REACTION OF DIKETENE WITH LACTIM ETHERS[1)]

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Reaction of 2-methoxy-1-pyrroline (Ia) with diketene without solvent affords 7-hydroxy-2,3-dihydro-1H,5H-indolizin-5-one (IIa) and 8a-methoxy-2-methylene-3,4,6,7,8,8a-hexahydro-2H-pyrrolo[2,1-b]-1,3-oxazin-4-one (IIIa) which, on treatment with sodium ethoxide, is transformed to 8a-methoxy-2-methyl-6,7,8,8a-tetrahydro-4H-pyrrolo[2,1-b]-1,3-oxazin-4-one (IVa).

Similarly, 2-methoxy-3,4,5,6-tetrahydropyridine (Ib) gives 2-hydroxy-6,7,8,9-tetrahydro-4H-quinolizin-4-one (IIb) and 9a-methoxy-2-methyl-7,8,9,9a-tetrahydro-4H,6H-pyrido-[2,1-b]-1,3-oxazin-4-one (IVb).

Reaction of 2-methoxy-4,5,6,7-tetrahydro-3H-azepine (Ic) gives 10a-methoxy-2-methyl-6,7,8,9,10,10a-hexahydro-4H-azepino[2,1-b]-1,3-oxazin-4-one (IVc).

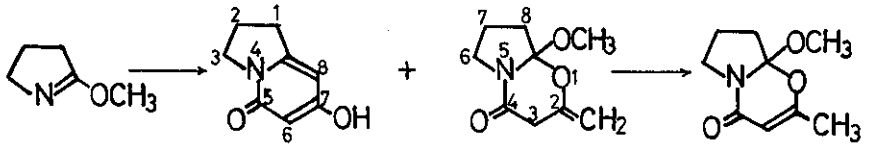
We have previously reported that imidates react with diketene to give the 1,3-oxazine derivatives.[2)] On the other hand, N-substituted imidates such as N-benzylacetimidate and lactim ethers react with diketene in glacial acetic

acid to give the 1,6-naphthyridine derivatives.[3] In the present paper we wish to report a novel reaction of diketene with lactim ethers to give the bicyclic 1,3-oxazine and α-pyridone derivatives.

A mixture of 2-methoxy-1-pyrroline (Ia) and an equimolar amount of diketene was kept in a refrigerator overnight, and crystals separated were collected by suction. Recrystallization from ethanol gave 7-hydroxy-2,3-dihydro-1H,5H-indolizin-5-one (IIa), $C_8H_9O_2N$, colorless prisms of mp 213-215° (decomp.), in 11% yield. IR ν_{max}^{KBr} cm^{-1}: 1640 (shoulder), 1620. NMR (CF_3CO_2H, ppm): 2.20-2.75 (2H, m, 2-CH_2), 3.35 (2H,t, J=8 Hz, 1-CH_2), 4.43 (2H, t, J=8 Hz, 3-CH_2), 6.59 (1H, d, J=3 Hz, 6-H), 6.76 (1H, d, J=3 Hz, 8-H).

The filtrate was purified by vacuum distillation to give 8a-methoxy-2-methylene-3,4,6,7,8,8a-hexahydro-2H-pyrrolo[2,1-b]-1,3-oxazin-4-one (IIIa), $C_9H_{13}O_3N$, a pale yellow oil of bp 98-99° (1.5 mm Hg), in 73% yield. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1690, 1645. NMR ($CDCl_3$, ppm): 1.80-2.60 (4H, m, CH_2), 3.30 (3H, s, OCH_3), 3.10-3.90 (4H, m, CH_2), 4.12 (1H, m, exomethylene), 4.44 (1H, m, exomethylene).

A solution of IIIa in methanol in the presence of a catalytic amount of sodium methoxide was allowed to stand at room temperature. After 2 hr the mixture was neutralized with 10% HCl, condensed in vacuo, and the residue was distilled to give 8a-methoxy-2-methyl-6,7,8,8a-tetrahydro-4H-pyrrolo[2,1-b]-1,3-oxazin-4-one (IVa), $C_9H_{13}O_3N$, a colorless oil of bp 90-92° (0.05 mm Hg), in 74% yield. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1667, 1630. NMR ($CDCl_3$, ppm), 2.00 (3H, s, 2-CH_3), 1.45-2.70 (4H, m, 7,8-CH_2), 3.28 (3H, s, OCH_3), 3.40-3.80 (2H, m, 6-CH_2), 5.27 (1H, s, 3-H).



