

## THE OXIDATION REACTION OF INDOLES WITH THALLIUM(III) TRINITRATE

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Sapporo, 060 JapanDedicated to Professor *Kyosuke Tsuda* on the occasion of his 75th birthday

Abstract - Some indole derivatives were submitted to the oxidation with thallium(III) trinitrate[TTN] to give the corresponding oxindole and isatin derivatives. Indole-3-propionic acid derivatives were oxidized with TTN to afford the spiro- $\gamma$ -lactones in good yields.

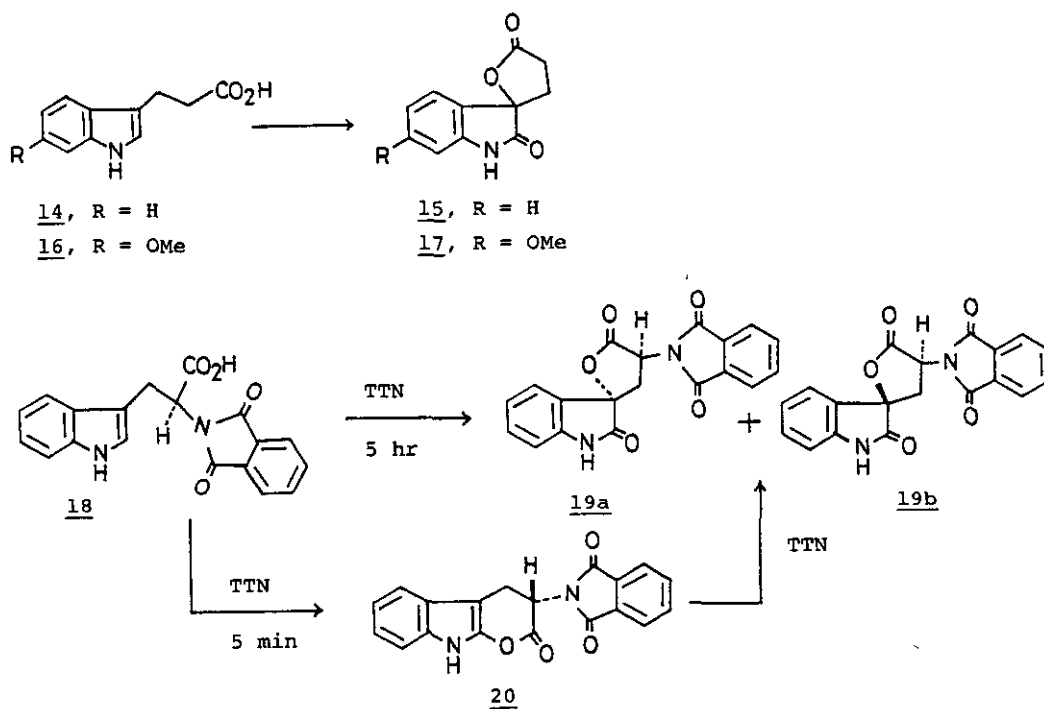
During the past decade, the investigation of oxidation reaction of olefinic compounds with thallium(III) reagents has been extensively made by McKillop and Taylor,<sup>1</sup> who clarified the unique useful properties of this reagent to be unattainable with any other oxidizing reagents for organic syntheses. Although oxidation reactions at C<sub>2</sub>,C<sub>3</sub>-double bond of indole derivatives for generation of the corresponding oxindoles with a variety of oxidizing agents have been known,<sup>2</sup> these methods are not always useful because of low overall yields accompanied by unfavored by-products under rather drastic conditions.

We describe here the new oxidation method of some indole derivatives with thallium(III) trinitrate[TTN]<sup>3</sup> giving the notable results. Table I summarizes the conversion of indoles(1, 2, 7, and 8) with TTN into the corresponding C<sub>3</sub>-disubstituted oxindoles(3,<sup>4</sup> 4,<sup>5</sup> 5, and 6) and isatin derivatives(9 and 10),<sup>6</sup> while oxidations of the same compounds performed with Tl(OAc)<sub>3</sub> and Tl(OCOCF<sub>3</sub>)<sub>3</sub> were not satisfactory. In the cases of 5 and 6, it was presumed that the nitro group was introduced to C<sub>3</sub>-position of the oxindoles based on their spectral data[5, mp 149-151°, IR(CHCl<sub>3</sub>) 1745 and 1550 cm<sup>-1</sup>; MS m/e 192(M<sup>+</sup>) and 146(M<sup>+</sup>-NO<sub>2</sub>, base peak): 6, IR(CHCl<sub>3</sub>) 1730 and 1555 cm<sup>-1</sup>; MS m/e 278(M<sup>+</sup>) and 232(M<sup>+</sup>-NO<sub>2</sub>, base peak)] and the elemental analyses. The oxidation of oxindole 11 with TTN in methanol at 25° afforded 3 in a high yield. When this oxidation was conducted in dry acetonitrile and then treated with water,<sup>7</sup> a nitrate group was introduced to give the 3-nitroxindole 13[mp 110°, IR(CHCl<sub>3</sub>) 3200, 1735, and 1640 cm<sup>-1</sup>; MS m/e 208(M<sup>+</sup>) and 162(M<sup>+</sup>-NO<sub>2</sub>, base peak)], and 12[mp 155-157°(lit<sup>8</sup> 161-162°)] as its hydrolyzed product



