A green and facile route to γ- and δ-lactones *via* efficient Pinner-cyclization of hydroxynitriles in water.

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SUPPORTING INFORMATION

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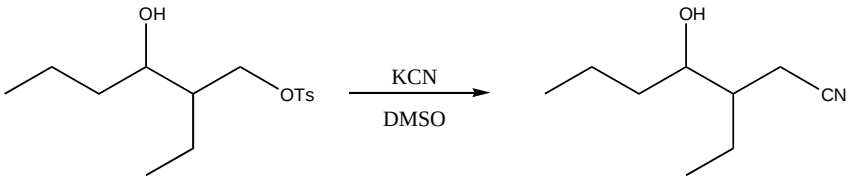
1. General Experimental Details

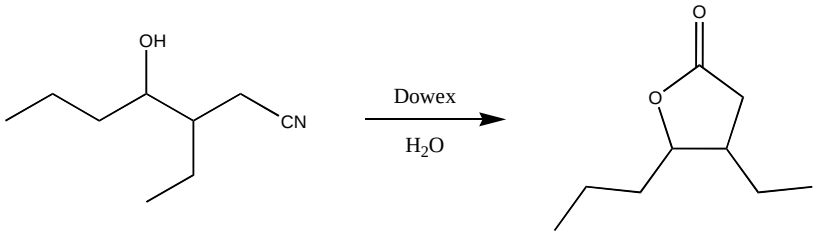
Deionized water was used in all reactions. All chemicals were used as received from the supplier. The Dowex 50W×8-200 (H^+) cation exchange resin has a density of 0.8 g/mL and maximum exchange quantity (meq) of 1.7/mL. The resin was washed with methanol then water until neutral pH, and finally dried in air before use. Reactions in sealed tubes were performed in thickened glass tubes (120x15 mm) fitted with a Teflon screw-cap. The tubes were immersed 2/3 into the oil baths set at the noted temperature. Flash chromatography was performed on normal phase silica gel, 35-70 μ, 60Å. Purity has been documented by providing a ^{13}C-NMR spectra for each of the products (see below). The preparation of the previously not reported compounds **1e** and **3e** is described herein together with analytical data. All other compounds are either commercially available (**1d**, **3c**, **3d**, **3f**) or previously reported in the literature (**1a**,[1] **1b**,[2] **1c**,[3] **1f**,[4] **3a**,[5] **3b**[6]) and gave consistent ^{1}H- and ^{13}C-NMR data.

[1] Ortuño, R. M.; Alonso, D.; Cardellach, J.; Font, J. *Tetrahedron* **1987**, 43, 2191.
[2] Menard, M.; Martel, A. *U.S. Patent* **1981**, 4,272,437.
[3] Jones, R. M.; Van De Water, R. W.; Lindsey, C. C.; Hoarau, C.; Ung, T.; Pettus, T. R. R. *J. Org. Chem.* **2001**, *66*, 3435.
[4] Katsumi, N.; Kunio, S.; Minoru, S.; Coll, S.; Shizuoka, P. *Jap. Chem. & Pharm. Bulletin* **1977**, *25*, 2396.
[5] Takahata, H.; Uchida, Y.; Momose, T. *J. Org. Chem.* **1994**, 59, 7201.
[6] Taylor, S. K.; Atkinson, R. F.; Almli, E. P.; Carr, M. D.; Van Huis, T. J.; Whittaker, M. R. *Tetrahedron Asym.* **1995**, 6, 157.

2. Experimental details for new compounds



3-ethyl-4-hydroxyheptanonitrile (1e). To a stirred mixture of 2-ethyl-3-hydroxyhexyl 4-methylbenzenesulfonate[7] (526 mg, 1.8 mmol) in DMSO (12 mL) was added KCN (234 mg, 3.6 mmol). The reaction mixture was stirred at 60 °C over night. Cold water (15 mL) was added to the reaction mixture, which was extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (heptane/ethyl acetate = 5/1), to give **1e** (184.0 mg, 66%). ^{1}H NMR ($CDCl_3$, 300 MHz, mixture of diastereomers): δ (ppm) 3.80 (m), 3.67-3.62 (m), 2.57-2.49 (m), 2.39 (dd, *J*=5.9, 16.9), 1.8-1.3 (m), 0.96 (m); ^{13}C NMR ($CDCl_3$, 75 MHz, mixture of diastereomers): δ (ppm) 119.8, 119.8, 72.5, 71.9, 42.8, 42.6, 37.1, 35.7, 23.3, 21.5, 19.5, 19.1, 18.1, 17.1, 14.2, 11.9, 11.4; HRMS, calcd for $C_9H_{17}NO$ (M+H) 156.1388, found 156.1385.



