JOC The Journal of Organic Chemistry

J. Org. Chem., 1998, 63(24), 8634-8635, DOI:10.1021/jo9816358

An Approach to Controlled Oligomerization via Iterative Diels-Alder Cycloadditions on Solid Supports

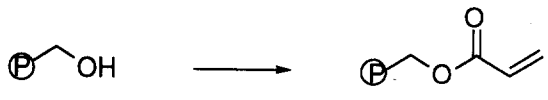
Jeffrey D. Winkler* and Young-Shin Kwak

Department of Chemistry, The University of Pennsylvania, Philadelphia, PA 19104

Supporting Information:

Experimental procedures and spectroscopic data for compounds **6-14** (17 pages).

Polymer-Bound Acrylate 6:

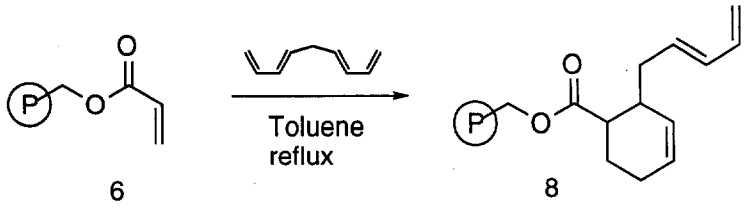


6

1.740 g of well-dried (vacuum oven, 50°C, 18 h) hydroxymethyl resin (0.37 mmol/g) was soaked and swollen for 20 min in dry methylene chloride (15ml) under argon. Then it was cooled in an ice bath and stirred. It is important to note that stirring in all of these reactions was performed magnetically at a very gentle rate. Vigorous stirring led to significantly lower yields via destruction of the polymer. Similar results were observed by Professor Ley and co-workers and we thank them for sharing this information with us prior to publication. Diisopropylamine (1.3 ml, 9.3 mmol, 15 eq) was added and after 5 min freshly distilled acryloyl chloride (0.5 ml, 6.2 mmol, 10 eq) was added dropwise into the stirred mixture. The color of reaction turned a little yellow and it was warmed to room temperature and stirred for 12 hours. Then it was diluted with diethyl ether and filtered. The yellow powder was washed with water, DMF and methylene chloride (20 mL each in this and in all of the workups described), and dried under vacuum for 12 hours to give 1.774 g (90%) of **6**, the creamy powder of acrylate on polymer.

FT-IR (KBr pellet, cm^{-1}): 1725.2 cm^{-1}.

Diels-Alder Adduct 8:

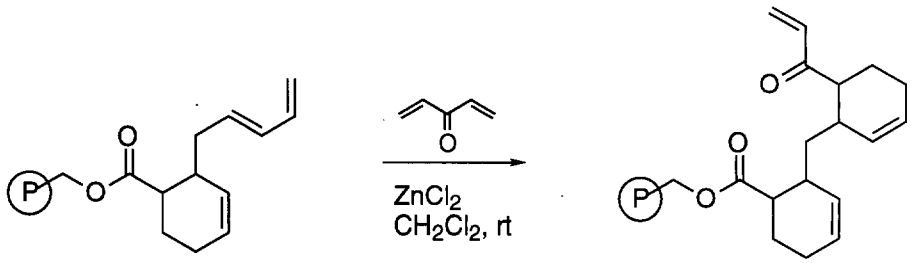


6 8

Masked bisdiene (800 mg, 4.3 mmol, 6 eq) was refluxed in toluene (25 ml) under argon and after 1 hour TLC analysis showed a complete conversion of starting material to bisdiene **7**. This solution of bisdiene was cooled to room temperature and creamy powder of polymer-bound acrylate **6** (2.0 g, 0.72mmol) was quickly added into the solution. Then the mixture was resubject to heating at reflux for 4 hours. The resulted slighly-yellow mixture was cooled to room temperature and filtered washing with methylene chloride, DMF and methylene chloride, and dried under vacuum for 6 hours to give 2.7 g of **8**.

FT-IR (KBr pellet, cm^{-1}): 1725.1 cm^{-1}.

Polymer-Bound Acrylate 11:

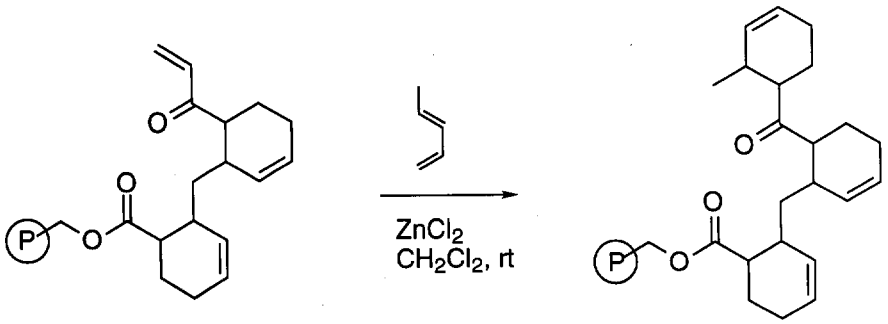


8 11

Freshly distilled divinyl ketone (360 mg, 4.4 mmol, 6.5 eq) was added into a stirred and anhydrous suspension of resin **8** (1.70 g, 0.68 mmol) swollen in dry methylene chloride (25 ml) at room temperature in argon atmosphere. To this stirred mixture 10 ml of 1.0 M solution of zinc chloride in ether was added dropwise at room temperature. The reaction mixture was stirred at same temperature for 12 hours, diluted with ether and quenched with pH 7 buffer. The suspension was filtered on a filter paper in a Buchner funnel and the solid was washed with methylene chloride, water, acetone and methylene chloride again. The resulted resin was dried under vacuum overnight to give a slightly yellow powder of 1.74 g of product **11**.

FT-IR (KBr pellet, cm^{-1}): 1724.9 cm^{-1}.

