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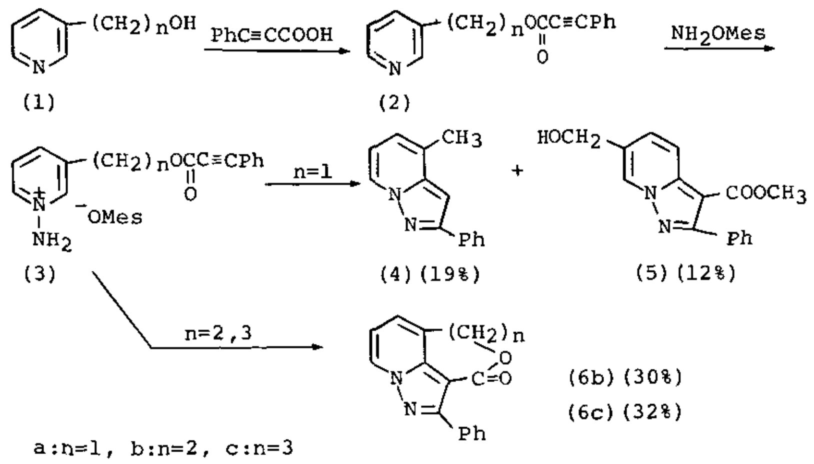
INTRAMOLECULAR 1,3-DIPOLAR CYCLOADDITION OF 3-PHENYLPROPIOLOYLOXYALKYLPYRIDINIUM N-IMINES

Yasuyoshi Miki,* Michiko Konishi, Noriko Nishikubo, Toshihiko Yoshimaru, and Shoji Takemura
Faculty of Pharmaceutical Sciences, Kinki University, 3-4-1
Kowakae, Higashi-Osaka, 577, Japan

Abstract —— Treatment of N-aminopyridinium salt (3a) with base in methanol gave unexpected product (4) but the salts (3b,c) in acetonitrile yielded normal adducts with 7- or 8-membered lactone (6b,c).

Few intramolecular 1,3-dipolar cycloadditions of pyridinium N-imines with an unsaturated substituent on pyridine ring have been known.[1] Here, we describe on the intramolecular 1,3-dipolar cycloaddition of 3-phenylpropioloyloxyalkylpyridinium N-imines.

Reaction of 3-ω-hydroxyalkylpyridines (1) with phenylpropiolic acid in the presence of N,N'-dicyclohexylcarbodiimide at -10°C afforded esters (2),[2] which were aminated with O-mesitylenesulfonylhydroxylamine[3] to give the N-amine salts (3) in



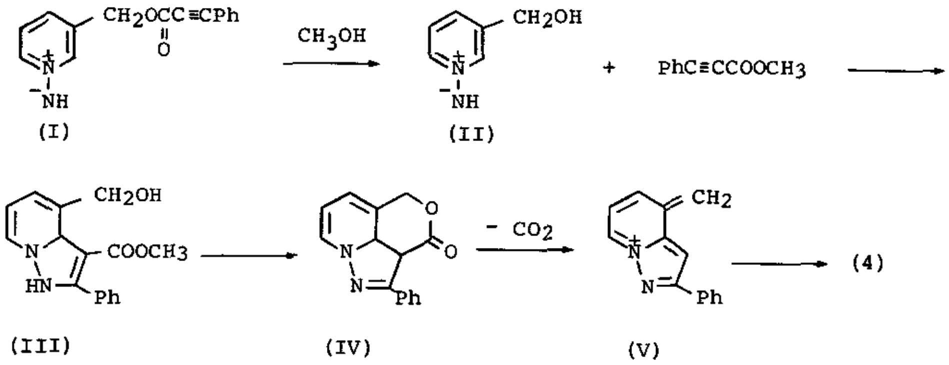
72-82% yields from (1).

The N-amine salt (3a) was treated with potassium carbonate in various solvents giving no isolable product but in methanol at room temperature yielding a mixture of 4-methyl-2-phenylpyrazolo[1,5-a]pyridine (4), mp 77-78°C, and 3-carbomethoxy-6-hydroxymethyl-2-phenylpyrazolo[1,5-a]pyridine (5), mp 128-129°C.

