Brief Communications

Studies on condensation of chlorocarbonyl phenyl ketene with *N*-unsubstituted amides: synthesis of some new 1,3-oxazin-6-ones

H. Sheibani, K. Saidi, and H. Foroughi*

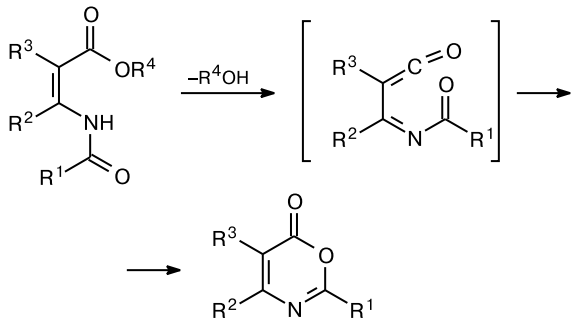
Shahid Bahonar University of Kerman, Department of Chemistry, Kerman, 76169 Iran.
Fax: +98 341 322 1452. E-mail: hsheibani@mail.uk.ac.ir

A series of 1,3-oxazin-6-one derivatives has been synthesized upon treatment of *N*-unsubstituted amides with chlorocarbonyl phenyl ketene under reflux in toluene for several minutes. In this simple way, 2,5-disubstituted derivatives of 1,3-oxazin-6-ones have been obtained in high yields.

Key words: chlorocarbonyl phenyl ketene, *N*-unsubstituted amides, 1,3-oxazin-6-ones.

1,3-Oxazin-6-ones (3-aza-α-pyrones) are six-membered heterocyclic compounds, which are known as important substrates in heterocyclic transformations, especially in the reactions of [4+2]-cycloaddition of their 2-azadiene fragment with many dienophiles, leading to pyridines after elimination of CO_2.[1] The synthesis of the first member of the series, 4-hydroxy-6*H*-1,3-oxazin-6-one, has been described[2] together with a detailed review of preparative methods for the substituted derivatives. The most common method for the synthesis of 1,3-oxazin-6-ones is the cyclization of 3-acylaminoacrylic acids and esters, as a rule, under thermal conditions, presumably through the intermediate formation of acylimino ketenes, which undergo electrocyclization into the 1,3-oxazin-6-one derivatives (Scheme 1).[3]

Scheme 1



Recently,[4] we have discovered a reaction of chlorocarbonyl ketenes with *N*-substituted cinnamic amides, leading to 2-vinyl-1,3-oxazinium-4-olates, as well as their conversion into 3-azabicyclo[3.1.1]heptanetriones by sequential facile ring opening and recyclization through the reaction of [2+2]-cross-cycloaddition (Scheme 2).

Chlorocarbonyl ketenes proved very efficient 1,3-dielectrophilic agents, capable of undergoing the reaction

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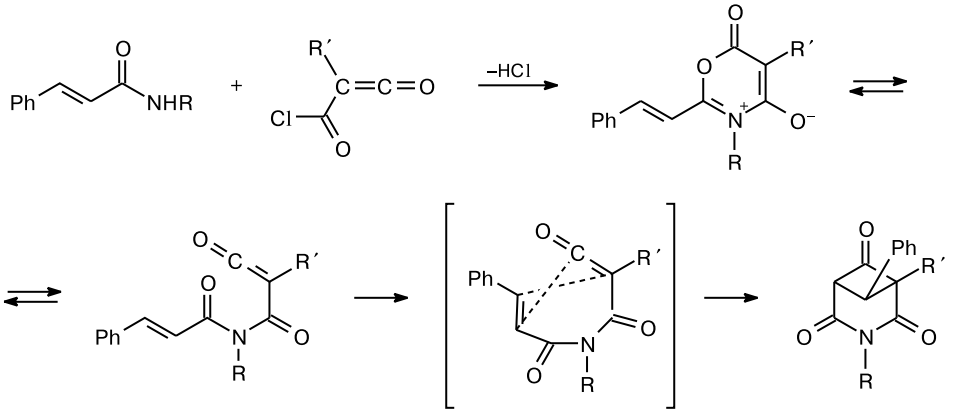
Scheme 2



