5-Acyl-4-amino-2-phenyl-1,3-oxazin-6-ones

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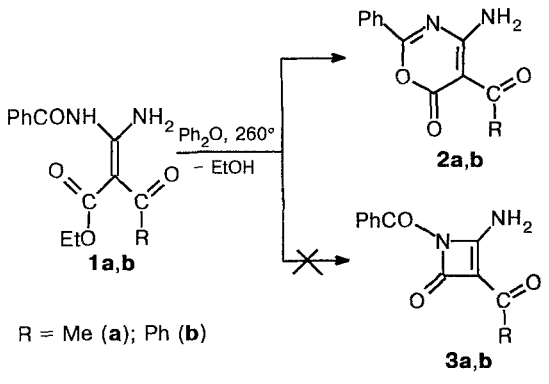
Intramolecular cyclization of acyl(ethoxycarbonyl)ketene *N*-benzoylaminals in boiling Ph_2O gives 5-acyl-4-amino-2-phenyl-1,3-oxazin-6-ones.

Key words: intramolecular cyclization, acyl(ethoxycarbonyl)ketene *N*-benzoylaminals, 5-acyl-4-amino-2-phenyl-1,3-oxazin-6-ones, ^{17}O NMR.

Azoles and azines containing vicinal amino and acyl groups are convenient building blocks for synthesizing condensed nitrogen-containing systems. We have previously found convenient methods for the synthesis of new reagents of this type belonging to triazole,[1] pyrazole,[2] pyridine,[3] and pyrimidine[4–6] series from acyl-, diacyl-, and acyl(ethoxycarbonyl)ketene aminals or *N,S*-acetals containing one or two unsubstituted NH_2 groups.[7–9]

In the present work we studied one of the possible approaches to the synthesis of substituted 1,3-oxazines from ketene aminals, which are readily obtained from alkyl β-ketocarboxylates and benzoylcyanamide in the presence of catalytic amounts of $Ni(acac)_2$.[8] We have found that refluxing of acyl(ethoxycarbonyl)ketene *N*-benzoylaminals (**1a,b**) in Ph_2O results in intramolecular cyclization with elimination of EtOH to give crystalline products, which, according to the spectral data (IR, ^1H, ^{13}C, and ^{15}N NMR), are 4-amino-5-acyl-2-phenyl-1,3-oxazin-6-ones (**2a,b**).



The alternative structure of 1*H*-azet-2-one derivatives (**3a,b**) was unambiguously ruled out based on ^{17}O NMR data recorded in CD_3CN. For example, the spectrum of the product obtained from **1a** displays signals at 235, 308, and 487 ppm. The first should obviously be attributed[10] to the O(1) atom of the oxazine ring in compound **2a**. However, this signal cannot be ascribed to any of the O atoms of the carbonyl groups in compound **3a**.

The yields of oxazinones **2a,b** are as high as 60—67 %. According to IR spectroscopic data (in CH_2Cl_2) and ^1H NMR spectra (in $CDCl_3$) for these compounds, one of the H atoms of the amino group is involved in an N—H···O=CR intramolecular hydrogen bond.

Previously,[11] acylation of diaminomethylenemalonic ester and ethyl diaminomethylenecyanoacetate with PhCOCl gave heterocyclization products, which were regarded to be the corresponding derivatives of 1*H*-azet-2-one (*cf.* **3a,b**). The structure of these compounds seems to require additional consideration.

4-Amino-2-aryl-1,3-oxazin-6-ones substituted at the exocyclic N atom have been obtained[12] by thermolysis of 2-(*N*-aroyl)diaminomethylene derivatives of Meldrum's acid. However, the possibility of an azetone-type alternative structure was not discussed.

In addition, the interest in the chemistry of 1,3-oxazinones is, to a considerable extent, determined by their ability to undergo various transformations during nucleophilic attack of the ring (for reviews see Refs. 13 and 14). Therefore, compounds **2a,b** can be used both in reactions involving annelation of the pyridine or pyrimidine ring and in reactions with ring transformations.

Experimental

^1H NMR spectra were recorded on a Bruker WM-250 spectrometer. ^{13}C, ^{15}N, and ^{17}O NMR spectra were obtained on a Bruker AM-300 instrument. IR spectra were recorded on an UR-20 spectrophotometer. Mass spectra were measured on a Varian MAT-311A mass spectrometer (EI, 70 eV). Acyl(ethoxycarbonyl)ketene aminals **1a,b** were synthesized according to a known procedure.[8]

Intramolecular cyclization of keteneaminals 1a,b (general procedure). A solution of keteneaminal **1a,b** (0.01 mol) in Ph_2O (25 mL) was refluxed for 1.5 h under Ar and cooled to

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~20 °C. Hexane (60 mL) was added, and the resulting precipitate was filtered off and purified by column chromatography ($CHCl_3/CCl_4$ 1:1, SiO_2) to give oxazinones **2a,b**, which were then recrystallized from benzene.

4-Amino-5-acetyl-2-phenyl-1,3-oxazin-6-one (2a). Yield 67 %, m.p. 165—166 °C (benzene). Found (%): C, 62.67; H, 4.40; N, 12.19. $C_{12}H_{10}N_2O_3$. Calculated (%): C, 62.60; H, 4.38; N, 12.17. MS, *m/z*: 230 $[M]^{+\cdot}$. IR (CH_2Cl_2), ν/cm^{-1}: 3465, 3250 br (NH); 1765, 1740 (C=O), 1636, 1615, 1596, 1580. ^1H NMR ($CDCl_3$), δ: 2.67 (s, 3 H, Me); 6.21 (s, 1 H, NH); 7.50—8.30 (m, 5 H, Ph); 10.45 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 31.99 (q, Me, J = 129 Hz); 90.94 (s, C(5)); 128.95, 129.0, 129.3, 134.4 (Ph); 159.14 (s, C(4)); 164.91 (s, C(6)); 165.29 (t, C(2), J = 3 Hz); 199.27 (q, CO, J = 7 Hz); ^{15}N NMR (DMSO-d_6), δ: −163.4 (d, C=N, J = 7 Hz); −268.70 (t, NH_2, J = 91 Hz). ^{17}O NMR (CD_3CN), δ: 235.00 (O—C=O), 308.00 (O—C=O), 487.00 (MeCO).

4-Amino-5-benzoyl-2-phenyl-1,3-oxazin-6-one (2b). Yield 60 %, m.p. 185—187 °C (benzene). Found (%): C, 69.93; H, 4.09; N, 9.71. $C_{17}H_{12}N_2O_3$. Calculated (%): C, 69.85; H, 4.14; N, 9.59. MS, *m/z*: 292 $[M]^{+\cdot}$. IR (CH_2Cl_2), ν/cm^{-1}: 3470, 3275 br (NH), 1760 sh, 1745 (CO), 1628, 1598, 1580. ^1H NMR, $CDCl_3$, δ: 9.90 (s, 1 H, NH), 7.30—8.40 (m, 10 H, 2 Ph), 6.23 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 89.58 (s, C(5)), 127.85, 128.92, 129.74, 131.31, 134.39, 140.63 (2 Ph), 158.60 (s, C(4)), 165.26 (s, C(6)), 165.74 (s, C(2)), 195.88 (CO).

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