Piperylene Diels-Alder Adduct 12:

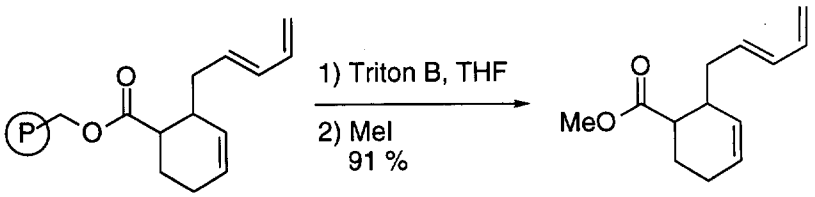


11 12

1 ml of piperylene (10 mmol, 16 eq) was added to a stirred and anhydrous suspension of resin **11** (1.7 g, 0.61 mmol) swollen in dry methylene chloride (25 ml) at room temperature in argon atmosphere. To this stirred mixture 10 ml of 1.0 M solution of zinc chloride in ether was added dropwise at room temperature. The reaction mixture was stirred at same temperature for 12 hours, diluted with ether and quenched with pH 7 buffer. The suspension was filtered on a filter paper in a Buchner funnel and the solid was washed with methylene chloride, water, acetone and methylene chloride again. The resulting resin was dried under vacuum overnight to give 1.74 g of **12**.

FT-IR (KBr pellet, cm^{-1}): 1721.5 cm^{-1}.

Mono Diels-Alder Cleavage Product 9:



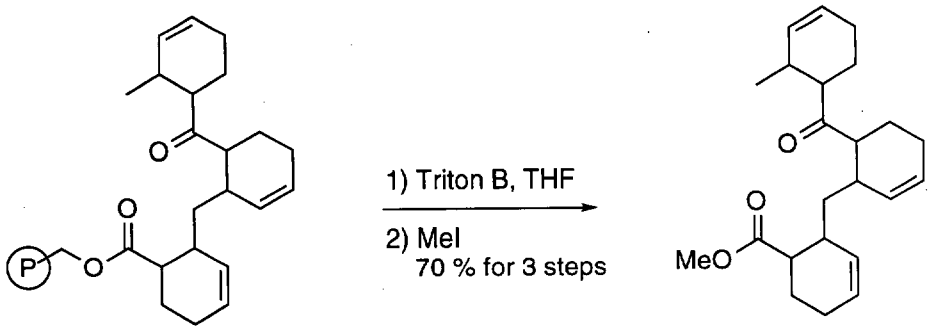
8 9

To a stirred and swollen resin **8** (200 mg, 0.081mmol) in anhydrous THF (2 ml) was added 0.3 ml of Triton B (25% solution in methanol) dropwise at ambient temperature. It was stirred for 18 hours and excess of methyl iodide (0.8 ml) was added. It was stirred for additional 6 hours and diluted with petroleum ether to precipitate the salts. The resin and the salts were filtered off and the filtrate was condensed in vacuo to afford a yellow oil, which was purified on silica gel (petroleum ether : ethyl acetate = 20 : 1) to give the product **9** as a colorless oil (15 mg, 0.073

mmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$, * denotes minor diastereoisomer peak): 6.26 (m, 1H); 6.00 (dd, 1H); 5.51-5.68 (m, 3H); 5.06 (d, 1H); 4.93 (d, 1H); 3.62 and 3.63* (two s's, 3H); 2.68 (ddd, 1H); 2.54 (m, 1H); 1.95-2.14 (m, 4H); 1.80-1.85 (m, 1H); 1.69-1.78 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, showing major peaks only here): 174.82; 136.93; 132.57; 129.50; 126.75; 115.27; 115.21; 51.27; 42.92; 36.37; 36.37; 35.27; 24.52; 20.30. FT-IR (thin film, cm^{-1}): 2948.1; 1737.5; 1175.4 cm^{-1}.

HRMS calculated for $C_{13}H_{18}O_2$ (M+H): 207.1385, found: 207.1390.

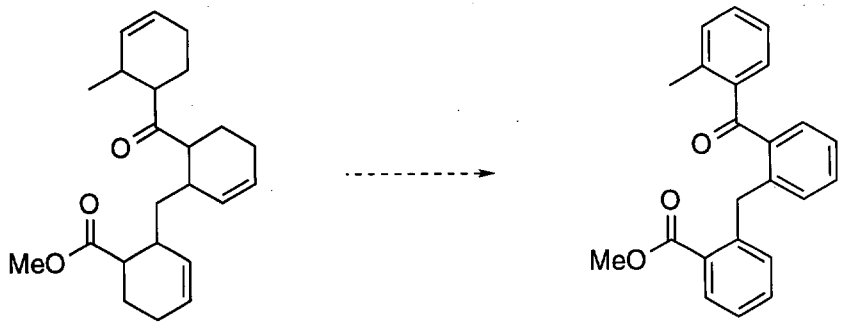
Final Cleavage Product 13:



