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THE REACTIONS AND SYNTHESES WITH ORGANOMETALLIC COMPOUNDS IV. THE NEW SYNTHESIS OF OXINDOLE DERIVATIVES BY UTILIZATION OF ORGANONICKEL COMPLEX

Miwako Mori and Yoshio Ban

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, 060 Japan

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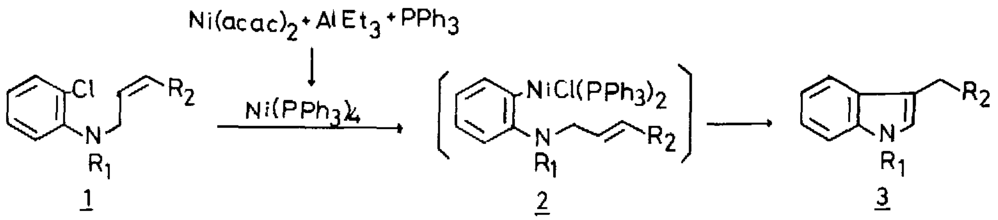
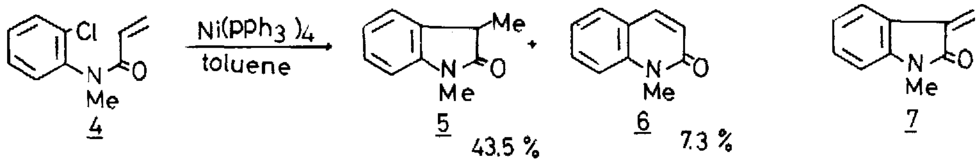
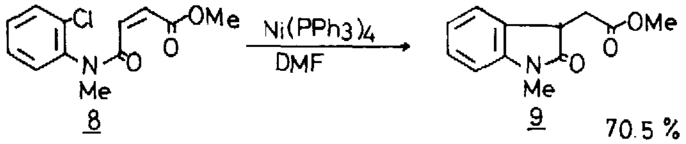
In the preceding communication,$^{1)}$ we described a new synthesis of indole derivatives from 2-chloro-N-alkyl-N-allylaniline by using tetrakis(triphenylphosphine)nickel[$Ni(PPh_3)_4$].

It was expected that this method could be extended to a new synthesis of oxindole derivatives when 2-chloro-N-alkyl-N-acrylanilides are chlosen as the starting materials. Thus, 2-chloro-N-methyl-N-acrylanilide(4) was mixed with $Ni(PPh_3)_4$ which was prepared *in situ* from $Ni(acac)_2$ and $AlEt_3$ in the presence of PPh_3 in toluene, and the mixture was heated at 50-60° for several hours to give 1,3-dimethyloxindole(5) in 43.5% yield with N-methylquinolone(6)(7.3%), but 1-methyl-3-methylene-oxindole(7) was never detected. Similarly, the compound(8), which was easily prepared from 2-chloro-N-methylaniline and maleic anhydride, was converted to N-methyl-2-hydroxyindolyl acetate(9) in a high yield(70.5%). In the case of 2-chloro-N-methyl-N-cinnamanilide(10), the reaction was relatively complicated. 1-Methyl-3-benzyloxindole(13) was a main product (57.4%) when toluene was used as a solvent, and the two stereoisomeric compounds(11 and 12)$^{2)}$ were obtained as minor products. When DMF was used as a solvent in place of toluene, the unsaturated compounds(11 and 12) became the main products as are shown in Table 1. These compounds(11 and 12) were easily reduced with $NaBH_4$ in EtOH to give 13.







