Supplementary Information For:

Synthesis of Enantiopure Chloroalcohols by Enzymatic Kinetic Resolution

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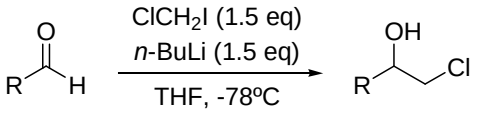
General procedure for the synthesis of substrates 1-7

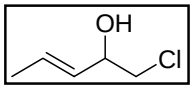
Substrates **1-7** were synthesized according to a literature procedure[1].



In a flamedried flask, a solution of aldehyde (typically 20 mmol) in freshly distilled THF (50 mL) was cooled down to −78 ºC. Chloroiodomethane (30 mmol) was then added, and subsequently *n*-butyllithium (30 mmol, 2.5 M in hexanes, 12 mL) was added dropwise to the solution over a period of 30 min. The reaction mixture was stirred until the starting material was fully converted (TLC), then quenched with NH_4Cl (sat.). After extraction with Et_2O (3x), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and solvents evaporated. The crude products thus obtained were further purified by flash chromatography.

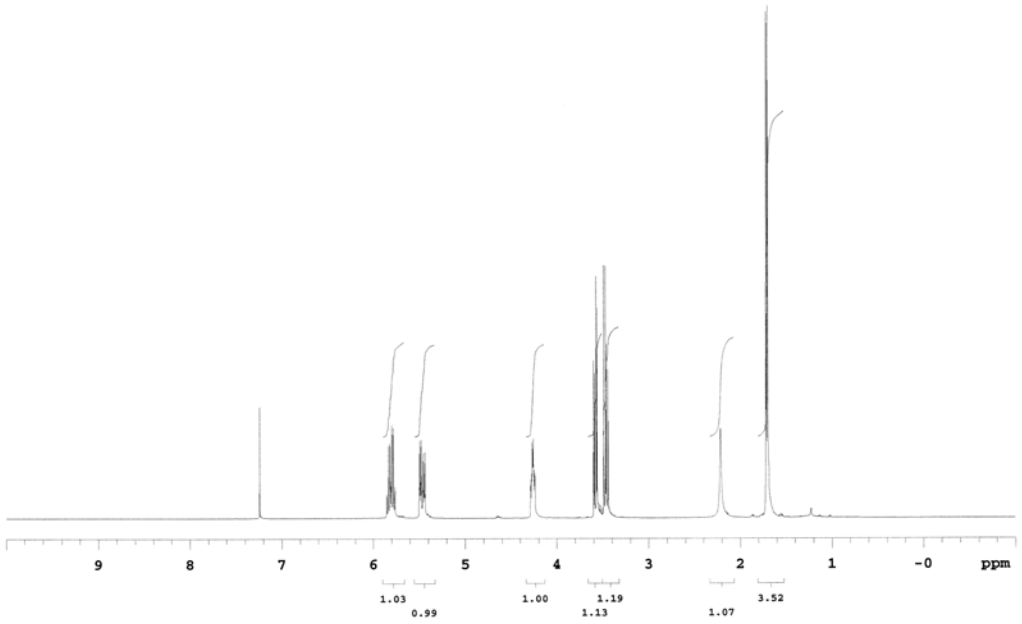
^{1}H and ^{13}C(APT) spectra for substrates 1-7

1-Chloro-pent-3-en-2-ol (1)[2]