12 13

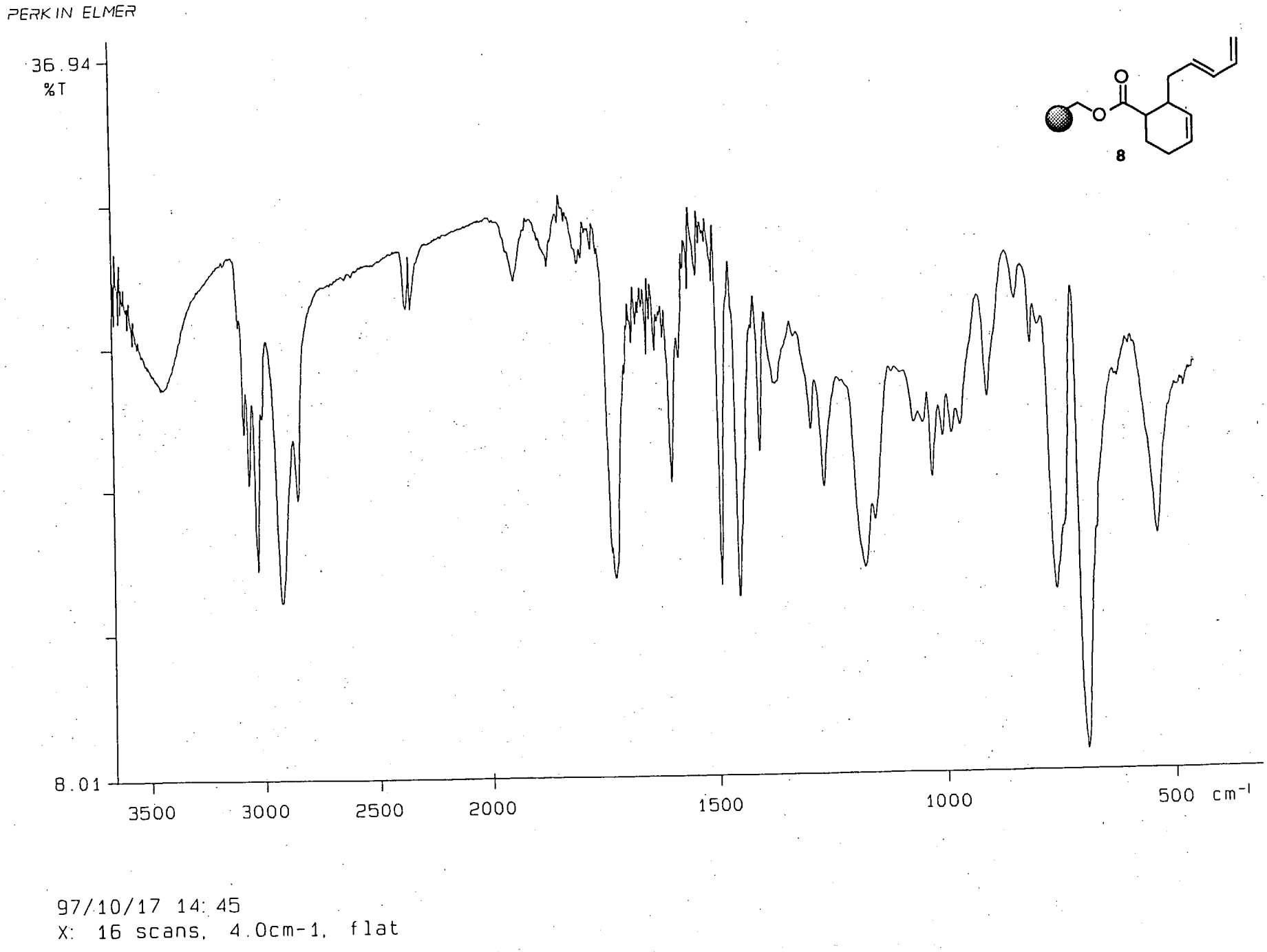
To the stirred and swollen resin **12** (130 mg, 0.045 mmol) in anhydrous THF (2 ml) was added 0.2 ml of Triton B (25% solution in methanol) dropwise at ambient temperature. It was stirred for 18 hours and excess of methyl iodide (0.5 ml) was added. It was stirred for additional 6 hours and diluted with petroleum ether to precipitate the salts. The resin and the salts were filtered off and the filtrate was condensed in vacuo to afford **13** as a yellow oil, which was purified on silica gel (petroleum ether : ethyl acetate = 20 : 1) to give the product as a colorless oil (12 mg, 0.033 mmol, 70%). ^{1}H NMR (500 MHz, $CDCl_3$): 5.47-5.75 (m, 6H); 3.65-3.68 (singlets, 3H); 2.55-2.68 (m, 4H); 2.33-2.45 (m, 2H); 2.18 (m, 1H); 1.84-2.15 (bs, 6H); 1.53-1.65 (m, 3H); 1.13-1.38 (m, 3H); 0.85-0.92 (m, 3H). FT-IR (thin film, cm^{-1}): 2927.0; 1734.5; 1703.7; 1161.7 cm^{-1}. HRMS calculated for $C_{23}H_{32}O_3$ (M+Na): 379.2249, found: 379.2257.

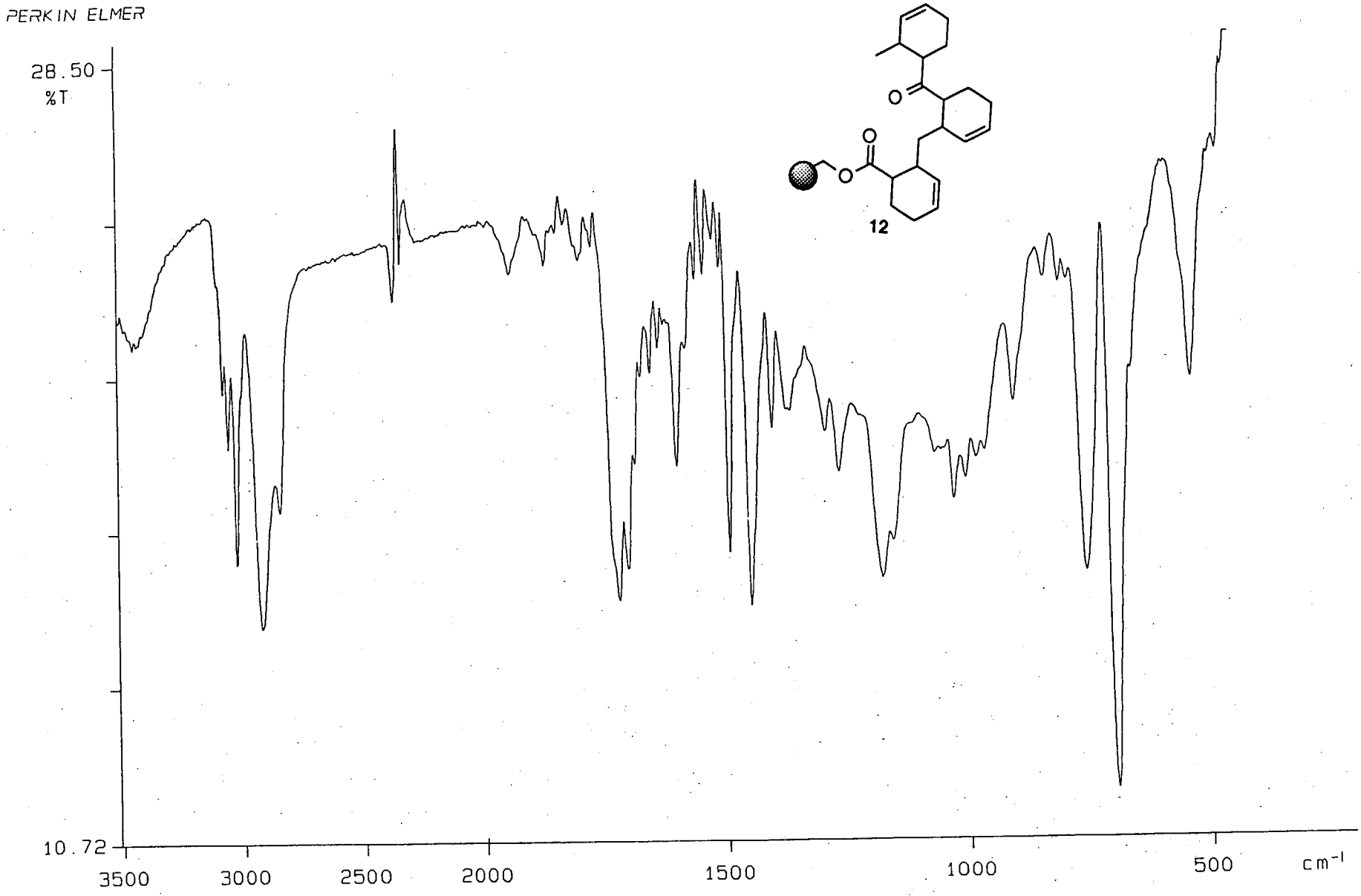
Aromatized Product 14:



