Facile, Direct Reaction of Benzaldehydes to 3-Arylprop-2-Enoic Acids and 3-Arylprop-2-Ynoic Acids in Aqueous Medium

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Abstract

Wittig reactions of benzaldehydes, alkanals, and cycloalkanals as well as of acetophenones are carried out with alkoxycarbonyl methylidenetriphenylphosphoranes in 10 w% aqueous NaOH, where the cinnamates and alkenoates produced are hydrolysed *in situ* and the corresponding acids are obtained after mostly simple extractive work-up, often without employing organic solvents. Under the same conditions, benzaldehydes are reacted with alkoxycarbonyl bromomethylidenephosphorane to produce 3-arylprop-2-ynoic acids (arylpropiolic acids).

Keywords

1. Introduction

Cinnamic acids and their derivatives have a wide range of uses. They can have antifungal [1] and/or antimicrobial [2] activity. Applications of cinnamic acid and derivatives can be found in the cosmetic industry, where they have been employed as firming agents in formulations used in skin care products [3]. Additionally, cinnamic acids and derivatives have found use as flavorants [4], and especially the alkoxylated and hydroxylated

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cinnamic acids are utilized as stabilizers in the food industry [5]. Also, they are key building blocks in various synthetic preparations in the industry. Cinnamic acid itself is an intermediate in the production of phenylalanine, and thus of aspartame [6]. The authors [7] [8] have communicated their interest in cinnamic acids previously, because some cinnamic acids [7]-[9] and especially dihydroxycinnamic acid derivatives show anti-cancer activity.

Cinnamic acids have been prepared in a number of ways. Among them, the reaction of benzaldehydes with malonic acid is the most common (Knoevenagel reaction with subsequent decarboxylation [10]-[11]). This strategy has been augmented recently by the reaction of benzaldehydes with Meldrum's acid [12]. Also, cinnamic acids can be prepared by the reaction of benzaldehydes with acetic anhydride/sodium acetate (Perkin reaction [13]), and of iodoarenes with acrylates via Heck reaction [14] with subsequent hydrolysis in a two-step sequence. Some of the reactions above give variable yields and others require special catalysts [12]. Therefore, the Wittig olefination reaction of benzaldehydes with stabilized alkoxymethylidenetriphenylphosphoranes remains an alternative in the preparation of cinnamic acids, and so has been used extensively, too [15].

Conventional Wittig reactions with stabilized phosphoranes have been carried under elevated temperature in organic solvents such as THF and benzene, sometimes under acid catalysis (Bestmann variation) [16]. In more recent times, so-called non-classical reaction conditions [17] have been forwarded for the Wittig olefination, such as carrying out reactions under solventless [18] conditions or in ionic liquids [19]. Often, this has been combined with microwave irradiation or ultrasonication. Also, water soluble phosphoranes [20]-[22] have been developed to carry out the reactions in aqueous solutions. Afterwards, it was seen that olefination reactions could also be performed in water with stabilized and semi-stabilized, non-water soluble phosphoranes [23]-[34], with one communication on a Wittig reaction utilizing semi-stabilized and non-stabilized phosphoranes in a biphasic mixture under phase transfer conditions (PTC) [35]. Nevertheless, almost all of these cases involve extractive work-up and often chromatographic separations using organic solvents. Mostly, such work-up utilizes greater amounts of organic solvent than does the reaction itself, if it were run in organic medium. Before, the authors had developed a biphasic reaction system of water and hexane for the Wittig olefination with stabilized and semi-stabilized phosphoranes [36]. Here, the reaction proceeds mostly at the solvent interface [37], giving the product after simple evaporation of the hexane phase, where the organic solvent can be recycled. Nevertheless, possibilities of using such a strategy are rare.

In the following, a methodology is introduced which involves a one-pot olefination-hydrolysis sequence, where the unsaturated carboxylic acid is the final product, which can be isolated by acidification of the reaction medium, and, in the case of the cinnamic acid products, by simple filtration. The reaction sequence is well-suited for educational laboratories also, and has been shown to give reproducible good yields with our undergraduate students.

2. Experimental

2.1. Chemicals and Instruments

Experimental

General Remarks. Melting points were measured on a Stuart SMP 10 melting point apparatus and are uncorrected. Infrared spectra were measured with a Thermo/Nicolet Nexus 470 FT-IR ESP spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Varian 400 NMR spectrometer (^{1}H at 395.7 MHz, ^{13}C at 100.5 MHz). The assignments of the carbon signals were aided by DEPT 90 and DEPT 135 experiments (DEPT = Distortionless Enhancement by Polarisation Transfer). The chemical shifts are relative to TMS (solvent CDCl$_3$, unless otherwise noted). Mass spectra were measured with a JMS-01-SG-2 spectrometer, and with an Agilent QTOF 6540 UHD. Column chromatography, where necessary, was performed on silica gel (S, 0.063 mm - 0.1 mm, Riedel de Haen and Merck grade 9385).

2-Methoxybenzaldehyde (**1a**), 2,4-dimethoxybenzaldehyde (**1g**) and 4-benzyloxybenzaldehyde (**1x**) were prepared from the corresponding, commercially available hydroxybenzaldehydes (KOH, DMSO, CH$_3$I or PhCH$_2$Br) [38]. Benzaldehydes **1n** and **1o** were synthesized by bromination (NBS, DMF, rt) of 2-hydroxy- and 4-hydroxybenzaldehydes, respectively, followed by alkylation (KOH, DMSO, CH$_3$I). The other benzaldehydes were acquired commercially. The 4-haloacetophenones **7b-d** and 1-acetylanthracene (**8**) were obtained by acetylation (AcCl, AlCl$_3$) of the parent acetophenones and anthracene, respectively. Phosphoranes **2a** [39] and **2b** [40] were prepared according to literature procedures.

20 and **22** were prepared by Wittig olefination, starting from 2-benzyloxybenzaldehyde and benzoylmethyli-denetriphenylphosphorane and from 2-benzyloxycinnamaldehyde (**24**) and toluoylmethylidenetriphenylphos-phorane.

2.2. General Procedure A

(*E*)-Cinnamic acid (**3f**). To a mixture of benzaldehyde (**1f**, 1.60 g, 15.1 mmol) and ethoxycarbonylmethylidene-triphenylphosphorane (**2a**, 6.82 g, 19.5 mmmol) was given an aq. NaOH solution (9.1 w%, 3.5 g (87.5 mmol) NaOH in 35 mL H_2O) and the resulting suspension was stirred at 75˚C for 23 h. Triphenylphosphine oxide was filtered off the cooled solution. Thereafter, the filtrate was acidified carefully with 15 w% aq. HCl. The resulting suspension was cooled and filtered. The solid obtained was dried in air to give cinnamic acid (**3f**, 1.89 g, 77%) as a colorless solid; mp. 132˚C [Lit. 132˚C - 135˚C [41]]; v_{max} (KBr/cm^{-1}) 1690 (C=O), 1631, 1454, 1312, 1290, 1225, 771, 714; δ_H (270 MHz, DMSO-d^6) 6.51 (1H, d, ^3J = 16.0 Hz), 7.39 (2H, m), 7.57 (1H, d, ^3J = 16.0 Hz), 7.59 - 7.66 (3H, m), 12.35 (1H, bs); δ_C (67.8 MHz, DMSO-d^6) 119.7, 128.6 (2C), 129.3 (2C), 130.7, 134.7, 144.4, 168.0; MS (EI, 70 eV) m/z (%) 148 (M$^+$) (100), 77 (40).

(*E*)-2-Methoxycinnamic acid (**3a**) (Procedure A). Colorless solid; mp. 187˚C [Lit. 183˚C - 186˚C [41]]; v_{max} (KBr/cm^{-1}) 1682 (C=O), 1620 (C=C), 1489, 1463, 1426, 1332, 1282, 1248, 1220 (C-O), 1025, 994, 941, 755, 696, 596, 567; δ_H (400 MHz, DMSO-d^6) 3.84 (3H, s, OCH$_3$), 6.48 (1H, d, ^3J = 16.0 Hz), 6.96 (1H, dd, ^3J = 7.6 Hz, ^3J = 7.2 Hz), 7.06 (1H, d, ^3J = 8.4 Hz), 7.36 - 7.40 (1H, m), 7.64 - 7.66 (1H, m), 7.81 (1H, d, ^3J = 16.0 Hz); δ_C (100.5 MHz, DMSO-d^6) 56.1, 112.2, 119.7, 121.2, 122.9, 128.9, 132.2, 139.1, 158.2, 168.3; MS (EI, 70 eV) m/z (%) = 178 (M$^+$, 89), 147 (M$^+$-OCH$_3$, 100).

(*E*)-4-Methoxycinnamic acid (**3b**) (Procedure A). Colorless solid; mp. 173˚C [Lit. 173˚C [41]]; v_{max} (KBr/cm^{-1}) 1694 (C=O), 1596 (C=C), 1336, 826, 685, 566, 527, 513; δ_H (400 MHz, CDCl$_3$) 3.85 (3H, s, OCH$_3$), 6.33 (1H, d, ^3J = 16.0 Hz), 6.92 (2H, d, ^3J = 8.8 Hz), 7.51 (2H, d, ^3J = 8.8 Hz), 7.75 (1H, d, ^3J = 16.0 Hz); δ_C (100.5 MHz, CDCl$_3$) 55.4 (OCH$_3$), 114.4 (2C, CH), 114.6 (CH), 126.8 (C$_{quat}$), 130.1 (2C, CH), 146.7 (CH), 161.7 (C$_{quat}$), 172.2 (C$_{quat}$, CO); MS (70 eV, EI) m/z (%) 178 (M$^+$, 65).

(*E*)-4-Ethoxycinnamic acid (**3c**) (Procedure A). Colorless solid, mp. 196˚C [Lit. mp. 195˚C - 199˚C [41]]; δ_H (400 MHz, DMSO-d^6) 1.30 (3H, t, ^3J = 7.2 Hz, CH$_3$), 4.02 (2H, q, ^3J = 7.2 Hz, OCH$_2$), 6.34 (1H, d, ^3J = 16.0 Hz), 6.92 (2H,. d, ^3J = 8.4 Hz), 7.51 (1H, d, ^3J = 16.0 Hz), 7.59 (2H, d, ^3J = 8.4 Hz); δ_C (100.5 MHz, DMSO-d^6) 15.0 (CH$_3$), 63.7 (CH$_2$), 115.2 (2C, CH), 116.8 (CH), 127.1 (C$_{quat}$), 130.4 (2C, CH), 144.2 (CH), 160.7 (C$_{quat}$), 168.3 (C$_{quat}$, CO); MS (EI, 70 eV) m/z (%) = 192 (M$^+$, 61), 146 (54), 118 (100).