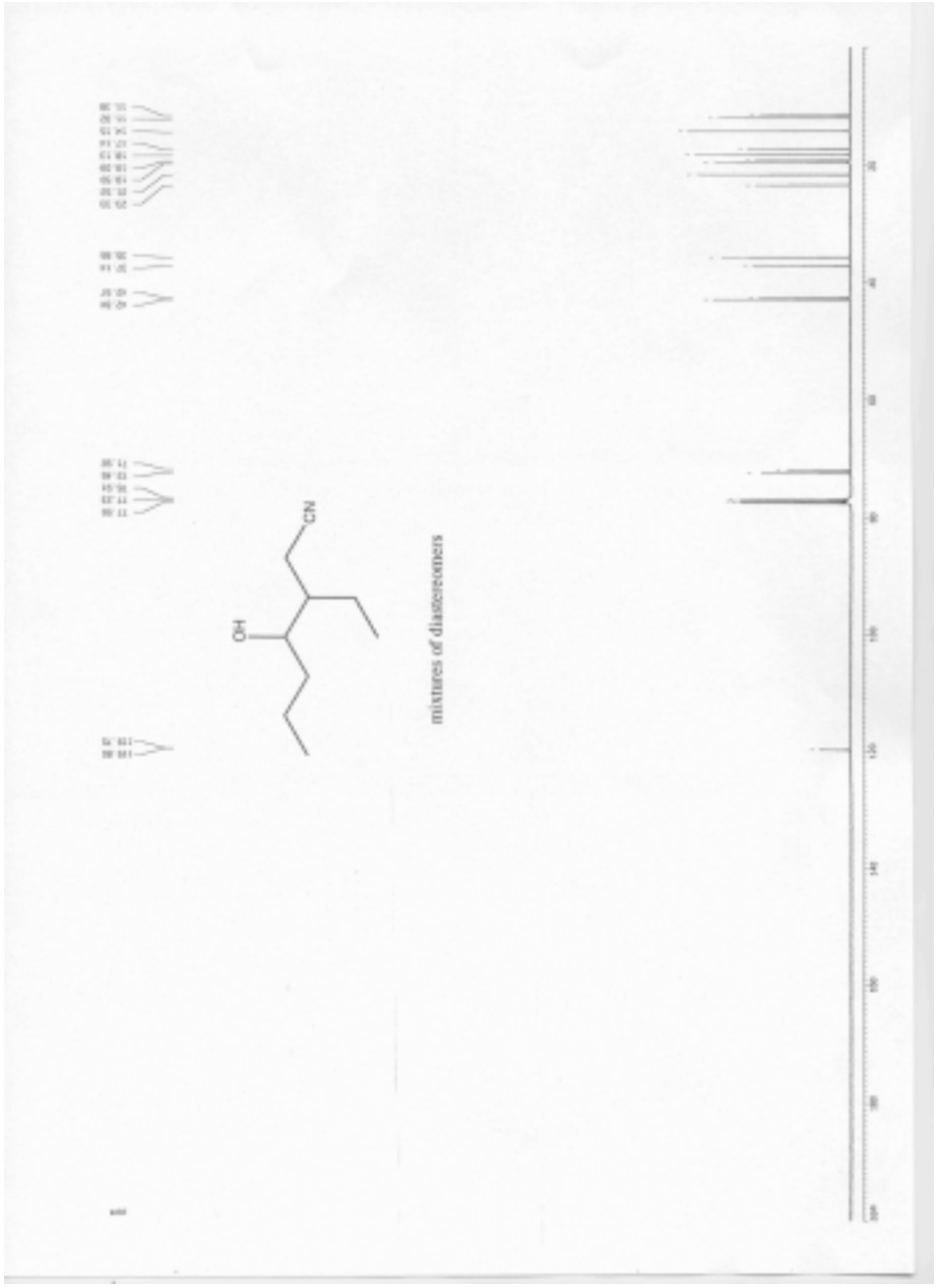
3-ethyl-4-propyl-γ-butyrolactone (3e). To a mixture of 3-ethyl-4-hydroxyheptanonitrile (**1e**) (22.1 mg, 0.142 mmol) in H_2O (1 mL) was added cationic exchange resin (220 mg, Dowex

