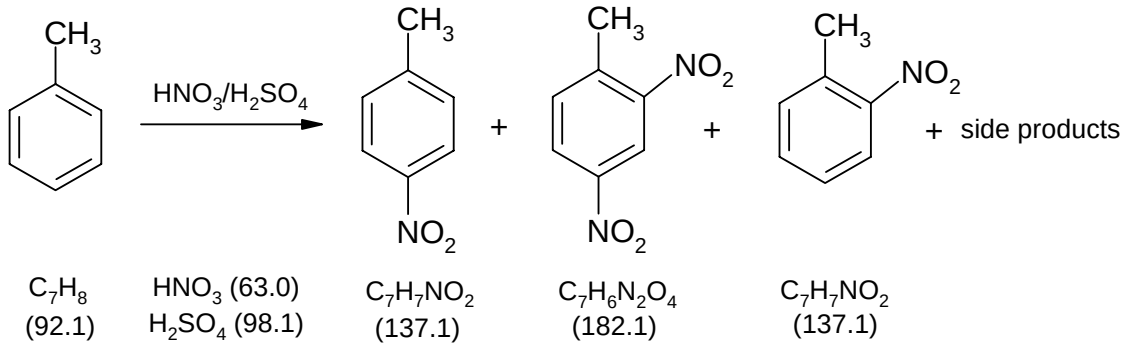
1001 Nitration of toluene to 4-nitrotoluene, 2-nitrotoluene and 2,4-dinitrotoluene



C_7H_8 (92.1) | HNO_3 (63.0), H_2SO_4 (98.1) | $C_7H_7NO_2$ (137.1) | $C_7H_6N_2O_4$ (182.1) | $C_7H_7NO_2$ (137.1)

Classification

Reaction types and substance classes

electrophilic substitution of aromatics, nitration of aromatics
nitroaromatics, aromatics

Work methods

distilling under reduced pressure, adding dropwise with an addition funnel, working with wash bottles, extracting, shaking out, recrystallizing, filtering, evaporating with rotary evaporator, stirring with magnetic stir bar, draining of gases, use of a cooling bath, heating with oil bath

Instruction (batch scale 100 mmol)

Equipment

250 mL wide-neck Erlenmeyer flask, 250 mL three-neck flask, separating funnel, internal thermometer, 2 wash bottles, adapter with ground-glass joint and hose coupling, addition funnel with pressure balance, Buechner funnel, suction flask, vacuum pump, distillation apparatus, desiccator, heatable magnetic stirrer with magnetic stir bar, rotary evaporator, ice/sodium chloride cooling bath, oil bath

Substances

toluene (bp 111 °C) (distilled from sodium)	9.21 g (10.6 mL, 100 mmol)
sulfuric acid (conc.)	12.5 mL (228 mmol)
nitric acid (conc.)	10.6 mL (153 mmol)
aqueous sodium hydroxide solution (2 N)	100 mL
cyclohexane (bp 81 °C)	60 mL
sodium hydrogen carbonat	about 1 g (for 10 mL saturated aqueous solution)

sodium sulfate for drying	about 5 g
ethanol (bp 78 °C) for recrystallization	
methanol (bp 65 °C) for recrystallization	
sodium chloride for cooling bath	
ice	

Reaction

Preparation of the nitrating acid: 12.5 mL (228 mmol) concentrated H_2SO_4 are slowly added under constant shaking and ice cooling to 10.6 mL (153 mmol) ice cold concentrated HNO_3, which was placed in a 250 mL wide-necked Erlenmeyer flask. Using an ice-salt cooling bath, cool the nitrating acid subsequently to -5 °C.

The reaction apparatus consists of a 250 mL three-neck flask with magnetic stirring bar, an internal thermometer and a dropping funnel with pressure balance. Connect the remaining opening of the flask to a rubber tube as outlet for possibly formed nitrous gases using an adapter with ground-glass joint. The rubber tubing connects to a safety wash bottle, which is connected to another wash bottle, which contains 100 mL of aqueous NaOH solution.

Charge the reaction flask with 9.21 g (10.6 mL, 100 mmol) toluene, which was freshly distilled from sodium. Cool the toluene in the reaction flask to -10 °C with an ice-salt cooling mixture. The cooled nitrating acid is placed in small portions (to avoid its warming up) into the dropping funnel of the reaction set up and is added dropwise under cooling to keep the internal temperature of the reaction mixture below 5 °C. It takes approx. 1.5 hours to add the entire nitrating acid. After complete addition the reaction mixture, still placed in an ice water cooling bath, is allowed to slowly warm up to room temperature. Warming up must be so slow to avoid the formation of nitrous gases. After reaching room temperature, stir the reaction mixture for additional 2 hours.

