A SIMPLE SYNTHESIS OF 1,3-BENZOXAZIN-4-ONE DERIVATIVES

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Treatment of salicyl chloride (2), prepared from salicylic acid and oxalyl chloride, with isoquinoline (1) gave the isoquinolobenzoxazinone (3). Reaction of (2) with 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (4), 3,4-dihydro-6-methoxy-β-carboline (6), and 3,4-dihydro-6-methyl-β-carboline (8) afforded the corresponding 1,3-benzoxazin-4-one derivatives (5), (7), and (9) respectively.

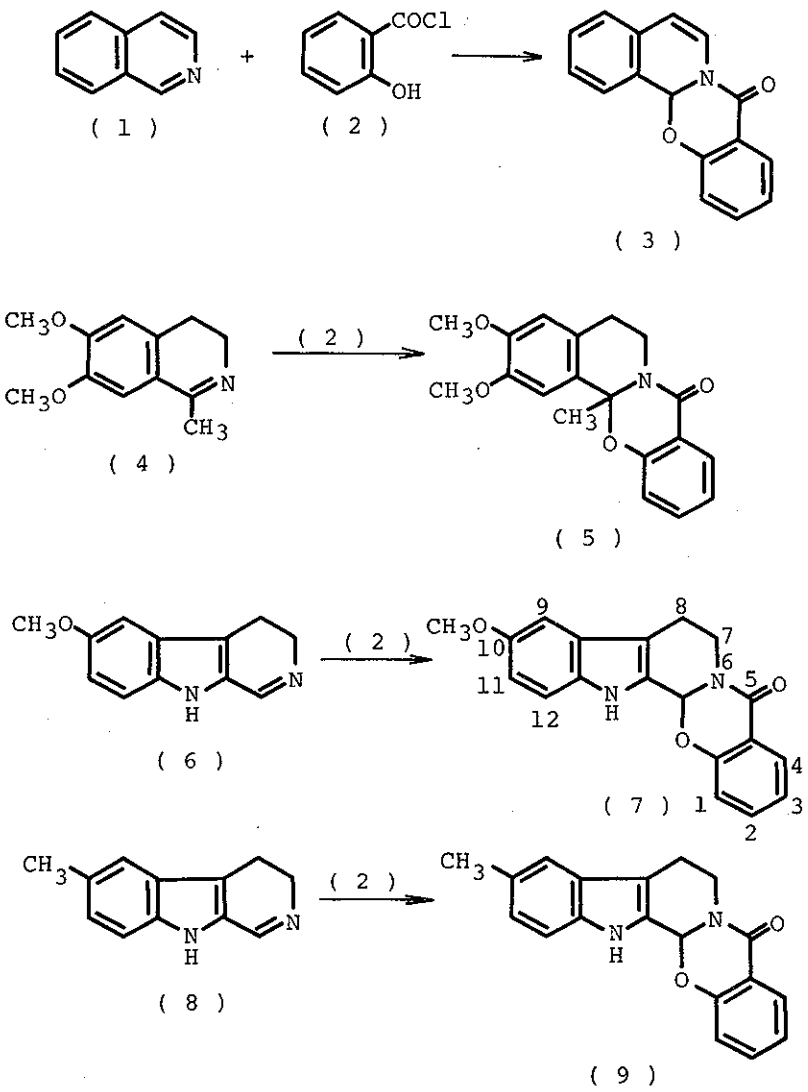
Previously we reported a novel synthetic method for 1,3-benzoxazin-4-one derivatives using the reaction of salicyl chloride, prepared from salicylic acid and thionyl chloride, with either imines or amides.[1] Carrying out further studies on this method, we found that the condition for the reaction of salicylic acid with thionyl chloride is difficult and the chlorination by thionyl chloride is therefore unsuitable for the preparation of salicyl chloride to be used in situ in its reaction with either imines or amides.

Adams and Ulich[2] reported the preparation of salicyl chloride from salicylic acid and oxalyl chloride without specifying clearly the reaction conditions. We then prepared salicyl chloride by the following procedure, somewhat adapted from that of Adams and Ulich: a mixture of 2 mmol of salicylic acid and 5 mmol of oxalyl chloride in 20 ml of dry benzene was refluxed for 2 hr. Evaporation of the solvent and the excess of oxalyl chloride at 25° under reduced pressure afforded salicyl chloride (2) which was treated with 2.2 mmol of isoquinoline (1) in dry benzene. The resulting mixture was then set aside overnight at room temperature. Filtration afforded recovered isoquinoline hydrochloride and the filtrate was washed with 5 % sodium carbonate solution and water respectively. Evaporation of the solvent gave the isoquinolobenzoxazinone (3), in 87 % yield (calculated from salicylic acid), whose melting point and spectral data are identical with those reported.[1] The fact that this yield is higher than that previously reported one[1] by us proves that the new method is an effective one.

Treatment of salicyl chloride (2), prepared from salicylic acid and oxalyl chloride, with 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (4) afforded, in 85 % yield, the corresponding 1,3-benzoxazin-4-one (5), identical with the authentic sample.[1]

Similarly the reaction of 3,4-dihydro-6-methoxy-β-carboline (6) with salicyl chloride (2) in dry benzene gave, in 83 % yield, the condensation product (7), $C_{19}H_{16}O_3N_2$ [Calcd.: C, 71.24; H, 5.03; N, 8.75. Found: C, 70.75; H, 4.84; N, 8.55] as colourless crystals, m.p. 225 - 227° (from ethyl acetate-n-hexane), [ν_{max} ($CHCl_3$) 1660 (CON<), 3499 cm^{-1} (NH); δ ($CDCl_3$) 2.63 - 3.40 (4H, m, CH_2CH_2),

Scheme



3.86 (3H, s, OCH_3), 6.43 (1H, s, $-CH<^{N<}_{O-}$), 6.76 - 7.80 (6H, m, ArH), 8.07 (1H, q, J 2 Hz and J 7 Hz, C_4-H).

The reaction of salicyl chloride (2) with 3,4-dihydro-6-methyl-β-carboline (8) gave the corresponding 1,3-benzoxazin-4-one (9) as yellow crystals, m.p. 174 - 176° (from ethyl acetate-n-hexane), [ν_{max} ($CHCl_3$): 1660 (CON<), 3499 cm^{-1} (NH); δ ($CDCl_3$): 2.46 (3H, s, CH_3), 2.60 - 3.40 (4H, m, CH_2CH_2), 6.36 (1H, s, $-CH<^{N<}_{O-}$), 6.56 - 7.66 (6H, m, ArH), 8.00 (1H, q, J 2 Hz and J 7 Hz, C_4-H); m/e (M^+) 304.

Thus we have succeeded in improving our synthetic procedure for 1,3-benzoxazin-4-one derivatives to make it a reliable and effective one.

References

1. T. Kametani, T. Higa, C. V. Loc, M. Ihara, and K. Fukumoto, Heterocycles, 1977, 6, 255.

2. R. Adams and L. H. Ulich, J. Amer. Chem. Soc., 1920, 42, 599.

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