

**A TANDEM COPE-CLAISEN REARRANGEMENT REACTION OF  
MESO-3,3'-DIPHENYLLEUCOISOINDIGOS**

Tetsuo Suyama,<sup>a\*</sup> Takeshi Kato,<sup>a</sup> Yutaka Morita,<sup>a</sup>  
and Hiroshi Miyamae<sup>b</sup>

Faculty of Pharmaceutical Sciences<sup>a</sup>

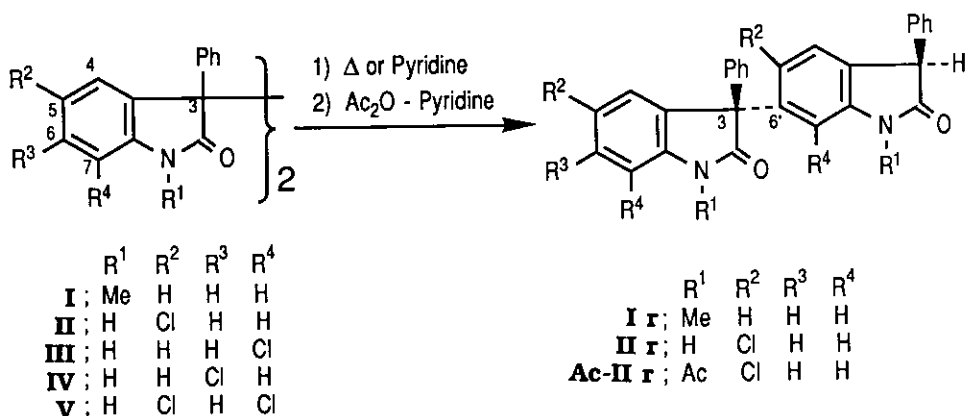
and Faculty of Science<sup>b</sup>,

Josai University, Keyakidai 1-1, Sakado, Saitama

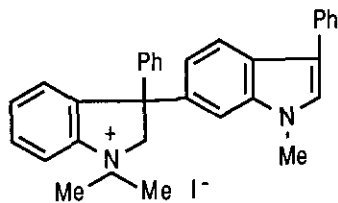
350-02, Japan

**Abstract** --- A unique and new rearrangement reaction of meso-3,3'-diphenylleucoisoindigos was examined. Structures of the products were determined as 3,6'-biindolinones by X-ray analyses. The formal reaction mechanism was supposed to be a tandem Cope-Claisen type rearrangement.

In the course of our study on leucoisoindigos,<sup>1</sup> an interesting rearrangement reaction of meso-3,3'-diphenylleucoisoindigos (I and II) to 3,6'-biindolinones (Ir - IIr) happened to be observed.<sup>2</sup>



The rearrangement reactions proceeded in moderate yields (65-80 %) by heating neat leucoisoidindigos at 150-180°C or leaving stand in methylene chloride or acetic anhydride with a small amount of pyridine. meso-1,1'-Dimethyl-3,3'-diphenylleucoisoidindigo (**I**)<sup>1a,1b,3</sup> was rearranged to a compound (**Ir**)<sup>4</sup> having a methine proton ( $\delta$  4.56 ppm) corresponded to C(3)-H of 3-phenylindolinone in <sup>1</sup>H-nmr spectrum, a methine carbon ( $\delta$  51.5 ppm) in <sup>13</sup>C-nmr spectrum, and the molecular peak ( $m/z$  444) in ms spectrum that were not observed in the spectra of **I**. Lithium aluminum hydride reduction of **Ir** gave a product<sup>5</sup> which had absorption maxima for indole and indoline in the uv spectrum and molecular peak at  $m/z$  414 in the ms spectrum. Lithium aluminum deuteride reduction of **Ir** introduced three D's in the reduced product by extinguishing the AB type quartet for two H's around  $\delta$  3.96 ppm and one H in the aromatic region observed in the <sup>1</sup>H-nmr spectrum of the hydride reduced product, and giving molecular peak at  $m/z$  417 in the ms spectrum. The hydride reduced product was converted into



**VI**

its methiodide and the structure was determined by X-ray analysis<sup>6</sup> with a final R value of 0.1116 as 1,1-dimethyl-3-(1'-methyl-3'-phenylindol-6'-yl)-3-phenylindolinium iodide (**VI**).<sup>7</sup> The 3,6'-biindolinone linkage in the rearrangement product was clearly suggested by the structure of **VI**. For the determina-

tion of C(3) and C(3') configurations, X-ray analysis<sup>6</sup> was carried out on **AcIIr**<sup>8</sup> which was obtained from meso-5,5'-dichloro-3,3'-diphenylleucoisoidindigo (**II**). The structure was determined with the final R of 0.1109 as [3R(S), 3'R(S)]-1-acetyl-3-(1'-acetyl-5'-chloro-3'-phenylindolinon-6'-yl)-5-chloro-3-phenylindolinone (**AcIIr**). The ORTEP drawing of an enantiomer of **AcIIr** having 3R, 3'R-configurations was depicted in the Figure. The rearrangement reaction did not proceed with compounds **III**, **IV**, and **V**.

