STERIC EFFECTS IN THE RING CLOSURE REACTIONS OF 2-(2-PYRIDYLAMINOMETHYLENE)SUCCINATES

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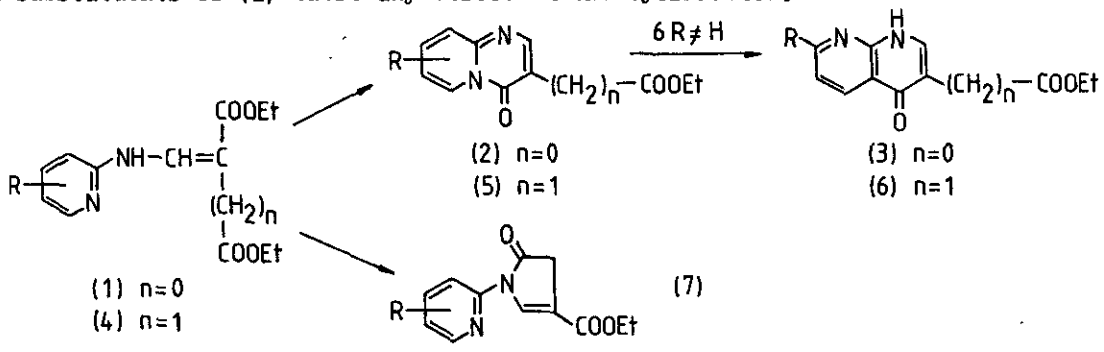
The ring closure of the 6-substituted (2-pyridylaminomethylene)malonates (1) leading to naphthyridines (3) and not to pyridopyrimidines (2), was explained by the steric hindrance effect of the 6-substituent of (1) [JACS 1948, 70, 3348]. Later it was shown that the naphthyridines (3) are formed not directly from (1) but from (2) [JCS Perkin I, 1977, 789]. It remained uncleared, whether the 6-substituents of (1) exert any effect on the cyclization.



R=H, Me, COOEt, 4,6-diMe, 3-OH, 6-OH, 5-Cl, 3,5-diCl, 3-NO_2, 5-NO_2, 6-NHAc

The *homologous* 2-(2-pyridylaminomethylene)succinates (4) by giving rise to pyridopyrimidines (5) and pyridylpyrrolinones (7) in competitive reactions, offered an opportunity to study the steric effect of the 6- and 3-substituents.

Cyclization of (4) was effected by heating in Dowtherm A; by $POCl_3$-PPA; and by sodium ethoxide in ethanol. Cyclic products (5), (6) and (7) arose in good overall yields. The ratio of the products depended on the reaction conditions and on the substituent (R). In the thermal ring closures,at 250 °C, practically no steric hindrance was observed. In the $POCl_3$-PPA ring closures, at 110 °C, a pronounced steric hindrance appeared. In sodium ethoxide, at 25 °C, the 6- and 3-substituents fully inhibited the formations of the respective cyclic products.