# A Convenient Synthetic Method for β-Alkoxy- and β-Phenoxyacrylic Acids and 3,4-Dihydro-2*H*-pyran-5- and 2,3-Dihydrofuran-4-carboxylic Acids

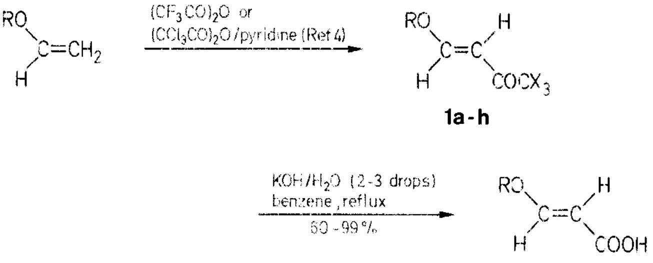
Masaru Hojo*, Ryōichi Masuda, Syūhei Sakaguchi, Makoto Takagawa

Department of Industrial Chemistry, Faculty of Engineering, Kobe University, Kobe, 657, Japan

*trans*-β-Trihaloacetylvinyl ethers **1** are easily hydrolyzed by wet potassium hydroxide in benzene, yielding the corresponding acids **2** in excellent yields. This synthetic method also can be applicable to cyclic vinyl ethers **3** and **5** to yield **4** and **6** in high yields.

Although methods[1,2,3] have been reported for synthesis of β-alkoxy- and β-phenoxyacrylic acids (**2**), yields in these procedures are not generally satisfactory, and starting materials are not readily available.

In earlier papers[4], we reported that commercial vinyl ethers react with trifluoroacetic anhydride or trichloroacetyl chloride quite readily at room temperature to give almost quantitative yields of *t*-β-trihaloacetylvinyl ethers **1**. In the course of subsequent studies in this field, we have found that **1** is easily hydrolysed to **2** in excellent yields (Scheme A) by a newly developed method; i.e., hydrolysis in the presence of wet potassium hydroxide in benzene.



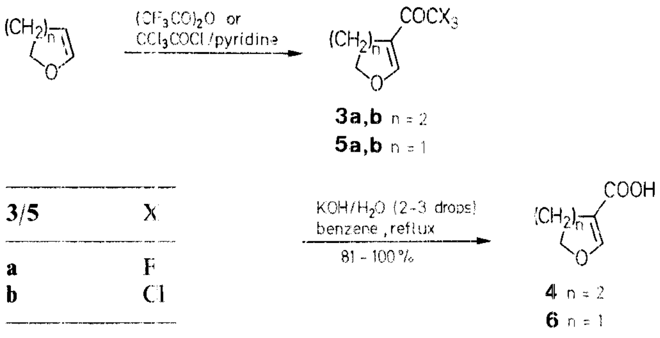
| 1 | R | X |
|---|---|---|
| a | $C_2H_5$ | F |
| b | $C_2H_5$ | Cl |
| c | $i$-$C_4H_9$ | F |
| d | $i$-$C_4H_9$ | Cl |
| e | $n$-$C_4H_9$ | F |
| f | $n$-$C_4H_9$ | Cl |
| g | $C_6H_5$ | F |
| h | $C_6H_5$ | Cl |

| 2 | R |
|---|---|
| a | $C_2H_5$ |
| b | $i$-$C_4H_9$ |
| c | $n$-$C_4H_9$ |
| d | $C_6H_5$ |

Scheme A

This synthetic method is also applicable to cyclic vinyl ethers, (Scheme **B**). For example, starting from commercially available 3,4-dihydro-2*H*-pyran trihaloacetylation and subsequent hydrolysis gives a quantitative yield of 3,4-dihydro-2*H*-pyran-5-carboxylic acid (**4**). This compound, **4**, was reported[5] to be formed in low yields with many by-products by treating 3,4-dihydro-2*H*-pyran with phosgene. We now wish to communicate a new convenient synthetic method for carboxylic acids, **2**, **4**, and **6** (Table 1).

Attempted hydrolysis of the β-trihalogenoacetylvinyl ethers (**1**, **3**, **5**) with saturated aqueous potassium hydroxide in ethanol resulted in the formation of the corresponding acids (**2**, **4**, **6**) in much lower yields. In the case of **3a**, 2-ethoxytetrahydropyran-3-carboxylic acid (**7**) was produced



| 3/5 | X |
|---|---|
| a | F |
| b | Cl |

Scheme **B**

**Table 1.** Syntheses of Compounds **2a–d**, **4**, **6**

| Substrate | Reaction Time [h] | Product[a] | m.p. [°C] | Yield [%] |
|---|---|---|---|---|
| **1a** | 1 | **2a** | 107–8[b] | 60 |
| **1b** | 5 | **2a** | 107–8[b] | 90 |
| **1c** | 7 | **2b** | 70 | 77 |
| **1d** | 7 | **2b** | 70 | 91 |
| **1e** | 8 | **2c** | 63 | 80 |
| **1f** | 8 | **2c** | 63 | 99 |
| **1g** | 1 | **2d** | 127–8[c] | 81 |
| **1h** | 8 | **2d** | 127–8[c] | 96 |
| **3a** | 7 | **4** | 73 | 100 |
| **3b** | 7 | **4** | 73 | 100 |
| **5a** | 5 | **6** | 73–4 | 81 |
| **5b** | 5 | **6** | 73–4 | 87 |