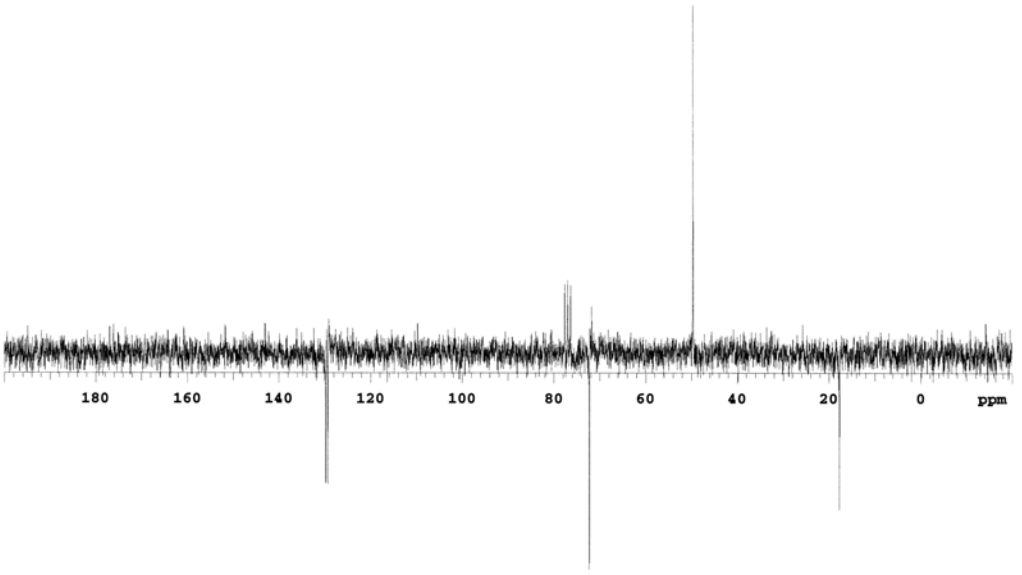


Prepared according to the general procedure, starting from 2.06 mL (1.75 g; 25 mmol) of crotonaldehyde. After flash chromatography over silica gel (pentane/Et_2O 4:1) a colorless oil was obtained (2.21 g; 18.3 mmol; 73%).

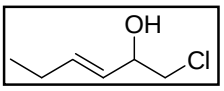
^{1}H NMR:



^{13}C NMR (APT):

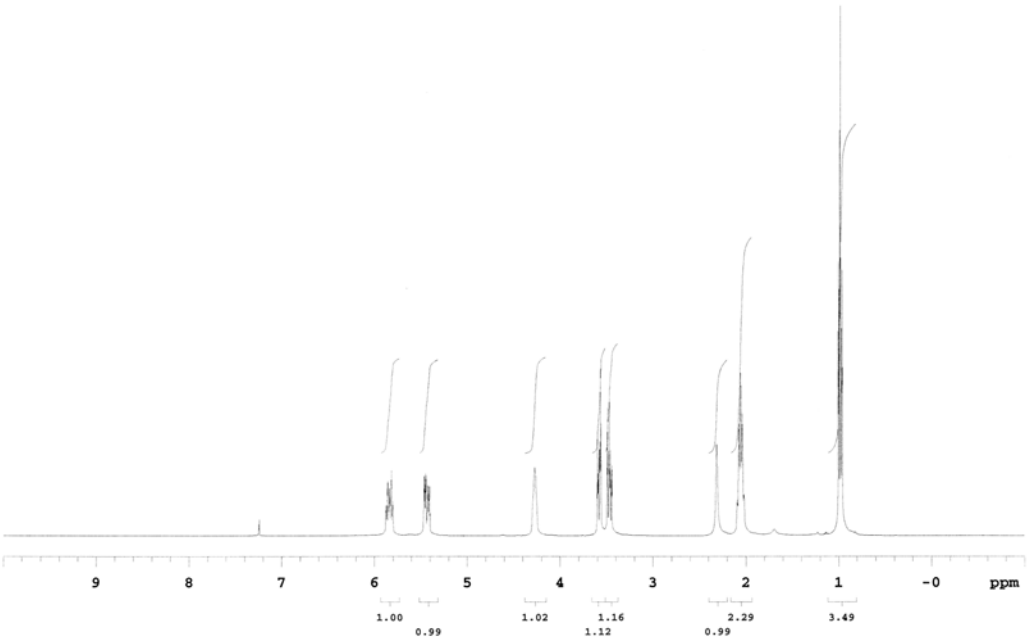


1-chloro-hex-3-en-2-ol (2)

