Palladium(II)-Catalyzed Asymmetric Cyclization of (*Z*)-4'-Acetoxy-2'-butenyl 2-Alkynoates. Role of Nitrogen-Containing Ligands in Palladium(II)-Mediated Reactions.

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Supporting Information:

Synthesis of (+)-α-(*Z*)-(1'-Acetoxy-6'-methylheptylidene)-β-hydroxymethyl-γ-butyrolactone (17). *N*-methylmorpholine *N*-oxide (1.1 equiv., 60% wt in water) and potassium osmate (VI) (1 mol %) were added to a solution of (+)-**2d** (84% ee, 700 mg, 2.5 mmol) in acetone-water (1:2, 14 mL). The reaction mixture was stirred for 15 h at 10 °C and, upon completion, was quenched with sodium bisulfite (347 mg), diluted with water and extracted with CH_2Cl_2 (4 × 50 mL). The combined CH_2Cl_2 portions were dried (Na_2SO_4), filtered and concentrated in vacuo below 30 °C. The residue was purified through a short silica gel column to afford a colorless oil which was added to a vigorously stirred suspension of SiO_2-supported $NaIO_4$ reagent[45] (4.55 g) in CH_2Cl_2 (23 mL). The reaction mixture was stirred at room temperature for 1.5 h, then filtered, washed with $CHCl_3$ and concentrated in vacuo to afford the aldehyde as an oil. The aldehyde was directly disssolved in MeOH (23 mL) without purification. Sodium borohydride (43 mg, 1.1 mmol) was added into the reaction mixture in portions at -2 °C. The reaction mixture was stirred for 1 h at the temperature, upon completion, diluted with water,

and extracted with CH_2Cl_2 (4 × 60 mL). The combined CH_2Cl_2 portions were dried (Na_2SO_4), filtered and concentrated in vacuo below 30 °C. The residue was submitted to colum chromatography on silica gel to afford pure **17** as the product (498 mg, 70.1% in total yield). $[\alpha]^{20}_D$ +59.4° (c, 0.945, $CHCl_3$). IR (neat) 3484, 2956, 1758, 1676, 1368, 1211, 1159. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.30 (d, J = 3.8 Hz, 2H), 3.69 (m, 2H), 3.32 (m, 1H), 2.70 (br, 1H), 2.42-2.29 (m, 2H), 2.27 (s, 3H), 1.56-1.50 (m, 3H), 1.38-1.31 (m, 2H), 1.22-1.17 (m, 2H), 0.88 (d, J = 7.2 Hz, 6H). MS (m/z) 285 (M^+ + 1), 267, 243 (100), 225, 211. HRMS Calcd for $C_{15}H_{24}O_5$ 284.1623, Found 284.1614.

Synthesis of (+)-α-(6'-Methylheptanoyl)-β-hydroxymethyl-γ-butyrolactone [(+)-A-factor]. To a solution of (+)-**17** (58 mg, 0.20 mmol) in MeOH (9 mL) was added 4-(dimethylamino)pyridine (5 mg, 0.04 mmol). The reaction mixture was stirred for 20 h at 9 °C. Most of the solvent was removed in vacuo below 30 °C, the residue was then submitted to column chromatography on silica gel (petroleum ether:ethyl acetate 3:1), affording the product as a waxy solid (40 mg, 82%). $[\alpha]^{22}_D$ +10.9° (c 1.40, $CHCl_3$) (lit[36b] $[\alpha]^{22}_D$ +12.7°). IR (neat) 3458, 2956, 1766, 1717, 1648, 1384, 1171, 1026 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.26 (small peak), 4.5-3.9 (m, 2H), 3.8-3.5 (m, 2H), 3.3-2.2 (m, 3H), 2.0-1.0 (m,9H), 0.87 (d, J = 6.6 Hz, 6H). MS (m/z) 243 (M^+ + 1, 100), 225, 211, 153, 143, 127, 109, 85, 67.

6-(1-Methoxy-2,2-dimethylpropyl)-2,2′-bipyridine.[41] colorless needles: mp 46-48 °C. IR (KBr) 1581, 1563, 1430, 1106, 771 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (dt, J = 4.8, 0.8 Hz, 1H), 8.39 (d, J = 8.0 Hz, 1H), 8.25 (dt, J = 7.8, 0.7 Hz, 1H), 7.82-7.76 (m, 2H), 7.37 (dd, J = 7.8, 0.6 Hz, 1H), 7.29-7.24 (m, 1H), 4.04 (s, 1H), 3.27 (s, 3H), 0.96 (s, 9H). MS (m/z) 257 (M^+ + 1), 241, 199, 185(100), 170, 155, 78, 57, 41. Anal. Calcd for $C_{16}H_{20}N_2O$ C, 74.94; H, 7.86; N, 10.93. Found C, 74.95; H, 7.75; N, 10.88.