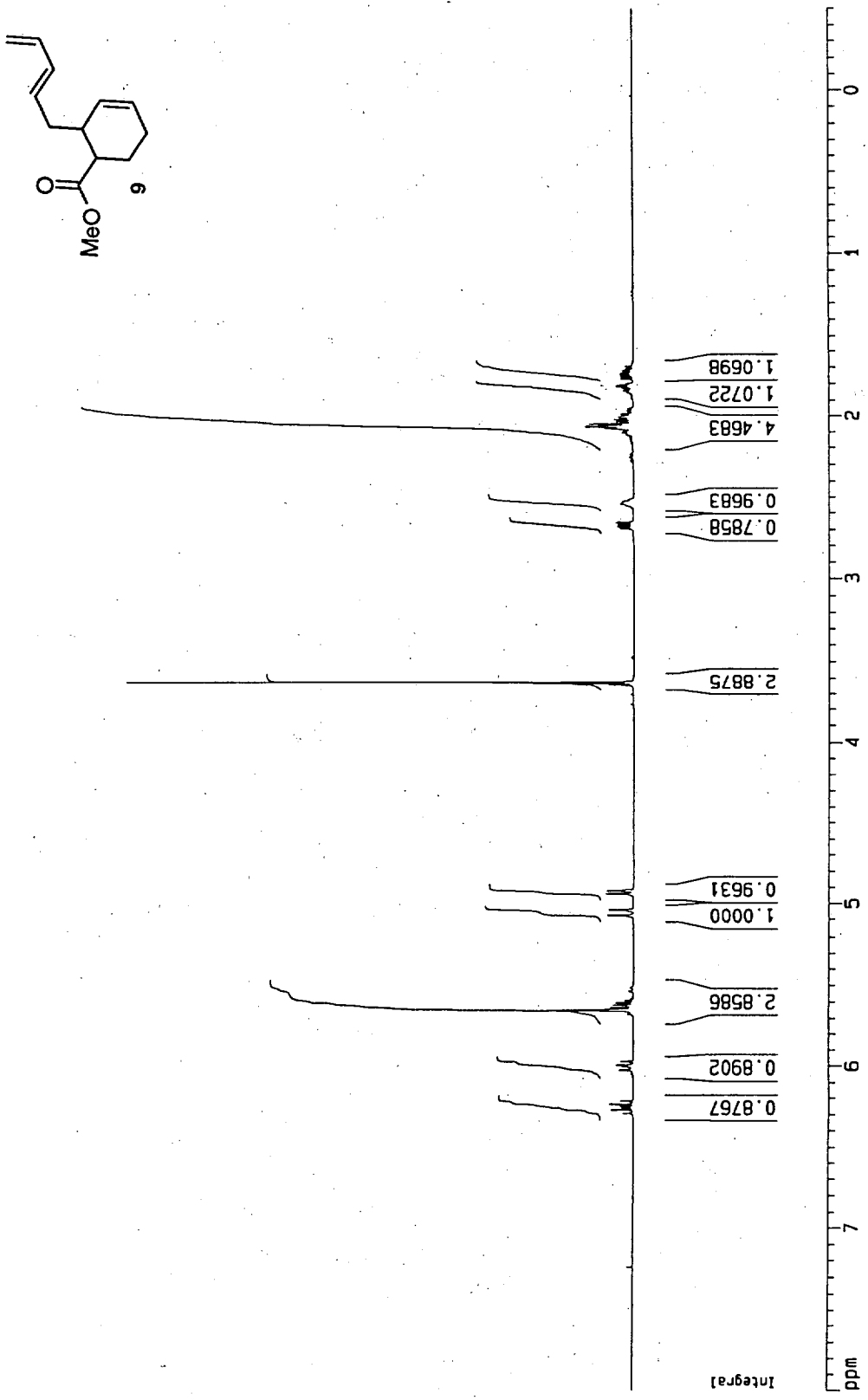
13 14

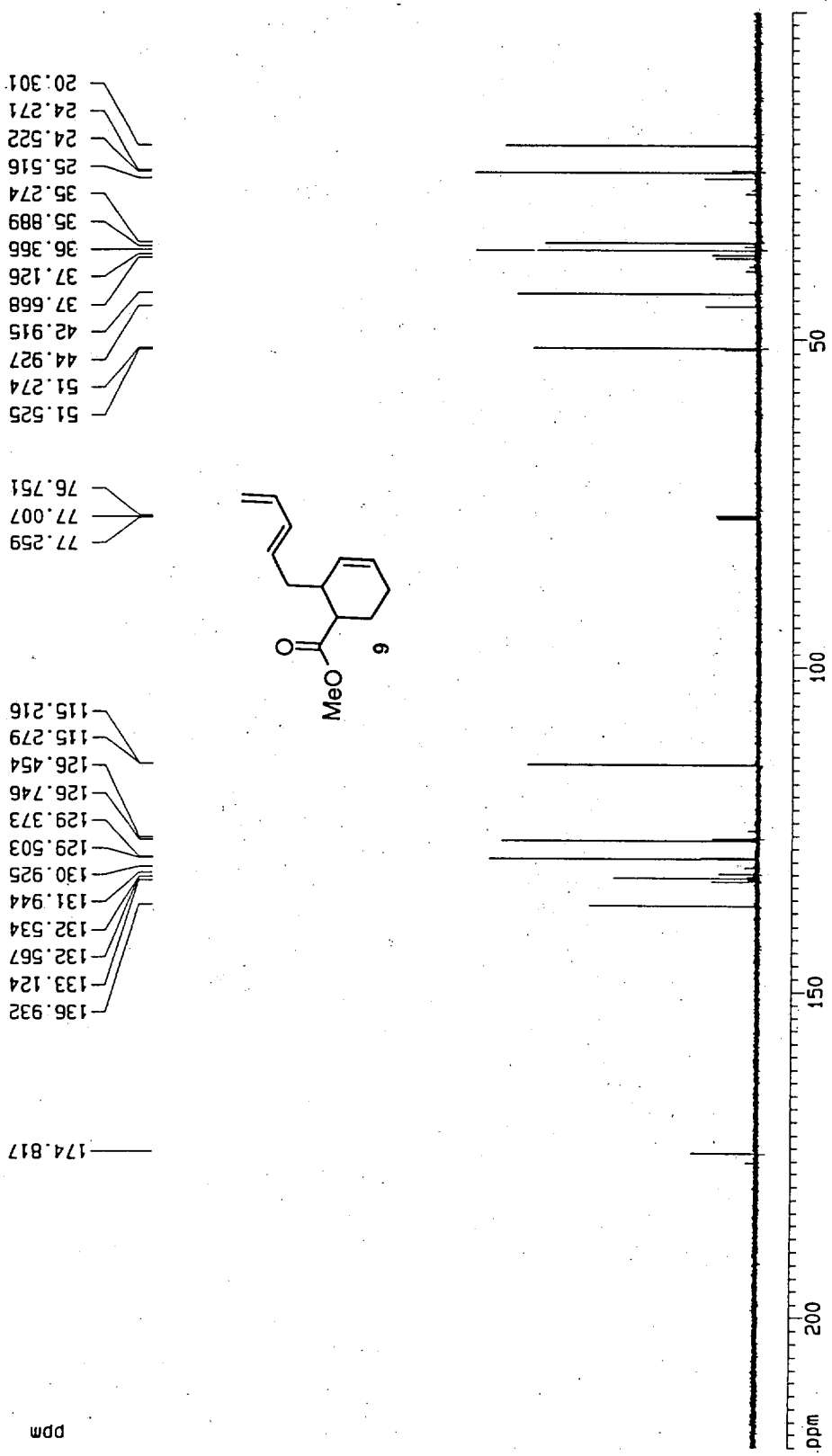
15 mg of **13** was dissolved in 4 ml of 1,3-dichlorobenzene and stirred. Palladium on activated carbon (30 mg) was added to the solution and the mixture was heated at reflux for 12 hours. TLC analysis showed a complete disappearance of starting material but 500 MHz pmr experiment of the crude material showed an existence of some partially aromatized products. The mixture was retreated with same condition for another 12 hours to complete the aromatization. 1,3-dichlorobenzene was removed by a simple distillation in vauo and the resulted green residue was purified on silica gel (petroleum ether : ethyl acetate = 20 : 1) to give the product **14** (10.9 mg, 75%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): 7.85 (dd, 1H); 32-7.37 (m, 4H); 7.27 (dd, 1H); 7.19-7.24 (m, 3H); 7.14 (t, 1H); 7.09 (d, 1H); 7.05 (d, 1H); 4.50 (s, 2H); 3.75 (s, 3H); 2.36 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): 200.46; 141.84; 140.73; 138.61; 138.53; 131.91; 131.65; 131.38; 131.10; 131.01; 130.71; 130.66; 130.59; 130.26; 130.02; 126.19; 125.77; 125.28; 51.85; 37.47; 20.62. FT-IR (thin film, cm^{-1}): 2948.1; 1721.2; 1661.7; 1252.4 cm^{-1}. HRMS calculated for $C_{23}H_{20}O_3$ (M+H): 345.1490; found: 345.1484.

