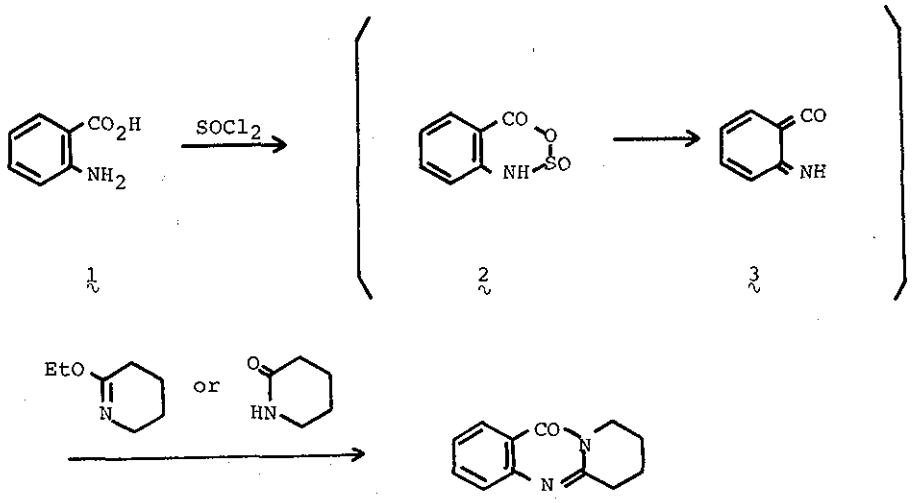
A NOVEL AND SIMPLE SYNTHESIS OF 1,3-BENZOXAZIN-4-ONE DERIVATIVES

Tetusji Kametani,* Terumi Higa, Chu Van Loc, Masataka Ihara,
and Keiichiro Fukumoto
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan

Treatment of salicyl chloride (6) with 3,4-dihydro-β-carboline (7) gave indolo[2^1,3^1:3,4]pyrido[2,1-b][1,3]-benzoxazin-4-one (9), which was also obtained by a reaction of 6 with N-formyltryptamine (8). The same reaction of 6 with 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (11) and isoquinoline (13) afforded the corresponding pyridobenzoxazinones (12) and (14), respectively.

Previously we have developed a new and one-step synthesis of quinazolones (4) by a cycloaddition reaction of the iminoketene 3, generated *in situ* from anthranilic acid 1 *via* the sulfinamide anhydride 2, to imines[1,2] and amides[3]. In a continuation of this work, we examined a reactivity of salicylic acid (5), instead of antharanilic aicd (1), on the basis of our finding[1-3], and now we wish to report a novel and simple synthetic method for 1,3-benzoxazin-4-one system by the reaction with imines or amide.

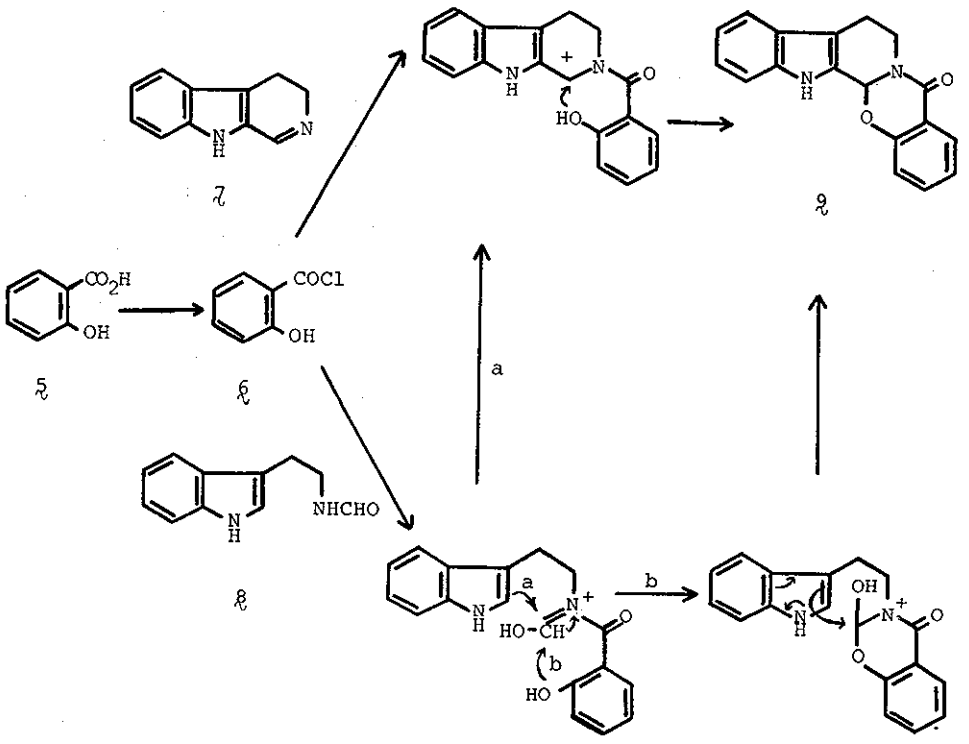
Chart 1



Heating salicylic acid (5) with an excess of thionyl chloride in dry benzene in a current of nitrogen for 4 hr gave salicyl chloride (6)[4], whose treatment with an equimolar amount of 3,4-dihydro-β-carboline (7) in dry benzene at room temperature for 2 hr, followed by silica gel column chromatography using benzene as eluant, afforded the condensation product, $C_{18}H_{14}N_2O_2$ [microanalysis and mass spectrometry, m/e 290 (M^+)], mp 234 ∿ 235° (from ethyl acetate-hexane), as colourless crystals in 81.4 % yield. The ir [ν_{max} ($CHCl_3$) 3500 (NH) and 1660 cm^{-1} (CON<)] and nmr [δ($CDCl_3$) 2.8 ∿ 3.6 (4H, m, CH_2CH_2), 6.4 (1H, s, $ArCH<^{N=}_{O-}$) and 7.2 ∿ 8.1 (8H, m, ArH) indicated this compound to be indolo-[2^1,3^1:3,4]pyrido[2,1-b][1,3]benzoxazin-4-one (9). Treatment of salicyl