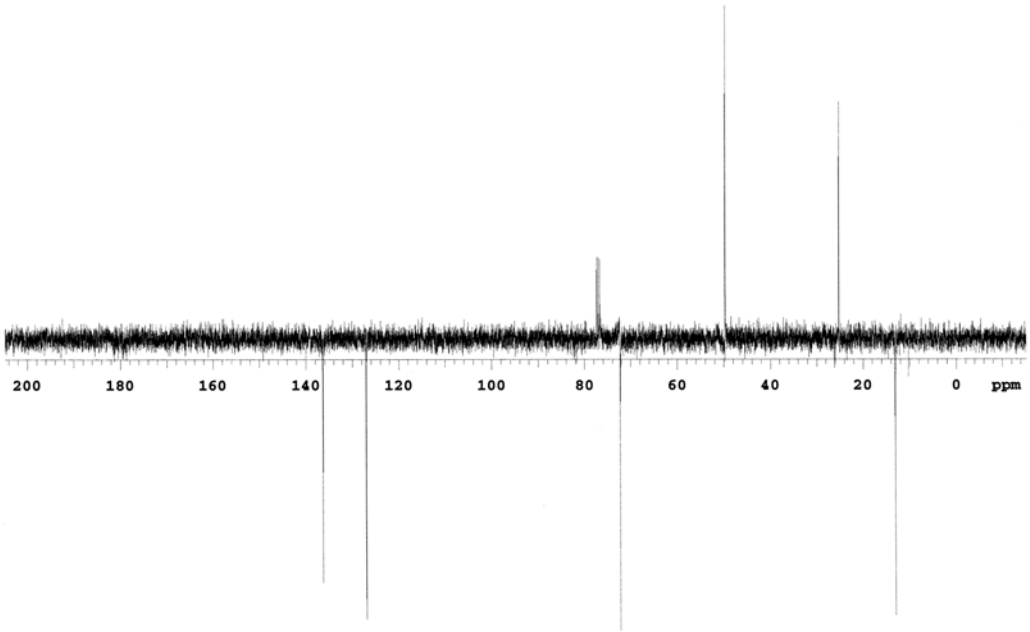


Prepared according to the general procedure, starting from 1.96 mL (1.68 g; 20 mmol) of pent-2-enal. After flash chromatography over silica gel (pentane/Et_2O 6:1, gradient to 4:1) a colorless oil was obtained (1.77 g; 13.2 mmol; 66%).

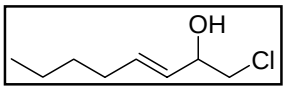
^{1}H NMR:



^{13}C NMR (APT):

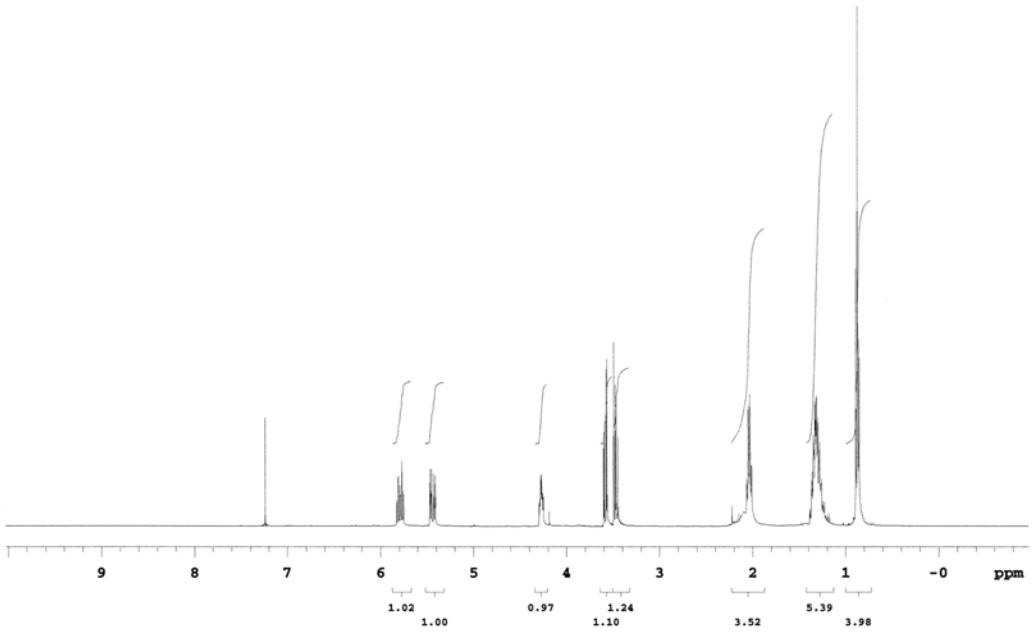


1-Chloro-oct-3-en-2-ol (3)[1,3]