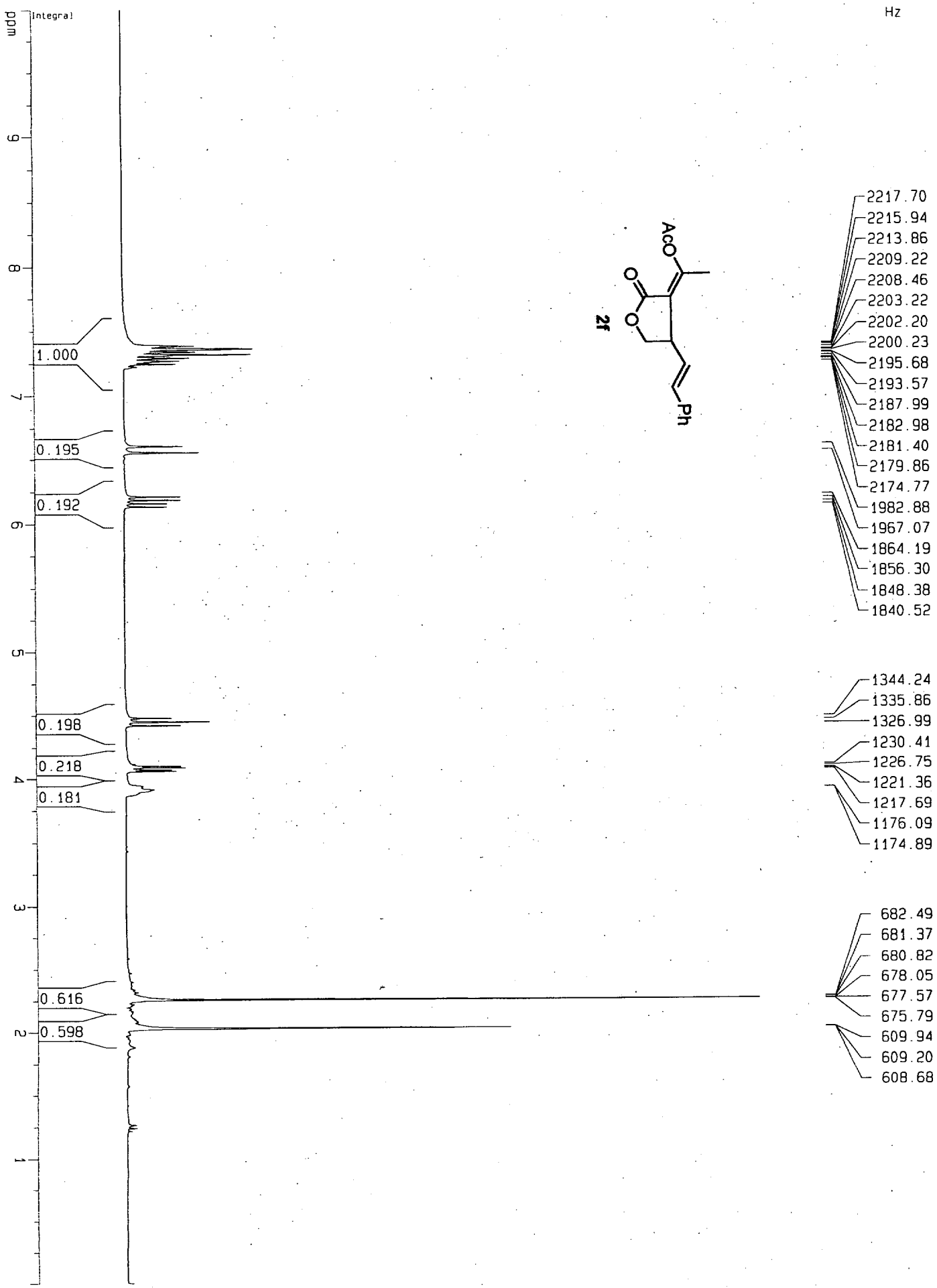
The Specific Rotation of the Optically Active γ-Butyrolactones 2

γ-butyrolactones (**2**)	ee%[a]	$[\alpha]^{20}_D$ in chloroform
2a	92	+36.8° (c 3.15)
2b	81	+21.6° (c 2.45)
2c	81	+128.5° (c 1.94)
2d	84	+25.4° (c 2.10)
2e	87	+57.7° (c 3.00)

[a] Determined by chiral HPLC using the chiralcel column OJ eluting with hexane:2-propanol (8:2, v:v), (λ = 214 nm).