(*E*)-4'-Propoxycinnamic acid (**3d**) (Procedure A). Colorless solid, mp. 155˚C [Lit. 155˚C [42]]; δ_H (400 MHz, DMSO-d^6) 0.96 (3H, t, ^3J = 7.2 Hz, CH$_3$), 1.70 (qt, ^3J = 7.2 Hz, ^3J = 6.4 Hz), 3.95 (2H, t, ^3J = 6.4 Hz), 6.34 (1H, d, ^3J = 16.0 Hz), 6.94 (2H, d, ^3J = 8.8 Hz), 7.51 (1H, d, ^3J = 16.0 Hz), 7.59 (2H, d, ^3J = 8.8 Hz); δ_C (100.5 MHz, DMSO-d^6) 14.1, 19.1, 67.8, 115.2 (2C), 116.8, 127.1, 130.4, 144.2, 160.9, 168.3.

(*E*)-4'-(*N,N*-Dimethylamino)cinnamic acid (**3e**) (Procedure A). Colorless solid, mp. 226˚C; [Lit. 227 - 228˚C [41]]; v_{max} (KBr/cm^{-1}) 2922 (CH), 1679 (C=O), 1598 (C=C), 1230, 1202, 815; δ_H (400 MHz, DMSO-d^6) 2.94 (6H, s, 2 CH$_3$), 6.19 (1H, d, ^3J = 16.0 Hz), 6.68 (2H, d, ^3J = 9.2 Hz), 7.43 (1H, d, ^3J = 16.0 Hz), 7.45 (2H, d, ^3J = 9.2 Hz), 11.93 (bs, 1H, OH); δ_C (100.5 MHz, CDCl$_3$) 39.4 (2C, CH$_3$), 111.8 (2C, CH), 113.1 (CH), 121.6 (C$_{quat}$), 129.6 (2C, CH), 144.6 (CH), 151.6 (C$_{quat}$), 168.0 (C$_{quat}$, CO); MS (EI, 70 eV) m/z (%) 191 (M$^+$, 100), 147 (17).

(*E*)-2,4-Dimethoxycinnamic acid (**3g**) (Procedure A). Colorless solid, mp. 191˚C; [Lit. 192˚C - 194˚C [41]]; δ_H (400 MHz, DMSO-d^6/CDCl$_3$) 3.81 (3H, s, OCH$_3$), 3.86 (3H, s, OCH$_3$), 6.33 (1H, d, ^3J = 16.0 Hz), 6.51 (2H, m), 7.47 (1H, d, ^3J = 8.0 Hz), 7.80 (1H, d, ^3J = 16.0 Hz); δ_H (100.5 MHz, DMSO-d^6/CDCl$_3$) 55.2 (OCH$_3$), 55.3 (OCH$_3$), 98.1 (CH), 105.9 (CH), 115.9 (C$_{quat}$), 116.3 (CH), 129.6 (CH), 138.8 (CH), 159.4 (C$_{quat}$), 162.7 (C$_{quat}$), 168.3 (C$_{quat}$, CO).

(*E*)-2,5-Dimethoxycinnamic acid (**3h**) (Procedure A). Colorless solid; mp. 149 ˚C; [Lit. 148˚C - 150˚C [41]]; v_{max} (KBr/cm^{-1}) 1697 (C=O), 1627 (C=C), 1581, 1503, 1430, 1323, 1228 (C-O), 1189 (C-O), 1052, 1019, 988, 941, 858, 788, 700, 629, 537, 487, 456; δ_H (400 MHz, DMSO-d^6) 3.72 (3H, s, OCH$_3$), 3.78 (3H, s, OCH$_3$), 6.53 (1H, d, ^3J = 16.4 Hz), 6.97 (1H, d, ^3J = 6.4 Hz), 6.99 (1H, d, ^3J = 6.4 Hz), 7.21 (1H, d, ^4J = 3.2 Hz), 7.78 (1H, d, ^3J = 16.4 Hz); δ_C (100.5 MHz, CDCl$_3$) 56.0 (OCH$_3$), 57.0 (OCH$_3$), 112.5, 113.5, 117.8, 118.0, 123.6, 142.2, 153.2 (C$_{quat}$), 153.6 (C$_{quat}$), 173.0 (C$_{quat}$, CO); MS (EI, 70 eV) m/z (%) = 208 (M$^+$, 100), 177 (M$^+$-OCH$_3$, 33).

4-Bromo-2,5-dimethoxycinnamic acid (**3i**) (Procedure A) as a mixture of *E*- and *Z*-isomers (72/28), pale yellow solid, mp. 177˚C - 180˚C (for the *E*-/*Z*-mixture); v_{max} (KBr/cm^{-1}) [*E*/*Z*-mixture] 3502 - 2829 (bs, OH),

1687 (C=O), 1677 (C=O), 1629 (C=C), 1565, 1499, 1441, 1392, 1329, 1255, 1207, 1052, 987, 917, 867, 822, 739, 696, 638, 617, 541; (*Z*)-isomer δ_H (400 MHz, CDCl$_3$) 3.80 (3H, s, OCH$_3$), 3.84 (3H, s, OCH$_3$), 6.01 (1H, d, ^3J = 12.8 Hz), 7.07 (1H, s), 7.23 (1H, d, ^3J = 12.8 Hz), 7.39 (1H, s); δ_C (100.5 MHz, CDCl$_3$) 56.2 (OCH$_3$), 56.3 (OCH$_3$), 113.5 (C$_{quat}$), 114.8 (CH), 115.8 (CH), 119.0 (CH), 123.0 (C$_{quat}$), 140.4 (CH), 149.3 (C$_{quat}$), 151.8 (C$_{quat}$), 170.9 (C$_{quat}$, CO); (*E*)-isomer δ_H (400 MHz, CDCl$_3$) 3.85 (3H, s, OCH$_3$), 3.89 (3H, s, OCH$_3$), 6.51 (1H, d, ^3J = 16.0 Hz), 7.03 (1H, s), 7.13 (1H, s), 8.00 (1H, d, ^3J = 16.0 Hz); δ_C (100.5 MHz, CDCl$_3$) 56.3 (OCH$_3$), 56.8 (OCH$_3$), 111.6 (CH), 115.3 (C$_{quat}$), 116.9 (CH), 118.0 (CH), 122.6 (C$_{quat}$), 141.5 (CH), 150.2 (C$_{quat}$), 153.0 (C$_{quat}$), 172.2 (C$_{quat}$, CO); MS (EI, 70 eV) *m/z* (%) = 288 ([^{81}BrM$^+$, 11), 286 ([^{79}BrM$^+$, 13).

(*E*)-4-Methylcinnamic acid (3j) (Procedure A). Colorless solid, mp. 195°C - 199°C [Lit. 196°C - 198°C [41]]; ν_{max} (KBr/cm^{-1}) 3550 - 2330 (bs, OH), 1678 (C=O), 1624 (C=C), 1423, 1312, 1285, 1223, 987, 944, 812, 687, 554, 495; δ_H (400 MHz, CDCl$_3$) 2.38 (3H, s, CH$_3$), 6.40 (1H, d, ^3J = 16.0 Hz), 7.21 (2H, d, ^3J = 8.0 Hz), 7.45 (2H, d, ^3J = 8.0 Hz), 7.76 (1H, d, ^3J = 16.0 Hz); δ_H (400 MHz, DMSO-d^6) 2.33 (3H, s, CH$_3$), 6.49 (1H, d, ^3J = 16.0 Hz), 7.23 (2H, d, ^3J = 8.4 Hz), 7.57 (2H, d, ^3J = 8.4 Hz), 7.58 (1H, d, ^3J = 16.0 Hz), 12.3 (1H, bs, OH); δ_C (100.5 MHz, DMSO-d^6) 30.0 (CH$_3$), 118.1 (CH), 128.2 (2C, CH), 129.6 (2C, CH), 131.6 (C$_{quat}$), 140.2 (C$_{quat}$), 144.0 (CH), 167.6 (C$_{quat}$, CO); MS (EI, 70 eV) *m/z* (%) = 162 (100) (M$^+$), 115 (43).

(*E*)-3-Chlorocinnamic acid (3k) (Procedure A). Colorless crystals, mp. 165°C; [Lit. 161°C - 164°C [41]]; ν_{max} (KBr/cm^{-1}) 1677 (C=O), 1632 (C=C), 1430, 1323, 1301, 1283, 1230, 1200, 943, 864, 727, 680, 669, 597, 550; δ_H (400 MHz, DMSO-d^6) 6.59 (1H, d, ^3J = 16.4 Hz), 7.41 - 7.45 (2H, m), 7.55 (1H, d, ^3J = 16.4 Hz), 7.63 - 7.65 (1H, m), 7.78 - 7.79 (1H, m); ^{13}C NMR (100.5 MHz, DMSO-d^6) 121.4, 127.2, 128.3, 130.2, 131.1, 134.2, 137.0, 142.7, 167.8; MS (EI, 70 eV) *m/z* (%) = 182 ([^{81}Cl]M$^+$, 100), 181 ([^{79}ClM$^+$], 77), 147 (36).

3-Bromocinnamic acid (3L) (Procedure A). Colorless solid; mp. 170°C [Lit. 177°C [41]]; ν_{max} (KBr/cm^{-1}) 3050 - 2550 (bs, OH), 2972 (C-H), 1694 (C=O), 1629 (C=C), 1424, 1318, 1219 (C-O), 977, 936, 784, 720, 664, 542; δ_H (400 MHz, DMSO-d^6) 6.57 (1H, d, ^3J = 16.4 Hz), 7.35 (1H, dd, ^3J = 8.0 Hz, ^3J = 8.0 Hz), 7.52 - 7.62 (2H, m), 7.52 (1H, d, ^3J = 16.4 Hz), 7.67 (1H, bd, ^3J = 8.0 Hz), 7.89 (1H, m); δ_C (100.5 MHz, DMSO-d^6) 121.3, 122.7, 127.5, 131.1, 131.4, 133.2, 137.2, 142.7, 167.8 (CO); MS (EI, 70 eV) *m/z* (%) = 228 (95) ([^{81}Br]M$^+$), 226 (100) ([^{79}Br]M$^+$), 147 (61).

