

A simple synthesis of 7-substituted 1-acetyl-2,3-dihydroindoles

著者	Somei Masanori, Kawasaki Toshiya, Ohta Toshiharu
journal or publication title	Heterocycles
volume	27
number	10
page range	2363-2365
year	1988-01-01
URL	http://hdl.handle.net/2297/4312

A SIMPLE SYNTHESIS OF 7-SUBSTITUTED 1-ACETYL-2,3-DIHYDROINDOLES¹

Masanori Somei,* Toshiya Kawasaki, and Toshiharu Ohta
 Faculty of Pharmaceutical Sciences, Kanazawa University
 13-1 Takara-machi, Kanazawa 920, Japan

Abstract ——— 7-Cyano-, 7-hydroxy-, 7-methoxycarbonyl-, 7-methyl-, 7-nitro-, and 7-phenyl-1-acetyl-2,3-dihydroindoles are prepared in two steps (or one pot) from 1-acetyl-2,3-dihydroindole.

Although 7-substituted 1-acetyl-2,3-dihydroindoles are suitable building blocks for the synthesis of biologically interesting indole alkaloids² having a substituent at the 7-position, they are available only through a laborious multistep route. We now wish to describe a simple synthesis method for them utilizing (1-acetyl-2,3-dihydroindol-7-yl)thallium bis(trifluoroacetate) (2), readily available from 1-acetyl-2,3-dihydroindole (1) as reported previously.³

We first applied our stannation-thallation (tin-thall) reaction⁴ for obtaining 7-alkyl and 7-aryl substituted compounds. Treatment of 2 with tetramethyltin in the presence of a catalytic amount of palladium acetate (Pd(OAc)₂) in N,N-dimethylformamide (DMF) at 120°C for 4 h afforded 1-acetyl-2,3-dihydro-7-methylindole⁵ (3, mp 89-90°C) and 1 in 32% and 45% yields, respectively. Similarly, 1-acetyl-2,3-dihydro-7-phenylindole (4, mp 125.5-126°C) was prepared in 35% yield together with 63% yield of 1 by the reaction of 2 with tetraphenyltin.

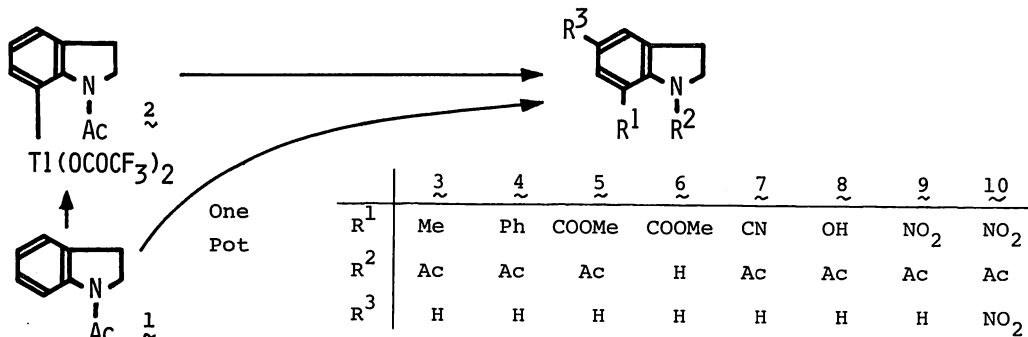
Introduction of methoxycarbonyl group into the 7-position under the usual reaction conditions^{6a,b} was not satisfactory. Thus, the reaction of 2 with carbon monoxide in the presence of a catalytic amount of Pd(OAc)₂ in methanol at 80°C for 3 h, followed by the treatment with ethereal diazomethane, afforded methyl 1-acetyl-2,3-dihydroindole-7-carboxylate (5, mp 103-104°C) and 1 in 27% and 44% yields, respectively. Interestingly, addition of chromium hexacarbonyl to the above reaction medium was newly found to improve the yield of the desired product (5) remarkably. Using one molar equivalent of chromium hexacarbonyl, 5 was obtained in 52% yield together with methyl 2,3-dihydroindole-7-carboxylate (6, mp 69-69.5°C) and 1 in 11% and 23%

yields, respectively.

1-Acetyl-2,3-dihydroindole-7-carbonitrile (2, mp 133.5-134°C, lit.⁷ mp 124°C) could be produced in 69% yield by the reaction of 2 with five molar equivalents of cuprous cyanide^{6b,c} in DMF at 120°C for 6 h. On the other hand, our phenol synthesis method⁸ from thallium compound was successfully applied to 2 and its reaction with cupric sulfate pentahydrate in DMF-H₂O (1:1, v/v) at 125°C for 6 h afforded 1-acetyl-2,3-dihydro-7-hydroxyindole (8, mp 114.5-115°C; lit.⁹ mp 112-114°C) in 62% yield. One pot synthesis of 8 from 1 could be readily carried out in 42% overall yield by the initial thallation with thallium tris(trifluoroacetate), followed by the reaction with cupric sulfate pentahydrate.

