# Improved Synthesis of (*E*)-3-Alkoxy- and (*E*)-3-Phenoxyacryloyl Chlorides

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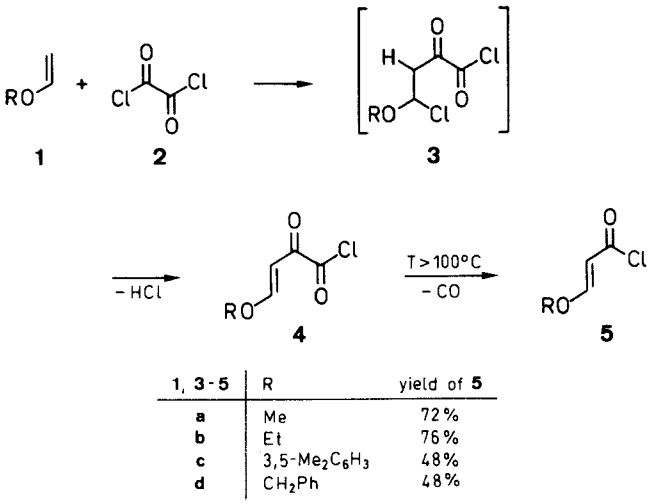
A one-step preparation of (*E*)-3-alkoxy- and (*E*)-3-phenoxyacryloyl chlorides by reaction of vinyl ethers and oxalyl chloride with subsequent decarbonylation is presented.

(*E*)-3-Alkoxy- and (*E*)-3-phenoxyacryloyl chlorides are valuable intermediates in organic syntheses,[1-9] inter alia in alkaloid synthesis[1] 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-phenoxyacryloyl chlorides can be prepared by reaction of vinyl ethers and phosgene[10,11] 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 Effenberger[13] 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-phenoxyacryloyl 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 ethoxyacryloyl chlorides **5a** and **b**, but also the phenoxy- and benzyloxyacryloyl 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 $\delta = 5.50-5.70$ 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 phenoxyacryloyl 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-phenoxyacryloyl chlorides.




| 1, 3-5 | R | yield of 5 |
|---|---|---|
| a | Me | 72 % |
| b | Et | 76 % |
| c | 3,5-$Me_2C_6H_3$ | 48 % |
| d | $CH_2Ph$ | 48 % |

**Scheme 1**

$^1$H and $^{13}$C NMR: Varian XL-200, VXR-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-Phenoxyacryloyl 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 Vigreux column.

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

IR (film): $\nu$ = 1744 (C=O), 1618 $cm^{-1}$ (C=C).

$^1H$ NMR ($CDCl_3$/TMS): $\delta$ = 3.84 (s, 3 H, OMe), 5.53 (d, $J$ = 12.5 Hz, 1 H, 2-H), 7.84 (d, $J$ = 12.5 Hz, 1 H, 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.[4] bp 105–107 °C/37–38 Torr).

IR (film): $\nu$ = 1744 (C=O), 1614 $cm^{-1}$ (C=C).

$^1H$ NMR ($CDCl_3$/TMS): $\delta$ = 1.40 (t, $J$ = 7.0 Hz, 3 H, $CH_3$), 4.04 (q, $J$ = 7.0 Hz, 2 H, $CH_2$), 5.50 (d, $J$ = 12.5 Hz, 1 H, 2-H), 7.78 (d, $J$ = 12.5 Hz, 1 H, 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′-Dimethylphenoxy)acryloyl Chloride* **(5c)**:
Reaction of 3,5-dimethylphenyl vinyl ether and oxalyl chloride. Yield: 48 %; bp 130 °C/0.4 mbar.

UV (MeCN): $\lambda_{max}$ (log $\varepsilon$) = 196 (4.563), 262 nm (4.064).

IR (film): $\nu$ = 1752 (C=O), 1614 $cm^{-1}$ (C=C).

$^1H$ NMR (nucleosides/TMS): $\delta$ = 2.35 (s, 6 H, 2 × $CH_3$), 5.75 (d, $J$ = 12.5 Hz, 1 H, 2-H), 6.68 ($m_c$, 2 H, 2′-, 6′-H), 6.87 ($m_c$, 1 H, 4′-H), 7.96 (d, $J$ = 12.5 Hz, 1 H, 3-H).

$^{13}C$ NMR ($CDCl_3$): $\delta$ = 21.21 (2 × $CH_3$), 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 (dimethylphenoxy, 10), 105 (dimethylphenyl, 19).

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

UV (MeCN): $\lambda_{max}$ (log $\varepsilon$) = 192 (4.470), 204 (4.082), 236 nm (4.100).

IR (film): $\nu$ = 1746 (C=O), 1612 $cm^{-1}$ (C=C).

$^1H$ NMR ($CDCl_3$/TMS): $\delta$ = 5.00 (s, 2 H, benzyl-H), 5.60 (d, $J$ = 12.5 Hz, 1 H, 2-H), 7.37 ($m_c$, 5 H, H-aromatic), 7.82 (d, $J$ = 12.5 Hz, 1 H, 3-H).

$^{13}C$ NMR ($CDCl_3$): $\delta$ = 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).

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