Ia IIa IIIa IVa

Similar reaction of 2-methoxy-3,4,5,6-tetrahydropyridine (Ib) with diketene afforded a 10% yield of 2-hydroxy-6,7,8,9-tetrahydro-4H-quinolizin-4-one (IIb), $C_9H_{11}O_2N$, colorless prisms of mp 220-223° (decomp.) (lit[4] mp 223-225°), and a 43% yield of 9a-methoxy-2-methyl-7,8,9,9a-tetrahydro-4H,6H-pyrido[2,1-b]-1,3-oxazin-4-one (IVb), $C_{10}H_{15}O_3N$, a pale yellow oil of bp 83-88° (0.05 mm Hg).

IIb: IR ν_{max}^{KBr} cm^{-1}: 1650, 1616. NMR (CF_3CO_2H, ppm), 1.70-2.37 (4H, m, 7,8-CH_2), 3.10 (2H, t, J=8 Hz, 9-CH_2), 4.28 (2H, t, J=8 Hz, 6-CH_2), 6.68 (2H, s, 1-H, 3-H).

IVb: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1673, 1630. NMR ($CDCl_3$, ppm), 1.20-3.00 (6H, m, CH_2), 1.94 (3H, s, CH_3), 3.25 (3H, s, OCH_3), 3.30-4.60 (2H, m, 6-CH_2), 5.12 (1H, s, 3-H).

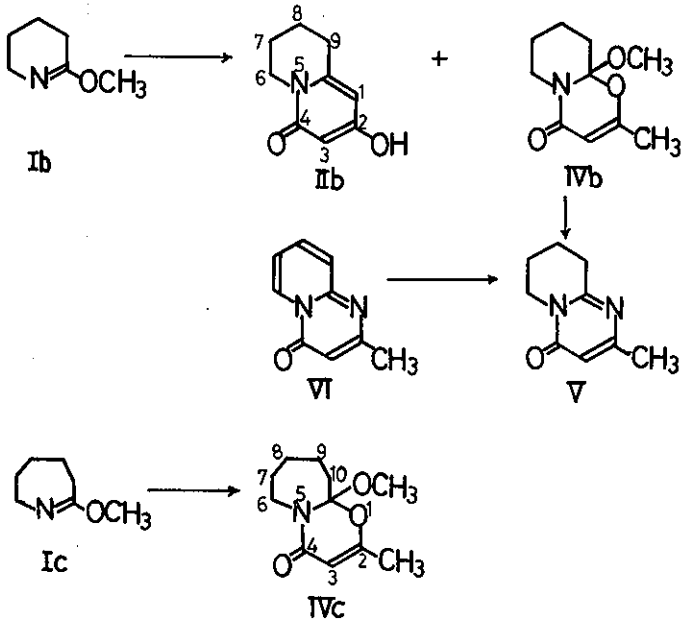
Compound IVb was heated with conc. NH_4OH in a sealed tube for 3 hr. After evaporation, the residue was purified by silica-gel column chromatography, using petroleum ether as an eluant to give a 20% yield of 2-methyl-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-one (V), $C_9H_{12}ON_2$, colorless needles of mp 80-83°, undepressed on admixture with a sample prepared by the catalytic reduction of 2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (VI)[5] with Raney Ni. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1667, 1605. NMR ($CDCl_3$, ppm): 1.60-2.10 (4H, m, 7,8-CH_2), 2.22 (3H, s, CH_3), 2.70-3.00 (2H, m, 9-CH_2), 3.78-4.05 (2H, m, 6-CH_2), 6.16 (1H, s, 3-H).

In this reaction product corresponding to III was not isolated.

Similarly, 2-methoxy-4,5,6,7-tetrahydro-3H-azepine (Ic) was allowed to react with diketene to give 10a-methoxy-2-methyl-6,7,8,9,10,10a-hexahydro-4H-azepino-[2,1-b]-1,3-oxazin-4-one (IVc), $C_{11}H_{17}O_3N$, a pale yellow oil of bp 90-95° (0.001 mm Hg), in 45% yield. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680, 1640. NMR ($CDCl_3$, ppm): 1.20-3.00 (8H, m, 7,8,9,10-CH_2), 1.98 (3H, s, CH_3), 3.25 (3H, s, OCH_3), 3.70-4.60 (2H, m, 6-CH_2), 5.22 (1H, s, 3-H).

In this reaction, the pyridone derivative corresponding to IIa and IIb

could not be detected.



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