[7] Horner, L.; Schmitt, R. E. *Phosphorous and Sulfur and the Related Elements* **1982**, *13*, 189.

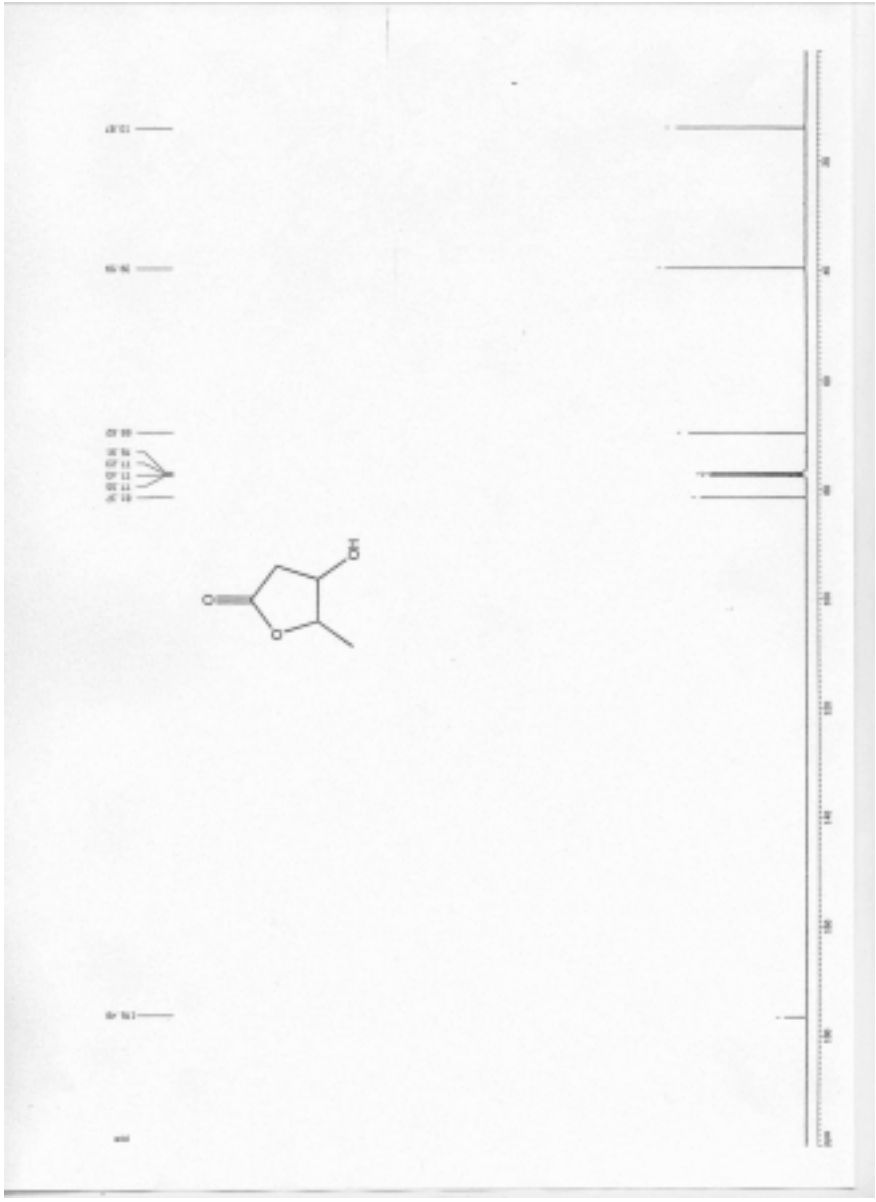
50W×8-200). The reaction mixture was stirred vigorously in a sealed tube at 135 °C for 1 h. after cooling, the catalyst was then filtered off and washed with ethanol. The filtrate was concentrated with gentle heating under reduced pressure to give 3-ethyl-4-propyl-γ-butyrolactone (**3e**) (14.8 mg**,** 65%) and small traces of imidate. ^{1}H NMR ($CDCl_3$, 300 MHz, mixture of diastereomers): δ (ppm) 4.50 (m), 4.11 (m), 2.71-2.53 (m), 2.46-2.34 (m), 2.32-2.15 (m), 2.11-1.98 (m), 1.68-1.20 (m), 0.97-0.90 (m); ^{13}C NMR ($CDCl_3$, 75 MHz, mixture of diastereomers): δ (ppm) 177.2, 177.0, 85.9, 83.5, 42.9, 40.7, 37.1, 35.1, 34.3, 32.1, 26.2, 21.4, 19.4, 19.2, 14.1, 14.1, 12.3, 12.1; HRMS: calcd for $C_9H_{17}O_2$ (M+H) 157.1229, found 157.1191.