Retention time of 2 in the HPLC analysis. Enantiomers were separated by HPLC using the chiralcel OJ column eluting with hexane:2-propanol (8:2, v:v), (λ = 214 nm).

sample	time (min)	
	(*S*)-	(*R*)-
2a	13.7	15.5
2b	12.0	13.5
2c	9.8	11.4
2d	32.1	36
2e	17.7	20.1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Ph
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2208.46
2203.22
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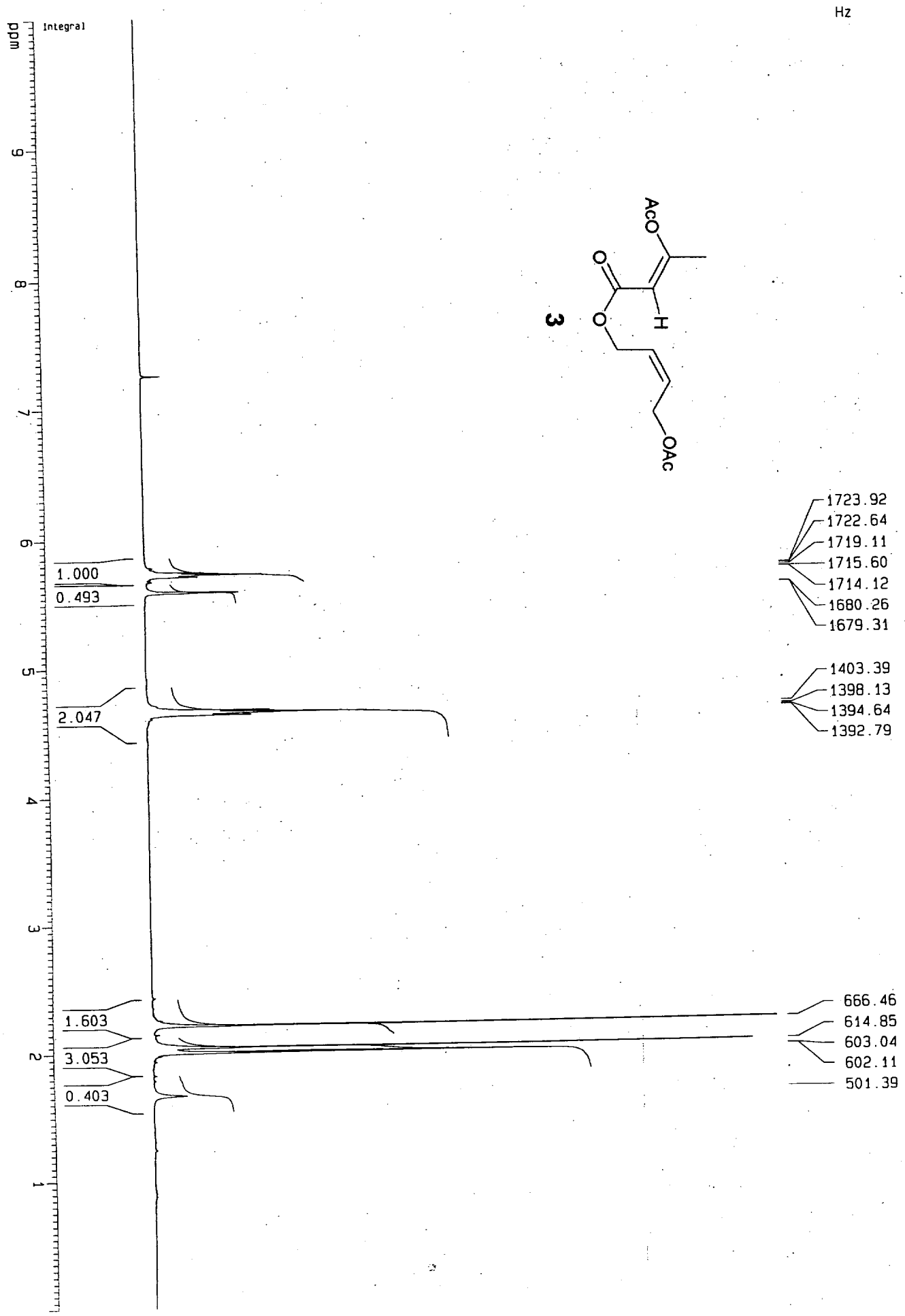
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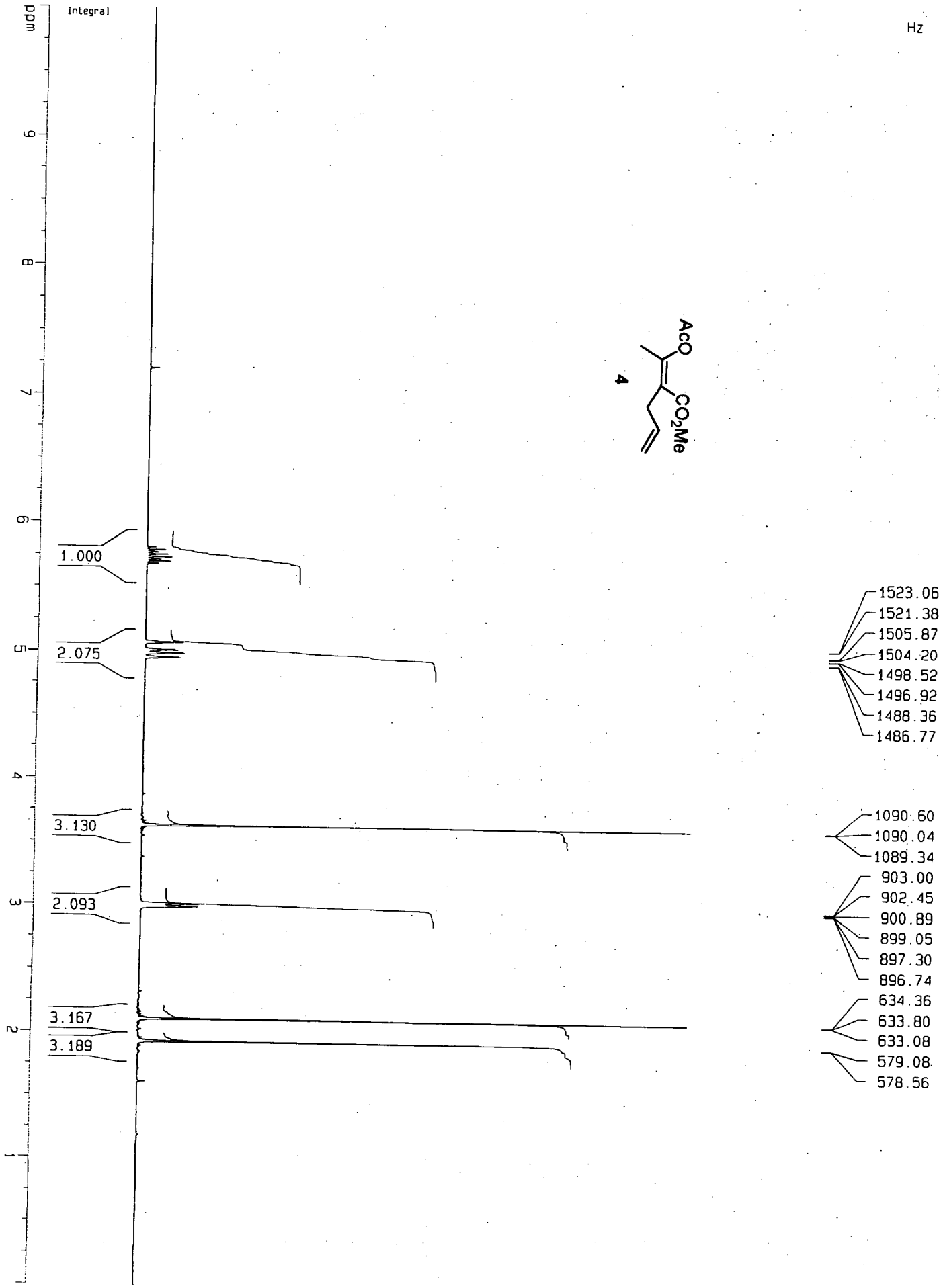
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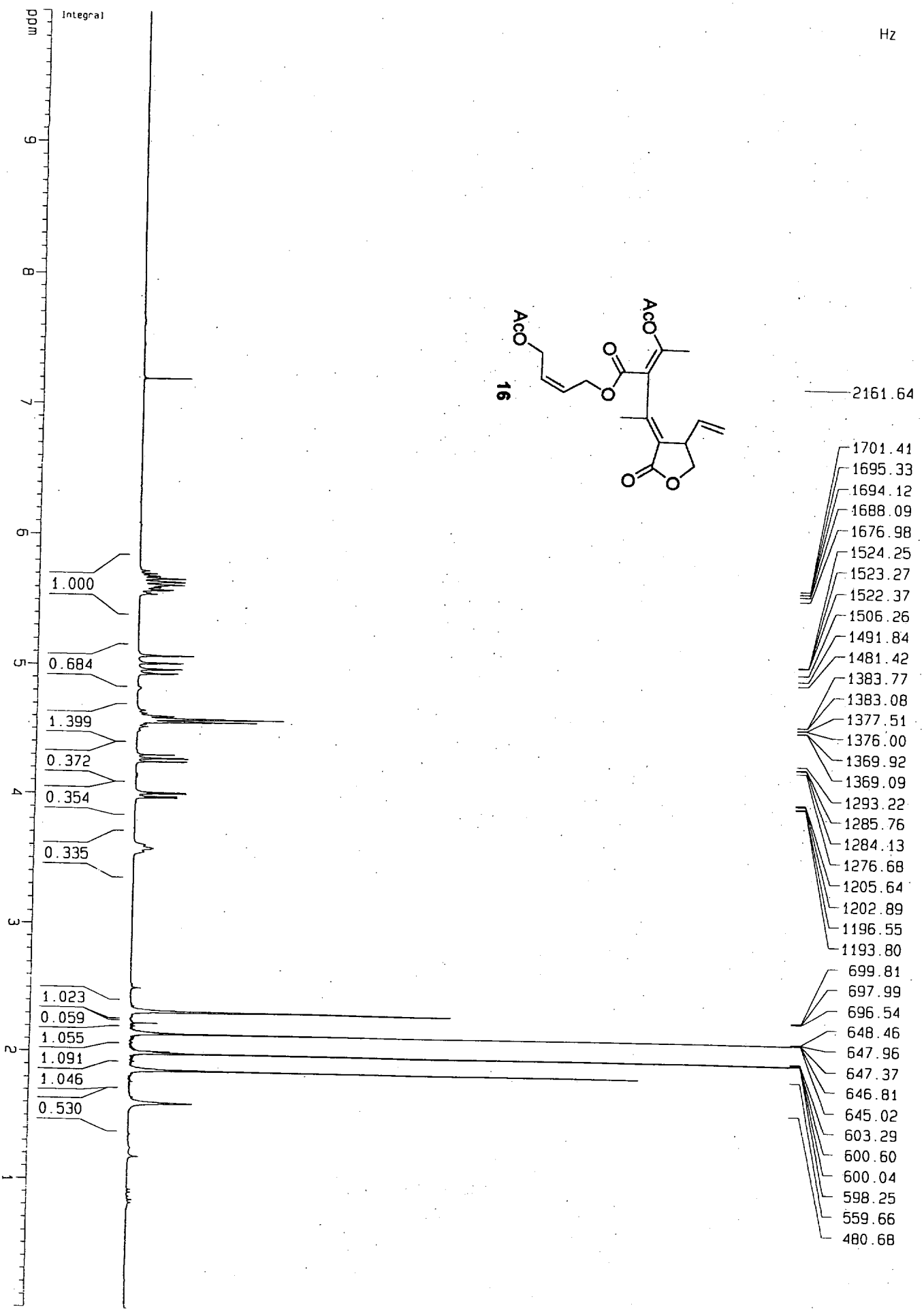