(*E*)-3-Fluorocinnamic acid (3m) (Procedure A).Colorless solid; mp. 168°C - 169°C [Lit. 167°C - 170°C [41]]; ν_{max} (KBr/cm^{-1}) 1693 (C=O), 1632, 1588, 1295, 1249, 940, 859, 782, 552; δ_H (400 MHz, DMSO-d^6) 6.57 (1H, d, ^3J = 16.0 Hz), 7.19 - 7.24 (1H, m), 7.40 - 7.56 (3H, m), 7.50 (1H, d, ^3J = 16.0 Hz); δ_C (100.5 MHz, DMSO-d^6) 114.8 ($^2J_{CF}$ = 21.7 Hz), 117.3 ($^2J_{CF}$ = 21.0 Hz), 121.3, 125.1, 131.3 ($^3J_{CF}$ = 8.2 Hz), 137.2 ($^3J_{CF}$ = 8.2 Hz), 143.0, 162.8 ($^1J_{CF}$ = 243 Hz), 167.9 (CO); MS (EI, 70 eV) *m/z* (%) = 166 (100) (M$^+$), 149 (30), 121 (33).

(*E*)-3,5-Dibromo-4-methoxycinnamic acid (3n) [43] (Procedure A). Colorless solid; mp. 198°C. ν_{max} (KBr/cm^{-1}) 3100 - 2597 (bs, OH), 1703 (C=O), 1633 (C=C), 1472, 1424, 1268, 1217, 978, 851, 747; δ_H (400 MHz, CDCl$_3$) 3.92 (3H, s, OCH$_3$), 6.37 (1H, d, ^3J = 16.4 Hz), 7.59 (1H, d, ^3J = 16.4 Hz), 7.69 (2H, s); δ_C (100.5 MHz, CDCl$_3$) 60.8 (OCH$_3$), 118.8 (2C, C$_{quat}$), 119.0 (CH), 132.3 (2C, CH), 143.3 (CH), 155.8 (C$_{quat}$), 170.9 (C$_{quat}$, CO).

(*E*)-2-Bromo-4,5-dimethoxycinnamic acid (3o) (Procedure A).Colorless solid, mp. 240°C - 244°C [Lit. 246°C - 247°C [44]]; ν_{max} (KBr/cm^{-1}) 3496 - 2578 (bs, OH), 1697 (C=O), 1596 (C=C), 1512, 1390, 1310, 1267, 1206, 1163, 1027, 969, 854, 814; δ_H (400 MHz, CDCl$_3$) 3.87 (3H, s, OCH$_3$), 3.90 (3H, s, OCH$_3$), 6.55 (1H, d, ^3J = 16.0 Hz), 6.58 (1H, s), 6.77 (1H, s), 7.60 (1H, d, ^3J = 16.0 Hz); δ_C (100.5 MHz, CDCl$_3$) 56.0 (OCH$_3$), 56.2 (OCH$_3$), 114.1 (CH), 115.4 (C$_{quat}$), 118.3 (CH), 122.0 (CH), 131.6 (C$_{quat}$), 144.6 (CH), 148.5 (C$_{quat}$), 150.3 (C$_{quat}$), 167.7 (C$_{quat}$, CO). Found: C, 45.70%; H, 3.86%. Calcd. for 46.02%; H, 3.86%.

(2*E*,4*E*)-5-Phenylpenta-2,4-dienoic acid (3p) (Procedure A). Pale yellow solid, mp. 165°C - 166°C [Lit. mp. 165°C [45]]; ν_{max} (KBr/cm^{-1}) 3500 - 2850 (bs, OH), 1678 (C=O), 1609 (C=C), 1582, 1285; δ_H (400 MHz, CDCl$_3$) 6.00 (1H, d, ^3J = 15.0 Hz), 6.90 - 6.96 (2H, m), 7.21 - 7.56 (6H, m); δ_C (100.5 MHz, CDCl$_3$) 120.1, 126.1, 127.3, 128.9, 129.3, 135.9, 141.7, 146.9, 171.8; MS (EI, 70 eV) *m/z* (%) = 174 (21) (M$^+$), 129 (100).

(*E*)-3-(Thien-2-yl)acrylic acid (3q) (Procedure A). Colorless solid, mp. 145°C; [Lit. 145°C - 148°C [41]]. ν_{max} (KBr/cm^{-1}) 3200 - 2500 (bs, OH), 1677 (C=O), 1615 (C=C), 1410, 1308, 1274, 1244, 1218, 1190, 972, 925, 860, 834, 715, 598, 531; δ_H (400 MHz, CDCl$_3$) 6.24 (1H, d, ^3J = 15.6 Hz), 7.08 (1H, dd, ^3J = 5.2 Hz, ^3J = 4.0 Hz), 7.31 (1H, d, ^3J = 4.0 Hz),7.43 (1H, d, ^3J = 5.2 Hz), 7.88 (1H, d, ^3J = 15.6 Hz); δ_C (100.5 MHz, CDCl$_3$) 115.9 (CH), 128.2 (CH), 129.3 (CH), 131.7 (CH), 139.2 (C$_{quat}$), 139.4 (CH), 172.2 (C$_{quat}$, CO); MS (FAB, 3-nitrobenzyl alcohol) *m/z* (%) = 155 (17) (MH$^+$).

(*E*)-5-Bromothien-2-ylacrylic acid (3r) (Procedure A). Colorless solid, mp. 207°C [Lit. 209°C - 210°C [46]];

ν_{max} (KBr/cm^{-1}) 3430 - 2597 (bs, OH), 1688 (C=O), 1615 (C=C), 1433, 1407, 1298, 1268, 1211, 966, 795, 533; δ_H (400 MHz, DMSO-d^6) 6.11 (1H, d, ^3J = 16.0 Hz), 7.22 (1H, d, ^3J = 4.4 Hz), 7.29 (1H, d, ^3J = 4.4 Hz), 7.62 (1H, d, ^3J = 16.0 Hz); δ_C (100.5 MHz, DMSO-d^6) 115.4, 118.6, 132.3, 132.9, 136.3, 141.1, 167.6.

(*E*)-3,4-Dimethoxycinnamic acid (3s) (Procedure A). Colorless solid, mp. 183˚C [Lit. 181˚C - 183˚C [41]]; ν_{max} (KBr/cm^{-1}) 3300 - 2500 (bs, OH), 1677 (C=O), 1624, 1596, 1517, 1463, 1426, 1340, 1250, 1140, 1025, 975, 840, 579, 536; δ_H (400 MHz, DMSO-d^6) 3.78 (3H, s, OCH$_3$), 3.80 (3H, s, OCH$_3$), 6.41 (1H, d, ^3J = 16.0 Hz), 6.86 (1H, d, ^3J = 8.0 Hz), 7.10 (1H, s), 7.13 (1H, d, ^3J = 8.0 Hz), 7.50 (1H, d, ^3J = 16.0 Hz), 12.19 (1H, bs, OH); δ_C (100.5 MHz, DMSO-d^6) 56.0, 56.1, 110.7, 112.0, 117.2, 123.1, 127.5, 144.6, 149.4, 151.2, 168.3; MS (EI, 70 eV) *m/z* (%) = 208 (M$^+$, 100), 193 (M$^+$-CH$_3$, 21).

(*E*)-3,4-Diethoxycinnamic acid (3t) (Procedure A). Colorless solid, mp. 154˚C [Lit. 156˚C [47]] δ_H (400 MHz, CDCl$_3$) 1.46 (6H, t, ^3J = 6.8 Hz, 2 CH$_3$), 4.12 (2H, q, ^3J = 6.8 Hz, OCH$_2$), 4.13 (2H, q, ^3J = 6.8 Hz, OCH$_2$), 6.28 (1H, d, ^3J = 16.0 Hz), 6.85 (1H, d, ^3J = 8.0 Hz), 7.07 (1H, s), 7.08 (1H, d, ^3J = 8.0 Hz), 7.70 (1H, d, ^3J = 16.0 Hz); δ_C (100.5 MHz, CDCl$_3$) 14.6, 14.7, 64.5, 64.6, 111.9, 112.6, 114.6, 123.1, 126.9, 147.1, 148.8, 151.3, 172.4.

(*E*)-3,4-(Methylenedioxy)-cinnamic acid (3u) (Procedure A). Mp. 214˚C [Lit. 242˚C - 244˚C [41]]; ν (KBr/cm^{-1}) 3200 - 2500 (bs, OH), 1693 (C=O), 1624 (C=C), 1495, 1446, 1314, 1251, 1100, 1036, 924, 805; δ_H (400 MHz, DMSO-d^6) 6.08 (2H, s), 6.39 (1H, d, ^3J = 15.6 Hz), 6.95 (1H, d, ^3J = 8.0 Hz), 7.16 (1H, dd, ^3J 8.0 Hz, ^4J = 1.6 Hz), 7.37 (1H, d, ^4J = 1.6 Hz), 7.51 (1H, d, ^3J = 15.6 Hz); δ_C (100.5 MHz, DMSO-d^6) 101.4, 106.6, 108.4, 117.0, 124.5, 128.6, 143.7, 147.9, 149.0, 167.7; MS (EI, 70 eV) *m/z* (%) = 192 (M$^+$, 100), 145 (13).

(*E*)-2-Chlorocinnamic acid (3v) (Procedure A). Colorless solid; mp. 200˚C [Lit. mp. 208˚C - 210˚C [41]]; ν_{max} (KBr/cm^{-1}) 3050 - 2500 (bs, OH), 2971 (C-H), 1687 (C=O), 1622 (C=C), 1427, 1281, 1224, 1041, 978, 921, 727, 595, 560; for *E*-3v: δ_H (400 MHz, DMSO-d^6) 6.57 (1H, d, ^3J = 16.0 Hz), 7.51 (1H, dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz), 7.35 – 7.45 (2H, m), 7.84 (1H, d, ^3J = 16.0 Hz), 7.89 (1H, dd, ^3J = 7.6 Hz, ^4J = 2.0 Hz); δ_C (100.5 MHz, DMSO-d^6) 122.7, 128.3, 128.6, 130.4, 132.2 (2C), 134.0, 139.2, 167.7 (C$_{quat}$, CO); for *Z*-3v: δ_H (400 MHz, DMSO-d^6) 6.10 (1H, d, ^3J = 12.0 Hz), 7.03 (1H, d, ^3J = 12.0 Hz), 7.26 - 7.45 (4H, m); δ_C (100.5 MHz, DMSO- d^6) 124.2, 127.1, 129.3, 131.1, 132.3 (2C), 134.5, 138.5, 167.2 (C$_{quat}$, CO); MS (EI, 70 eV) *m/z* (%) = 182 (15) ([^{35}Cl]M$^+$), 147 (100).