5. ^{13}C-NMR spectra demonstrating purity of products.

1e:



3a:



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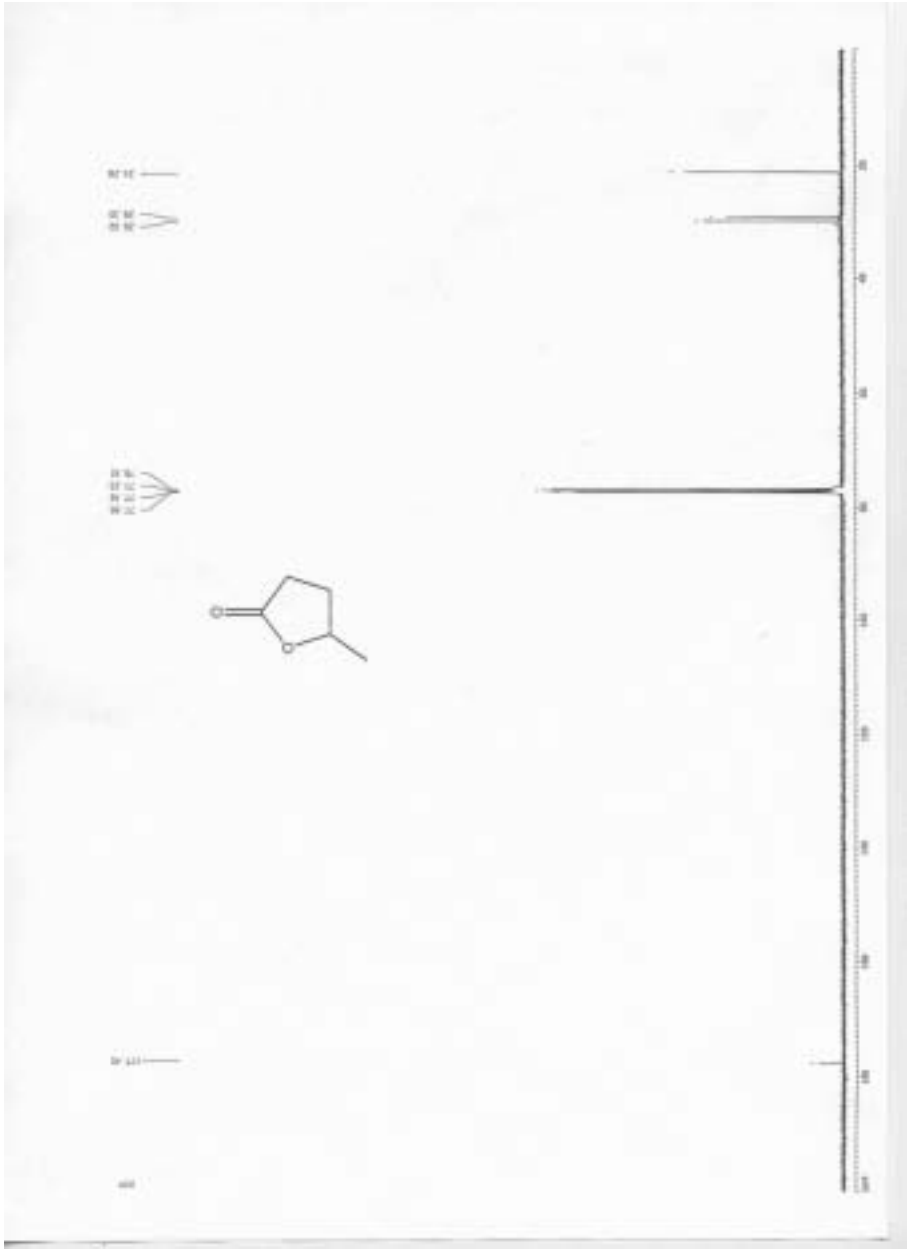