Work up

Pour the reaction mixture into a 250 mL beaker containing 50 g of ice. Then place the mixture into a separating funnel, and extract it once with 40 mL, and twice with 10 mL of cyclohexane. The combined organic phases are washed subsequently with 10 mL water, 10 mL saturated aqueous $NaHCO_3$-solution and again with 10 mL water. The organic phase is dried over Na_2SO_4 (1-2 tee spoons), the drying agent is removed by filtration and the solvent is removed using the rotary evaporater. The crude product remains as an oily residue.
Yield of the crude product: 10.1 g.

Purify the crude product by distillation at 20 hPa. The receiving flasks must be cooled. The desired product distills over in a boiling temperature range of 100–130 °C (20 hPa) yielding 8.50 g of the yellow product as a liquid and 1.30 g distillation residue.

The liquid product of the distillation crystallizes at -20 °C. Isolate the crystalline material by filtration over a cooled Buechner funnel and recrystallize it from a few mL of methanol. Repeat the recrystallization step, if necessary.
Yield: 1.80 g (13.1 mmol, 13%) 4-nitrotoluene; mp 49 °C

Recrystallize the solid residue of the distillation from a few mL of ethanol. Collect the crystalline product by filtation with a Buechner funnel and dry it in an evacuated desiccator over silica gel.
Yield: 500 mg (2.75 mmol, 3%) 2,4-dinitrotoluene; mp 69 °C

Comments
The yield of 2-nitrotoluene cannot be specified, due to incomplete separation of the products.

Downscaling of the reaction to 10 mmol is not recommended. It is difficult to separate the crude product into the pure isomeric products.

Waste management

Recycling
The evaporated cyclohexane of the reaction mixture is collected and redistilled.

Waste disposal

Waste	Disposal
aqueous phases	solvent water mixtures, halogen free
methanol and ethanol (mother liquors)	organic solvents, halogen free
sodium sulfate	solid waste, free from mercury
aqueous solution from the wash bottle	aqueous waste, neutral to alkaline

Time
5 hours, without recristallization

Break
Before distillation

Degree of difficulty
Difficult

Instruction (batch scale 500 mmol)

Equipment
500 mL wide-neck Erlenmeyer flask, 500 mL three-neck flask, separating funnel, internal thermometer, 2 wash bottles, adapter with ground-glass joint and hose coupling, addition funnel with pressure balance, Buechner funnel, suction flask, vacuum pump, distillation apparatus, desiccator, heatable magnetic stirrer with magnetic stir bar, rotary evaporator, ice/sodium chloride cooling bath, oil bath

Substances

toluene (bp 111 °C) (distilled from sodium)	46.1 g (53.0 mL, 500 mmol)
sulfuric acid (conc.)	61.0 mL (1.11 mol)
nitric acid (conc.)	53.0 mL (0.766 mol)
aqueous sodium hydroxide solution (2 N)	500 mL

cyclohexane (bp 81 °C)	280 mL
sodium hydrogen carbonat	about 4 g (for 40 mL saturated aqueous solution)
sodium sulfate for drying	about 20 g
ethanol (bp 78 °C) for recrystallization	
methanol (bp 65 °C) for recrystallization	
sodium chloride for cooling bath	
ice	

Reaction

Preparation of the nitrating acid: 61.0 mL (1.11 mol) concentrated H_2SO_4 are slowly added under constant shaking and ice cooling to 53.0 mL (0.766 mol) ice cold concentrated HNO_3, which was placed in a 500 mL wide-necked Erlenmeyer flask. Using an ice-salt cooling bath, cool the nitrating acid subsequently to -5 °C.

The reaction apparatus consists of a 500 mL three-neck flask with magnetic stirring bar, an internal thermometer and a dropping funnel with pressure balance. Connect the remaining opening of the flask to a rubber tube as outlet for possibly formed nitrous gases using an adapter with ground-glass joint. The rubber tubing connects to a safety wash bottle, which is connected to another wash bottle, which contains 500 mL of aqueous NaOH solution.

Charge the reaction flask with 46.1g (53.0 mL, 500 mmol) toluene, which was freshly distilled from sodium. Cool the toluene in the reaction flask to -10 °C with an ice-salt cooling mixture. The cooled nitrating acid is placed in small portions (to avoid its warming up) into the dropping funnel of the reaction set up and is added dropwise under cooling to keep the internal temperature of the reaction mixture below 5 °C. It takes approx. 2 hours to add the entire nitrating acid. After complete addition the reaction mixture, still placed in an ice water cooling bath, is allowed to slowly warm up to room temperature. Warming up must be so slow to avoid the formation of nitrous gases. After reaching room temperature, stir the reaction mixture for additional 3 hours.