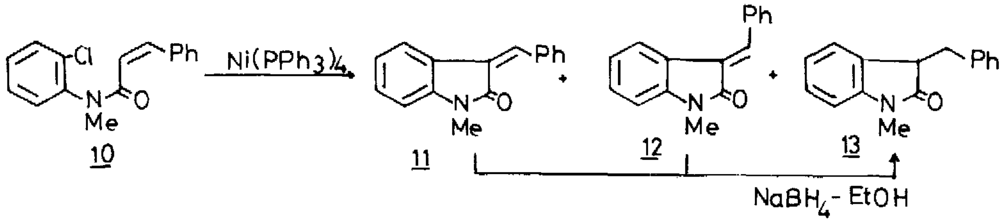
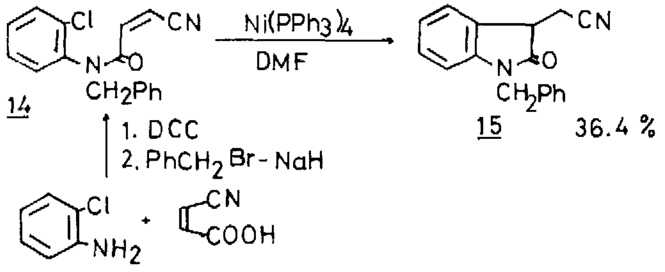
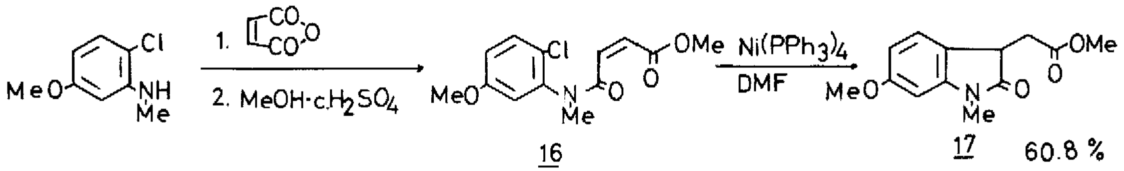


Table 1

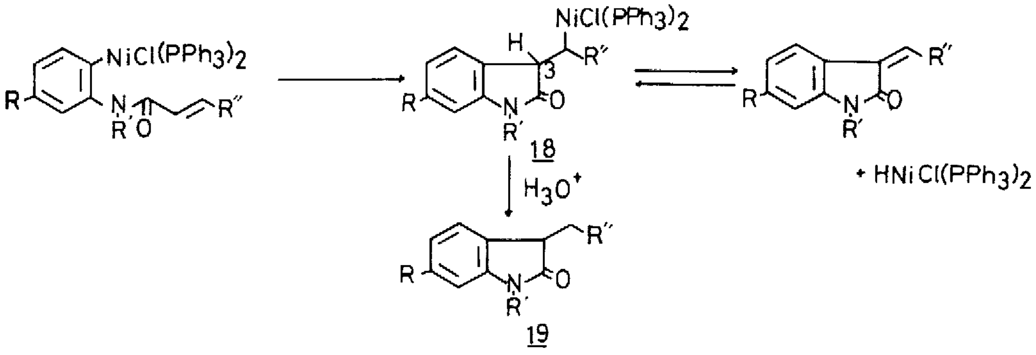
Solvent	Total Yield	Yield of 11	12	13	11 + 12 / 13
DMF	86.6 %	55.0 %	10.9 %	20.7 %	3/1
Toluene	84.0	24.3	2.3	57.4	1/2



Moreover, the compound (14), which was prepared by condensation of 2-chloroaniline with β-cyanoacrylic acid, followed by benzylation with NaH and benzyl bromide, was reacted with $Ni(PPh_3)_4$ in the same manner to afford 15 in 36.4% yield. This compound might be a very useful intermediate for the synthesis of indole alkaloids.[3)] The present method is particularly advantageous for the synthesis of oxindole derivatives with the substituents on the benzene ring, because the direction of cyclization is destined for the position of the original aromatic halide. Therefore, the preparation of 6-methoxyoxindole derivatives, which was necessary for the synthesis of the natural alkaloids, was attempted with success according to this method. Thus the compound (16) was warmed with $Ni(PPh_3)_4$ in DMF at 50-60° for 5 hours to provide 17 in 60.8% yield.



One of the reason why the reduced products (5, 9, 13, 15 and 17) were generated, may be due to the result that $AlEt_2(acac)$ acted as a reducing agent during the reaction. Therefore, $Ni(PPh_3)_4$ was carefully separated from the reaction mixture under the stream of argon to make it free from $AlEt_2(acac)$, but even with this pure crystalline $Ni(PPh_3)_4$, the reduced products were still obtained. It may be assumed that 18 was relatively stable since C-3 hydrogen of that compound (18) could not be easily removed as a hydride, and it was decomposed with 10% HCl to give the reduced product (19).



These results exhibit that the various oxindole derivatives could be easily synthesized according to this method. Further studies are in progress.

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References and Notes:

1. M. Mori and Y. Ban, Tetrahedron Letters, the preceding communication.
2. The structures of the isomeric compounds (11 and 12) were deduced on the basis of Antey's report. R. L. Antrey and F. C. Tahk, Tetrahedron, **23**, 901 (1967).
3. Y. Ban, T. Ohnuma, M. Nagai, Y. Sendo and T. Oishi, Tetrahedron Letters, 5023 (1972).