Ethyl (*E*)-4-nitrocinnamate (3w) and (*E*)-4-nitrocinnamic acid (3x). A mixture of 4-nitrobenzaldehyde (1w, 1.51 g, 10 mmol) and phosphorane 2a (4.87 g, 14 mmol) in chloroform (0.5 mL) was heated to 120˚C for 45 min. The cooled solution is subjected directly to column chromatography on silica gel (CHCl$_3$/ether/hexane 1:1:1) to give 3w (1.97 g, 89%) as a light yellow solid; mp. 140˚C; [Lit. 138˚C - 140˚C [41]]; ν_{max} (KBr/cm^{-1}) 3106, 3079 (C-H$_{arom.}$), 2983 (C-H$_{aliph}$), 2939 (C-H$_{aliph}$), 1712 (C=O), 1645, 1594, 1340 (NO$_{2(s)}$), 1189, 1177, 1110, 1029, 1189, 1171, 1110, 1028, 978, 845, 759; δ_H (400 MHz, CDCl$_3$) 1.35 (3H, t, ^3J = 7.2 Hz), 4.29 (2H, q, ^3J = 7.2 Hz), 6.55 (1H, d, ^3J = 16.4 Hz), 7.70 (1H, d, ^3J = 16.4 Hz), 7.66 (2H, d, ^3J = 8.8 Hz), 8.25 (2H, d, ^3J = 8.8 Hz). A solution of 3w (1.95 g, 8.82 mmol) in a mixture of aq. NaOH (10w%, 50 mL) and methanol (10 mL) was heated at 65˚C for 12h. Thereafter, the solution was filtered, and the filtrate was acidified with half-conc. aq. HCl. The formed precipitate was filtered, washed with water (3 × 20 mL) and air-dried to give 3x (1.62 g, 95%) as a light yellowish solid; mp. 287˚C [Lit. mp. 289˚C [40]]; ν_{max} (KBr/cm^{-1}) 3500 - 2499 (bs, OH), 1686 (C=O), 1628 (C=C), 1522 (NO$_{2(as)}$), 1426, 1350 (NO$_{2(s)}$), 1308, 1283, 1222, 985, 836, 716; δ_H (400 MHz, DMSO-d^6) 6.69 (1H, d, ^3J = 16.0 Hz), 7.64 (1H, d, ^3J = 16.0 Hz), 7.92 (2H, d, ^3J = 8.8 Hz), 8.20 (2H, d, ^3J = 8.8 Hz); δ_C (100.5 MHz, DMSO-d^6) 124.4 (2C, CH), 129.7 (2C, CH), 123.9 (CH), 141.1 (C$_{quat}$), 141.8 (CH), 148.4 (C$_{quat}$), 167.5 (C$_{quat}$, CO); MS (EI, 70 eV) *m/z* (%) 193 (M$^+$, 65), 176 (18), 147 (15).

(*Z*)-4-Benzyloxycinnamic acid (3y) (Procedure A). Colorless solid; mp. 168˚C; δ_H (400 MHz, DMSO-d^6) 5.11 (2H, s, OCH$_2$), 5.79 (1H, d, ^3J = 12.8 Hz), 6.80 (1H, d, ^3J = 12.8 Hz), 6.98 (2H, d, ^3J = 8.8 Hz), 7.40 (2H, d, ^3J = 8.4 Hz), 7.57 (2H, d, ^3J = 8.4 Hz), 7.67 (2H, d, ^3J = 8.8 Hz); δ_C (100.5 MHz, DMSO-d^6) 68.8 (OCH$_2$), 114.7 (2C, CH), 118.9, 121.4, 128.0, 129.2, 130.3 (2C, CH), 131.8 (2C, CH), 132.4 (2C, CH), 136.8, 141.2, 159.2 (C$_{quat}$), 168.0 (C$_{quat}$, CO); MS (Ion trap): *m/z* 255 (MH$^+$).

Ethyl 3(*E*)-(9-anthranyl)propenoate (3z-Et). A mixture of 9-anthranylcarbaldehyde (1y, 1.0 g, 4.85 mmol) and ethoxycarbonylmethylidenephosphorane (2a, 2.36 g, 6.79 mmol) is heated at 130˚C for 3h. Thereafter, an additional amount of 2a (348 mg, 1.0 mmol) is added and the reaction mixture heated for another hour at 135˚C. The cooled solution is subjected directly to column chromatography on silica gel (eluent: M^{t}BE/CHCl$_3$/hexane 1:1:7) to give 3z-Et as a yellow-orange solid (1.23 g, 92%), mp. 80˚C [Lit. 80˚C [48]]; δ_H (400 MHz, CDCl$_3$) 1.35 (3H, t, ^3J = 7.2 Hz), 4.31 (2H, q, ^3J = 7.2 Hz, OCH$_2$), 6.36 (1H, d, ^3J = 16.0 Hz), 7.43 (4H, m), 7.95 (2H,

m), 8.17 (2H, m), 8.39 (1H, s), 8.57 (1H, d, ^3J = 16.0 Hz); δ_C (100.5 MHz, CDCl$_3$) 14.5, 61.0, 125.2, 125.4, 127.2, 128.2, 128.8, 129.3, 129.4, 131.2, 141.9, 166.5; MS: Found: 299.1040 (C$_{19}$H$_{16}$O$_2$+Na)$^+$; Calcd. for C$_{19}$H$_{16}$O$_2$Na: 299.1048.

Alternatively, to the reaction mixture of **1y** and **2a**, aq. NaOH (10 w%, 15 mL) was added after 4h, and the resulting solution was kept at reflux for 14 h. Thereafter, the solution was cooled and the precipitate was filtered off. The precipitate which contains both triphenylphosphine oxide and sodium 3(*E*)-(9-anthranyl)propenoate (**3z-Na**, see below) was washed diligently with hot water, to dissolve the remainder of the salt. Acidification of the cool filtrate with half conc. aq. HCl provides a precipitate, which was filtered, washed with water and dried to yield 3-(9-anthranyl)propenoic acid (**3z**) (1.02 g, 85%) as a yellow solid; mp. 242˚C [Lit. mp. 245˚C [49]]; ν_{max} (KBr/cm^{-1}) 3500 - 2495 (bs, OH), 3424, 3051 (C-H$_{arom.}$), 3003 (C-H$_{arom.}$), 2898 (C-H$_{aliph}$), 1690 (C=O), 1630, 1425, 1307, 1200, 725; δ_H (400 MHz, DMSO-d^6) 6.32 (1H, d, ^3J = 16.4 Hz), 7.57 (4H, m), 8.12 (4H, m), 8.46 (1H, d, ^3J = 16.4 Hz), 8.64 (1H, s), 12.75 (bs, OH); δ_C (100.5 MHz, DMSO-d^6) 125.3 (CH), 126.0 (CH), 127.2 (CH), 128.4 (C$_{quat}$), 128.8 (C$_{quat}$), 129.1 (CH), 129.3 (CH), 129.5 (C$_{quat}$), 131.2 (CH), 141.0 (CH), 157.3 (C$_{quat}$, CO).

When heated with 10 w% aq. NaOH, 3-(9-anthranyl)propenoic acid (**3z**) gives sodium 3(*E*)-(9-anthranyl) propenoate (**3z-Na**) as golden, shiny leaflets ν_{max} (KBr/cm^{-1}) 3620 - 2850 (bs, OH), 3611 (v), 1635, 1540 (s), 1441, 1392, 1285, 991, 881, 734; δ_H (400 MHz, CDCl$_3$) 6.14 (1H, d, ^3J = 16.0 Hz), 7.50 (4H, m), 7.90 (1H, d, ^3J = 16.0 Hz), 8.07 (2H, m), 8.20 (2H, m), 8.50 (1H, s).

4-Nitrobenzoic acid (**4**) and **4-nitrobenzyl alcohol** (**5**). 4-Nitrobenzaldehyde (**1w**, 1.51 g, 10 mmol) and phosphorane **2a** (4.87 g, 14 mmol) was given to an aq. NaOH solution (9.1 w%, 3.5 g (87.5 mmol) NaOH in 35 mL H$_2$O) and the resulting suspension was stirred at 75˚C for 20 min. With the addition of 4-nitrobenzaldehyde, the solution turned dark-red. The solution was filtered, and the filtrate was extracted with dichloromethane (3 × 25 mL). Then, the aqueous solution was acidified with half-conc. aq. HCl to give 4-nitrobenzoic acid (**4**) (800 mg, 48%) as a colorless solid, mp. 237˚C [Lit. 237˚C - 240˚C [41]]; ν (KBr/cm^{-1}) 3065 (OH), 2672, 1695 (C=O), 1609 (C=C), 1543, 1433; δ_H (400 MHz, CDCl$_3$) 8.13 (2H, d, ^3J = 9.2 Hz), 8.28 (2H, d, ^3J = 9.2 Hz); δ_C (100.5 MHz, DMSO-d^6) 123.5 (2C, CH), 131.1 (2C, CH), 136.4 (C$_{quat}$), 150.5 (C$_{quat}$), 166.8 (C$_{quat}$, CO). Thereafter the filter cake of the first filtration was taken up in CHCl$_3$ (50 mL) and combined with the CH$_2$Cl$_2$ extract. The combined extract was dried over anhydrous MgSO$_4$ and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel (CHCl$_3$-hexane-ether 1:1:1) to give 4-nitrobenzyl alcohol (**5**, 540 mg, 35%) as a colorless solid, mp. 93˚C [Lit. 92˚C - 94˚C [48]]; ν (KBr/cm^{-1}) 3550 (bs, OH), 2954 (C-H), 2925 (C-H), 1508 (NO$_{2(a)}$), 1458 (NO$_{2(s)}$); δ_H (400 MHz, CDCl$_3$) 2.11 (1H, t, ^3J = 5.6 Hz, OH), 4.83 (2H, d, ^3J = 5.6 Hz), 7.52 (2H, cd, ^3J = 8.8 Hz), 8.21 (2H, cd, ^3J = 8.8 Hz); δ_H (400 MHz, CDCl$_3$) 64.0 (CH$_2$), 123.7 (2C, CH), 127.1 (2C, CH), 147.3 (C$_{quat}$), 148.4 (C$_{quat}$); MS (EI, 70 eV) *m/z* (%) 153 (55, M$^+$), 77 (100).