Work up

Pour the reaction mixture into a 600 mL beaker containing 250 g of ice. Then place the mixture into a separating funnel, and extract it once with 170 mL, and twice with 40 mL of cyclohexane. The combined organic phases are washed subsequently with 50 mL water, 40 mL saturated aqueous $NaHCO_3$-solution and again with 40 mL water. The organic phase is dried over Na_2SO_4, the drying agent is removed by filtration and the solvent is removed using the rotary evaporater. The crude product remains as an oily residue.
Yield of the crude product: 62.5 g.

Purify the crude product by distillation at 20 hPa. The receiving flasks must be cooled. The desired product distills over in a boiling temperature range of 100–130 °C (20 hPa) yielding yellow product as a liquid and a solid distillation residue.

The liquid product of the distillation crystallizes at -20 °C. Isolate the crystalline material by filtration over a cooled Buechner funnel and recrystallize it from a methanol. Repeat the recrystallization step, if necessary.
Yield: 3.20 g (23.3 mmol, 5%) 4-nitrotoluene; mp 49 °C

Recrystallize the solid residue of the distillation from ethanol. Collect the crystalline product by filtation with a Buechner funnel and dry it in an evacuated desiccator over silica gel.
Yield: 2.60 g (14.3 mmol, 3%) 2,4-dinitrotoluene; mp 69 °C

Comments
The yield of 2-nitrotoluene cannot be specified, due to incomplete separation of the products.

Because of a complex reaction to products the cyclohexane phase may become supersaturated during the extraction (separation of three phases). This problem can be resolved by adding more cyclohexane.

Waste management

Recycling
The evaporated cyclohexane of the reaction mixture is collected and redistilled.

Waste disposal

Waste	Disposal
aqueous phases	solvent water mixtures, halogen free
methanol and ethanol (mother liquors)	organic solvents, halogen free
sodium sulfate	solid waste, free from mercury
aqueous solution from the wash bottle	aqueous waste, neutral to alkaline

Time
1 day, without recristallization

Break
Before distillation

Degree of difficulty
Difficult

Analytics

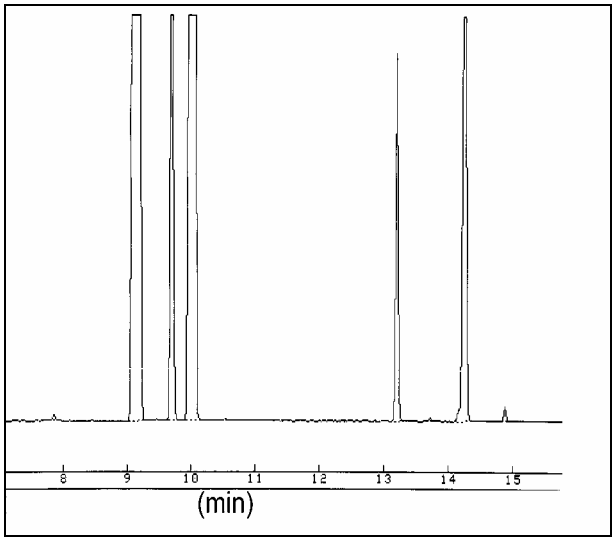
GC

GC conditions:

column:	5CB Low Blend/MS, L=30 m, d=0.32 mm, film=0.25 μm
inlet:	injector 210 °C, split injection, injected volume 0.1 μL
carrier gas:	H_2, precolumn pressure 50 kPa
oven:	60 °C (2 min), 10 °C/min, isotherm 240 °C (30 min)
detector:	FID, 310
integration:	Shimadzu

Percent concentration was calculated from peak areas

GC of the crude product



Retention time (min)	Substance	Peak area %
9.10	2-nitrotoluene	52.10
9.70	3-nitrotoluene	3.30
10.00	4-nitrotoluene	37.90
13.20	2,6-dinitrotoluenel	1.70
14.30	2,4-dinitrotoluene	4.90

