, (**3b**), (**3c**), and (**3d**) were obtained from the irradiation of 1-ethyl- **1b**, 1-propyl- **1c**, and 1-butylisatins **1d** in degassed solutions.[12]
It is noteworthy that the excitation is localized on the carbonyl group of benzoyl moiety of 1-alkylisatins.

REFERENCES AND NOTES

1. J. C. N-Ferreira and J. C. Scaiano, *Photochem. Photobiol.*, 1991, **54**, 17; D. R. Boate, L. J. Johnston, P. C. Kwong, E. Lee-Ruff, and J. C. Scaiano, *J. Am. Chem. Soc.*, 1990, **112**, 8858; T. Mosandl and C. Wentrup, *J. Org. Chem.*, 1993, **58**, 747.
2. O. Buchardt, "*Photochemistry of Heterocyclic Compounds*," John Wiley & Sons. Inc., New York, 1976; W. M. Horspool and G. D. Khandelwal, *Chem. Commun.*, **1970**, 257; V. Dvorak, J. Kok, and J. Michl, *Tetrahedron Lett.*, **1972**, 3443; W. Friedrichsen, *Ann.*, **1975**, 1545; J. B. Stanford and J. K. Sugden, *Chemist and Druggist*, August 11, 1973.
3. For a review of isatin chemistry see F. D. Popp, *Adv. Heterocycl. Chem.*, 1975, **18**, 1-56.
4. K. C. Joshi, R. T. Pardasani, A. Dandia, and S. Bhagat, *Heterocycles*, 1991, **32**, 1491.
5. K. C. Joshi, R. Jain, and S. Arora, *Indian J. Heterocycl. Chem.*, 1991, **1**, 95.
6. Typical conditions for preparation of 1-methylisatin are as follows: Sodium hydride

0.48g(12 mmol) free from mineral oil is added to isatin 1.47g(10 mmol) in DMF (20 ml) under an inert atmosphere. After 30 min, methyl iodide 0.68g(11 mmol) is added slowly as a solution in DMF (2 ml) and the solution stirred at room temperture for 1 h to give a dark red solution. The reaction is quenched by careful addition of water (30 ml) and 1-methylisatin is extracted with dichloromethane. The dichloromethane layer is washed with distilled water. After drying the dichloromethane layer and removal of solvent, the residue is purified by column chromatography.

7. J. Tatsugi, *Chemistry and Chemical Industry*, 1992, **45**, 482.
8. Selected spectroscopic data for **2a**: ir(KBr) ν cm^{-1} : 3288(OH), 1694(CO); ^{1}H-nmr ($CDCl_3$, 400 MHz) δ ppm: 3.19(3H, s, CH_3), 3.84(1H, s, OH), 5.09(1H, s, CH), 6.83(1H, d, J = 8.0 Hz, aromatic-H), 7.11(1H, t, J = 8.0 Hz, aromatic-H), 7.34(1H, t, J = 8.0 Hz, aromatic-H), 7.47(1H, d, J = 8.0 Hz, aromatic-H); ms : m/z 163(M$^+$, 23), 161(86), 133(34), 105(70), 104(100). **3a**: ir(KBr) ν cm^{-1} 1703(CO); ^{1}H-nmr (DMSO-d_6, 400 MHz) δ ppm: 3.11(3H, s, CH_3), 3.53(2H, s, CH_2), 6.96(1H, d, J = 8.0 Hz, aromatic-H), 7.00(1H, t, J = 8.0 Hz, aromatic-H), 7.14(1H, t, J = 8.0 Hz, aromatic-H), 7.28(1H, d, J = 8.0 Hz, aromatic-H); ms : m/z 147(M$^+$, 100), 132(15), 119(18), 91(21).
9. H.Hata, S. Simizu, S. Hattori, and H. Yamada, *J. Org. Chem.*, 1990, **55**, 4377.
10. P. G. Gassman and T. J. van Bergen, *J. Am. Chem. Soc.*, 1974, **96**, 5508.
11. Selected spectroscopic data for 1-methyl-4-hydroxyoxindole: ir(KBr) ν cm^{-1}: 3258(OH), 1682(CO); 1H-nmr($CDCl_3$, 400MHz) δ ppm: 3.20(3H, s, CH_3), 3.50(2H, s, CH_2), 4.92(1H, d, OH), 6.47(1H, d, J = 8.0 Hz, aromatic-H), 6.52(1H, d, J = 8.0 Hz, aromatic-H), 7.27(1H, d, J = 8.0 Hz, aromatic-H); ms : m/z 163(M$^+$, 100), 135(27), 134(64).
12. Satisfactory analytical and spectral data were obtained for all compounds.

Received, 28th August, 1995