(***E***)-**4-Hydroxycinnamic acid** (**6**) [50]. A mixture of **1z** (835 mg, 6.84 mmol) and **2a** (3.35 g, 9.63 mmol) was heated at 135˚C for 1h. Thereafter, aq. NaOH (10 w%, 10 mL) was added to the cooled mixture, and it was stirred for 12 h at rt. The precipitated triphenylphosphine oxide was filtered off, and the filter-cake was washed with water (2 × 15 mL). The filtrate, combined with the washings, was acidified with half-conc. aq. HCl. The formed precipitate was filtered, washed with water (2 × 15 mL) and air-dried to yield **6** (850 mg, 74%) as a colorless solid, mp. 211˚C - 212˚C; IR (KBr/cm^{-1}) ν_{max} 3379 (bs, OH), 1672 (C=O), 1628, 1602 (C=C), 1512, 1449, 1313, 1244 (C-O), 1214 (C-O), 1172, 978, 832, 690; δ_H (400 MHz, DMSO-d^6) 6.23 (1H, d, ^3J = 16.0 Hz), 6.76 (2H, d, ^3J = 8.8 Hz), 7.19 (1H, d, ^3J = 16.0 Hz), 7.34 (2H, d, ^3J = 8.8 Hz); δ_H (100.5 MHz, DMSO-d^6) 115.0 (CH), 115.9 (2C, CH), 127.2 (C$_{quat}$), 129.3 (2C, CH), 138.9 (CH), 158.7 (C$_{quat}$), 171.0 (C$_{quat}$, CO).

While general procedure A was used for the preparation of **8b**, **8d/8e**, and **8f**, the *E*- and *Z*-isomers of **8b** and **8f** and compound **8d** and **8e** were separated by column chromatography on silica gel (CHCl$_3$/ether 10:1) and crystallized from a mixture of CHCl$_3$-hexane (1:4).

(***E***)-**3-Phenylbut-2-enoic acid** (**8a**) (Procedure A). Colorless solid, mp. 129˚C - 131˚C [Lit. 131˚C [51]]; δ_H (400 MHz, DMSO-d^6) 2.49 (3H, d, ^4J = 1.6 Hz), 6.10 (1H, q, ^4J = 1.6 Hz), 7.40 - 7.42 (3H, m), 7.55 - 7.57 (2H, m), 12.27 (1H, bs, OH); δ_C (100.5 MHz, DMSO-d^6) 17.7 (CH$_3$), 117.9 (CH), 126.6 (2C, CH), 129.1 (2C, CH), 129.5 (CH), 141.9 (C$_{quat}$), 154.2 (C$_{quat}$), 168.0 (C$_{quat}$, CO).

(***Z***)-**3-(4-Chlorophenyl)but-2-enoic acid** (***Z*-8b**) [52] (Procedure A). ν (KBr/cm^{-1}) 3150 - 2550 (bs, OH), 1678 (C=O), 1617 (C=C), 1432, 1289, 1210, 1073, 819, 713; δ_H (400 MHz, DMSO-d^6) 2.11 (3H, d, ^4J = 1.6 Hz, CH$_3$), 5.92 (1H, q, ^4J = 1.6 Hz), 7.25 (2H, d, ^3J = 8.8 Hz), 7.39 (2H, d, ^3J = 8.8 Hz); δ_H (400 MHz, DMSO-d^6) 26.7 (CH$_3$), 119.4 (CH), 128.2 (CH, 2C), 129.4 (CH, 2C), 132.6, 139.9, 152.6, 166.8 (C$_{quat}$, CO). (***E***)-**3-(4-**

Chlorophenyl)but-2-enoic acid (*E*-**8b**). Beige solid, mp. 133˚C [Lit. 135˚C]; δ_H (400 MHz, DMSO-d^6) 2.47 (3H, d, ^4J = 1.6 Hz, CH$_3$), 6.12 (1H, q, ^4J = 1.6 Hz), 7.47 (2H, d, ^3J = 8.8 Hz), 7.59 (2H, d, ^3J = 8.8 Hz), 12.2 (1H, bs, OH); δ_C (100.5 MHz, DMSO-d^6) 17.5 (CH$_3$), 118.6 (CH), 128.5 (CH, 2C), 129.0 (CH, 2C), 134.2, 140.7, 152.6, 167.8 (CO, C$_{quat}$).

(*E*)-3-(4-Bromophenyl)but-2-enoic acid (**8c**) (Procedure A). Colorless solid, mp. 116˚C [Lit. 116˚C [11]]; ν (KBr/cm^{-1}) 3150 - 2550 (bs, OH), 1681 (C=O), 1610 (C=C), 817; δ_H (400 MHz, DMSO-d^6) 2.47 (3H, q, ^4J = 1.2 Hz, CH$_3$), 6.12 (1H, d, ^4J = 1.2 Hz), 7.51 (2H, d, ^3J = 8.4 Hz), 7.60 (2H, d, ^3J = 8.4 Hz), 12.30 (1H, bs, OH); δ_C (100.5 MHz, DMSO-d^6) 17.5, 118.6, 122.9, 128.8 (2C), 131.9 (2C), 141.0, 152.7, 167.8.

(*E*)-3-(4-Iodophenyl)but-2-enoic acid (**8d**) (Procedure A) [53]. Colorless solid; mp. 161˚C; ν (KBr/cm^{-1}) 3150 - 2550 (bs, OH), 1683 (C=O), 1608 (C=C), 1436, 1278 (C-O), 1208 (C-O), 994, 814, 708; δ_H (400 MHz, DMSO-d^6) 2.45 (3H, q, ^4J = 1.2 Hz, CH$_3$), 6.11 (1H, q, ^4J = 1.2 Hz), δ_H (400 MHz, CDCl$_3$) 2.58 (3H, q, ^4J = 1.2 Hz, CH$_3$), 6.15 (1H, q, ^4J = 1.2 Hz), 7.36 (2H, d, ^3J = 8.4 Hz), 7.43 (2H, d, ^3J = 8.4 Hz); δ_C (100.5 MHz, DMSO-d^6) 17.4, 96.1, 118.4, 128.8 (2C), 137.8 (2C), 141.4, 152.9, 167.8; δ_C (100.5 MHz, CDCl$_3$) 18.2 (CH$_3$), 116.5 (CH), 127.7 (CH, 2C), 128.9 (CH, 2C), 135.4 (C$_{quat}$), 140.3 (C$_{quat}$), 157.1 (C$_{quat}$), 171.6 (C$_{quat}$, CO), and 3-(4-iodophenyl)but-3-enoic acid (**8e**) as a colorless solid, mp. 143˚C; ν (KBr/cm^{-1}) 3150 - 2550 (bs, OH), 1685 (C=O); δ_H (400 MHz, CDCl$_3$) 3.51 (2H, s), 5.28 (1H, s), 5.57 (1H, s), 7.17 (2H, d, ^3J = 6.4 Hz), 7.65 (2H, d, ^3J = 6.4 Hz); δ_C (100.5 MHz, CDCl$_3$) 40.4 (CH$_2$), 117.5 (CH$_2$), 127.6 (2C, CH), 133.1 (C$_{quat}$), 137.6 (2C, CH), 138.9 (C$_{quat}$), 139.4 (C$_{quat}$), 174.9 (C$_{quat}$, CO).

(*E*)-3-Phenylpent-2-enoic acid (*E*-**8f**) (Procedure A). Colorless solid, mp. 93˚C [Lit. 95˚C [54]]; ν (KBr/cm^{-1}) 3150 - 2550 (bs, OH), 1698 (C=O); δ_H (400 MHz, CDCl$_3$) 1.09 (3H, t, ^3J = 7.6 Hz, CH$_3$), 3.13 (2H, q, ^3J = 7.6 Hz), 6.06 (1H, s), 7.38 - 7.40 (3H, m), 7.46 - 7.47 (2H, m), 11.7 (1H, s, OH); δ_C (100.5 MHz, CDCl$_3$) 13.6 (CH$_3$), 24.5 (CH$_2$), 115.8 (CH), 126.7 (CH, 2C), 128.6 (CH, 2C), 129.2 (CH), 140.9 (C$_{quat}$), 165.0 (C$_{quat}$), 171.2 (C$_{quat}$); and **(*Z*)-3-phenylpent-2-enoic acid** (*Z*-**8f**) as a colorless solid, mp. 74 ˚C; ν (KBr/cm^{-1}) 3180 - 2550 (bs, OH), 1687 (C=O); δ_H (400 MHz, CDCl$_3$) 1.04 (3H, t, ^3J = 7.2 Hz, CH$_3$), 2.44 (2H, q, ^3J = 7.2 Hz), 5.86 (1H, s), 7.13 - 7.15 (2H, m), 7.30 - 7.35 (3H, m); δ_C (100.5 MHz, CDCl$_3$) 12.0 (CH$_3$), 33.8 (CH$_2$), 115.3 (CH), 127.0 (CH, 2C), 127.8 (CH), 128.0 (CH, 2C), 139.8 (C$_{quat}$), 163.8 (C$_{quat}$), 170.0 (C$_{quat}$).

(*E*)-4-Phenylbut-2-enoic acid (**8g**) (procedure A). Beige solid, mp. 96˚C [Lit. 97˚C [55]]; ν_{max} (KBr/cm^{-1}) 3054, 1702 (C=O), 1409, 1218 (C-O), 977, 914, 745, 692; δ_H (400 MHz, DMSO-d^6) 3.23 (2H, d, ^3J = 7.2 Hz), 6.28 (1H, dd, ^3J = 16.4 Hz, ^3J = 7.2 Hz), 6.46 (1H, d, ^3J = 16.4 Hz), 7.20 (1H, m), 7.28 (2H, dd, ^3J = 7.2 Hz, ^3J = 7.2 Hz), 7.38 (2H, d, ^3J = 7.2 Hz); δ_H (400 MHz, CDCl$_3$) 3.30 (2H, d, ^3J = 8.4 Hz), 6.29 (1H, dd, ^3J = 15.6 Hz, ^3J = 8.4 Hz), 6.52 (1H, d, ^3J = 15.6 Hz), 7.25 (1H, m), 7.32 (2H, m), 7.39 (2H, m); δ_C (100.5 MHz, DMSO-d^6) 38.3 (CH$_2$), 123.6 (CH), 126.4 (2C, CH), 127.9 (CH), 129.1 (2C, CH), 132.7 (CH), 137.1 (C$_{quat}$), 173.2 (CO); δ_C (100.5 MHz, CDCl$_3$) 38.1 (CH$_2$), 120.9 (CH), 126.3 (2C, CH), 127.7 CH), 128.6 (2C, CH), 134.0 (CH), 136.6 (C$_{quat}$), 177.8 (C$_{quat}$, CO).

