REACTION OF DIKETENE WITH LACTIM ETHERS

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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-quinolinizin-4-one (IIb) and 9a-methoxy-2-methyl-7,8,9a-tetrahydro-4H,6H-pyrindo-[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. 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. 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), C₈H₈O₂N, colorless prisms of mp 213-215° (decomp.), in 11% yield. IRKBr cm⁻¹: 1640 (shoulder), 1620. NMR (CF₃CO₂H, ppm): 2.20-2.75 (2H, m, 2-CH₂), 3.35 (2H, t, J=8 Hz, 1-CH₂), 4.43 (2H, t, J=8 Hz, 3-CH₂), 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), C₉H₁₃O₃N, a pale yellow oil of bp 98-99° (1.5 mm Hg), in 73% yield. IRCHCl₃ cm⁻¹: 1690, 1645. NMR (CDCl₃, ppm): 1.80-2.60 (4H, m, CH₂), 3.30 (3H, s, OCH₃), 3.10-3.90 (4H, m, CH₂), 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), C₉H₁₃O₃N, a colorless oil of bp 90-92° (0.05 mm Hg), in 74% yield. IRCHCl₃ cm⁻¹: 1667, 1630. NMR (CDCl₃, ppm), 2.00 (3H, s, 2-CH₃), 1.45-2.70 (4H, m, 7,8-CH₂), 3.28 (3H, s, OCH₃), 3.40-3.80 (2H, m, 6-CH₂), 5.27 (1H, s, 3-H).

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\text{Ia} \quad \rightarrow \quad \text{IIa} + \quad \text{IIIa} \quad \rightarrow \quad \text{IVa}
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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-quinolinizin-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 v_KBr cm^{-1}: 1650, 1616. NMR (C_F_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 v_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}O_2N, colorless needles of mp 80-83°, undepressed on admixture with a sample prepared by the catalytic reduction of 2-methyl-4H-pyridine[1,2-a]pyrimidin-4-one (VI) with Raney Ni. IR v_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 v_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.

\[ \text{Ib} \xrightarrow{} \text{IIb} + \text{IVb} \]

\[ \text{Ic} \xrightarrow{} \text{IVc} \]

REFERENCES
1 This forms Part LXXX of "Studies on Ketene and Its Derivatives", by T. Kato.

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