Conversion of carbon-thallium bond to carbon-nitrogen bond is reported by the reaction with sodium nitrite.¹⁰ However, the attempted nitration of 2 according to the reported method¹⁰ gave 1-acetyl-2,3-dihydro-7-nitroindole (9, mp 163-164°C) in poor yield (3-26%) under various reaction conditions in addition to variable yields (0-26%) of 1-acetyl-2,3-dihydro-5,7-dinitroindole (10, mp 217-218°C, lit.¹¹ mp 210-212°C). Although Taylor¹² and Uemura¹⁰ reported that the reaction of thallium compounds with nitronium ion could not change the carbon-thallium bond to a carbon-nitrogen bond, we expected that the addition of cupric (or cuprous) ion would alter the reaction to the desired direction. Based on this idea, we finally found a new method which produced the desired mononitro compound (9) selectively. Thus, treatment of 2 with two molar equivalents of cupric nitrate trihydrate in DMF-acetic anhydride (1:1, v/v) at 80°C for 5 h afforded 46% yield of 9 without any detectable amount of 10. Generalization of this reaction is now in progress.

In conclusion, various 7-substituted 2,3-dihydroindoles are easily available utilizing 2 as a common synthetic intermediate, though optimum reaction conditions are not made. Since the isolation of 2 is not necessary and one pot operation is possible,^{3d} the present method should find considerable application in organic synthesis.



REFERENCES AND NOTES

1. This report is part XLVI of a series entitled "The Chemistry of Indoles".
Part XLV: M. Somei, S. Sayama, K. Naka, and F. Yamada, Heterocycles, 27, 1585 (1988).
2. N.B. Perry, J.W. Blunt, and M.H.G. Munro, Tetrahedron, 44, 1727 (1988); K. Takeshi, H. Shibata, Y. Matsushima, and T. Iijima, Agric. Biol. Chem., 51, 3445 (1987); N. Kawahara, K. Nozawa, S. Nakajima, and K. Kawai, J. Chem. Soc., Chem. Commun., 1986, 1495; J.E. Swagzdis, R.W. Wittendorf, R.M. DeMarinis, and B.A. Mico, J. Pharm. Sci., 75, 925 (1986); C.M. Maes, P.S. Steyn, R. Vleggaar, G.W. Kirby, D.J. Robins, and W.M. Stark, J. Chem. Soc., Perkin I, 1985, 2489. See also reference 3.
3. a) M. Somei and Y. Saida, Heterocycles, 23, 3113 (1985); b) M. Somei, T. Funamoto, and T. Ohta, ibid., 26, 1783 (1987); c) M. Somei, Y. Saida, and N. Komura, Chem. Pharm. Bull., 34, 4116 (1986); d) M. Somei, Y. Saida, T. Funamoto, and T. Ohta, ibid., 35, 3146 (1987).
4. M. Somei, F. Yamada, and K. Naka, Chem. Pharm. Bull., 35, 1322 (1987).
5. R. Ikan and Y. Fetal, J. Chem. Eng. Data, 16, 125 (1971) [Chem. Abstr., 74, 76253h (1971)].
6. a) R.C. Rarock and C.A. Fellows, J. Am. Chem. Soc., 104, 1900 (1982); b) F. Yamada and M. Somei, Heterocycles, 26, 1173 (1987); c) E.C. Taylor and A.H. Katz, Tetrahedron Lett., 25, 5473 (1984).
7. R. Ikan and E. Rapaport, Tetrahedron, 23, 3823 (1967).
8. M. Somei, E. Iwasa, and F. Yamada, Heterocycles, 24, 3065 (1986).
9. R.R. Hunt and R.L. Rickard, J. Chem. Soc., (C), 1966, 344.
10. S. Uemura, A. Toshimitsu, and M. Okano, Bull. Chem. Soc. Japan, 49, 2582 (1976); Idem, J. Chem. Soc., Perkin Trans. I, 1978, 1076; B. Davies and C.B. Thomas, ibid., 1975, 65; E.C. Taylor, R.H. Danforth, and A. McKillop, J. Org. Chem., 38, 2088 (1973).
11. W.E. Noland and K.R. Rush, J. Org. Chem., 29, 947 (1964)
12. E.C. Taylor, H.W. Altland, and A. McKillop, J. Org. Chem., 40, 3441 (1975).

Received, 12nd July, 1988