A New One-Step Conversion of Ketoximes into α-Acyloxyketones

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α-Hydroxy functions are present in a number of naturally occurring ketones and other biologically active carbonyl compounds. Although a variety of methods are available for the conversion of ketones into α-acyloxyketones, these methods may have certain drawbacks such as poor yields[1-4], multistep procedures[5-8], or non-compatibility with other functional groups present[9,10]. We report here a new one-step conversion of dialkyl ketoximes into α-acyloxyketones.

We have previously reported the transformation of oximes (**1**) into α′- and α-acyloxyenimides (**2, 3**) by reaction with a mixture of acetyl chloride, acetic anhydride, and a tertiary base such as pyridine, 2,4,6-trimethylpyridine, or *N,N*-dimethylaniline (Path A)[11,12]. Hydrolysis of the enimides **2** and **3** under mild conditions affords α-acyloxyketones (**4**; Path B). We have now combined the two steps of this sequence (Path A + Path B) to provide a single-step method (Path C) for the conversion of dialkyl ketoximes (**1**) into α-acyloxyketones (**4**). We have further found that treatment of the isolated enimides **2** and **3** with dry hydrogen chloride in acetic anhydride at 100 °C leads to the formation of 1,3-oxazoles (**5**; Path D)[13].

3-Acetoxy-2-diacetylaminocyclohexene (2a) and 1-Acetoxy-2-diacetylaminocyclohexene (3a); Typical Procedure for the Reaction of Path A:
Cyclohexanone oxime (**1a**; 11.32 g, 0.1 mol) is dissolved in pyridine (7.91 g, 0.1 mol) and acetic anhydride (10 ml). To this solution, a mixture of acetyl chloride (5.5 g, 0.07 mol) and acetic anhydride (10 ml) is added slowly, with stirring at 0 °C. The mixture is then heated on a boiling water bath for 10 h, cooled, poured onto crushed ice (200 g), and extracted with dichloromethane (6 × 30 ml). The organic extract is washed with water (100 ml) and saturated sodium chloride solution (60 ml), dried with sodium sulfate, and concentrated by distillation at atmospheric pressure. The residual oil is distilled in vacuo to give a mixture of **2a** and **3a** as a colorless liquid; yield: 18.5 g (77%); boiling range: 130–139 °C/2–3 torr.

2-Acetoxycyclohexanone (4a); Typical Procedure for the Reaction of Path B:
90% Acetic acid (30 ml) and ammonium chloride (5 g) are added to the mixture of enimides **2a** and **3a** (2.4 g, 0.01 mol) and the mixture is heated on a boiling water bath for 30–60 min. It is then cooled, diluted with water (50 ml), and extracted with dichloromethane (4 × 20 ml). The organic extract is washed with water (75 ml) and saturated sodium chloride solution (40 ml), dried with sodium sulfate, and evaporated in vacuo. The residual brown liquid is submitted to short-path distillation to give **4a** as a colorless liquid; yield: 1.4 g (91%); b.p. 85–86 °C/2 torr.

Direct Conversion of Dialkyl Ketoximes (1) into α-Acetoxyketones (4) According to Path C; General Procedure:
The ketoxime **1** (0.01 mol) is dissolved in a tertiary base (0.01 mol) and acetic anhydride (3 ml). To this is added slowly, with stirring at 0 °C, a mixture of acetyl chloride (0.942 g, 0.012 mol) and acetic anhydride (2 ml). The resultant mixture is heated on a boiling water bath for 2–10 h and then cooled. Water (10 ml) is added slowly (exothermic reaction) and heating is continued for 30 min. The mixture is then cooled, diluted with water (40 ml), and extracted with dichloromethane (4 × 20 ml). The organic extract is washed with water (35 ml) and saturated sodium chloride solution (20 ml), dried with magnesium sulfate, and evaporated in vacuo. The residual product **4** is purified by distillation in vacuo or preparative T.L.C.

2-Acetoxycyclohexanone (4a); Typical Procedure for the Reaction of Path C:
Cyclohexanone oxime (**1a**; 11.3 g, 0.1 mol) is dissolved in 2,4,6-trimethylpyridine (12.12 g, 0.1 mol) and acetic anhydride (30 ml). To this solution, a mixture of acetyl chloride (9.42 g, 0.12 mol) and acetic anhydride (20 ml) is gradually added, with stirring at 0 °C. The resultant mixture is

