Pergamon

Tetrahedron Letters, Vol. 35, No. 8, pp. 1283-1284, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0053-Z

Manganese(III) Acetate Initiated Oxidative Free Radical Reaction Between *N*-Aroylindoles And Dimethyl Malonate

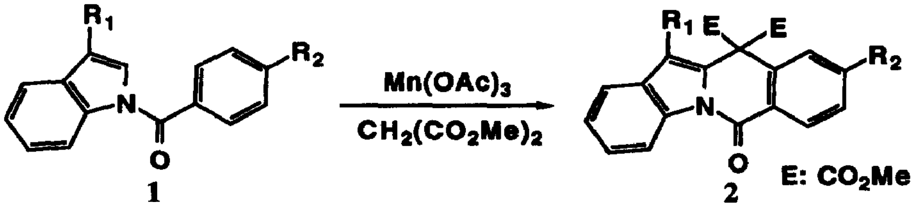
Che-Ping Chuang* and Sheow-Fong Wang

Department of Chemistry, National Cheng Kung University, Tainan, Taiwan, 70101, R.O.C.

Abstract: The manganese(III) initiated oxidative free radical reaction between *N*-aroylindoles and dimethyl malonate giving indolo[2,3-a]isoquinolines is described.

The free radical cyclization reaction is increasingly being used in the formation of ring systems.[1] The manganese(III) - based oxidative free radical reaction have been studied by several groups.[2,3] These reactions can be performed intermolecularly and intramolecularly. The free radical addition of carbon center radical to aromatic ring system has been reported.[4,5] We describe here our results of manganese(III) initiated oxidative free radical reaction between *N*-aroylindoles and dimethyl malonate.

We began our studies with the reaction shown in equation 1. Thus, treatment of indole **1a** and dimethyl malonate with manganese(III) acetate in acetic acid gave isoquinoline **2a** in 83% yield (Eq. 1). The generality of this reaction is illustrated in Table I. This free radical reaction presumably occurs via the addition of malonyl radical generated from the oxidation of malonate by manganese(III) acetate to indole ring and aryl ring consecutively. A typical experimental procedure is described for the reaction between indole **1a** and dimethyl malonate; A mixture of **1a** (0.47 mmol), dimethyl malonate (2.79 mmol) and manganese(III) acetate dihydrate (2.79 mmol) in acetic acid (10ml) was heated at 80°C for 24 h. The reaction mixture was diluted with ethyl acetate, washed with sat. aqueous sodium bicarbonate and water successively and then dried (Na_2SO_4). The crude product was purified by column chromatograph to afford **2a**.[6]



(Eq. 1)

Table I: The Free Radical Reaction Between *N*-Aroylindoles and Dimethyl Malonate

Entry	Substrate 1		Yield
	R_1	R_2	
a	CO_2Me	H	83%
b	CO_2Me	H	74%
c	CO_2Me	Ph	81%
d	CN	H	59%
e	CN	Me	57%
f	CN	OMe	62%
g	COMe	H	48%
h	COMe	Me	52%
i	COMe	Ph	42%

In Conclusion, this oxidative free radical reaction provides a novel method for the synthesis of indolo[2,3-a]isoquinolines from readily available *N*-aroylindoles.

Acknowledgement. The authors wish to thank the National Science Council, R.O.C. for financial support (NSC 82-0208-M006-25).

References:

1 (a) Hart, D. J. *Science (Washington, D. C.)*, **1984**, *223*, 883. (b) Neumann, W. P. *Synthesis*, **1987**, 665. (c) Curran, D. P. *Synthesis*, **1988**, 417 and 489.

2 (a) Heiba, E. I.; Dessau, R. M.; Koehl, W. J. *J. Am. Chem. Soc.* **1968**, *90*, 5905. (b) Nikishin, G. I.; Vinogradov, M. G.; Fedorova, T. M. *J. Chem. Soc.* **1973**, 693. (c) Corey, E. J.; Kang, M. C. *J. Am. Chem. Soc.* **1984**, *106*, 5384. (d) Peterson, J. R.; Do, H. D.; Surjasasmita, I. B. *Synth. Commun.* **1988**, *18*, 1985.

3 (a) Snider, B.B.; Mohan, R.; Kates, S. A. *J. Org. Chem.* **1985**, *50*, 3659. (b) Merritt, J. E.; Sasson, M.; Kates, S. A.; Snider, B. B. *Tetrahedron Lett.* **1988**, *29*, 5209. (c) Oumar-Mahamat, H.; Moustrou, C.; Surzur, J.-M.; Berstrand, M. P. *J. Org. Chem.* **1989**, *54*, 5684. (d) Snider B. B.; Wan, B. Y. F.; Buckman, B. O.; Foxman, B. M. *J. Org. Chem.* **1991**, *56*, 328.

4 (a) Citterio, A.; Santi, R.; Fiorani, T.; Strologo, S. *J. Org. Chem.* **1989**, *54*, 2703. (b) Citterio, A.; Sebastiano, R.; Marion, A. *J. Org. Chem.* **1991**, *56*, 5328. (c) Citterio, A.; Sebastiano, R.; Carvayal, M. C. *J. Org. Chem.* **1991**, *56*, 5335. (d) Citterio, A.; Sebastiano, R.; Nicolini, M. *Tetrahedron*, **1993**, *49*, 7743.

5 (a) Bowman, W. R.; Heaney, H.; Jordan, B. M. *Tetrahedron*, **1991**, *47*, 10119. (b) Ziegler, F. E.; Jeronic, L.O. *J. Org. Chem.* **1991**, *56*, 3479. (c) Chuang, C. -P. *Tetrahedron Lett.* **1992**, *33*, 6311.

6 The Spectra data for **2a**: IR ($CHCl_3$) 3028, 1780, 1758, 1704, 1454, 1330 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.61 (s, 6H, CH_3), 3.95 (s, 3H, OCH_3), 7.42-7.53 (m, 2H, ArH), 7.62 (td, J = 7.6, 1.0 Hz, 1H, ArH), 7.73 (td, J = 7.7, 1.5 Hz, 1H, ArH), 8.18 (dm, J = 7.7 Hz, 1H, ArH), 8.23 (dm, J = 6.8 Hz, 1H, ArH), 8.48 (dd, J = 7.8, 1.4 Hz, 1H, ArH), 8.81 (dm, J = 6.9 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 51.4 (q), 53.6 (q), 57.5 (s), 111.4 (s), 116.9 (d), 121.5 (d), 125.2 (s), 125.4 (d), 125.9 (d), 126.8 (s), 127.8 (d), 129.3 (d), 129.5 (d), 133.1 (s), 134.3 (d), 134.6 (s), 139.5 (s), 159.7 (s), 164.7 (s), 166.3 (s); exact mass calcd for $C_{22}H_{17}O_7N$ m/e 407.1005, found m/e 407.1006.

(*Received in Japan* 19 *October* 1993; *accepted* 17 *December* 1993)