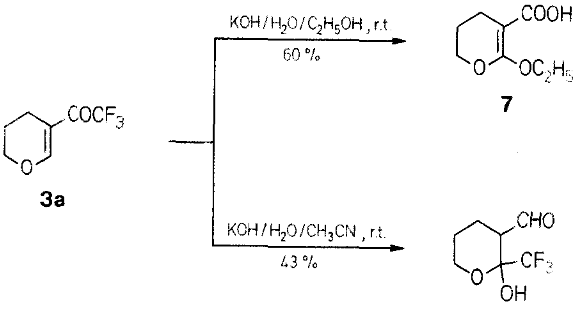
[a] All products are *trans*.
[b] Ref[1]., m.p. 109°C.
[c] Ref[3]., m.p. 127°C.

**Table 2.** Compounds **2a–d**, **4**, **6** Prepared

| Product | Molecular Formula[a] | IR (KBr) $\nu_{CO}$ [cm$^{-1}$] | $^1$H-NMR ($CDCl_3$/$TMS_{int}$) $\delta$ [ppm] |
|---|---|---|---|
| **2a** | $C_5H_8O_3$ (113.1) | 1697–1675 | 1.31 (q, 3H, $J$ = 7.0 Hz); 3.95 (q, 2H, $J$ = 7.0 Hz); 5.18 (d, 1H, $J$ = 12.0 Hz); 8.35 (s, 1H) |
| **2b** | $C_7H_{12}O_3$ (144.2) | 1690–1675 | 0.93 (d, 6H, $J$ = 7.0 Hz); 2.00 (m, 1H); 3.63 (d, 2H, $J$ = 7.0 Hz); 5.15 (d, 1H, $J$ = 12.0 Hz); 7.64 (d, 1H, $J$ = 12.0 Hz); 10.57 (s, 1H) |
| **2c** | $C_7H_{12}O_3$ (144.2) | 1685 | 0.74–1.88 (m, 7H); 3.82 (t, 1H, $J$ = 7.2 Hz); 5.08 (d, 1H, $J$ = 12.1 Hz); 7.55 (d, 1H, $J$ = 12.1 Hz); 11.50 (s, 1H) |
| **2d** | $C_9H_8O_3$ (164.2) | 1703; 1690 | 5.54 (d, 1H, $J$ = 12.0 Hz); 6.95–7.62 (m, 5H); 7.90 (d, 1H, $J$ = 12.0 Hz); 10.25 (s, 1H) |
| **4** | $C_6H_8O_3$ (128.1) | 1695–1650 | 1.93 (q, 2H, $J$ = 4.8 Hz); 2.27 (t, 2H, $J$ = 4.8 Hz); 4.07 (t, 2H, $J$ = 4.8 Hz); 7.69 (s, 1H); 10.23 (br. s, 1H) |
| **6** | $C_5H_6O_3$ (114.1) | 1670 | 2.74 (t, 2H, $J$ = 9.8 Hz); 4.50 (t, 2H, $J$ = 9.8 Hz); 7.12 (s, 1H); 10.52–10.69 (br. s, 1H) |

[a] Satisfactory microanalyses obtained: C ±0.36, H ±0.25.

in as much as 60 % yield, presumably by concurrent Michael type addition of ethanol. The use of *t*-butyl alcohol as solvent also resulted in low yields. Interestingly, when hydrolysis of **3a** was carried out with the use of a small amount of potassium hydroxide in wet acetonitrile at room temperature for 3 h, 2-trifluoromethyl-2-hydroxy-3-formyltetrahydropyran (**8**) was obtained 42 % yield (Scheme C). In contrast, the hydrolysis proceeded quite cleanly when the substrates (**1**, **3**, **5**) were refluxed in benzene in the presence of powdered wet potassium hydroxide for 1–8 h, giving the corresponding carboxylic acids (**2**, **4**, **6**) in excellent yields.



Scheme C

**trans-β-n-Butoxyacrylic acid (2c) from trans-n-butyl β-trichloroacetylvinyl ether; Typical Procedure:**

To a solution of *trans*-*n*-butyl β-trichloroacetylvinyl ether (0.519 g, 2.11 mmol) in benzene (30 ml), powdered potassium hydroxide (0.205 g, 3.65 mmol) and 2–3 drops of water are added. The mixture is refluxed for 8 h with stirring and then acidified with 6 normal hydrochloric acid and extracted with dichloromethane. After drying with sodium sulfate the solvent is removed *in vacuo* to yield **2c**, which is recrystallized from *n*-hexane; yield: 0.302 g (99 %); m.p. 63 °C.