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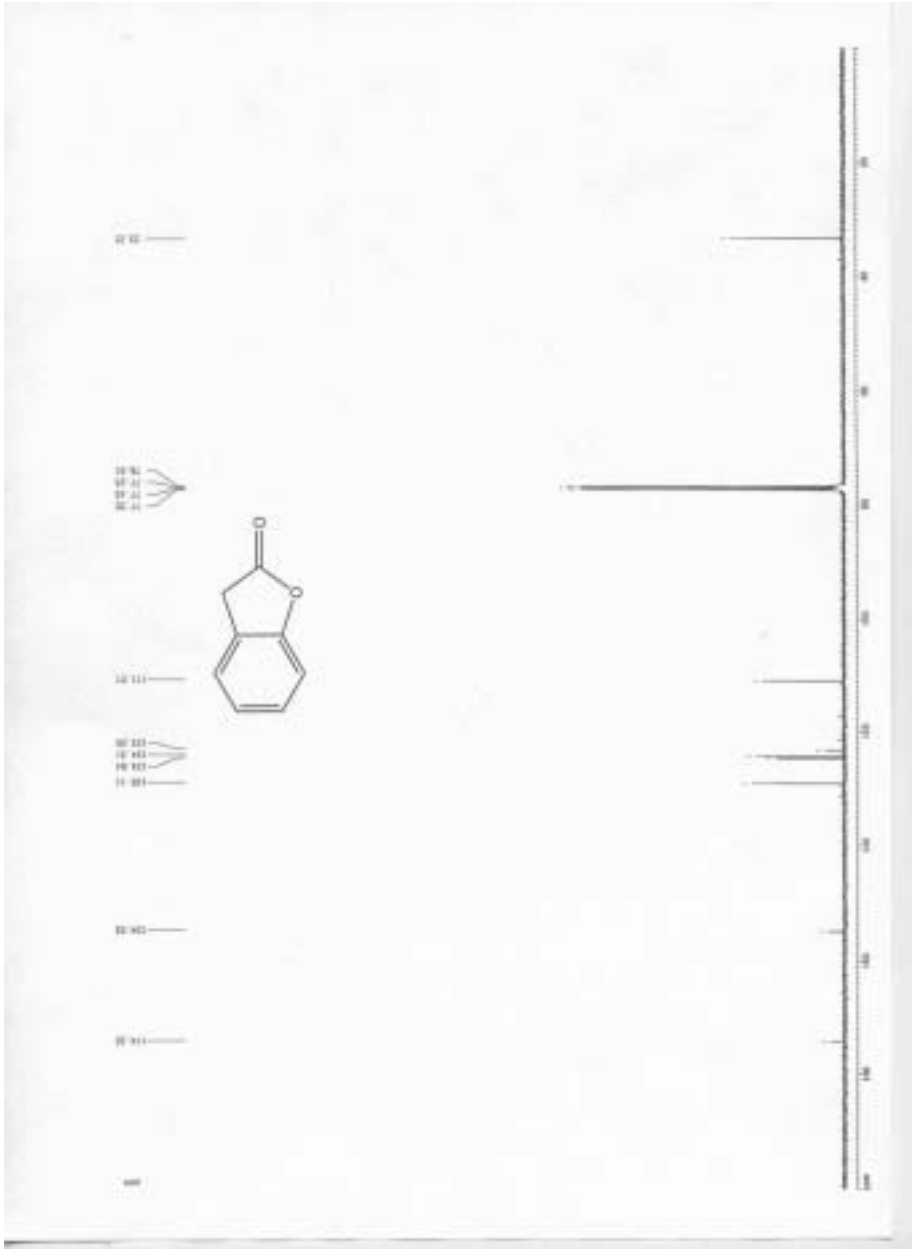