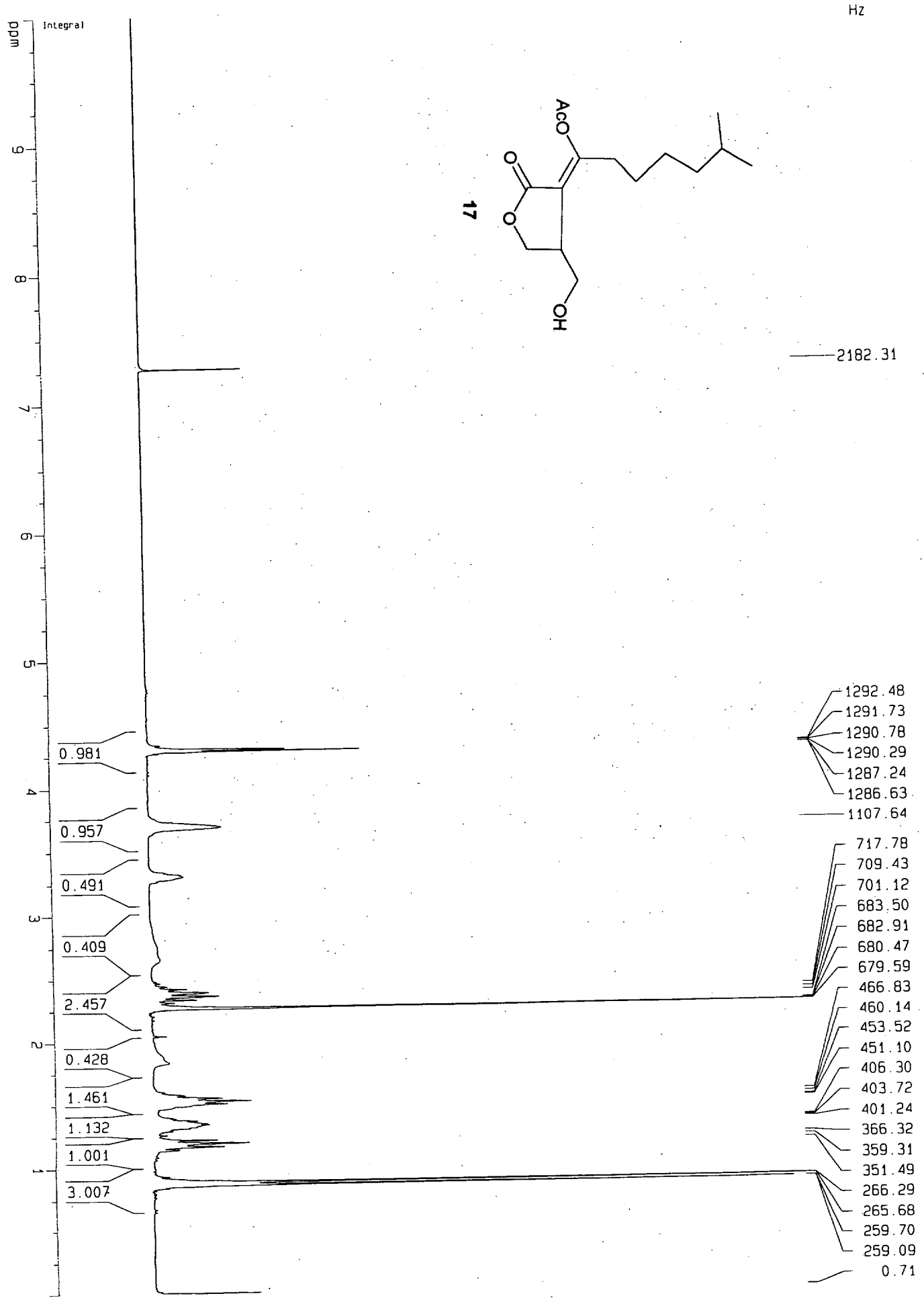
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