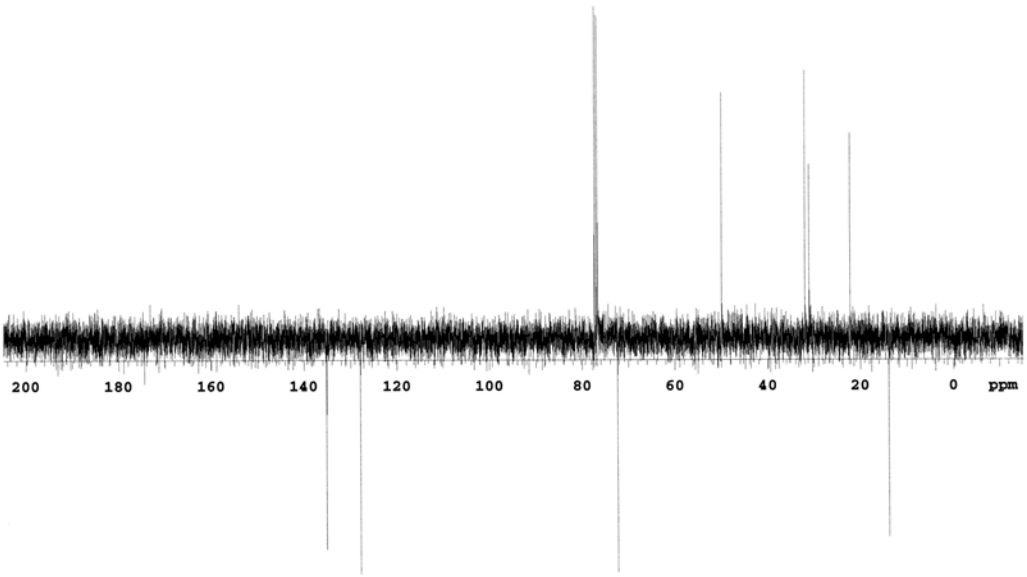


Prepared according to the general procedure, starting from 1.31 mL (1.12 g; 10 mmol) of hept-2-enal. After flash chromatography over silica gel (pentane/Et_2O 6:1; R_f = 0.32) a colorless oil was obtained (903 mg; 5.55 mmol; 56%).

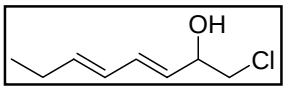
^{1}H NMR:



^{13}C NMR (APT):

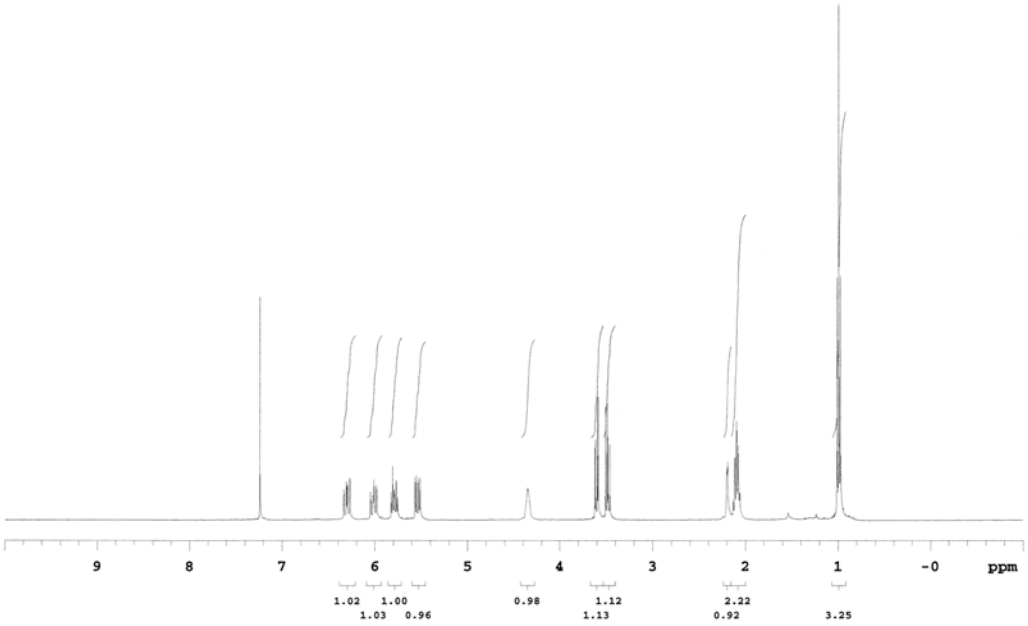


1-Chloro-3,5-octadien-2-ol (4)