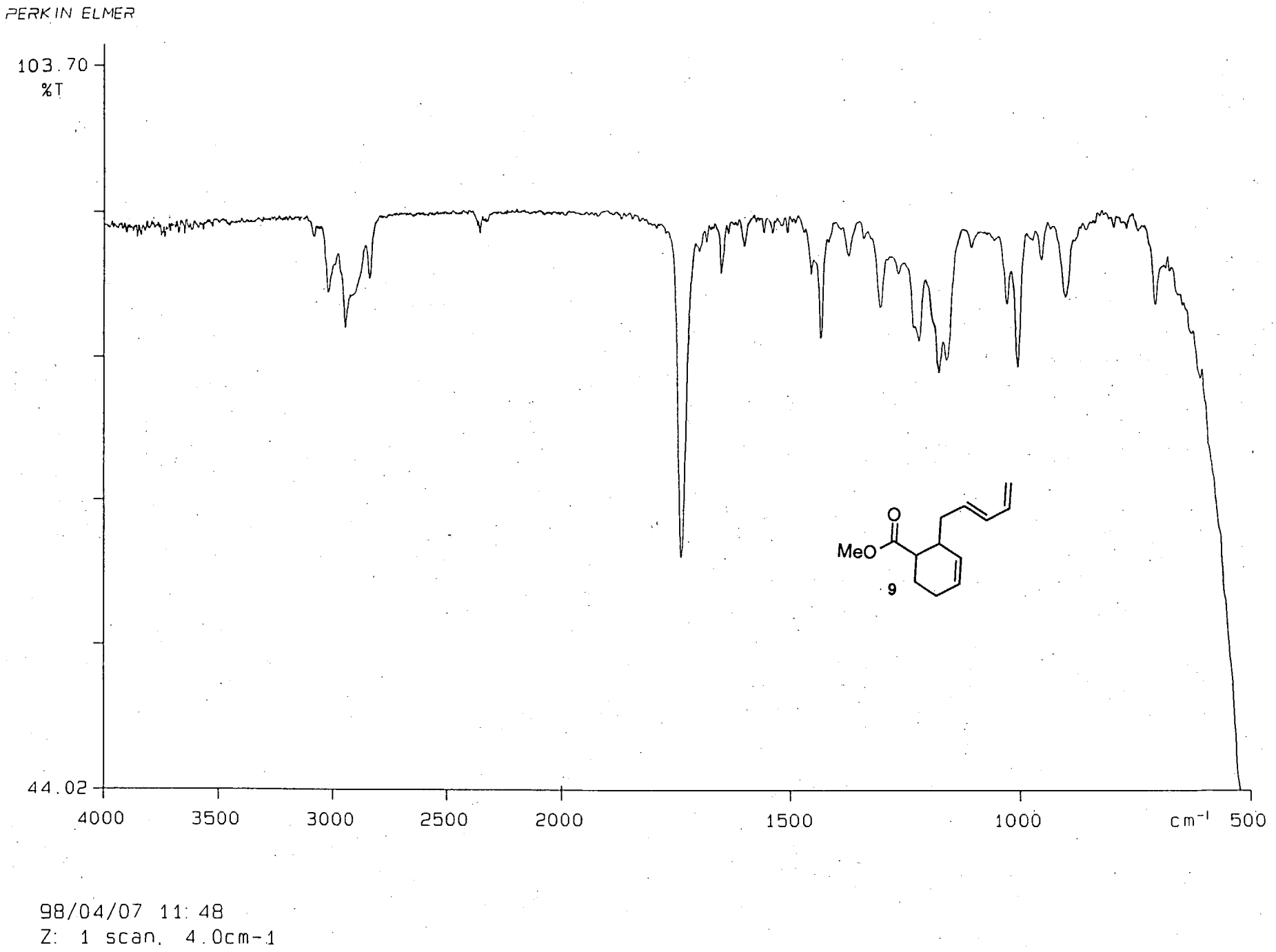


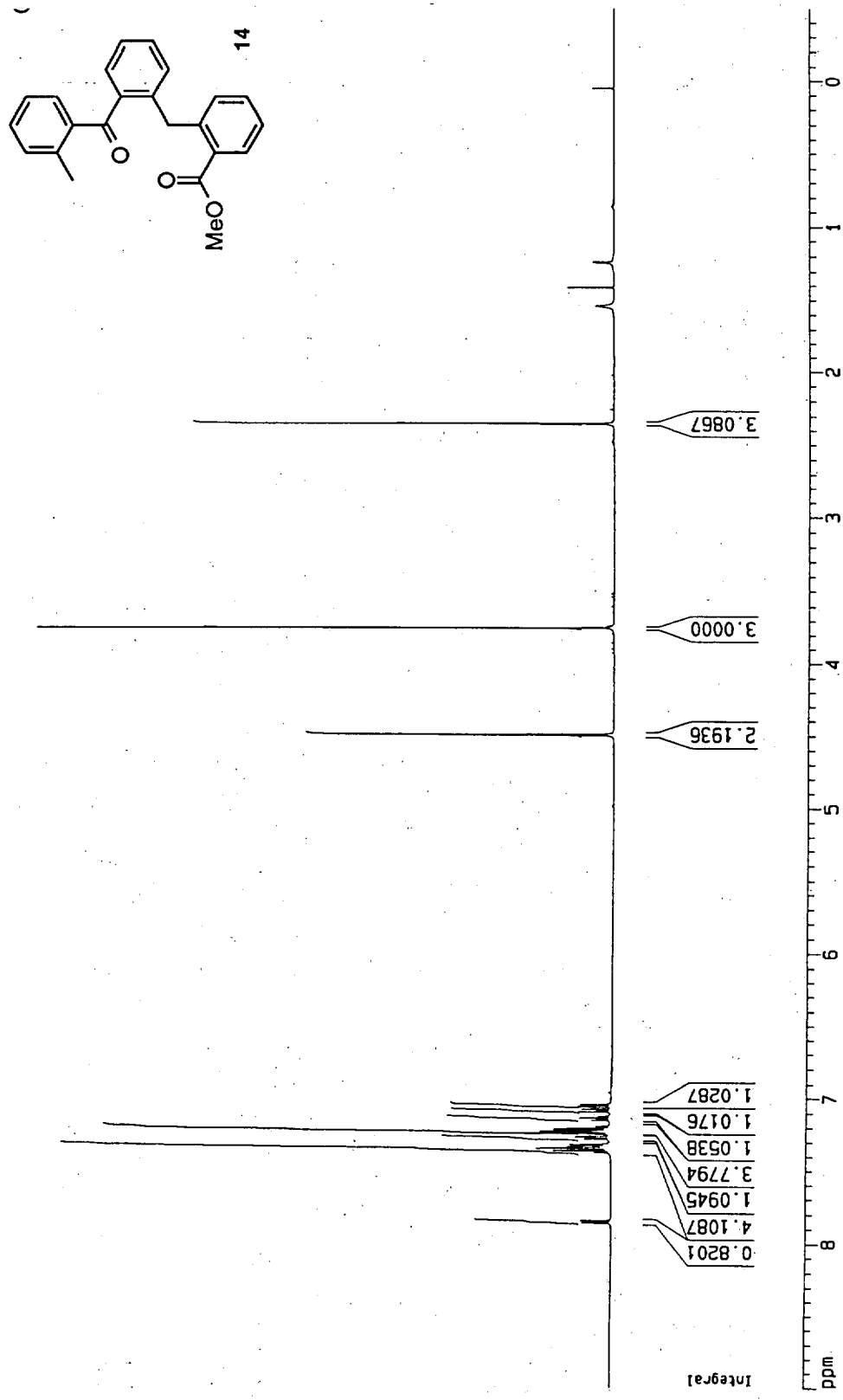