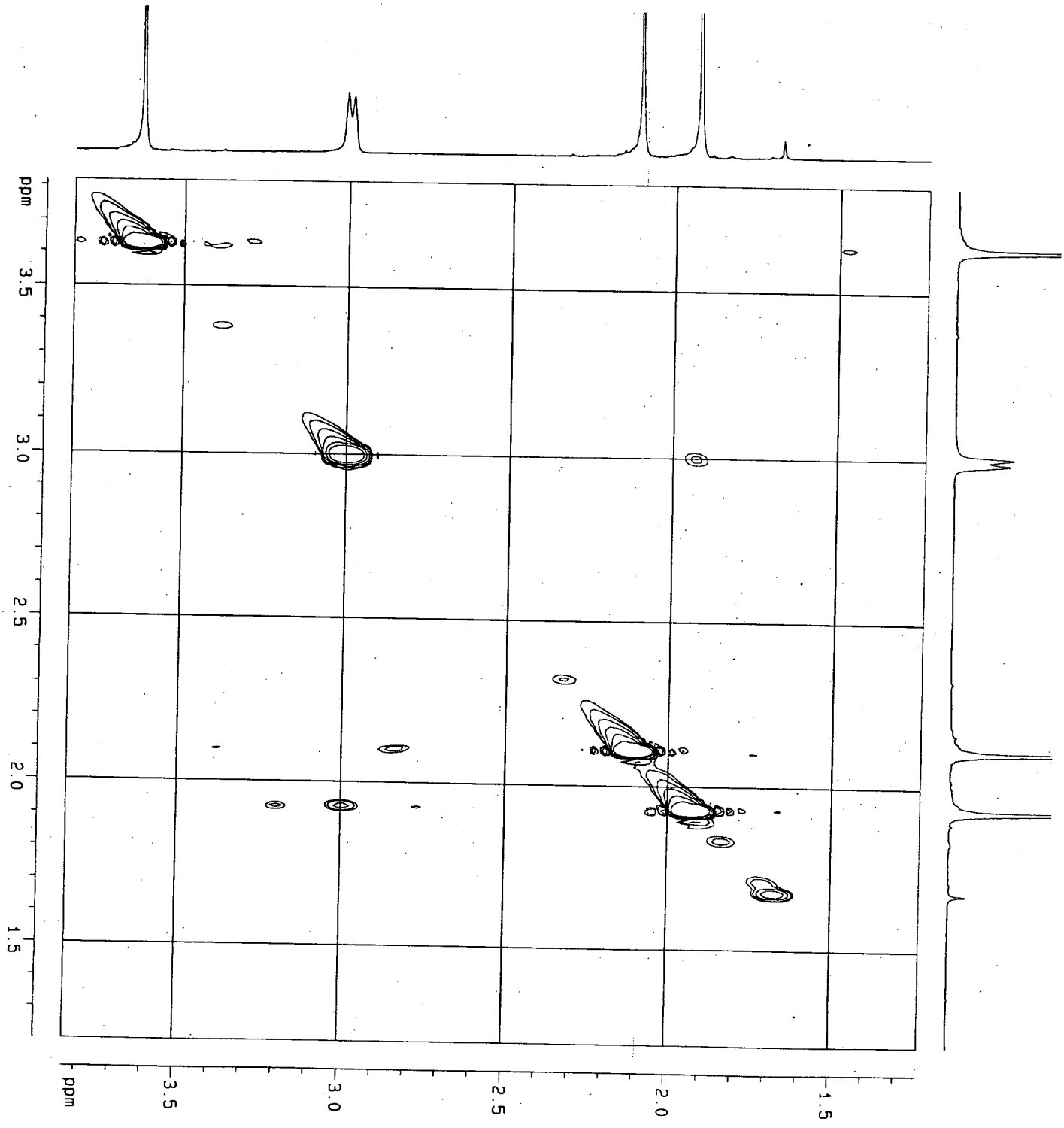