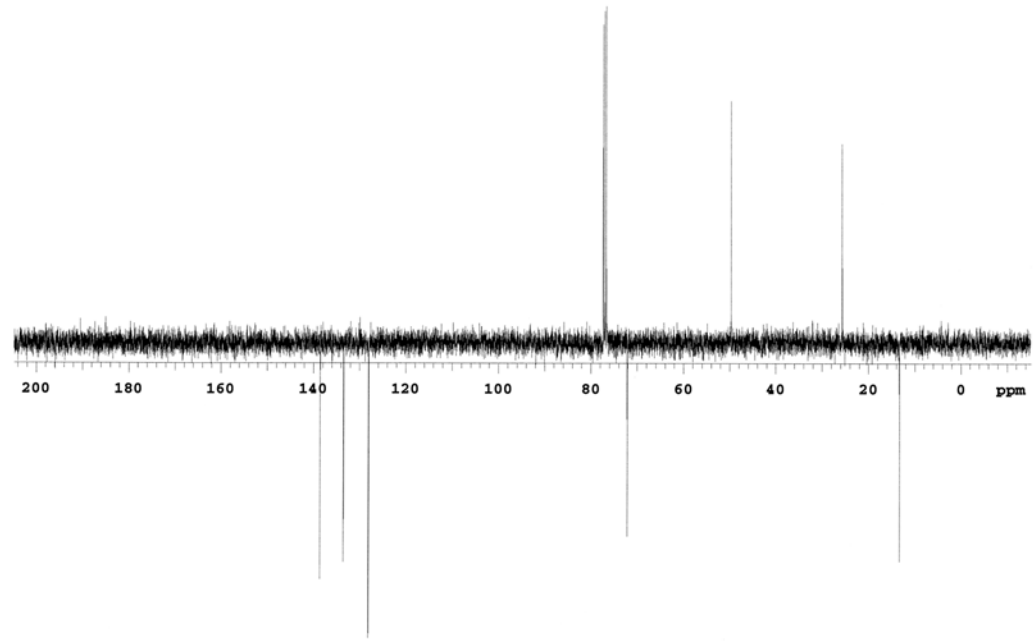


Prepared according to the general procedure, starting from 1.25 mL (1.10 g; 10 mmol) of *trans*,*trans*-hepta-2,4-dienal. After flash chromatography over silica gel (pentane/Et_2O 7:1; R_f = 0.26) a colorless oil was obtained (1.29 g; 8.0 mmol; 79%).

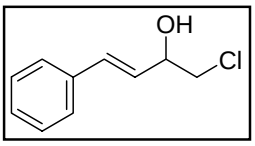
^{1}H NMR:



^{13}C NMR (APT):

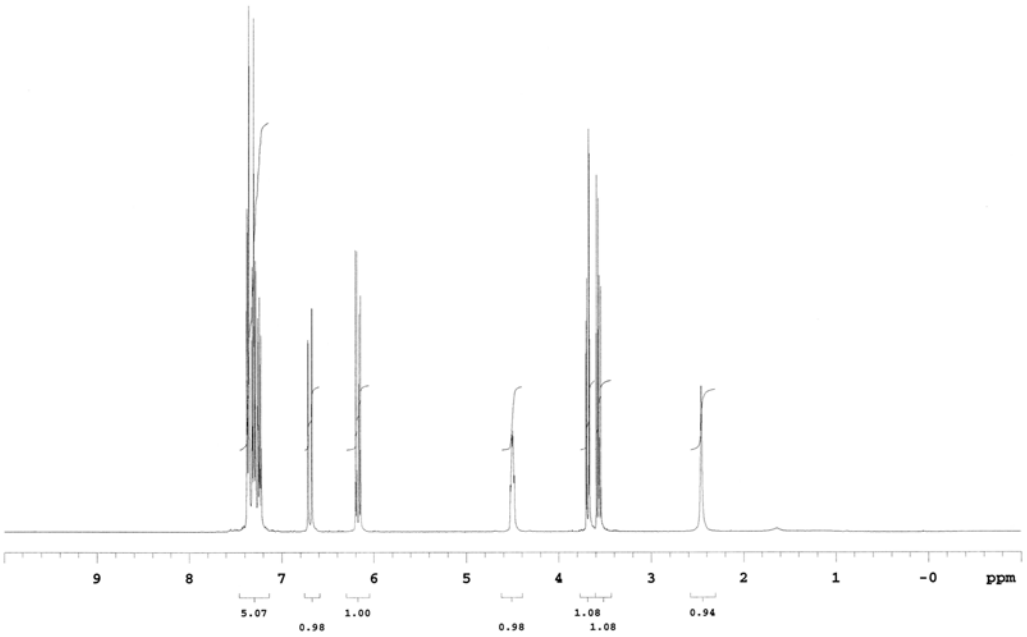


(*E*)-1-Chloro-4-phenyl-but-3-en-2-ol (5)[1,3,4,5,6]