$\text{CH}_3\text{CN}$ ,  $0^\circ \rightarrow \text{rt}$ , 5 h) gave two diastereomeric lactones, 19a (34%) [mp  $271-273^\circ$ ,  $[\alpha]_D^{20} -163^\circ$  (c 0.5, acetone)]<sup>11</sup> and 19b (16%) [mp  $261-263^\circ$ ,  $[\alpha]_D^{20} -220^\circ$  (c 0.5, acetone)],<sup>12</sup> whose stereochemistry at the spiro position was determined by comparison with the known optical rotations.<sup>13</sup> In this oxidation reaction, if the reaction time was limited to 5 min under a similar condition ( $0^\circ$ ), there was readily trapped the intermediate 20 (80%) [mp  $239-243^\circ$  (decomp),  $[\alpha]_D^{20} -38^\circ$  (c 0.5, acetone); IR (Nujol) 3300, 1780, 1750, and  $1720\text{ cm}^{-1}$ ;  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  5.73 (t, 1,  $J=10\text{Hz}$ ), 7.0-7.4 (m, 4), 7.96 (s, 4), and 11.65 (s, 1); MS  $m/e$  332 ( $\text{M}^+$ )], which was further treated with TTN in 5% aq  $\text{CH}_3\text{CN}$  to give a mixture of 19a and 19b in 62% yield.<sup>14</sup> Further studies are in progress.

Scheme 2



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4. The compound **3**, mp 120-122° (lit<sup>8</sup> 121-123°), IR(Nujol) 1745 and 1715 cm<sup>-1</sup>; <sup>1</sup>H NMR(CDCl<sub>3</sub>) δ 1.60(s, 3), 3.09(s, 3), 6.9-7.3(m, 4), and 9.11(broad, 1, D<sub>2</sub>O exchange); MS m/e 177(M<sup>+</sup>).
5. The compound **4**, IR(CHCl<sub>3</sub>) 3250 and 1720 cm<sup>-1</sup>; <sup>1</sup>H NMR(CDCl<sub>3</sub>) δ 1.20(t, 3, J=7Hz), 2.3(m, 4), 4.09(q, 2, J=7Hz), 4.2(broad, 1, D<sub>2</sub>O exchange), 7.2(m, 4), and 8.81(broad, 1, D<sub>2</sub>O exchange); MS m/e 249(M<sup>+</sup>).
6. The compounds, **9** [IR(Nujol) 1740, 1720, and 1700 cm<sup>-1</sup>; <sup>1</sup>H NMR(acetone-d<sub>6</sub>) δ 2.76(t, 2, J=7Hz), 4.02(t, 2, J=7Hz) and 7.0-7.8(m, 4); MS m/e 219(M<sup>+</sup>) and 132(base peak)], and **10** [mp 97.5°, IR(Nujol) 1740 cm<sup>-1</sup>; <sup>1</sup>H NMR(CDCl<sub>3</sub>) δ 2.71(t, 2, J=8Hz), 3.62(s, 3), 3.97(t, 2, J=8Hz), and 6.9-7.6(m, 4); MS m/e 233(M<sup>+</sup>) and 132(base peak)]. Furthermore, the compound **10** was identical with the sample obtained through N-alkylation of isatine with methyl acrylate in the presence of sodium hydride in THF-DME at room temperature.
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11. The compound **19a**, IR(Nujol) 3250, 1790, 1760, 1745, and 1700 cm<sup>-1</sup>; <sup>1</sup>H NMR(acetone-d<sub>6</sub>) δ 3.11(dd, 2, J=3, 10Hz), 5.71(t, 1, J=10Hz), 7.0-7.6(m, 4) and 7.95(s, 4); MS m/e 348(M<sup>+</sup>).
12. The compound **19b**, IR(Nujol) 3200, 1800, 1770, 1740, and 1710 cm<sup>-1</sup>; <sup>1</sup>H NMR(DMSO-d<sub>6</sub>) δ 2.8-3.2(m, 2), 5.83(dd, 1, J=10, 13Hz), 6.9-7.8(m, 4) and 7.92(s, 4); MS m/e 348(M<sup>+</sup>).
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14. In regard to this oxidative cyclization, a similar intermediate such as **20** was detected on oxidation with NBS. [T. Hino, H. Miura, T. Nakamura, R. Murata, and M. Nakagawa, Heterocycles, **3**, 805 (1975); cf. E. C. Taylor, J. G. Andrade, G. J. H. Rall, and A. McKillop, J. Org. Chem., **43**, 805 (1978).

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