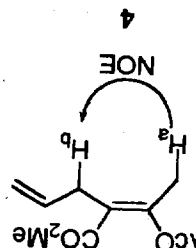

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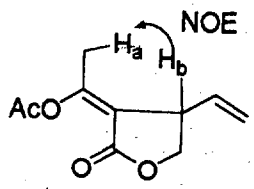
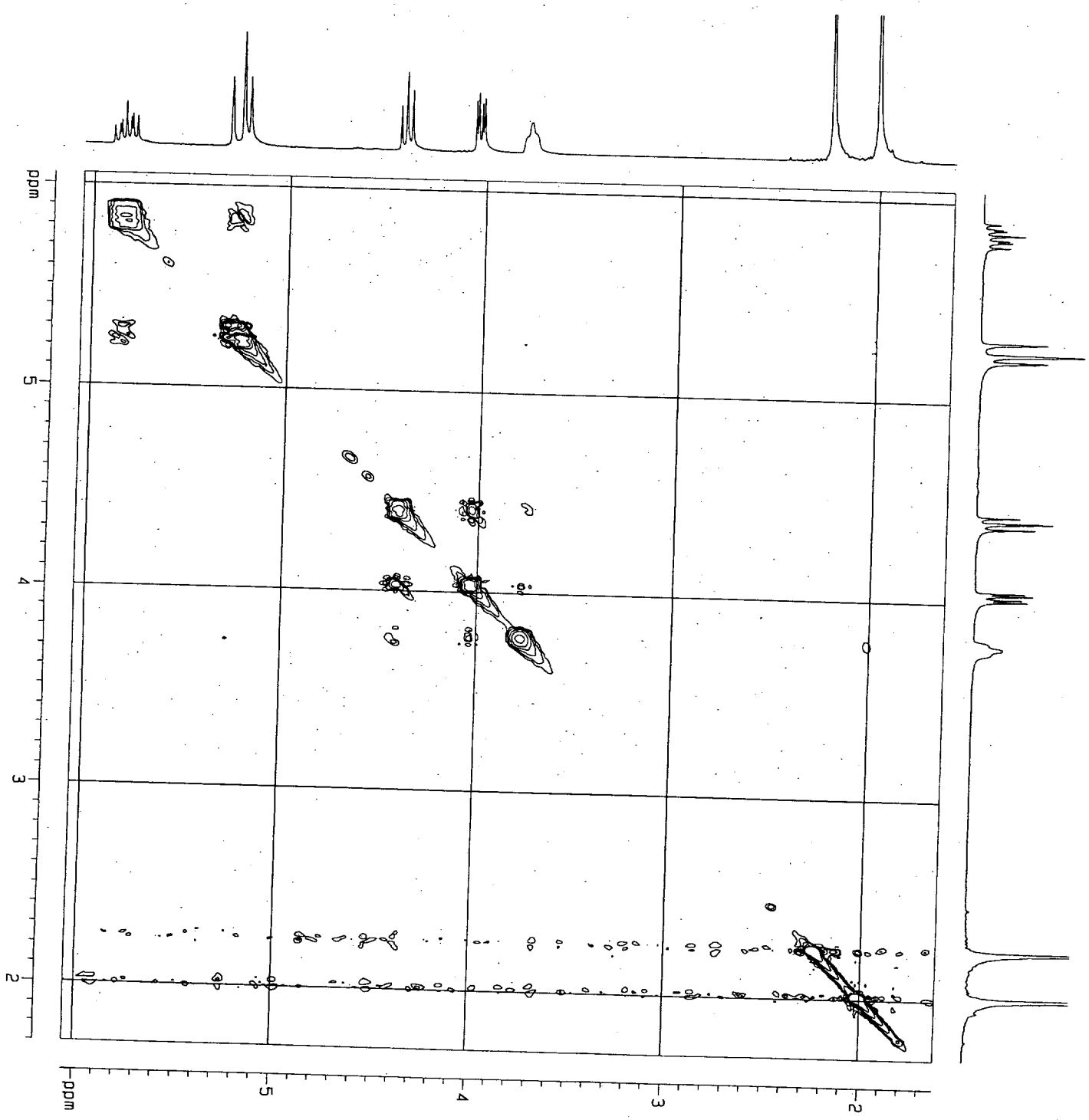
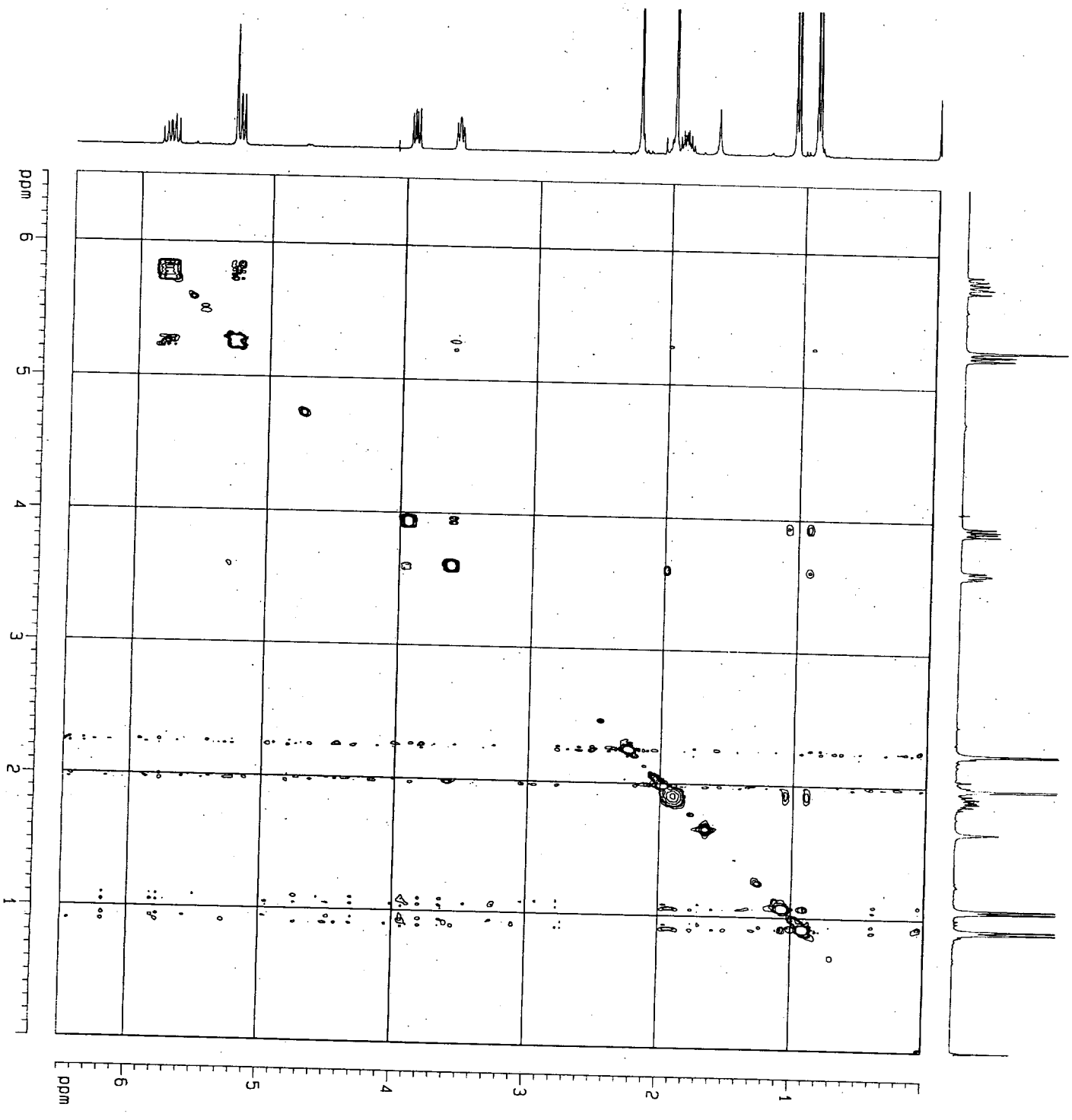
δ H_a: 1.93 (s, 3H)
δ H_b: 3.00 (d, J = 6.2 Hz, 2H)



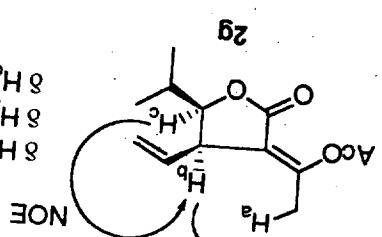
2a

δ H_a: 2.02 (d, J = 1.2 Hz, 3H)
δ H_b: 3.80-3.74 (m, 1H)

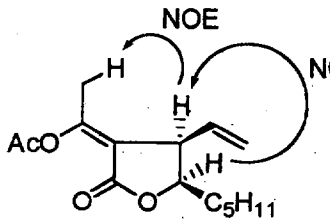




2g



δ H_a: 1.99 (s, 3H)
δ H_b: 3.63-3.59 (m, 1H)
δ H_c: 3.95 (dd, J = 10.3, 5.9 Hz, 1H)



2h

δ H_a: 1.99 (s, 3H)
δ H_b: 3.63 (t, J = 7.4 Hz, 1H)
δ H_c: 4.47-4.39 (m, 1H)