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

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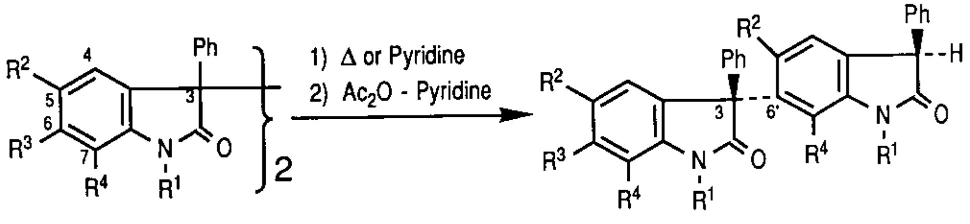
Abstract --- A unique and new rearrangement reaction of *meso*-3,3'-diphenylleucoisoindigos was examined. Structures of the products were determined as 3,6'-biindolinones by X-ray analyses. The formal reaction mechanism was supposed to be a tandem Cope-Claisen type rearrangement.

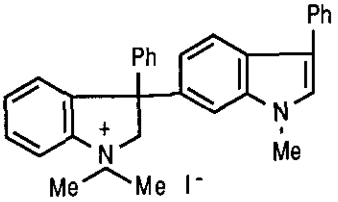
In the course of our study on leucoisoindigos,[1] an interesting rearrangement reaction of *meso*-3,3'-diphenylleucoisoindigos (I and II) to 3,6'-biindolinones (**Ir** - **IIr**) happened to be observed.[2]



| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **I** ; | Me | H | H | H |
| **II** ; | H | Cl | H | H |
| **III** ; | H | H | H | Cl |
| **IV** ; | H | H | Cl | H |
| **V** ; | H | Cl | H | Cl |

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **I r**; | Me | H | H | H |
| **II r**; | H | Cl | H | H |
| **Ac-II r** ; | Ac | Cl | H | H |

The rearrangement reactions proceeded in moderate yields (65-80 %) by heating neat leucoisoindigos 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'-diphenylleucoisoindigo (I)[1a,1b,3] was rearranged to a compound (Ir)[4] having a methine proton ( $\delta$ 4.56 ppm) corresponded to C(3)-H of 3-phenylindolinone in $^1$H-nmr spectrum, a methine carbon ( $\delta$ 51.5 ppm) in $^{13}$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[5] 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 $^1$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 its methiodide and the structure was determined by X-ray analysis[6] with a final R value of 0.1116 as 1,1-dimethyl-3-(1'-methyl-3'-phenylindol-6'-yl)-3-phenylindolinium iodide (**VI**).[7] The 3,6'-biindolinone linkage in the rearrangement product was clearly suggested by the structure of **VI**. For the determination of C(3) and C(3') configurations, X-ray analysis[6] was carried out on **AcIIr**[8] which was obtained from meso-5,5'-dichloro-3,3'-diphenylleucoisoindigo (**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.



**VI**

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[9] rearrangement via C(7a) involving two [3s,3s] sigmatropic shifts.[10]

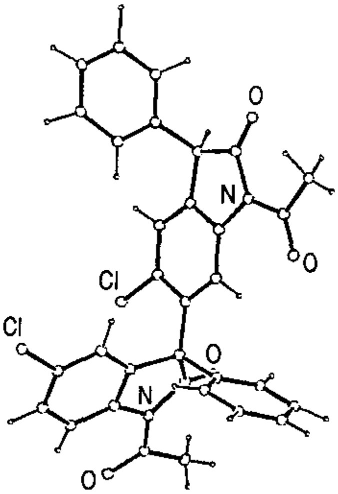


Figure The ORTEP drawing of an enantiomer of **AcIIr**.

REFERENCES AND NOTES

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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'-diphenylleucoisoindigo (**I**); plates (MeOH); mp 216°C; $C_{30}H_{24}N_2O_2$; uv $\lambda_{max}^{CHCl_3}$ nm(log ε) 242(4.22), 258(4.14), 290(3.55); monoclinic, $P2_1/a$, a=18.664, b=23.114, c=10.642Å, β=91.00°, Z=8. The crystal structure of **I** was determined by X-ray analysis with the R value of 0.0614 having the ± sc conformation.[1b]

4. Amorphous powder; $C_{30}H_{24}N_2O_2$; uv $\lambda_{max}^{CHCl_3}$ nm(log ε) 242(4.18), 258(4.10), 290(3.56).

5. Amorphous powder; uv $\lambda_{max}^{CHCl_3}$ nm(log ε) 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, β=97.3°, Z=4. Of the total of 5198 independent reflections of $2° < 2\theta < 60°$ obtained by the use of graphite-monochromated Cu-Kα 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, α=104.1, β=73.1, γ=136.9°, Z=2. 6634 of independent reflections of $2° < 2\theta < 120°$ 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.

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