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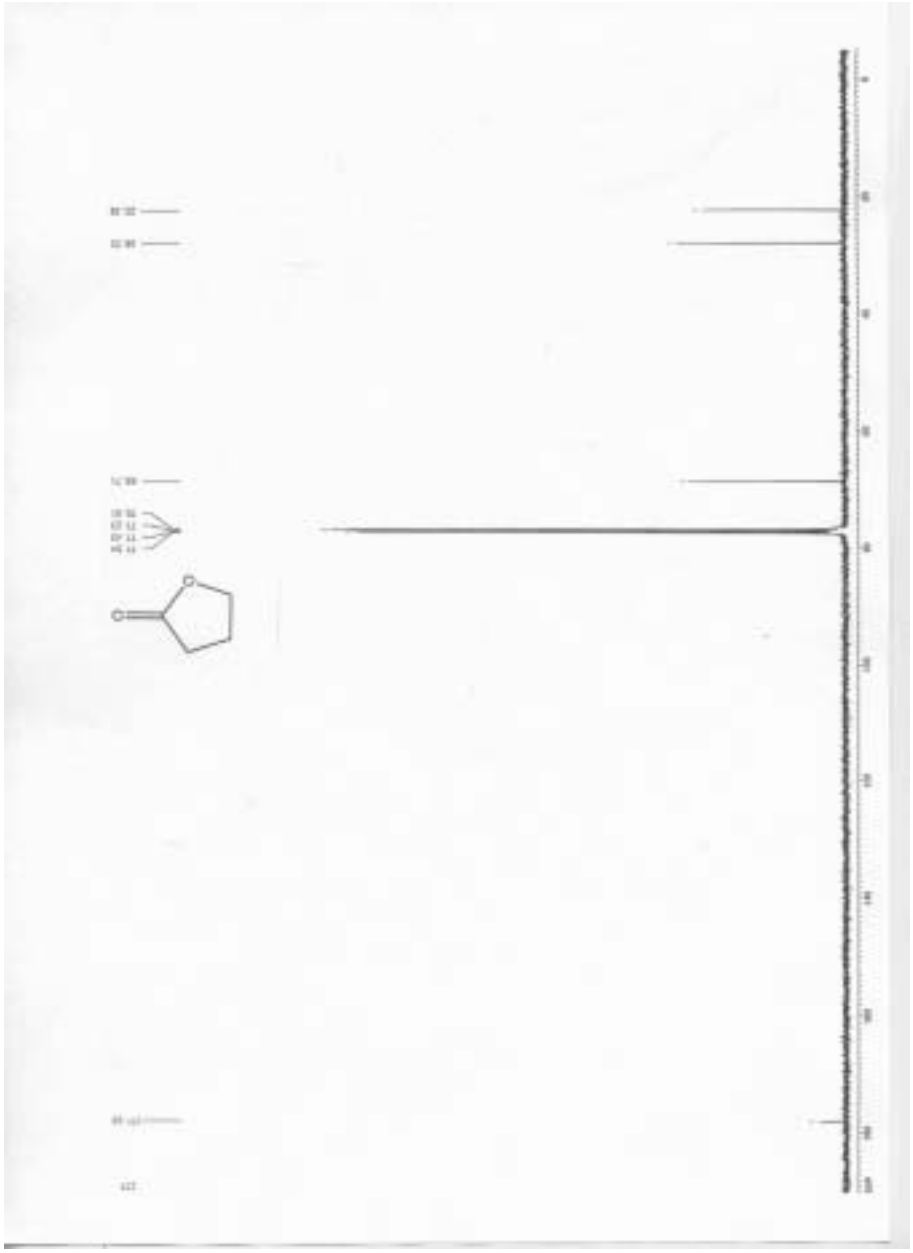