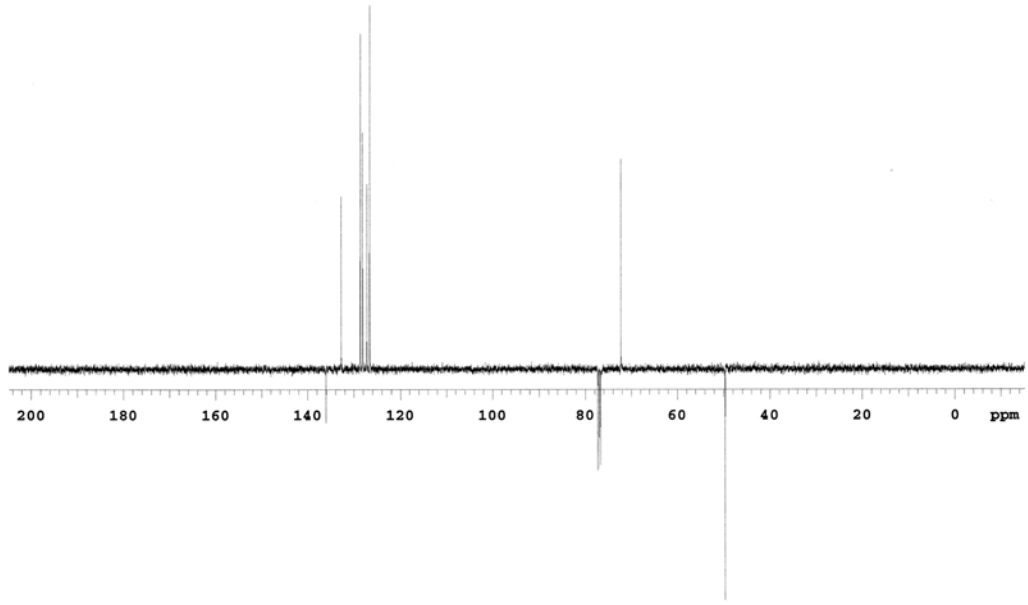


Prepared according to the general procedure, starting from 2.52 mL (2.64 g; 20 mmol) of cinnamaldehyde. After flash chromatography over silica gel (pentane/Et_2O 5:1; R_f = 0.24) a colorless oil was obtained (2.34 g; 12.8 mmol; 64%), which crystallized upon standing.

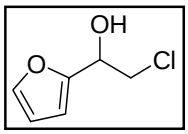
^{1}H NMR:



^{13}C NMR (APT):

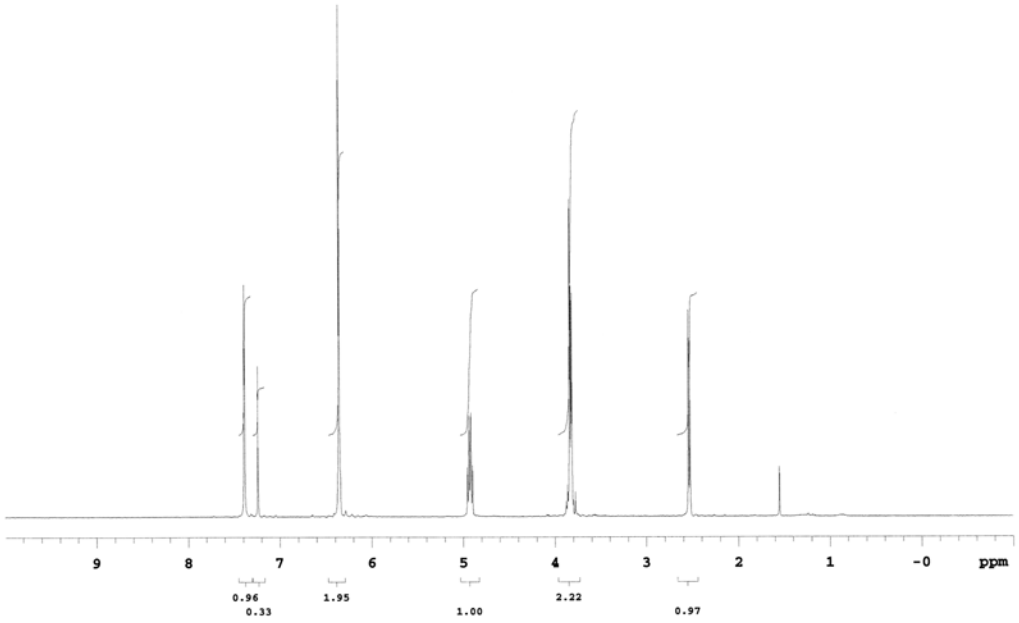


2-Chloro-1-furan-2-yl-ethanol (6)[4,7]

