The Synthesis of 7-Methoxyisoflavan-4α-ol[1]

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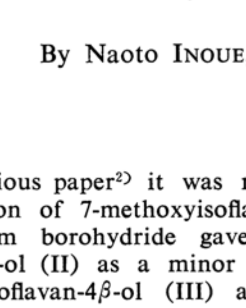
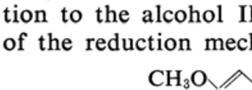
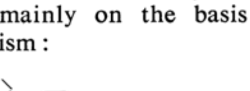
In a previous paper[2] it was reported that the reduction of 7-methoxyisoflavanone[3] (I) with sodium borohydride gave 7-methoxyisoflavan-4α-ol (II) as a minor product and 7-methoxyisoflavan-4β-ol (III) as the main product. Trans configuration was tentatively assigned to the alcohol II and cis configuration to the alcohol III, mainly on the basis of the reduction mechanism:



I



II



III

The following experiments were undertaken to find a synthetic method which affords only II in a good yield. A solution of 7-methoxyisoflavan[2] (0.25 g.) and lead tetraacetate (0.76 g.) in dry benzene (16.8 g.) was refluxed for 6 hr.; The reaction was run until an iodine-starch test for unreacted lead tetraacetate became negative. From this reaction there was obtained II-acetate (45 mg.), but no III-acetate. Acetic acid was not used as a solvent in this reaction, since the acetate of III had been found to be converted into the acetate of II by mild treatment with acetic acid.[2] 7-Methoxy-4-aminoisoflavan acetate (IV), m. p. 145°C (Found: C, 68.73; H, 6.63; N, 4.27. Calcd. for $C_{18}H_{21}O_4N$: C, 68.55; H, 6.71; N, 4.44%) was prepared from the oxime of I[3] by catalytic hydrogenation over a palladium charcoal catalyst in acetic acid. Hydrochloride (V), m. p. 220°C (Found: C, 65.98; H, 6.12; N, 4.47. Calcd. for $C_{16}H_{18}O_2NCl$: C, 65.86; H, 6.22; N, 4.83%). 7-Methoxy-4-aminoisoflavan, m. p. 111°C (Found: C, 75.38; H, 6.63; N, 5.25. Calcd. for $C_{16}H_{17}O_2N$: C, 75.27; H, 6.71; N, 5.49%). A solution of sodium nitrite (0.24 g. in 10 ml. water) was added, over a 30 min. period, to a stirred solution of V (0.49 g.) in 50% acetic acid (30 ml.) at 0°C. The mixture was then stirred for a further 30 min. at room temperature. After the usual treatment, II (70 mg.) was obtained and III was not.[5] With a view of obtaining II as the result of equilibration, III (300 mg.) was treated with aluminum isopropoxide (300 mg., molar ratio to III : 1.3) in a mixture of isopropyl alcohol (10 ml.) and acetone (0.1 ml.) at 95∼100°C for 96 hr. The reaction mixture was poured into ice-water (300 ml.) containing concentrated hydrochloric acid (1 ml.). The precipitates were collected, dried and recrystallized from ethyl alcohol. Needles with an m. p. of 111°C were obtained, and II was not found. The product with an m. p. of 111°C did not show a depression of melting point on admixture with the 4-isopropoxy-7-methoxyisoflavan which had been

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[1] Part VII of Studies of Synthetic Isoflavanones. Presented at the 16th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1963.

[2] Submitted for publication to this Bulletin.

[3] N. Inoue, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **79**, 218 (1958); N. Inoue, *Science Repts. Tohoku Univ.*, First Ser., XLV, 68 (1961).

[4] Cf. M. M. Bokadia, R. B. Brown and W. Cummings, *J. Chem. Soc.*, **1960**, 3380.

[5] Cf. R. Bognár, M. Rákosi, H. Fletcher, D. Kehoe, E. M. Philibin and T. S. Wheeler, *Tetrahedron*, **18**, 135 (1962).

obtained as a by-product in the Meerwein-Ponndorf reduction of I.[2] When the molar ratio of aluminum isopropoxide to III was 1 : 1, III was recovered unchanged.

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