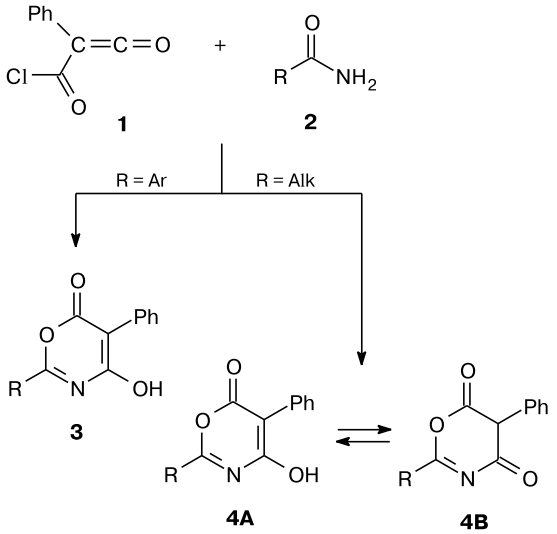
with a wide variety of binucleophiles under mild conditions. They were predominantly used in the synthesis of five- and six-membered heterocycles functionalized with hydroxy groups in 1,3-positions.[5,6] In continuation of our study on the reactions of chlorocarbonyl ketenes with 1,2-dinucleophiles (oximes[7] and hydrazones[8]) and 1,3-dinucleophiles (1,3-dicarbonyl compounds,[9,10] thioamides, and amides[11]), we studied a facile condensation of chlorocarbonyl phenyl ketene with *N*-unsubstituted amides and synthesized some new 1,3-oxazine derivatives (Scheme 3).

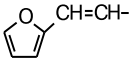
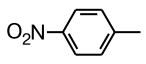
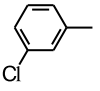
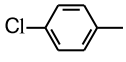
In comparison with other multistep methods, this synthesis is of interest for the simple and efficient *one-pot* procedure. Another advantage of the method consists in the availability of the starting compounds, short reaction time, and high yields of the target products. The condensation of isolable and stable ketene **1** with *N*-unsubstituted α,β-unsaturated amides or aromatic amides **2** in boiling toluene gives the high yields of 4-hydroxy-1,3-oxazin-6-ones **3a—d**. At the same time, *N*-unsubstituted aliphatic amides lead to a mixture of two tautomers: 1,3-oxazin-6-one **4A** and 1,3-oxazin-4,6-dione **4B** in good yields (see Scheme 3).

The structures of compounds **3a—d** and **4a,b** have been inferred from the IR, ^{1}H and ^{13}C NMR spectroscopic and mass spectrometric data. The IR spectrum of compound **3a** contains a broad band of the hydroxy group at 3180—2500 cm^{-1}, the band of the carbonyl group at 1741 cm^{-1}, and an intensive band at 1595 cm^{-1} related to the C=N bond. In the ^{1}H NMR spectrum of compound **3a**, four signals are present along with a downfield signal for the enolic OH group (δ 12.78). Such an assignment agrees with the literature data for similar compounds.

The ^{1}H and ^{13}C NMR spectra of compounds **4a,b** indicate the presence of two tautomers. Thus, in the ^{1}H NMR spectrum the signal at δ 11.64 is present, which corresponds to the OH group of tautomer **A** of compound **4a**, and the signal at δ 5.62, which has been assigned to the

Scheme 3



Compound	R	Yield (%)	Compound	R	Yield (%)
3a		75	**3d**		85
3b		90	**4a**	PhCHBrCHBr—	75
3c		92	**4b**		70

proton at C(5) of the minor tautomer **B** of compound **4a**.[12,13] The quantitative analysis of the mixtures was perform by the integration of signals in the ^{1}H NMR spectra.

Experimental

Commercially available reagents (Merck, Fluka) were used without additional purification. Melting points were measured using Gallenkamp apparatus (Great Britain) and were not cor-

rected. IR spectra were recorded on a Matson 1000 FT IR spectrometer (KBr pellets). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 spectrometer in DMSO-d_6. Chemical shifts marked with asterisk are given for two tautomers. Mass spectra were obtained on a Shimadzu QP2000A instrument (70 eV). Chlorocarbonyl phenyl ketene (**1**) was obtained similarly to the procedure reported earlier.[14]

Compounds 3a—d and 4a,b (general procedure). A solution of compound **1** (0.36 g, 2 mmol) in anhydrous THF (5 mL) was added dropwise over 2 min to a stirred boiling solution of *N*-unsubstituted amide **2** (2 mmol) in toluene (20 mL). An immediate precipitation of colored products **3** or **4** was observed. The reaction mixture was cooled, the precipitate was filtered off, washed with anhydrous diethyl ether, and recrystallized from anhydrous ethyl acetate—hexane.