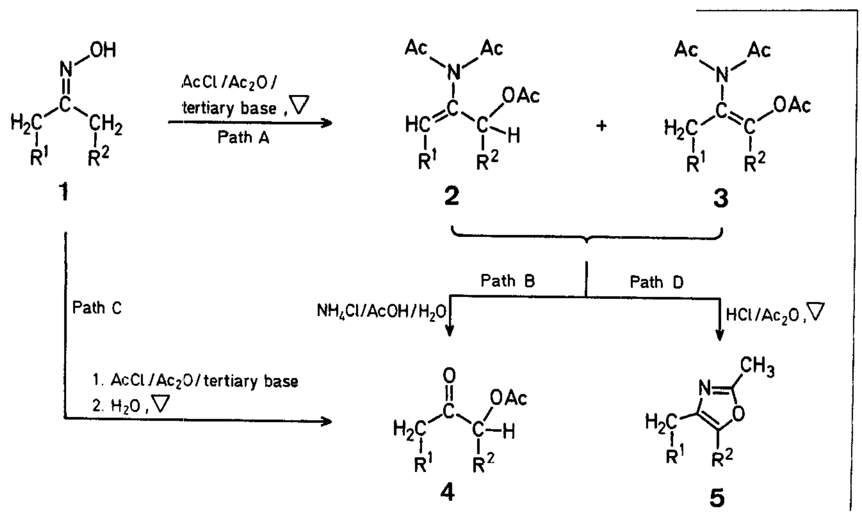

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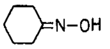
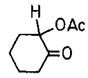
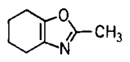
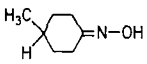
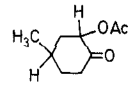
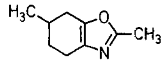
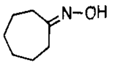
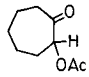
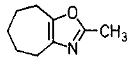
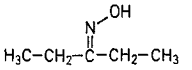
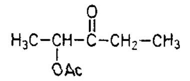
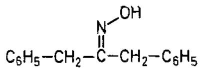
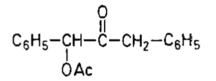
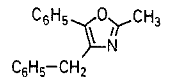
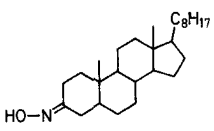
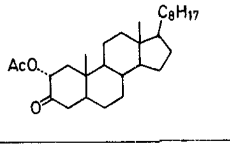
Table. Conversion of Dialkyl Ketoximes (**1**) into α-Acetoxyketones (**4**) [and 1,3-Oxazole Derivatives (**5**) as Side Products] via Path C

Oxime **1**	Products	Reaction time [h]	Yield [%]	m.p. or b.p./torr [°C]	
				found	reported or Molecular formula[a]
a 		2	60[b]	b.p. 85–86°/2	b.p. 123–126°/16[8]
			18[b]	b.p. 60–61°/2	b.p. 79.5°/10[15]
b 		3	52[b] 58[c]	b.p. 98°/2	b.p. 53–55°/0.25[18]
			16[b] 20[c]	b.p. 112–114°/4	$C_9H_{13}NO$ (151.2)
c 		3	58[c]	b.p. 93°/2	b.p. 120–122°/10[16]
			20[c]	b.p. 108°/4	$C_9H_{13}NO$ (151.2)
d  $H_3C{-}CH_2{-}\overset{N-OH}{\overset{\|}{C}}{-}CH_2{-}CH_3$	 $H_3C{-}\underset{OAc}{\underset{\|}{CH}}{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}CH_3$	4	40[c,d]	b.p. 87°/20	b.p. 56–59°/2–5[17]
e  $C_6H_5{-}CH_2{-}\overset{N-OH}{\overset{\|}{C}}{-}CH_2{-}C_6H_5$	 $C_6H_5{-}\underset{OAc}{\underset{\|}{CH}}{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}C_6H_5$	10	38[c,d]	b.p. 74–75°/2	b.p. 95°/5[19]
			16[c]	b.p. 132–134°/4	$C_{17}H_{15}NO$ (249.3)
f 		8	72[c]	m.p. 125°	m.p. 123–125°[14]

[a] The microanalyses were in good agreement with the calculated values: C, ±0.26; H, ±0.19; N, ±0.16.

[b] Purified by distillation.

[c] Isolated by preparative T.L.C. (silica gel; hexane/ethyl acetate 9/1).

[d] Rest of the material was the ketone corresponding to **1**.

heated on a boiling water bath for 2 h and then cooled. Water (100 ml) is added slowly (exothermic reaction) and heating is continued for 30 min. The mixture is then cooled, diluted with water (240 ml), and extracted with dichloromethane (8 × 20 ml). The organic extract is washed with water (150 ml) and saturated sodium chloride solution (80 ml), dried with magnesium sulfate, and evaporated in vacuo. The residual brown liquid is distilled in vacuo to give two products:

2-Methyl-4,5,6,7-tetrahydro-1,3-benzoxazole (**5a**); yield: 2.5 g (18%); b.p. 60–61 °C/2 torr.

2-Acetoxycyclohexanone (**4a**); yield: 9.3 g (60%); b.p. 85–86 °C/2 torr; purity: ≥99%, as determined by G.L.C. analysis (6 ft × 1/8 in. stainless steel comun; carbowax 10%; 185 °C).

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