Communications to the Editor

[Chem. Pharm. Bull. 32(4)1665—1666(1984)]

SYNTHESIS OF ANIBINE USING KETENE DITHIOACETAL

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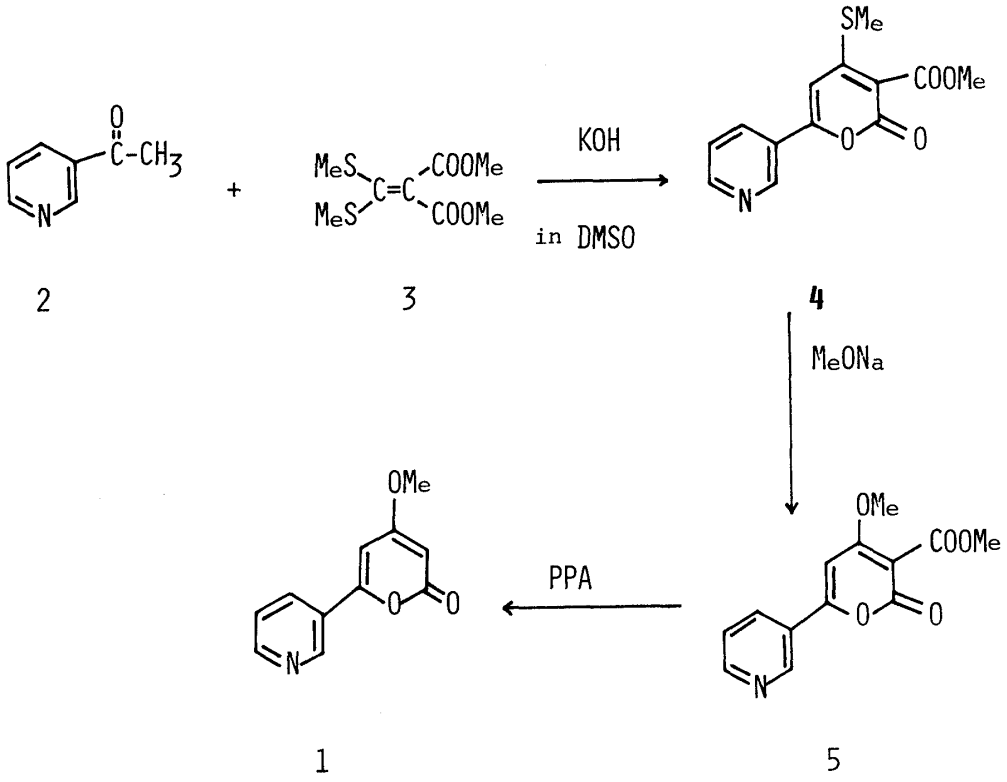
Synthesis of anibine using 3-acetylpyridine and dimethyl bis(methylthio)methylenemalonate is described.

KEYWORDS——anibine; ketene dithioacetal; 3-acetylpyridine; dimethyl bis(methylthio)methylenemalonate; Aniba rosaeodora Duke

A number of 4-hydroxy-2H-pyran-2-ones and their methyl ethers have been isolated from natural source and synthesized by many groups.[1] Mostly, they have phenyl or styryl groups at the 6-position of pyran-2-ones. Anibine (1) is unique alkaloid having a 2-oxo-2H-pyran-6-yl group. It was isolated from the wood of South American rosewood trees(Aniba rosaeodora Duke) by Djerassi et al. in 1957.[2-4] We now wish to report a simple total synthesis of anibine using ketene dithioacetal, dimethyl bis(methylthio)methylenemalonate (3).[5]

The key intermediate in this study was methyl 4-methylthio-2-oxo-6-(3-pyridyl)-2H-pyran-3-carboxylate (4). Recently, we reported the convenient synthesis of paracotoin and related naturally occurring 2H-pyran-2-ones by the condensation of aryl acetyl compounds with 3.[6-9] We applied that reaction to the preparation of anibine.

The reaction of 3-acetylpyridine (2) with 3 in the presence of powdered potassium hydroxide as a base in dimethyl sulfoxide gave 4 as pale yellow needles, mp 193°C, in 34% yield. This reaction was carried out at room temperature for 3 h with stirring. 4: IRν(KBr)cm^{-1}: 1750, 1688(C=O); UVλ_{max}^{EtOH}nm(log ε): 246(4.20), 325(4.23); NMR(DMSO-d_6)δ: 2,67(3H, s, SMe), 3.77(3H, s, OMe), 7.22(1H, s, 5-H), 7.59(1H, dd, J=5, 8 Hz, 5′-H), 8.36(1H, dd, J=1.5, 8 Hz, 4′-H), 8.78(1H, dd, J=2, 8 Hz, 6′-H), 9.24(1H, d, J=1.5 Hz, 2′-H). Compound 4 was allowed to react with sodium methoxide in methanol under refluxing to give methyl 4-methoxy-2-oxo-6-(3-pyridyl)-2H-pyran-3-carboxylate (5) as tan needles, mp 242°C, in 67% yield. The treatment of 5 with polyphosphoric acid (PPA) at 100°C for 5 h afforded anibine, 4-methoxy-6-(3-pyridyl)-2H-pyran-2-one (1) as colorless needles, mp 176°C (lit[2]: mp 178-180°C), in 86% yield. 5: IRν(KBr)cm^{-1}: 1763, 1713(C=O); UVλ_{max}^{EtOH}nm(log ε): 233(4.35), 266(3.80), 338 (4.23); NMR($CDCl_3$)δ: 3.91(3H, s, OMe), 4.09(3H, s, OMe), 6.77(1H, s, 5-H), 7.50(1H, dd, J=5, 8 Hz, 5′-H), 8.25(1H, bd, J=8 Hz, 4′-H), 8.75(1H, dd, J=2, 5 Hz, 6′-H), 9.13(1H, d, J=1.5 Hz, 2′-H). Anibine: NMR($CDCl_3$)δ: 3.89(3H, s, OMe), 5.60(1H, d, J=2.2 Hz, 3-H), 6.55(1H, d, J=2.2 Hz, 5-H), 7.58(1H, dd, J=5, 8 Hz, 5′-H), 8.32(1H, m, 4′-H), 8.72(1H, dd, J=1.5 5 Hz, 6′-H), 9.19(1H, d, J=1.5 Hz, 2′-H).



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(Received February 13, 1984)