4-Hydroxy-5-phenyl-2-[(*E*)-1-ethyl-2-(2-furyl)]-6*H*-1,3-oxazin-6-one (3a). The yield was 0.42 g (75%), orange crystals, m.p. 180—182 °C. Found (%): C, 68.12; H, 3.76; N, 4.69. $C_{16}H_{11}NO_4$. Calculated (%): C, 68.33; H, 3.94; N, 4.98. IR, ν/cm^{-1}: 3180—2500 (br, OH), 1741 (C=O), 1595 (C=N). ^{1}H NMR, δ: 12.78 (s, 1 H, OH); 7.97 (d, 1 H, β-CH, ^3J = 16 Hz); 7.96—6.70 (m, 8 H, H arom.); 6.44 (d, 1 H, α-CH, ^3J = 16 Hz). ^{13}C NMR, δ: 165.52 (C=O), 160.64, 150.79, 147.22, 131.73, 130.53, 130.34, 127.86, 127.11, 117.95, 114.75, 113.67, 94.72. MS, *m/z* (I_{rel} (%)): 281 $[M]^+$ (29), 280 $[M - H]^+$ (44), 253 $[M - CO]^+$ (15), 120 (100), 118 (29), 77 (15).

2-(3-Chlorophenyl)-4-hydroxy-5-phenyl-6*H*-1,3-oxazin-6-one (3b). The yield was 0.53 g (90%), yellow crystals, m.p. 214—216 °C. Found (%): C, 63.80; H, 3.23; N, 4.49. $C_{16}H_{10}ClNO_3$. Calculated (%): C, 64.12; H, 3.36; N, 4.67. IR, ν/cm^{-1}: 3200—2500 (br, OH), 1701 (C=O), 1615 (C=N). ^{1}H NMR, δ: 12.88 (s, 1 H, OH); 8.07—7.27 (m, 9 H, H arom.). ^{13}C NMR, δ: 165.49 (C=O), 160.89, 160.63, 134.21, 133.53, 131.51, 131.41, 131.34, 130.54, 127.95, 127.69, 127.00, 126.55, 95.75. MS, *m/z* (I_{rel} (%)): 301 $[M + 2]^+$ (28), 299 $[M]^+$ (100), 271 $[M - CO]^+$ (65), 139 (65), 105 (48), 78 (90), 77 (15).

2-(4-Chlorophenyl)-4-hydroxy-5-phenyl-6*H*-1,3-oxazin-6-one (3c). The yield was 0.55 g (92%), yellow crystals, m.p. 238—240 °C. Found (%): C, 64.05; H, 3.29; N, 4.56. $C_{16}H_{10}ClNO_3$. Calculated (%): C, 64.12; H, 3.36; N, 4.67. IR, ν/cm^{-1}: 3180—2500 (br, OH), 1695 (C=O), 1605 (C=N). ^{1}H NMR, δ: 12.90 (s, 1 H, OH); 8.11—7.26 (m, 9 H, H arom.). ^{13}C NMR, δ: 165.62 (C=O), 161.38, 160.71, 138.83, 131.43, 130.56, 130.20, 129.78, 128.56, 127.92, 127.31, 95.47. MS, *m/z* (I_{rel} (%)): 301 $[M + 2]^+$ (30), 299 $[M]^+$ (100), 271 $[M - CO]^+$ (60), 139 (65), 105 (48), 77 (15).

4-Hydroxy-2-(4-nitrophenyl)-5-phenyl-6*H*-1,3-oxazin-6-one (3d). The yield was 0.52 g (85%), yellow crystals, m.p. 230—232 °C. Found (%): C, 61.55 H, 3.11; N, 9.12. $C_{16}H_{10}N_2O_5$. Calculated (%): C, 61.94; H, 3.25; N, 9.03. IR, ν/cm^{-1}: 3200—2550 (br, OH), 1691 (C=O), 1595 (C=N). ^{1}H NMR, δ: 12.80 (s, 1 H, OH); 8.42—7.26 (m, 9 H, H arom.). ^{13}C NMR, δ: 166.57 (C=O), 165.39, 160.59, 150.37, 140.36, 135.31, 131.23, 130.53, 129.81, 129.28, 127.98, 124.57, 123.78, 96.25. MS, *m/z* (I_{rel} (%)): 310 $[M]^+$ (100), 282 $[M - CO]^+$ (65), 150 (97), 118 (79), 104 (25).

2-(1,2-Dibromo-2-phenylethyl)-5-phenyl-6*H*-1,3-oxazin-6-one (4a). The yield was 0.63 g (70%), yellow crystals, m.p. 150—152 °C. IR, ν/cm^{-1}: 3220—2800 (br, OH), 1717, 1690, 1660. MS, *m/z* (I_{rel} (%)): 451 $[M]^+$ (10), 423 $[M - CO]^+$ (20), 371 (18), 369 (20), 346 (22), 344 (35), 290 (60), 228 (100), 226 (95), 257 (25), 250 (40), 181 (70), 183 (95), 131 (55), 118 (70), 103 (35), 101 (20), 91 (10).