Ethyl (*E*)-3-anthran-1-ylbut-2-enoate (**10b**). A mixture of 1-acetylanthracene (300 mg, 1.36 mmol), phosphorane **2a** (760 mg, 2.18 mmol), and benzoic acid (30 mg, 0.25 mmol) in benzene (8 mL) was heated at 80˚C for 12 h. After 3 h, additional **2a** (300 mg, 0.87 mmol) was added. The cooled reaction mixture was concentrated *in vacuo* and subjected to column chromatography on silica gel (ether/CHCl$_3$/hexane 1:3:3) to give **10b** (25 mg, 6%) as a colorless oil. ν (neat/cm^{-1}) 1720 (C=O), 1634, 1170; δ_H (400 MHz, CDCl$_3$) 1.35 (3H, t, ^3J = 7.2 Hz), 2.70 (3H, d, ^4J = 1.2 Hz), 4.28 (2H, q, ^3J = 7.2 Hz), 6.07 (1H, q, ^4J = 1.2 Hz), 7.25 (1H, d, ^3J = 6.8 Hz), 7.42 (1H, dd, ^3J = 8.4 Hz, ^3J = 6.8 Hz), 7.47 - 7.48 (1H, m), 7.95 – 8.00 (3H, m), 8.41 (1H, s), 8.44 (1H, s); δ_C (100.5 MHz, CDCl$_3$) 14.3 (CH$_3$), 21.6 (CH$_3$), 60.0 (OCH$_2$), 120.6 (CH), 123.5 (CH), 124.2 (CH), 124.6 (CH), 125.6 (CH), 125.8 (CH), 126.8 (CH), 127.3 (C$_{quat}$), 127.6 (C$_{quat}$), 127.9 (CH), 128.5 (2C, CH), 128.7 (C$_{quat}$), 131.5 (C$_{quat}$), 131.8 (C$_{quat}$), 142.1 (C$_{quat}$), 166.8 (C$_{quat}$, CO).

For the preparation of **12a** - **12c**, general procedure A was used. After acidification of the reaction medium after completion of the reaction, the aqueous phase was extracted with CHCl$_3$. The organic phase was dried over MgSO$_4$, concentrated *in vacuo* and the residue was filtered over a small layer of silica gel (ether/CHCl$_3$ 1:1).

5,9-Dimethyldeca-2,8-dienoic acid (**12a**) [56] as a colorless oil; ν_{max} (neat/cm^{-1}) 3100 - 2550 (bs, OH), 2917, 1695 (C=O), 1648, 1428, 1282, 983, 938, 686; δ_H (3H, d, ^3J = 6.8 Hz), 0.95 (1H, m), 1.10 (1H, m), 1.35 (1H, m), 1.59 (3H, d, ^4J = 0.8 Hz), 1.68 (3H, d, ^4J = 0.8 Hz), 1.90 – 2.07 (2H, m), 2.22 - 2.24 (2H, m), 5.04 (1H, m), 5.82 (1H, d, ^3J = 15.6 Hz), 7.07 (1H, m); δ_C (100.5 MHz, CDCl$_3$) 17.7, 19.5, 32.0, 25.5, 25.9, 36.7, 39.7, 121.8, 124.3, 131.6, 151.3, 171.9 (CO).

(*E*)-Dec-2-enoic acid (**12b**) [57]. Colorless oil; ν_{max} (neat/cm^{-1}) 1698 (C=O), 1660, 1422, 1310, 1300, 980,

940; δ_H (400 MHz, CDCl$_3$) 0.83 (3H, t, ^3J = 5.6 Hz, CH$_3$), 1.22 (m), 1.41 (2H, m), 2.17 (2H, m), 5.76 (1H, d, ^3J = 15.2 Hz), 7.03 (1H, dt, ^3J = 15.2 Hz, ^3J = 5.6 Hz); δ_C (100.5 MHz, CDCl$_3$) 14.0 (CH$_3$), 22.6 (CH$_2$), 27.8 (CH$_2$), 29.0 (CH$_2$), 29.1 (CH$_2$), 31.7 (CH$_2$), 32.3 (CH$_2$), 120.6 (CH), 152.4 (CH), 172.1 (C$_{quat}$, CO); MS (EI, 70 eV) m/z (%) 170 (M$^+$, 13), 73 (65).

3-Cyclohexylpropenoic acid (12c). Colorless solid, mp. 53°C [Lit. 57°C - 58°C [58]], ν_{max} (neat) 3400 - 2550 (bs, OH), 2931, 2856, 1699 (C=O); δ_H (400 MHz, CDCl$_3$) 1.00 - 2.05 (10H, m), 2.20 (1H, m), 5.69 (1H, dd, ^3J = 16.0 Hz, ^4J = 2.0 Hz), 6.95 (1H, dd, ^3J = 16.0 Hz, ^3J = 6.8 Hz), 9.40 - 10.00 (1H, bs, OH); δ_C (100.5 MHz, CDCl$_3$) 25.6, 25.9, 31.6, 40.5, 118.5, 158.2, 172.9.

2.3. General Procedure B

Phenylpropiolic acid (13b). To a mixture of benzaldehyde (**1f**, 763 mg, 7.2 mmol) and ethoxycarbonylbromo-methylidenetriphenylphosphorane (**2b**, 4.0 g, 9.4 mmol) was given aq. NaOH solution (10 w%, 1.8 g NaOH in 18 mL H$_2$O) and the resulting suspension was stirred at 85°C for 16 h. Triphenylphosphine oxide was filtered off the cooled solution. Thereafter, the filtrate was acidified carefully with 15 w% aq. HCl. The resulting suspension was cooled and filtered. The solid obtained was dried in air to give phenylpropiolic acid (**13b**, 589 mg, 56%) as a colorless solid. An analytical sample gave mp. 133°C [Lit. 135°C - 137°C [41]]-ν_{max} (KBr/cm^{-1}) 3200 - 2500 (bs, OH), 2238, 2201 (C≡C), 1670 (C=O), 1489, 1417, 1305, 1208 (C-O), 919, 753, 683, 610, 533, 509; δ_H (400 MHz, CDCl$_3$) 7.39 - 7.42 (2H, m), 7.46 - 7.48 (1H, m), 7.60 - 7.62 (2H, m), 10.1 (bs, OH); δ_C (100.5 MHz, CDCl$_3$) 80.2 (C$_{quat}$), 88.8 (C$_{quat}$), 119.1 (C$_{quat}$), 128.8 (2C, CH), 131.1 (CH), 133.3 (2C, CH), 158.4 (C$_{quat}$, CO); MS (EI, 70 eV) m/z (%) 146 (M$^+$) (100), 76 (30).

4-Methoxyphenylpropiolic acid (13a) (Procedure B). Pale yellow solid, mp. 143°C [Lit. 144°C [59]]; ν_{max} (KBr/cm^{-1}) 2197 (C≡C), 1671 (C=O), 1602 (C=C), 1511, 1417, 1322, 1297, 1255, 1213, 1168, 1028, 923, 832, 799, 609, 565, 539; δ_H (400 MHz, CDCl$_3$) 3.84 (3H, s, OCH$_3$), 6.89 (2H, d, ^3J = 8.8 Hz), 7.56 (2H, d, ^3J = 8.8 Hz); δ_C (100.5 MHz, CDCl$_3$) 55.5 (OCH$_3$), 79.6 (C$_{quat}$), 90.0 (C$_{quat}$), 110.8 (C$_{quat}$), 114.4 (2C, CH), 135.3 (2C, CH), 158.4 (C$_{quat}$), 161.9 (C$_{quat}$, CO); δ_C (100.5 MHz, DMSO-d^6) 55.8 (OCH$_3$), 81.5 (C$_{quat}$), 85.9 (C$_{quat}$), 110.9 (C$_{quat}$), 115.1 (2C, CH), 135.1 (2C, CH), 155.1 (C$_{quat}$), 161.6 (C$_{quat}$, CO).

3-Chlorophenylpropiolic acid (13c) (Procedure B). Colorless solid, mp. 145°C [Lit. 144°C [60]]; ν_{max} (KBr/cm^{-1}) 3200 - 2500 (bs, OH), 2960, 2586, 2217 (C≡C), 1683 (C=O), 1475, 1420, 1310, 1208, 877, 784, 674, 611, 519; δ_H (400 MHz, CDCl$_3$); 9.0 (1H, bs, OH), 7.31 - 7.34 (1H, m), 7.44 - 7.49 (2H, m), 7.58 (1H, s); δ_C (100.5 MHz, DMSO-d^6) 81.0 (C$_{quat}$), 86.3 (C$_{quat}$), 121.0 (C$_{quat}$), 129.9 (CH), 131.3 (2C, CH), 132.8 (CH), 134.5 (C$_{quat}$), 157.4 (C$_{quat}$).
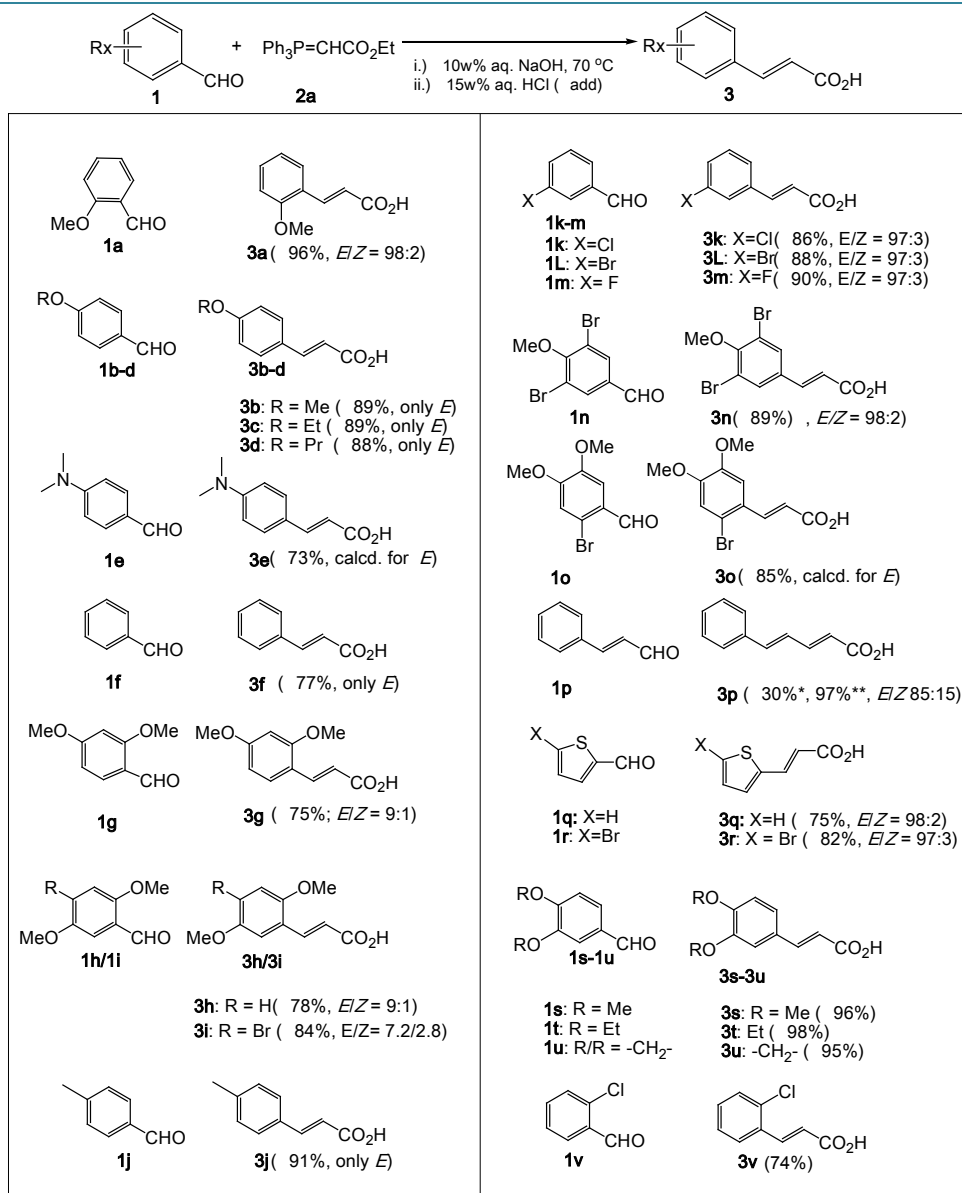
3,4-Dimethoxyphenylpropiolic acid (13d) (Procedure B). Colorless solid, mp. 154°C [Lit. 152°C - 153°C [61]]; ν_{max} (KBr/cm^{-1}) 3200 - 2500 (bs, OH), 2937, 2837, 2595, 2202 (C≡C), 1684 (C=O), 1625, 1596, 1517, 1312, 1252, 1165, 1140, 1022, 975, 839, 810, 723, 579, 540. δ_H (400 MHz, CDCl$_3$) 3.89 (3H, s, OCH$_3$), 3.92 (3H, s, OCH$_3$), δ_C (100.5 MHz, CDCl$_3$) 79.4 (C$_{quat}$), 89.8 (C$_{quat}$), 110.9 (C$_{quat}$), 111.0 (CH), 115.4 (CH), 127.7 (CH), 148.8 (C$_{quat}$), 151.9 (C$_{quat}$), 157.9 (C$_{quat}$).