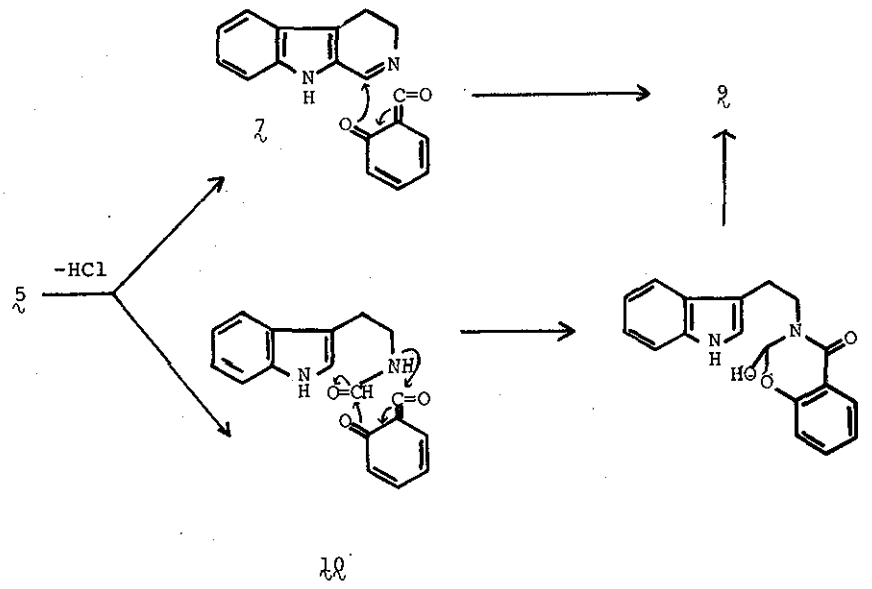
chloride (5) with 1.2 molar equivalent of N-formyltryptamine (8) in dry benzene and chloroform under the same conditions as above gave, in 73.6 % yield, the indolopyridobenzoxazepine (9) which was identical with the authentic sample, prepared from 7, in spectral and mp comparisons. These reaction would proceed as shown in Chart 2.

Chart 2



However, the following mechanism would not be ruled out; salicyl chloride (6) might be firstly converted into the more reactive oxoketene (10)[4,5] by an intramolecular elimination of hydrogen chloride and then the oxoketene (10) would react with 3,4-dihydro-β-carboline (7) or N-formyltryptamine (8) in a manner due to an intermolecular cycloaddition as indicated in Chart 3.

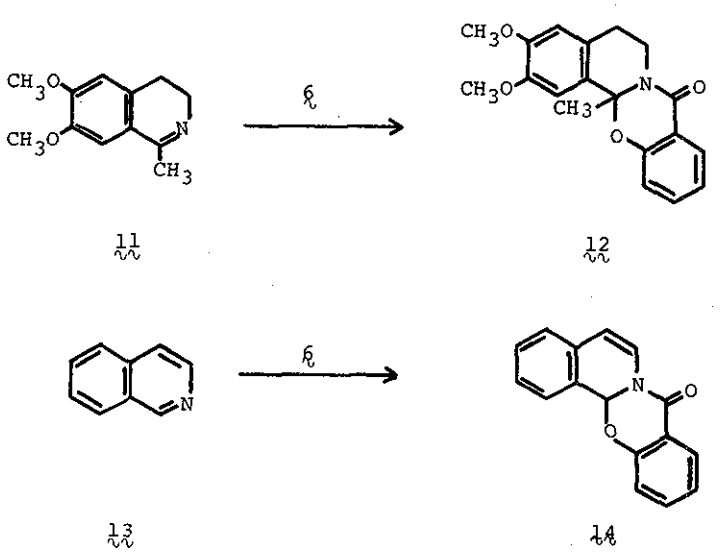
Chart 3



3,4-Dihydro-6,7-dimethoxy-1-methylisoquinoline (11) reacted with salicyl chloride (6) in dry benzene at room temperature for 16 hr to form the corresponding 1,3-benzoxazin-4-one (12), mp 153 ∿ 155° (from ethyl acetate-hexane) [ν_{max} ($CHCl_3$) 1650 cm^{-1} (CON<); δ($CDCl_3$)

1.85 (3H, s, CH_3), 2.5 ∿ 3.2 (4H, m, CH_2CH_2), 3.8 and 3.9 (each 3H, s, OCH_3) and 6.9 ∿ 8.6 (6H, m, ArH)] in 65 % yield. Similarly, the reaction of isoquinoline (13) with 6 in dry benzene under the same conditions afforded, in 75 % yield, the isoquinolobenzoxazinone (14), mp 130 ∿ 132° (from ethyl acetate) [ν_{max} ($CHCl_3$) 1675 cm^{-1} (CON<); δ($CDCl_3$) 5.75 (1H, d, J 8 Hz, ArCH=CHN), 6.7 (1H, s, ArCH<N=O-), 6.95 ∿ 7.6 (8H, m, ArH) and 7.95 (1H, d, J 8 Hz, ArCH=CHN).

Chart 4



We have developed a novel and simple synthetic procedure for 1,3-benzoxazin-4-one system, and a further extension[5] of this reaction using thiosalicylic acid, o-aminobenzyl alcohol and so on is now in progress.

References

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