Major tautomer, 2-(1,2-dibromo-2-phenylethyl)-4-hydroxy-5-phenyl-6*H*-1,3-oxazin-6-one (form **A**) (60%). ^{1}H NMR, δ: 11.64 (s, 1 H, OH); 7.91—7.04 (m, 20 H, H arom.)*; 5.91, 5.77 (both d, 1 H each, ^3J = 14 Hz). ^{13}C NMR, δ: 168.61, 165.38, 164.27, 160.16 (C=O, C(2), C(4))*, (139.22, 138.02, 130.56, 129.91, 129.80, 129.63, 129.33, 129.27, 129.14, 128.91, 128.69, 128.65, 128.49, 127.74)*, 96.05 (C(5)), (52.24, 51.49, 49.23, 48.04)*. Minor tautomer, 2-(1,2-dibromo-2-phenylethyl)-5-phenyl-4*H*-1,3-oxazin-4,6(5*H*)-dione (form **B**) (40%). ^{1}H NMR, δ: 5.51, 5.18 (both d, 1 H each, ^3J = 10 Hz); 5.62 (s, 1 H, H(5)). ^{13}C NMR, δ: 50.69 (C(5)).

2-Cyclohexyl-5-phenyl-6*H*-1,3-oxazine (4b). The yield was 0.40 g (75%), yellow crystals, m.p. 196—198 °C. Found (%): C, 70.65; H, 6.21; N, 5.03. $C_{16}H_{17}NO_3$. Calculated (%): C, 70.83; H, 6.32; N, 5.16. IR, ν/cm^{-1}: 3150—2700 (br, OH), 1727, 1690, 1650. MS, *m/z* (I_{rel} (%)): 271 $[M]^+$ (58), 245 (50), 243 $[M - CO]^+$ (30), 188 (20), 161 (20), 145 (22), 127 (58), 118 (100), 99 (35), 83 (65), 72 (25), 40 (45).

Major tautomer, 2-cyclohexyl-4-hydroxy-5-phenyl-6*H*-1,3-oxazin-6-one (form **A**) (70%). ^{1}H NMR, δ: 12.25 (s, 1 H, OH); 7.47—7.23 (m, 10 H, H arom.)*; 2.50—1.15 (m, 22 H, *cyclo*-C_6H_{13})*. ^{13}C NMR, δ: 177.75, 176.69, 172.48, 172.09, 170.03, 169.15, 165.44, 161.26 (C=O, C(2), C(4))*, (135.21, 130.48, 129.96, 129.85, 128.56, 128.47, 127.88, 127.10, 126.95, Ph)*, 94.35 (CM_5), (44.55, 44.06, 43.55, 42.80, 29.56, 28.88, 25.91, 25.70, 25.26, cyclohexyl)*. Minor tautomer, 2-cyclohexyl-5-phenyl-4*H*-1,3-oxazin-4,6(5*H*)-dione (form **B**) (30%). ^{1}H NMR, δ: 5.20 (s, 1 H, H(5)). ^{13}C NMR, δ: 59.21 (C(5)).

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* For two tautomers.

References

1. D. L. Boger, *Tetrahedron*, 1983, **39**, 2869.
2. A. Krantz, B. Hoppe, *J. Am. Chem. Soc.*, 1975, **97**, 6590.
3. H. McNab, K. Withell, *Tetrahedron*, 1996, **52**, 3163.
4. H. Sheibani, P. V. Bernhardt, C. Wentrup, *J. Org. Chem.*, 2005, **70**, 5859.
5. W. Ried, H. Nenninger, *Synthesis*, 1990, 167.
6. K. T. Potts, M. O. Dery, R. K. Kullnig, *J. Chem. Soc., Chem. Commun.*, 1987, 840.
7. K. Saidi, H. Sheibani, *Synth. Commun.*, 2001, **31**, 1809.
8. H. Sheibani, D. Lari, M. Islami, K. Saidi, *Izv. Akad. Nauk, Ser. Khim.*, 2003, 1335 [*Russ. Chem. Bull., Int. Ed.*, 2003, **52**, 1411].
9. H. Sheibani, M. R. Islami, H. Khabazzadeh, K. Saidi, *Tetrahedron*, 2004, **60**, 5931.
10. H. Sheibani, M. H. Mosslemin, S. Behzadi, M. R. Islami, K. Saidi, *Synthesis*, 2006, **3**, 435.
11. H. Sheibani, M. H. Mosslemin, S. Behzadi, M. R. Islami, H. Foroughi, K. Saidi, *ARKIVOC*, 2005, **15**, 88.
12. L. George, R. N. Veedu, H. Sheibani, A. A. Taherpour, R. Flammang, C. Wentrup, *J. Org. Chem.*, 2007, **72**, 1399.
13. W. Stadlbauer, E1-S. Badawey, C. Hojas, P. Roschger, T. Kappe, *Molecules*, 2001, **6**, 338.
14. S. Nakanishi, K. Butler, *Org. Prep. Proced. Int.*, 1975, **7**, 155.

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