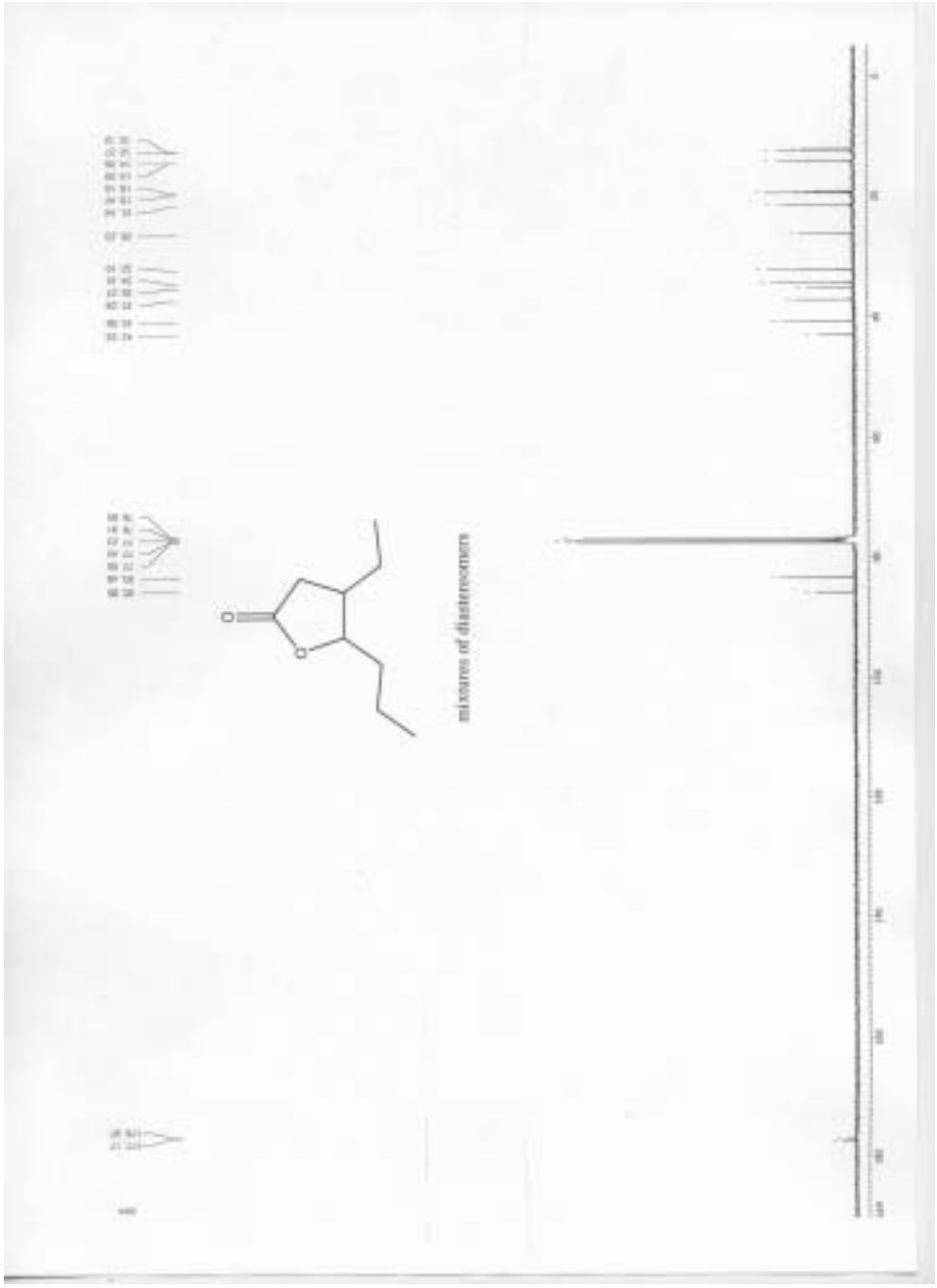


3e:



3f: