Improved Synthesis of (E)-3-Alkoxy- and (E)-3-Phenoxyacyryloyl Chlorides

L. F. Tietze*, C. Schneider, M. Pretor

Institut für Organische Chemie der Universität Göttingen, Tammanstraße 2, D-37077 Göttingen, Germany
Received 21 December 1992, revised 25 March 1993

A one-step preparation of (E)-3-alkoxy- and (E)-3-phenoxyacyryloyl chlorides by reaction of vinyl ethers and oxalyl chloride with subsequent decarbonylation is presented.

(E)-3-Alkoxy- and (E)-3-phenoxyacyrloyl chlorides are valuable intermediates in organic syntheses,1–9 inter alia in alkaloid synthesis1 and the de novo synthesis of nucleoside analogs,2–4 as well as reactive precursors to the corresponding acids, esters, and amides, which may be used for the synthesis of different heterocycles.9

3-Alkoxy- and 3-phenoxyacyrloyl chlorides can be prepared by reaction of vinyl ethers and phosgene10,11 as well as by nucleophilic addition of alcohols to propiolic esters.12 Both procedures have disadvantages: in the first case the use of toxic phosgene, and in the second case the expense of propiolic esters.

We report herein a simple one-step procedure which employs reasonably priced and easy to handle chemicals and which can be performed on a kilogram scale.

Nucleophilic addition of vinyl ethers 1 to oxalyl chloride 2 according to the procedure of Effenberger13 at room temperature affords via 3 the α-keto acid chlorides 4, which decarbonylate upon distillation to give the (E)-3-alkoxy- and (E)-3-phenoxyacyrloyl chlorides 5. The loss of carbon monoxide occurs smoothly at temperatures above 100 °C, so that heating of the crude 4 directly furnishes the pure acryloyl chlorides 5. The broad scope of the reaction is demonstrated by the successful preparation of not only the simple methoxy- and ethoxyacyrloyl chlorides 5a and b, but also the phenoxy- and benzylphenoxyacyrloyl chlorides 5c and d. Compounds 5a and b are obtained in over 70% yield; the somewhat lower yields of 5c and 5d (48%) are due to the high boiling points of these compounds and the necessary harsh conditions during distillation. The obtained acryloyl chlorides 5 have the (E)-configuration as demonstrated by the coupling constants (J = 12.4 Hz) for the signals of the two vinylic protons at δ = 5.50–5.70 and 7.78–7.96. The formation of the E-configuration can be explained either by a stereospecific transelimination of hydrogen chloride from the intermediate 3, or more likely by an isomerisation under the reaction conditions to give the more stable E-compound. The (E)-3-alkoxy- and phenoxyacyrloyl chlorides 5 can easily be transformed into the corresponding acids, esters and amides, by standard methods in almost quantitative yield.9 In conclusion, the described method represents an efficient and cheap synthetic route to the valuable (E)-3-alkoxy- and (E)-3-phenoxyacyrloyl chlorides.

![Scheme 1]

1H and 13C NMR: Varian XL-200, VX-200, and FT-80 A; multiplicities were determined with the APT pulse sequence. MS: Varian MAT 311 A. IR: Bruke IFS 25. UV: Varian Cary 219. Elemental analyses were carried out in the analytical laboratory of the University. Compounds 5c and d gave C ± 0.13, H ± 0.05. Reagents and materials were purchased from commercial suppliers and were used without further purification. All reactions were performed in flame-dried flasks under a positive pressure of nitrogen. (E)-3-Alkoxy- and (E)-3-Phenoxyacyrloyl Chlorides (5a–d); General Procedure:

Vinyl ether (0.10 mol) was slowly added to oxalyl chloride (12.9 mL, 0.15 mol) at 0°C. The reaction mixture was maintained for 2 h at
0°C and then warmed to r.t. over 12 h. Excess oxalyl chloride was distilled off, the black residue was heated at 120°C for 30 min and then purified by vacuum distillation through a short Viguere column.