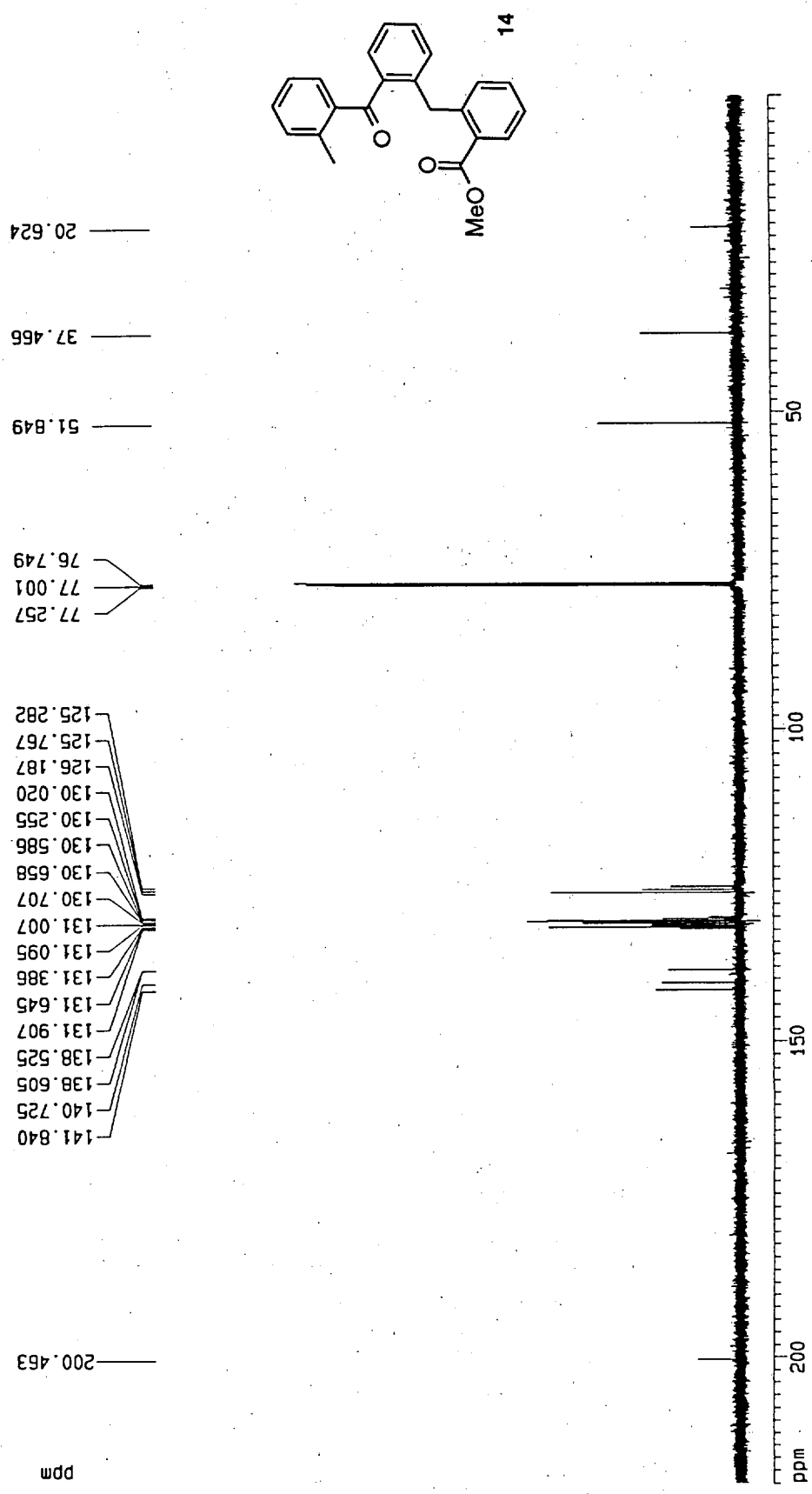
97/04/07 18:14
X: 16 scans, 8.0cm-1, flat

