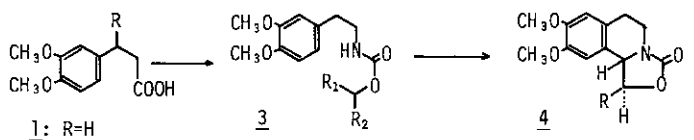
SYNTHESIS OF PYRIDINE AND ISOQUINOLINE DERIVATIVES BY CYCLIZATION OF N-ACYLIMINIUM ION INTERMEDIATES

Shinzo Kano, Yoko Yuasa, Tsutomu Yokomatsu, and Shiroshi Shibuya

Tokyo College of Pharmacy, 1432-1 Horinouchi, Hachioji, Tokyo 192-03, Japan

π Cyclization of α-oxaacyliminium ion intermediates, derived from the 3-arylpropionic acids (1 and 2), was applied to a synthesis of oxazolo[4,3-a]isoquinolines. Reduction of the carbamates (3a-3d) with DIBAH at -78°C or ozonolysis of the carbamates (3e-3g), followed by cyclization with formic acid afforded the corresponding oxazolo[4,3-a]isoquinolines (4). In a similar fashion, 6-aryloxazolo[4,3-a]isoquinolines (5) were obtained with high stereoselectivity. The method was extensively applied to a synthesis of pyrimido[6,1-a]isoquinolines (6).



1: R=H

2: R=

a: R_1=COOEt, R_2=H
b: R_1=COOEt, R_2=CH_3
c: R_1=COOEt, R_2=Et
d: R_1=$COOCH_2$, R_2=C_6H_5
e: R_1=CH=CH_2, R_2=H
f: R_1=CH=CH_2, R_2=CH_3
g: R_1=CH=CH_2, R_2=Et

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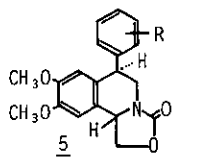
a: R=H
b: R=CH_3
c: R=Et
d: R=C_6H_5



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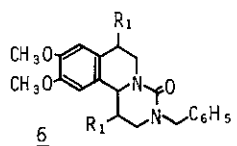
a: R=H, b: R=4-OCH_3
c: R=2-OCH_3, d: R=4-CH_3
d: R=3,4-$(OCH_3)_2$



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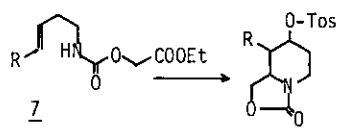
a: R_1=R_2=H
b: R_1=H, R_2=CH_3
c: R_1=C_6H_5, R_2=H
d: R_1=C_6H_5, R_2=CH_3

This π cyclization reaction was applied to a synthesis of pyridine and 4-phenyldecahydroisoquinoline derivatives. Reduction of 7 and 8 with DIBAH, followed by cyclization with p-toluenesulfonic acid in $CHCl_3$ gave 9 and 10, respectively. Treatment of 11 with paraformaldehyde in formic acid yielded the 6-oxygenated trans-4a-phenyldecahydroisoquinoline (12).



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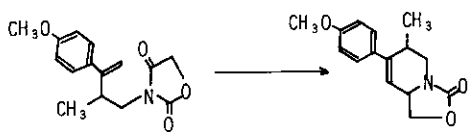
a: R=CH_3, b: R=Et

9



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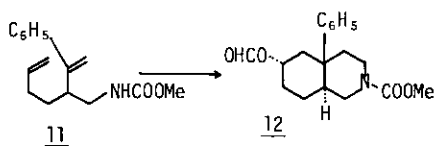

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