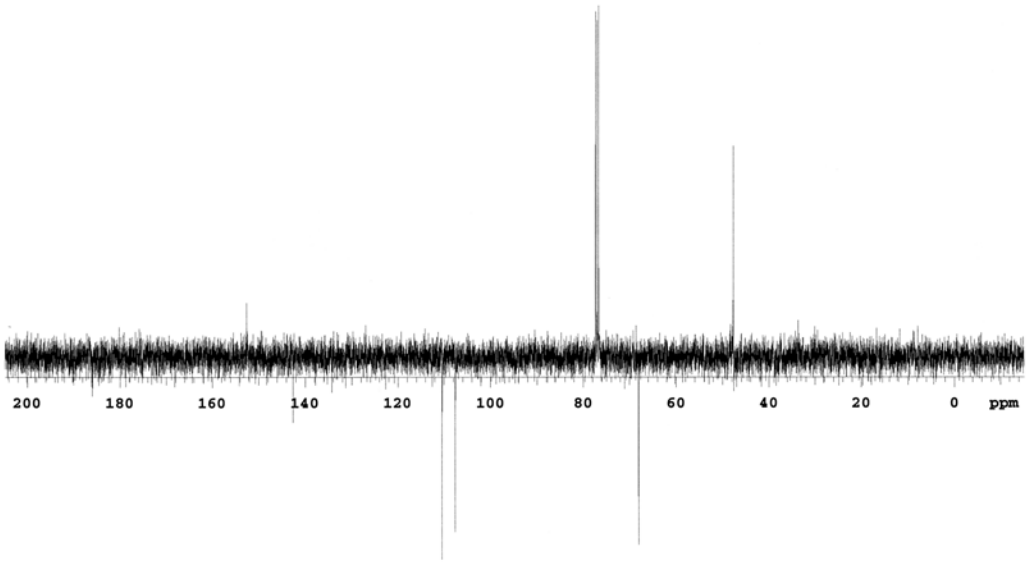


Prepared according to the general procedure, starting from 1.66 mL (1.92 g; 20 mmol) of freshly distilled furfural. After flash chromatography over silica gel (pentane/Et_2O 4:1, gradient to 3:1; $R_{f,\ 3:1}$ = 0.40) a light yellow oil (1.87 g; 12.7 mmol; 64%) was obtained.
For the resolution on 2.3 g scale, different preparations were combined.

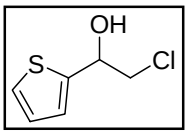
^{1}H NMR:



^{13}C NMR (APT):