**3,4-Dihydro-5-trifluoroacetyl-2*H*-pyran (3a):**

Trifluoroacetic anhydride (12.64 g, 60.2 mmol) is added dropwise to a stirred mixture of 3,4-dihydro-2*H*-pyran (2.52 g, 30.0 mmol) and pyridine (4.87 g, 61.3 mmol) in dichloromethane (20 ml) at room temperature, and the solution is allowed to stand for 1 d. After reaction, the mixture is added to an aqueous 10 % sodium carbonate solution (20 ml). After washing with water (2 × 30 ml) the dichloromethane layer is dried with sodium sulfate, and the solvent is evaporated to give **3a**; yield: 4.45 g (82 %); b.p. 64.6 °C/10.5 torr.

IR (liquid film): $\nu = 1680, 1600, 1180-1130\ \mathrm{cm}^{-1}$.

$^1$H-NMR ($CDCl_3/TMS_{int}$): $\delta = 2.02$ (q, 2 H, $J = 6.0$ Hz); 2.29 (t, 2 H, $J = 6.0$ Hz); 4.15 (t, 2 H, $J = 6.0$ Hz); 7.72 (s, 1 H).

**3,4-Dihydro-5-trichloroacetyl-2*H*-pyran (3b):**

A mixture of 3,4-dihydro-2*H*-pyran (1.69 g, 20.1 mmol, 1.5 eq.) of trichloroacetyl chloride (5.50 g, 30.3 mmol) and pyridine (1.49 ml) is stirred at room temperature for 3 h in chloroform (10 ml), to give **3b**; yield: 2.79 g (60 %); b.p. 132 °C/10 torr.

IR (liquid film): $\nu = 1670, 1600, 710-660\ \mathrm{cm}^{-1}$.

$^1$H-NMR ($CDCl_3/TMS_{int}$): $\delta = 2.03$ (q, 2 H, $J = 6.0$ Hz); 2.44 (t, 2 H, $J = 6.0$ Hz); 4.15 (t, 2 H, $J = 6.0$ Hz); 8.16 ppm (s, 1 H).

**2,3-Dihydro-4-trifluoroacetylfuran (5a):**

2,3-Dihydrofuran (3.07 g, 43.1 mmol) and 2 eq. of trifluoroacetic anhydride (17.88 g, 85.1 mmol) in the presence of pyridine (5.20 ml) are stirred at room temperature for 3 h in chloroform (20 ml) to give **5a**; yield: 6.21 g (73 %); b.p. 48.5 °C/10 torr.

IR (liquid film): $\nu = 1655, 1593, 1210-1130\ \mathrm{cm}^{-1}$.

$^1$H-NMR ($CDCl_3/TMS_{int}$): $\delta = 2.95$ (t, 2 H, $J = 9.8$ Hz); 4.66 (t, 2 H, $J = 9.8$ Hz); 7.63 ppm (s, 1 H).

**2,3-Dihydro-4-trichloroacetylfuran (5b):**

2,3-Dihydrofuran (2.98 g, 42.5 mmol) and 1.5 eq. of trichloroacetyl chloride (11.20 g, 61.6 mmol) in the presence of pyridine (4.92 ml) are stirred at room temperature for 3 h in chloroform (20 ml) to give **5b**; yield: 7.72 g (84 %); b.p. 123.3 °C/11.8 torr.

| | | | | |
|---|---|---|---|---|
| $C_6H_5Cl_3O_2$ | calc. | C 33.44 | H 2.34 | Cl 49.37 |
| (215.5) | found | 33.20 | 2.27 | 49.14 |

IR (liquid film): $\nu = 1660, 1585-1560, 800-600\ \mathrm{cm}^{-1}$.

$^1$H-NMR ($CDCl_3/TMS_{int}$): $\delta = 3.02$ (t, 2 H, $J = 9.8$ Hz); 4.65 (t, 2 H, $J = 9.8$ Hz); 7.82 ppm (s, 1 H).

**2-Ethoxytetrahydropyran-3-carboxylic Acid (7):**

A saturated aqueous solution of potassium hydroxide (5 ml) is added to a solution of **3a** (340 mg, 2 mmol) in ethanol (5 ml). The mixture is stirred at room temperature for 3 h and hydrochloric acid (6 normal) (10 ml) is added. After extraction with dichloromethane (20 ml), the organic layer is dried with sodium sulfate and evaporated to give **7**; yield: 208 mg (60 %); m.p. 102 °C.

| | | | |
|---|---|---|---|
| $C_8H_{14}O_4$ | calc. | C 55.16 | H 8.10 |
| (174.2) | found | 54.93 | 8.35 |

IR (KBr): $\nu = 3300-3400, 1710\ \mathrm{cm}^{-1}$.

$^1$H-NMR ($CDCl_3/TMS_{int}$): 1.19 (t, 3 H, $J = 7.2$ Hz), 1.40–2.05 (br, m, 4 H); 2.50–2.90 (br, m, 1 H); 3.62 (q, 2 H, $J = 7.2$ Hz); 3.30–3.95 (m, 2 H); 5.10 (d, 1 H, $J = 3.75$ Hz); 11.03 (s, 1 H).

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