3. Results and Discussion

When a mixture of benzaldehyde **1** and ethoxymethylidenetriphenylphosphorane (**2a**, 1.3 eq.) is heated in a 10 w% aq. NaOH solution, sodium cinnamates are formed by Wittig olefination and subsequent ester hydrolysis. Upon neutralization of the aqueous solutions with 10 w% - 15w% aq. HCl, cinnamic acids **3** are obtained by easy filtration and drying of the solids in air. With this procedure, cinnamic acids **3** could be synthesized (**Table 1**).

Even solid **3e** can be filtered off from the neutralized solution easily, as the anilinic nitrogen in **3e** is not basic enough to be protonated upon careful neutralization of the reaction mixture. Most of the cinnamic acids are produced in good *E*-selectivity. However, for phenylpenta-2,5-dienoic acid (**3p**), 2,4-dimethoxycinnamic acid (**3g**), 2,5-dimethoxycinnamic acid (**3h**) and especially 3-bromo-2,5-dimethoxycinnamic acid (**3i**) anoticable quantity of *Z*-isomer is formed.

4-Nitrobenzaldehyde (**1w**) is not an adequate substrate for this one-pot procedure, even though 4-nitroben-zaldehyde (**1w**) and ethoxymethylidenetriphenylphosphorane (**2a**) give the Wittig product**3w**facilely, when the reaction is performed in chloroform (**Scheme 1**). Also, the ester hydrolysis of **3w** in 10 w% aq. NaOH proceeds

Table 1. Substituted cinnamic acids via one pot Wittig olefination-hydrolysis reaction.

Reaction scheme:

$$Rx\text{-}C_6H_4\text{-}CHO \ (\mathbf{1}) + Ph_3P=CHCO_2Et \ (\mathbf{2a}) \xrightarrow[\text{ii.) } 15w\% \text{ aq. HCl (add)}]{\text{i.) } 10w\% \text{ aq. NaOH, 70 °C}} Rx\text{-}C_6H_4\text{-}CH=CH\text{-}CO_2H \ (\mathbf{3})$$

1a (2-OMe benzaldehyde) → **3a** (96%, *E/Z* = 98:2)

1b-d (4-RO benzaldehyde) → **3b-d**
3b: R = Me (89%, only *E*)
3c: R = Et (89%, only *E*)
3d: R = Pr (88%, only *E*)

1e (4-NMe₂ benzaldehyde) → **3e** (73%, calcd. for *E*)

1f (benzaldehyde) → **3f** (77%, only *E*)

1g → **3g** (75%; *E/Z* = 9:1)

1h/1i → **3h/3i**
3h: R = H (78%, *E/Z* = 9:1)
3i: R = Br (84%, E/Z = 7.2/2.8)

1j (4-Me benzaldehyde) → **3j** (91%, only *E*)

1k-m → **3k-m**
1k: X=Cl **3k**: X=Cl (86%, E/Z = 97:3)
1L: X=Br **3L**: X=Br (88%, E/Z = 97:3)
1m: X= F **3m**: X=F (90%, E/Z = 97:3)

1n → **3n** (89%) , *E/Z* = 98:2

1o → **3o** (85%, calcd. for *E*)

1p → **3p** (30%*, 97%**, *E/Z* 85:15)

1q: X=H **3q**: X=H (75%, *E/Z* = 98:2)
1r: X=Br **3r**: X = Br (82%, *E/Z* = 97:3)

1s-1u → **3s-3u**
1s: R = Me **3s**: R = Me (96%)
1t: R = Et **3t**: Et (98%)
1u: R/R = -CH₂- **3u**: -CH₂- (95%)

1v (2-Cl benzaldehyde) → **3v** (74%)

*no additive; **tetramethylammonium bromide (0.15 eq. Bu₄NBr) addad.

readily, and **3x** is obtained, which can be filtered off and dried after acidification of the reaction solution. Yet, in 10 w% aq. NaOH, 4-nitrobenzaldehyde (**1w**) undergoes a rapid Cannizzaro reaction, which would be expected to be the general competing pathway for benzaldehydes in aqueous basic media. However, with the exception of the nitro-substituted benzaldehydes, Cannizzaro is not noted to be a main side reaction for the benzaldehydes used. The reason for this may be that the Wittig olefination ensues rapidly in the lipotropic droplets formed by themixture of benzaldehyde and phosphorane, initially suspended in the aqueous solution. In the case of 4-nitrobenzaldehyde (**1r**) in 10 w% aq. NaOH, a deep red homogeneous solution is produced immediately, from which one of the Cannizzaro products, 4-nitrobenzoic acid (**4**), can be obtained facilely by extraction of the side product with CH₂Cl₂ and acidification of the aqueous phase with subsequent extraction of the phase and crystallization of the obtained product [62] [63]. Cannizaro reaction can also be noted for 2-nitrobenzaldehyde under the conditions, and the 2-nitrobenzoic acid can be obtained easily.

In the case of **1x** (**Figure 1**), only (*Z*)-*p*-benzyloxycinnamic acid (**3y**) was obtained as the cinnamic acid
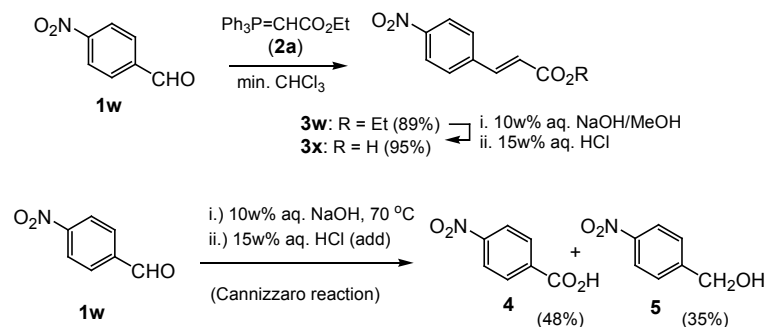
Scheme 1. Comparison of the sequential Wittig olefination–hydrolysis reaction of 4-nitrobenzaldehyde (1w) leading to cinnamic acid 3x and the reaction under one pot conditions leading to Cannizzaro products 4 and 5.
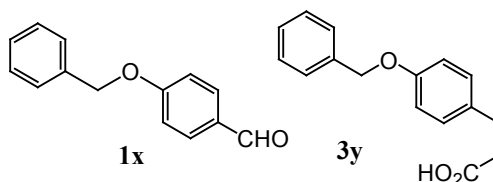

Figure 1. Reduction of alkenes carrying *O*-benzyl esterand/or *O*-benzyl ether functions.

fraction. The *E*-isomer could not be detected. At 70˚C, triphenylphosphine oxide and the Wittig product develop liquid hydrophobic micelles. Ester hydrolysis takes place at the micelle boundary, and it may be that the ethyl (*E*)- *p*-benzyloxycinnamate, more easily forming intermolecular layers within the micelle, is not as readily accessible as the *Z*-isomer. It must also be noticed that under the strongly basic conditions, the benzyloxy function is not sufficiently stable and is severed to provide the hydroxy-substituted compound. That micelles play a role in the ester hydrolysis can be seenin alkyl cinnamates with larger residues, such as in ethyl phenylpenta-2,4-dienoate, where the addition of tetramethylammonium bromide [$(CH_3)_4NBr$] leads to more yield in phenylpenta-2,4-dienoic acid (**3p**).