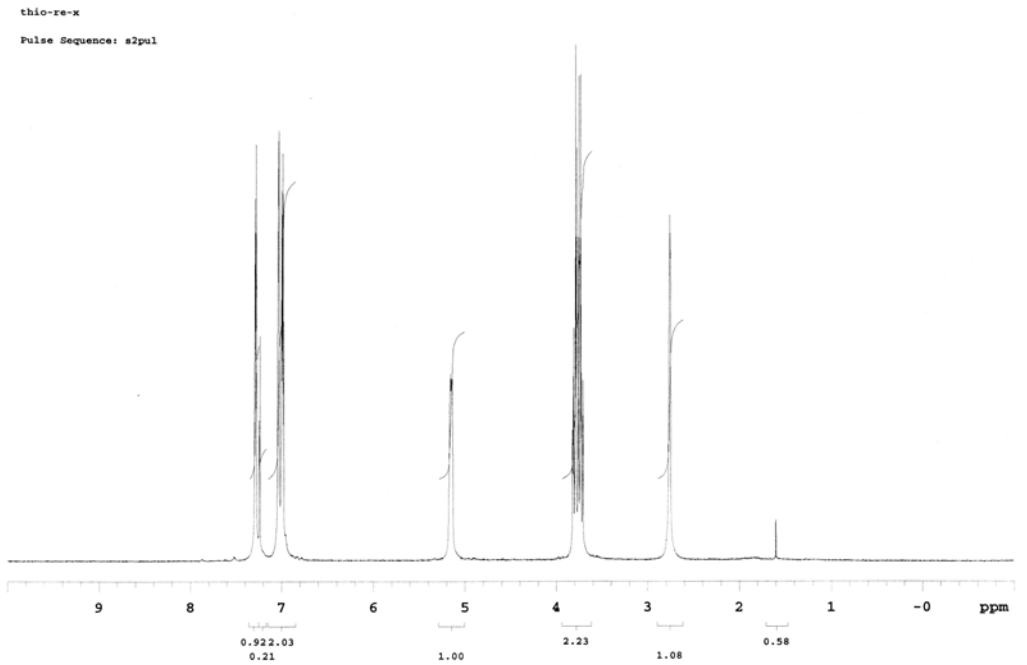


2-Chloro-1-thiophen-2-yl-ethanol (7)[4,8]

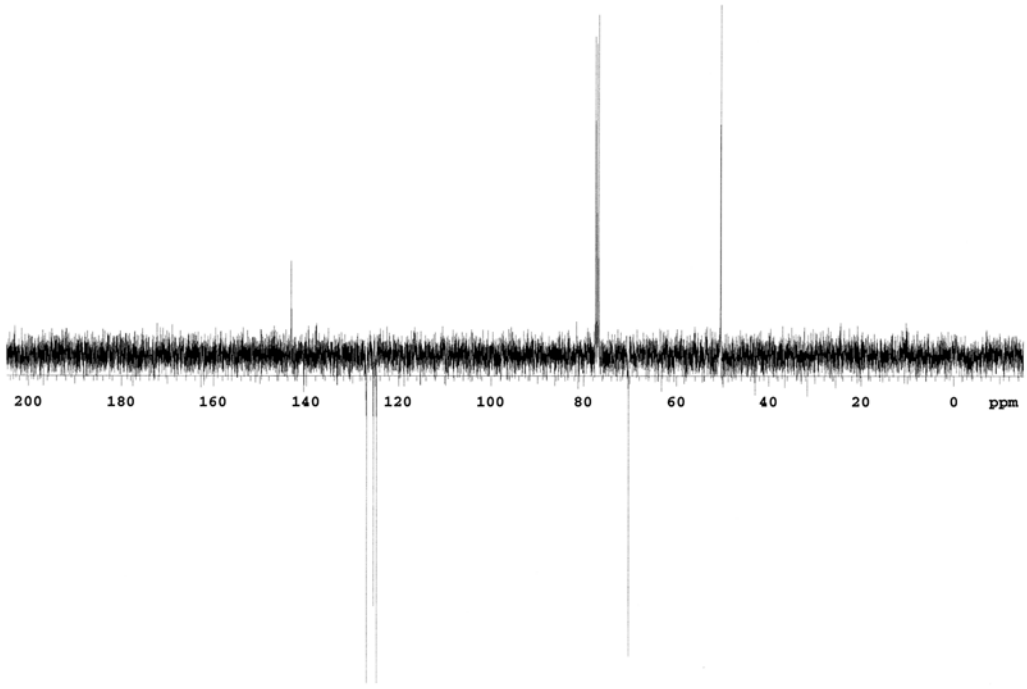


Prepared according to the general procedure, starting from 1.87 mL (2.24 g; 20 mmol) of 2-thiophene-carboxaldehyde. After flash chromatography over silica gel (pentane/Et_2O 4:1; R_f = 0.33) a colorless oil was obtained (2.86 g; 17.6 mmol; 88%).
For the 20 g scale resolution, this compound was prepared analogously (64%).

^{1}H NMR:



^{13}C NMR (APT):



References

[1] M. Lautens, M. L. Maddess, E. L. O. Sauer and S. G. Ouellet, *Org. Lett.*, 2002, **4**, 83.

[2] This compound has been reported in: Pudowik and Iwanow, *Zh. Obshch. Khim.*, 1956, **26**, 1910, Engl. Ed. 2129; Ponomarew *et al.*, *Zh. Obshch. Khim.*, 1957, **27**, 1226, Engl. Ed. 1309.

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[8] A. Kamal, G. B. R. Khanna, R. Ramu and T. Krishnaji, *Tetrahedron Lett.*, 2003, **44**, 4783; C. Corral, V. Darias, M. P. Fernández-Tomé, R. Madroñero and J. Del Río, *J. Med. Chem.*, 1973, **16**, 882; H. Hopff and R. Wandeler, *Helv. Chim. Acta*, 1962, **45**, 982.