**E)-3-Methoxyacryloyl Chloride (5a):**
Reaction of methyl vinyl ether and oxalyl chloride. Yield: 72%; bp 73–74°C/25 mbar (Lit.6 bp 77–79°C/20 Torr).

IR (film): ν = 1744 (C=O), 1618 cm⁻¹ (C=C).

1H NMR (CDCl₃/TMS): δ = 3.84 (s, 3H, OMe), 5.53 (d, J = 12.5 Hz, 1H, 2-H), 7.84 (d, J = 12.5 Hz, 1H, 3-H).

MS (70 eV): m/z (relative intensity) = 120 (M⁺, 8), 86 (M⁺ + 1 - Cl, 18), 85 (M⁺ - Cl, 100), 69 (M⁺ - OCl, 20).

**E)-3-Ethoxyacryloyl Chloride (5b):**
Reaction of ethyl vinyl ether and oxalyl chloride. Yield: 76%; bp 60–61°C/5 mbar (Lit.6 bp 105–107°C/37–38 Torr).

IR (film): ν = 1744 (C=O), 1614 cm⁻¹ (C=C).

1H NMR (CDCl₃/TMS): δ = 1.40 (t, J = 7.0 Hz, 3H, CH₃), 4.04 (q, J = 7.0 Hz, 2H, CH₂), 5.50 (d, J = 12.5 Hz, 1H, 2-H), 7.78 (d, J = 12.5 Hz, 1H, 3-H).

MS (70 eV): m/z (relative intensity) = 134 (M⁺, 2), 114 (17), 99 (M⁺ - Cl, 25), 91 (11), 66 (17), 64 (34).

**E)-3-(3,5-Dimethylphenoxo)acryloyl Chloride (5c):**
Reaction of 3,5-dimethylphenyl vinyl ether and oxalyl chloride. Yield: 48%; bp 130°C/0.4 mbar.

UV (MeCN): λ_max (log ε) = 196 (4.563), 262 nm (4.064).

IR (film): ν = 1752 (C=O), 1614 cm⁻¹ (C=C).

1H NMR (nucleosides/TMS): δ = 2.35 (s, 6H, 2 × CH₃), 5.75 (d, J = 12.5 Hz, 1H, 2-H), 6.68 (m, 2H, 2'-6'-H), 6.87 (m, 1H, 4'-H), 7.96 (d, J = 12.5 Hz, 1H, 3-H).

13C NMR (CDCl₃): δ = 21.21 (2 × CH₃), 107.2 (C-2), 115.7 (C-2', C-6'), 127.7 (C-4'), 140.3 (C-3', C-5'), 155.4 (C-1'), 164.2 (C-1), 165.3 (C-3).

MS (70 eV): m/z (relative intensity) = 210 (M⁺, 16), 175 (M⁺ - Cl, 100), 122 (dimethylphenoxo, 10), 105 (dimethylphenyl, 19).

**E)-3-Benzoxoxyacryloyl Chloride (5d):** Reaction of benzyl vinyl ether and oxalyl chloride. Yield: 47%; bp 125°C/0.4 mbar.

UV (MeCN): λ_max (log ε) = 192 (4.470), 204 (4.082), 236 nm (4.100).

IR (film): υ = 1746 (C=O), 1612 cm⁻¹ (C=C).

1H NMR (CDCl₃/TMS): δ = 5.00 (s, 2H, benzyl-H), 5.60 (d, J = 12.5 Hz, 1H, 2-H), 7.37 (m, 5H, H-aromatic), 7.82 (d, J = 12.5 Hz, 1H, 3-H).

13C NMR (CDCl₃): δ = 74.64 (benzyl-C), 103.8 (C-2), 127.9 (C-2', C-6'), 128.9 (C-3', C-5'), 129.1 (C-4'), 134.1 (C-1'), 164.5 (C-1), 167.7 (C-3).

MS (70 eV): m/z (relative intensity) = 197 (M⁺, 1), 161 (M⁺ - Cl, 5), 105 (M⁺-benzyl, 12), 92 (benzyl + 1, 39), 91 (benzyl, 100).