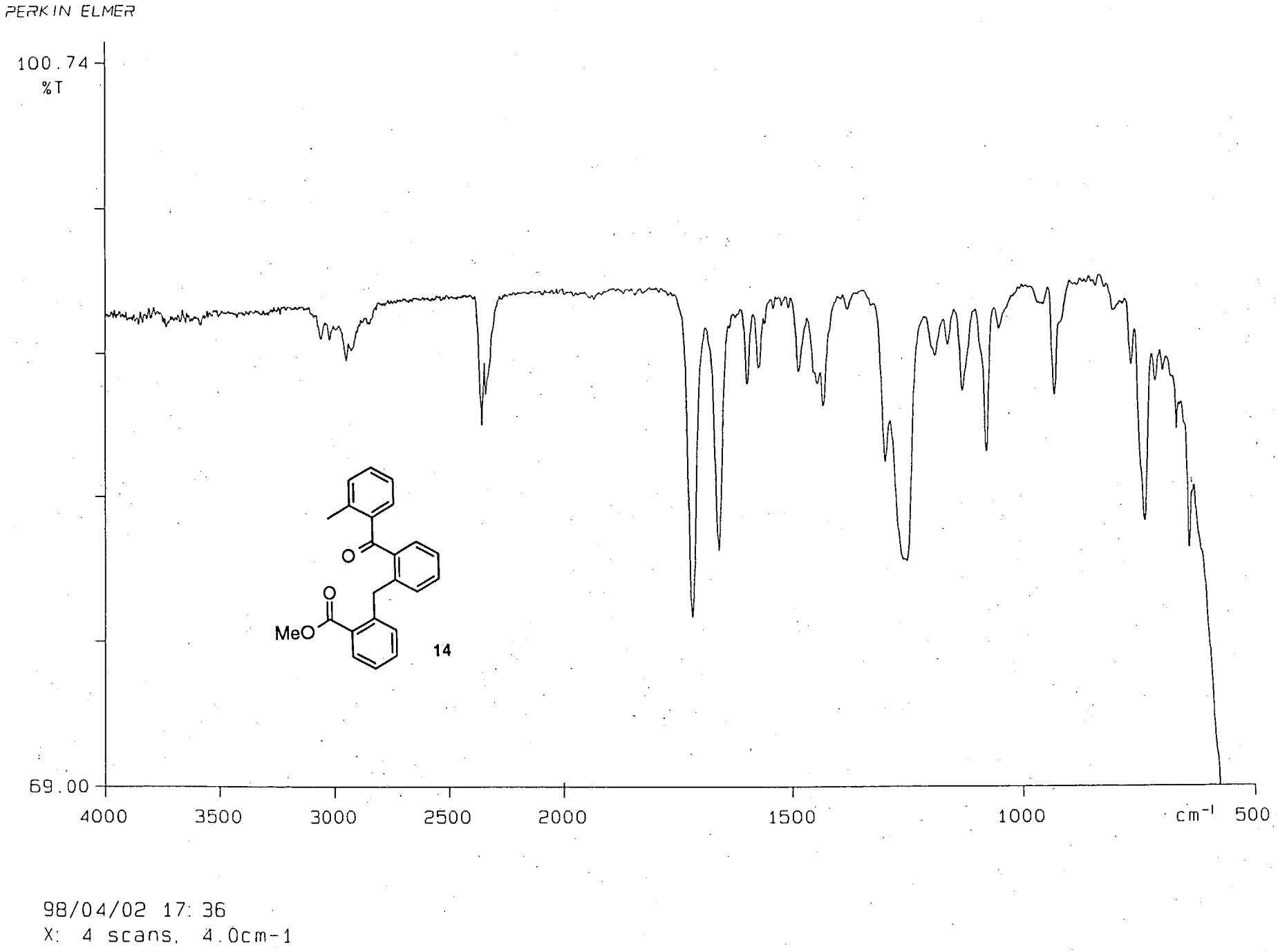

MeO
O
9
1.0698
1.0722
4.4683
0.9683
0.7858
2.8875
0.9631
1.0000
2.8586
0.8902
0.8767
Integral
ppm
0
1
2
3
4
5
6
7

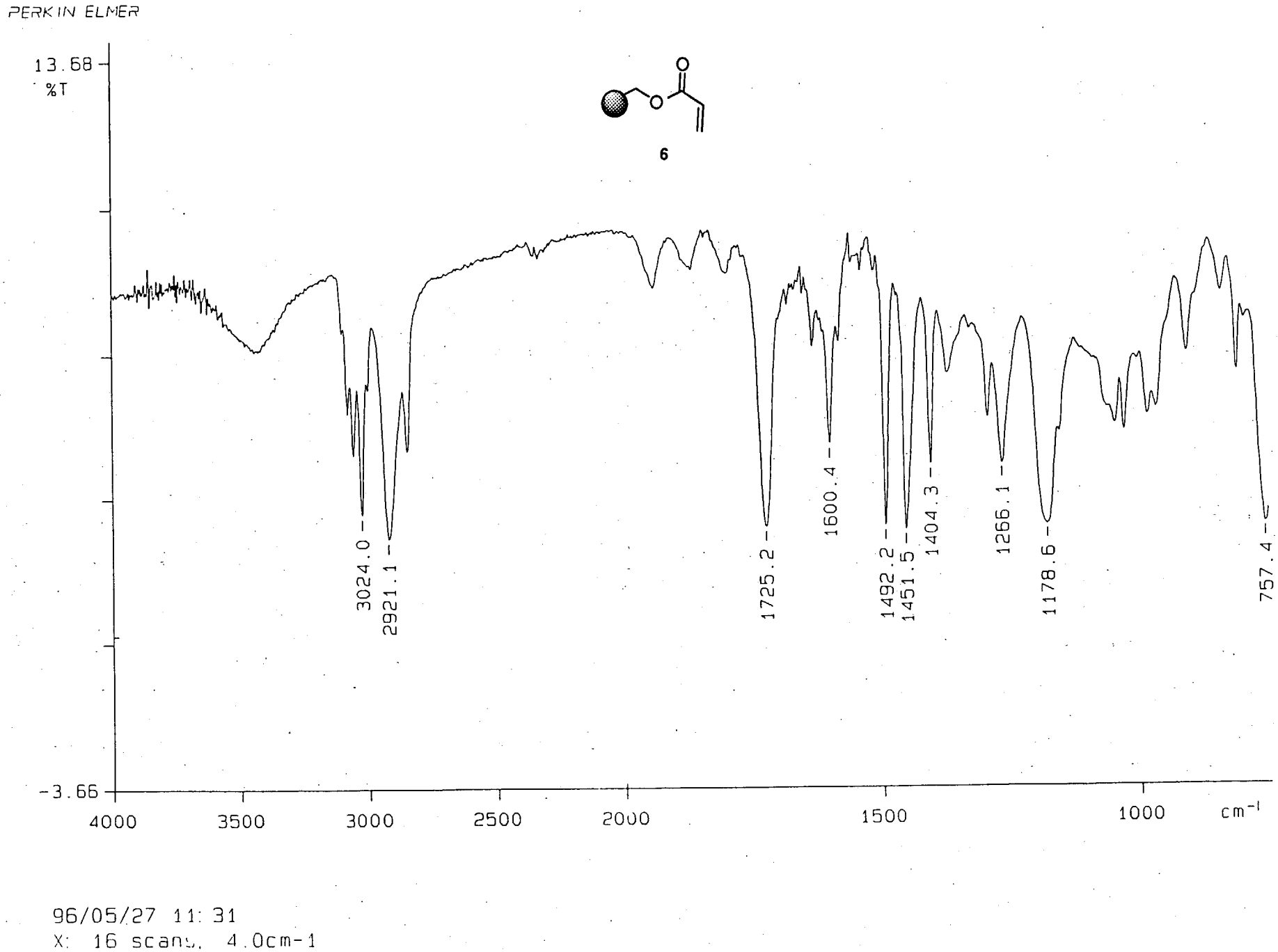

20.301
24.271
24.522
25.516
35.274
35.889
36.366
37.126
37.668
42.915
44.927
51.274
51.525
76.751
77.007
77.259
115.216
115.279
126.454
126.746
129.373
129.503
130.925
131.944
132.534
132.567
133.124
136.932
174.817
MeO
O
6
ppm
50
100
150
200
ppm











6