In case if the reaction would proceed via the inter-molecular mechanism, the rearrangement might be expected at least by **III** comparing the geometry around C(6) of it with that of **II**. None of the case gave the rearrangement product having the migrating moiety on C(4). Provided that the rearrangement proceeded via the intra-molecular mechanism in which the substituent on C(7) exerts the steric hindrance to the reaction intermediate, the plausible one might be a tandem Cope (or retro Claisen)-Claisen<sup>9</sup> rearrangement via C(7a) involving two [3s,3s] sigmatropic shifts.<sup>10</sup>

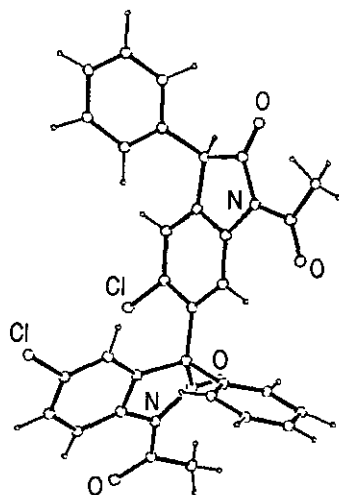


Figure The ORTEP drawing of an enantiomer of **AcIIr**.

#### REFERENCES AND NOTES

1. a) A. Inada and Y. Morita, *Heterocycles*, 1982, 19, 2193; b) T. Kato, Y. Morita, A. Inada, and H. Miyamae, The 104th Annual Meeting of Pharm. Soc. of Japan, Sendai, 1984; c) T. Kato, A. Inada, Y. Morita, and H. Miyamae, *Chem. Pharm. Bull.*, 1985, 33, 5270.
2. T. Suyama, T. Kato, H. Miyamae, and Y. Morita, *JUC Pharm. Sci.* '87, 1987, Poster Abstracts, S143.
3. meso-1,1'-Dimethyl-3,3'-diphenylleucoisoidindigo (**I**); plates (MeOH); mp 216°C; C<sub>30</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>; uv  $\lambda_{\text{max}}^{\text{CHCl}_3}$  nm(log  $\epsilon$ ) 242(4.22), 258(4.14), 290(3.55); monoclinic,  $P2_1/a$ ,  $a=18.664$ ,  $b=23.114$ ,  $c=10.642\text{\AA}$ ,  $\beta=91.00^\circ$ ,  $Z=8$ . The crystal structure of **I** was determined by X-ray analysis with the R value of 0.0614 having the  $\pm$  sc conformation.<sup>1b</sup>
4. Amorphous powder; C<sub>30</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>; uv  $\lambda_{\text{max}}^{\text{CHCl}_3}$  nm(log  $\epsilon$ ) 242(4.18), 258(4.10), 290(3.56).
5. Amorphous powder; uv  $\lambda_{\text{max}}^{\text{CHCl}_3}$  nm(log  $\epsilon$ ) 242(4.48), 265(4.33),

295(4.17).

6. UNICS III; T. Sakurai and K. Kobayashi, Rikagaku Kenkyusho Hokoku (Rep. Inst. Phys. Chem. Res. in Japanese), 1978, 55, 69: MULTAN; P. Main, S.E. Hull, L. Lessinger, G. Germain, J.P. Declercq, and M.M. Woolfson, 1978, MULTAN 78, A system of computer programs for the automatic solution of crystal structures for X-ray diffraction data, Univs. of York, England, and Louvain, Belgium.

7. Needles (MeOH), mp 167°C,  $C_{31}H_{29}N_2I$ , monoclinic,  $P2_1/c$ ,  $a=14.26$ ,  $b=13.89$ ,  $c=13.74$  Å,  $\beta=97.3^\circ$ ,  $Z=4$ . Of the total of 5198 independent reflections of  $2^\circ < 2\theta < 60^\circ$  obtained by the use of graphite-monochromated Cu-K $\alpha$  radiation with a computer-controlled Rigaku Denki AFC-5 four-circle auto-diffractometer, 1832 reflections with  $|F_o| > 3\sigma(F_o)$  were used for the calculation. The structure was solved using the heavy-atom method and refined by the block-diagonal least-squares procedure in UNICS III system.

8. Plates (Benzene), mp 165°C,  $C_{32}H_{22}N_2O_2Cl_2(C_6H_6)$ , triclinic,  $P\bar{1}$ ,  $a=18.14$ ,  $b=17.29$ ,  $c=8.60$  Å,  $\alpha=104.1$ ,  $\beta=73.1$ ,  $\gamma=136.9^\circ$ ,  $Z=2$ . 6634 of independent reflections of  $2^\circ < 2\theta < 120^\circ$  were measured and 4846 reflections of  $|F_o| > 3\sigma(F_o)$  were used for the further calculation. The structure was solved by the direct method using MULTAN 78 and refined by the block-diagonal least-squares procedure in UNICS III system.

9. R.P. Lutz, Chem. Revs., 1984, 84, 205 and literatures cited therein.

10. C.R. Frihart and N.L. Leonard, J. Am. Chem. Soc., 1973, 95, 7174.

Received, 30th October, 1991