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ONE-POT WITTIG SYNTHESIS OF METHYL-3-[5-(HYDROXYMETHYL)-2-FURYL]ACRYLATE FROM FRUCTOSE

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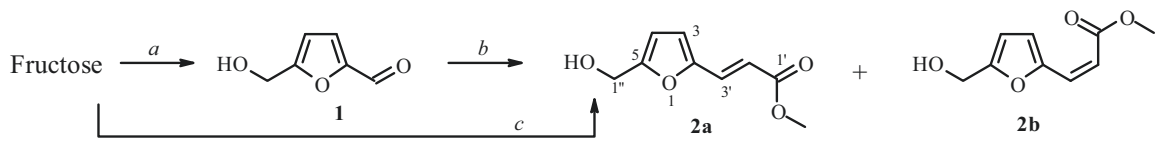
Exhaustion of nonrenewable natural resources has necessitated the development of alternative methods for processing renewable raw material sources. Carbohydrates represent a large part of yearly renewable biomass and are highly promising for such processing [1]. Furan compounds are especially interesting because they have many applications in the chemical industry [2–7]. The plant-derived furan 5-hydroxymethylfurfurol (**1**, 5-HMF) is being extensively used as a transformation platform. However, 5-HMF is labile [8] and requires certain storage conditions. Therefore, synthesis of stable 5-HMF derivatives directly from carbohydrates is a challenging problem for contemporary chemistry.

5-HMF was synthesized by refluxing fructose in DMSO for 2 h followed by a Wittig reaction with methyl(triphenylphosphoranylidene)acetate (Scheme 1). The latter reaction occurred at room temperature in 1 h. Flash chromatography over silica gel isolated two products **2a** and **2b** in a 4:1 ratio.



a. DMSO, 150°C; *b*. Ph_3=CHCOOMe; *c*. 1. DMSO, 150°C; 2. Ph_3P=CHCOOMe

Scheme 1

The structures of **2a** and **2b**, which were isolated pure, were elucidated using physicochemical analytical methods. The main indicators were disappearance of the 5-HMF aldehyde, which appeared in ^{13}C NMR spectra at 178.56 ppm, and formation of a multiple bond with resonances at 115.37 and 115.76 ppm in **2a** and at 114.09 and 118.04 ppm in **2b**.

Olefination of 5-HMF without isolation from DMSO gave analogous results. The best yield (56%) from both approaches was observed with a slight (1.2×) excess of the phosphorane calculated for starting fructose.

Thus, a one-pot synthesis of a stable 5-HMF derivative (platform compound) with good water-solubility was developed and made it highly promising for biological screening.

Preparation of 2a and 2b. Crystalline fructose (Sladis, 0.5 g, 2.8 mmol; natural fruit sugar, OOO Arkom) was dissolved in DMSO (2.5 mL) and heated at 150°C with constant stirring on an oil bath for 2 h (the yield was 67% if 5-HMF was isolated). The reaction mixture was cooled to room temperature, treated with methyl(triphenylphosphoranylidene)acetate, and stored for 1 h at room temperature. The products were isolated by column chromatography over silica gel using petroleum ether–EtOAc (7:3).

Methyl (2*E*)-3-[5-(Hydroxymethyl)-2-furyl]acrylate (2a). Powdery light-brown compound, mp 50°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 7.38 (1H, d, J = 15.8, H-2′), 6.54 (1H, d, J = 3.3, H-3), 6.36 (1H, d, J = 3.3, H-4), 6.28 (1H, d, J = 15.8, H-3′), 4.62 (2H, s, H-1″), 3.78 (3H, s, OCH_3), 2.19 (1H, br.s, OH). ^{13}C NMR spectrum ($CDCl_3$, δ, ppm): 51.70 (CH_3), 57.58 (CH_2), 110.19 (=CH), 115.37 (=CH), 115.76 (=CH), 131.11 (=CH), 150.72 (=C), 156.62 (=C), 167.58 (O=C). Found, %: C 59.39; H 5.58. $C_9H_{10}O_4$. Calcd, %: C 59.34; H 5.53; O 35.13.

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Methyl (2*Z*)-3-[5-(Hydroxymethyl)-2-furyl]acrylate (2b). Powdery white compound, mp 130°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 7.61 (1H, d, J = 3.3, H-2′), 6.74 (1H, d, J = 12.9, H-3), 6.39 (1H, d, J = 3.3, H-3′), 5.74 (1H, d, J = 12.9, H-4), 4.64 (2H, s, H-1″), 3.77 (3H, s, OCH_3), 2.01 (1H, br.s, OH). ^{13}C NMR spectrum ($CDCl_3$, δ, ppm): 51.36 (CH_3), 57.66 (CH_2), 110.61 (=CH), 114.09 (=CH), 118.04 (=CH), 130.54 (=CH), 150.62 (=C), 155.49 (=C), 166.42 (O=C). Found, %: C 59.29; H 5.56. $C_9H_{10}O_4$. Calcd, %: C 59.34; H 5.53; O 35.13.

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