In cases, where the arylcarbaldehydes undergo Wittig reaction with alkoxycarbonylmethylidene phosphoranes slowly and only at higher temperatures at which the phosphoranes are already hydrolysed, a variant of the reaction protocol can be employed. First, the aldehyde is reacted with the phosphorane under solventless conditions at higher temperatures. Thereafter, 10 w% aq. NaOH is added to the reaction mixture, and the reaction is completed. 9-Anthranylcarbaldehyde (**1t**) represents such a case, where the aldehyde undergoes Wittig olefination only sluggishly due to the steric congestion around the carbaldehyde function. **1t** can be reacted with **2a** under solventless conditions at 130˚C [64]. Subsequent addition of aq. NaOH to the reaction and heating of the mixture gives the 3-(anthran-9-yl)propenoic acid (**3z**) in 85% yield (**Scheme 2**). It must be noted that upon cooling of the reaction, sodium 3-(anthran-9-yl)propenoate (**3z-Na**) crystallizes in the aqueous solution, and the resulting solid, which is comprised of the sodium salt of the acid as well as triphenylphosphine oxide, must be washed diligently with hot water upon filtration of the triphenylphosphine oxide. The precipitation was also noted in the hydrolysis of isolated ethyl anthranylpropenoate (**3z-Et**, R = Et) in 10 w% aq. NaOH. In that case, the precipitate can be treated directly with aq. HCl to yield anthranylpropenoic acid (**3z**) as a filterable precipitate.

The same solventless procedure was followed, when reacting 4-hydroxybenzaldehyde (**1z**) with phosphorane **2a** at 140˚C for 90 min. Thereafter, the mixture was taken up in 10 w% aq. NaOH and stirred at rt for 30 min., after which the triphenylphosphine oxide was filtered off, and the filtrate acidified with half-conc. aq. HCl to give 4-hydroxycinnamic acid (**6**, *p*-coumaric acid) (**Scheme 3**). Previously, 4-hydroxycinnamic acid had been prepared by Horner Emmons olefination [65] with a subsequent, second hydrolysis step and via Wittig reaction with a polymer-bound Wittig reagent and a subsequent hydrolysis step [66].

Acetophenones **7** have been subjected successfully to the one-pot Wittig olefination-hydrolysis, too (**Table 2**). In these cases, a mixture of phosphorane **2a** and acetophenone **7** was heated, and thereafter an aq. NaOH solution was added. A workup identical to that described for the benzaldehydes provided the products as mixtures of
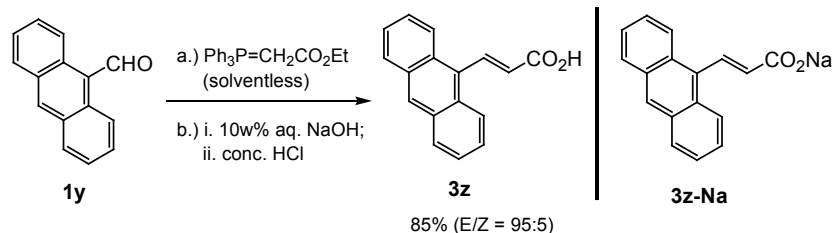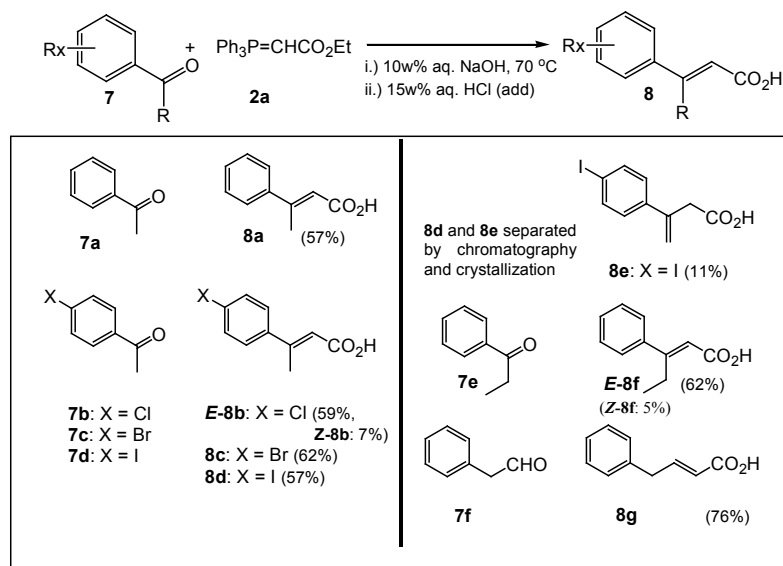
Scheme 2. Solventless Wittig reaction and subsequent hydrolysis without work-up of 3z.
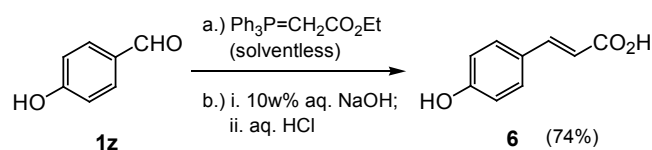
Scheme 3. Preparation of *p*-coumaric acid (6) by solventless Wittig-olefination with basic extractive work-up.

**Table 2.** One pot Wittig reaction and hydrolysis with acetophenone as starting material.

E/Z-isomers. The *E*-isomer could be obtained in pure form by recrystallization from 1:1 v/v CH$_2$Cl$_2$/hexane. In order to obtain both isomers in pure form, the mixture was subjected to chromatography on silica gel (hexane/EtOAc 2:1). The reaction is dependent on the steric bulkiness of the ketone, where bulkiness in the ketone leads to a sterically congested transition state in the Wittig olefination. Thus, 1-acetylanthracene (**9**) does not react under the conditions to the respective acid at all. **9** reacts with phosphorane **2a** sluggishly, and produces butenoate **10b** after 12 h in refluxing chloroform in the presence of benzoic acid as acid catalyst only in trace amounts. Under the conditions of the one-pot Wittig olefination–ester hydrolysis, much of the phosphorane **2a** hydrolyses before undergoing Wittig olefination with **9** (**Scheme 4**).

Alkanals and alicyclic carbaldehydes **11** have also been reacted in a one-pot Wittig olefination-hydrolysis reaction. The yields of the corresponding unsaturated acids **12** were slightly lower than for aromatic aldehydes. Also, the obtained carboxylic acids could not be purified simply by crystallization through addition of hydrochloric acid to the reaction mixture. Rather, they have to be extracted after the acidification of the reaction mixture and subjected to column chromatography on silica gel (**Scheme 5**).

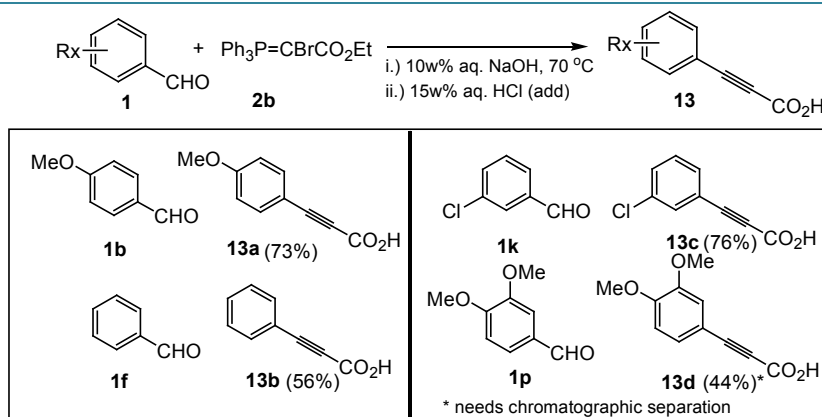When a mixture of (substituted) benzaldehyde **1** and ethoxybromomethylidenetriphenylphosphorane (**2b**, 1.3
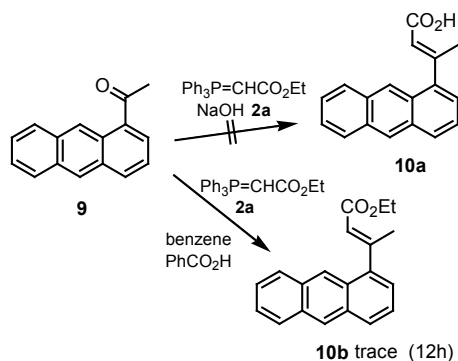
Scheme 4. Wittig reaction of 1-acetylanthracene (9) with phosphorane.
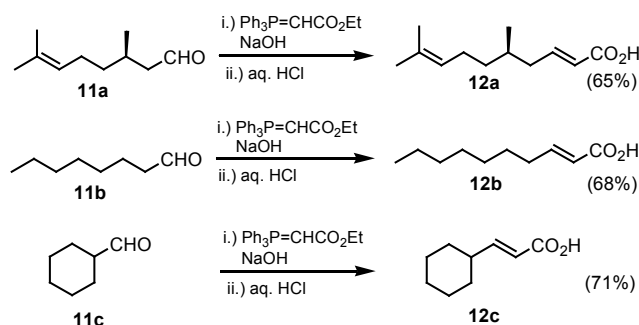
Scheme 5. One-pot transformation of alkanals and alicyclic aldehydes.

Table 3. Arylpropiolic acids from benzaldehydes in one pot synthesis in aq. solutions.

eq.) is heated in a 10 w% aq. NaOH solution, arylpropiolic acids **13** can be isolated upon careful neutralization of the aqueous solution (**Table 3**). In this case, the Wittig olefination is followed by ester hydrolysis and base catalysed dehydrobromination. Phenylpropiolic acids are usually prepared by bromination and dehydrobromination of cinnamic acids [60] or by Sonogashira coupling of haloarenes with propiolates [67]. In the present communication, we are showing a facile one-pot procedure to phenylpropiolic acids with a simple extractive work-up. For certain derivatives, cinnamic acids have been found as side-products. Nevertheless, the procedure in its yields compares well with that of Chenault and Dupin [59], who employ ethoxyiodomethylidenetriphenyl-phosphorane in Na_2CO_3/methanol, followed by subsequent acid catalysed hydrolysis of the phenylpropiolates.

4. Conclusions

We have developed two simple procedures from benzaldehydes to cinnamic acids and to phenylpropiolic acids,

respectively, utilizing a modified Wittig-olefination protocol. The reactions and the work-up are performed without any organic solvents in most cases here described. Yields are reproducibly good. The one-pot procedure of olefination and ester hydrolysis can be utilized with alkanals and acetophenones, also. Here, however, chromatographic separation of the products is necessary in some cases.

In former times, the Wittig olefination reaction has not been viewed as a green reaction due to its poor atom-economy. Recently, however, a dedicated effort has seen the development of numerous methods to recycle the toxic triphenylphosphine oxide [17] [68]-[70] that joins older methods [71], and some of them already established in industrial processes [17] [72]. The reaction procedure described above allows for an efficient separation of triphenylphosphine oxide from the mixture upon completion of the reaction by simple filtration. Then, triphenylphosphine oxide is dried and stored and can be recycled upon accumulation from a larger number of Wittig reactions.

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