(4): MS m/e 208 (M^+); NMR ($CDCl_3$) δ 2.43 (3H, s, CH_3), 6.58 (1H, t, H-6, J=6.5 Hz), 6.72 (1H, s, H-3), 6.80 (1H, br d, H-5, J=6.5 Hz), 7.2-7.6 (3H, m), 7.8-8.1 (2H, m), and 8.32 (1H, br d, H-7, J=6.5 Hz). (5): IR (nujol) 3400, 1695 cm^{-1}; NMR ($CDCl_3$) δ 2.50 (1H, s, OH, disappeared with D_2O), 3.83 (3H, s, $COOCH_3$), 4.70 (2H, s, $\underline{CH_2}OH$), 7.36 (1H, dd, H-5, J=9, 1 Hz), 7.4-7.5 (3H, m), 7.7-7.8 (2H, m), 8.47 (1H, br s, H-7), and 8.50 (1H, d, H-4, J=9, 1 Hz).

Formation of (4) and (5) probably proceeds by methanolysis of (I) and intermolecular 1,3-dipolar cycloaddition of the formed N-imine (II) with methyl phenylpropiolate. Product (4) arises by lactonization and isomerization of (III) to (IV) followed by decarboxylation and hydrogen shift.

mechanism



Contrary to the above results, treatment of (3b,c) with potassium carbonate in acetonitrile at room temperature gave 7- and 8-membered lactones; (6b), mp 200-201°C, (30%) and (6c), mp 194-195°C, (32%), respectively.

(6b): IR (nujol) 1685 cm^{-1}; NMR ($CDCl_3$) δ 3.3-3.4 (2H, m, $COOCH_2\underline{CH_2}$), 4.6-4.7 (2H, m, $COO\underline{CH_2}CH_2$), 6.92 (1H, t, H-10, J=7 Hz), 7.18 (1H, dd, H-9, J=7, 1 Hz), 7.4-7.5 (2H, m), 7.7-7.9 (3H, m), and 8.45 (1H, dd, H-11, J=7, 1 Hz). (6c): IR (nujol) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.7-2.5 (2H, br, $CH_2\underline{CH_2}CH_2$), 2.8-3.3 (2H, br, $Ar\underline{CH_2}CH_2$), 4.4-4.6 (2H, br s, $CH_2\underline{CH_2}OCO$), 6.85 (1H, t, H-11, J=7 Hz), 7.10 (1H, dd, H-10, J=7, 1 Hz), 7.3-7.5 (2H, m), 7.7-7.8 (3H, m), and 8.40 (1H, dd, H-12, J=7, 1 Hz).

The above results are explained on the basis of possibility of the orbital overlap of 1,3-dipole (pyridinium N-imine) and dipolarophile (acetylenic group) in the transition state. In the case of (3a), the distance between the 1,3-dipole and dipolarophile in (3) is not effective approach of the orbitals. On the contrary to the above, in the case of (3b,c), the orbital overlap of the moieties is so easy to give the lactones (6).

Further studies on the mechanism and synthetic applications are in progress.

REFERENCES AND NOTES

1. T. Tsuchiya and H. Sashida, J. Chem. Soc. Chem. Comm., 1109 (1980).
2. (2a): oil (picrate mp 142-143°C); IR (neat) 2150, 1700 cm^{-1}.
   (2b): oil (picrate mp 120-122°C); IR (neat) 2170, 1710 cm^{-1}; NMR ($CDCl_3$) δ 3.03 (2H, t, $\underline{CH_2}CH_2OCO$), J=7 Hz), 4.44 (2H, t, $CH_2\underline{CH_2}OCO$, J=7 Hz), 7.2-7.7 (6H, m, H-4 and Ph), 7.25 (1H, dd, H-5, J=8, 5 Hz), 8.50 (1H, dd, H-6, J=5, 1.5 Hz), and 8.53 (1H, d, J=1.5 Hz).
   (2c): oil (picrate mp 105-107°C); IR (neat) 2150, 1700 cm^{-1}.
3. Y. Tamura, J. Minamikawa, Y. Miki, S. Matsugashita, and M. Ikeda, Tetrahedron Letters, 4133 (1972).

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