TLC

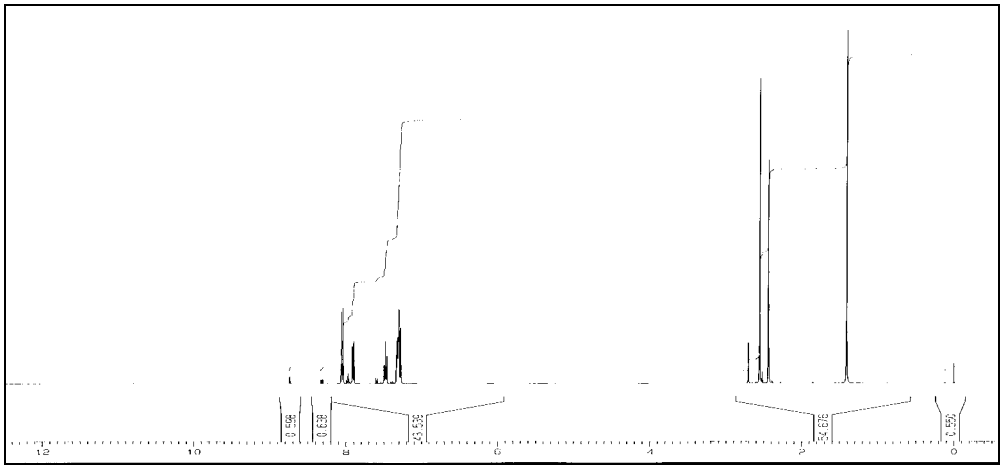
Sample preparation:
Samples were dissolved in (warm) methanol.

TLC conditions:

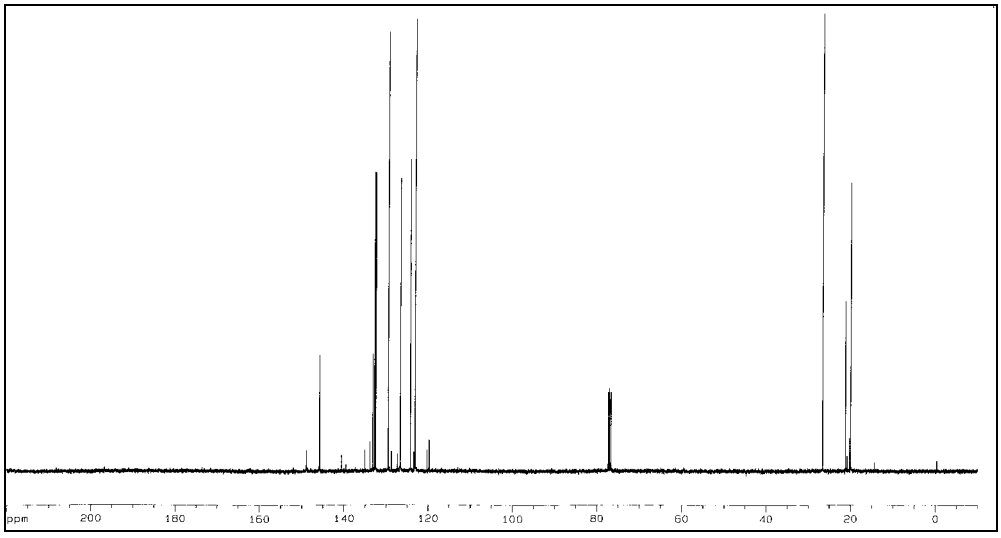
adsorbent:	Macherey and Nagel Polygram SilG/UV plates, 0.2 mm
elution solvent:	*n*-hexane/ethyl acetate 9:1

R_f	Substance
0.65	2-nitrotoluene
0.62	4-nitrotoluene
0.31	2,4-dinitrotoluene

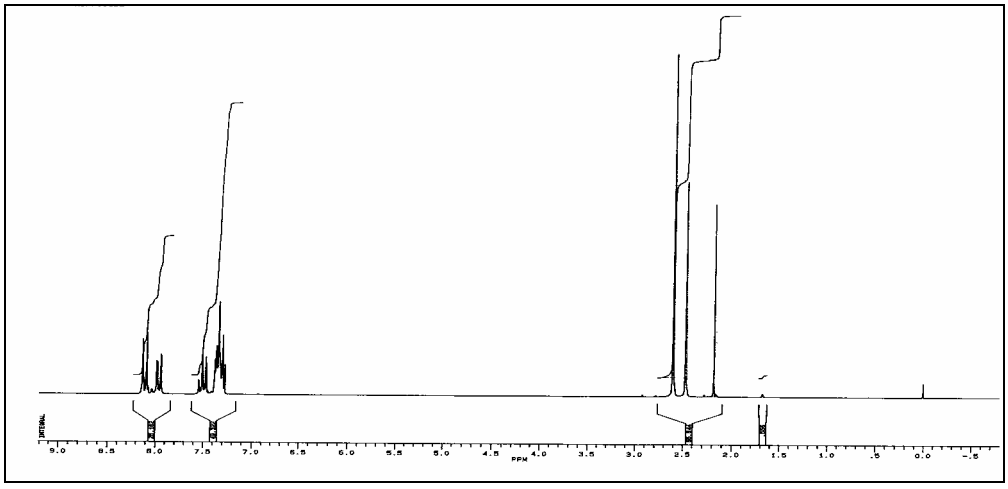
^{1}H NMR spectrum of the crude product (400 MHz, $CDCl_3$)



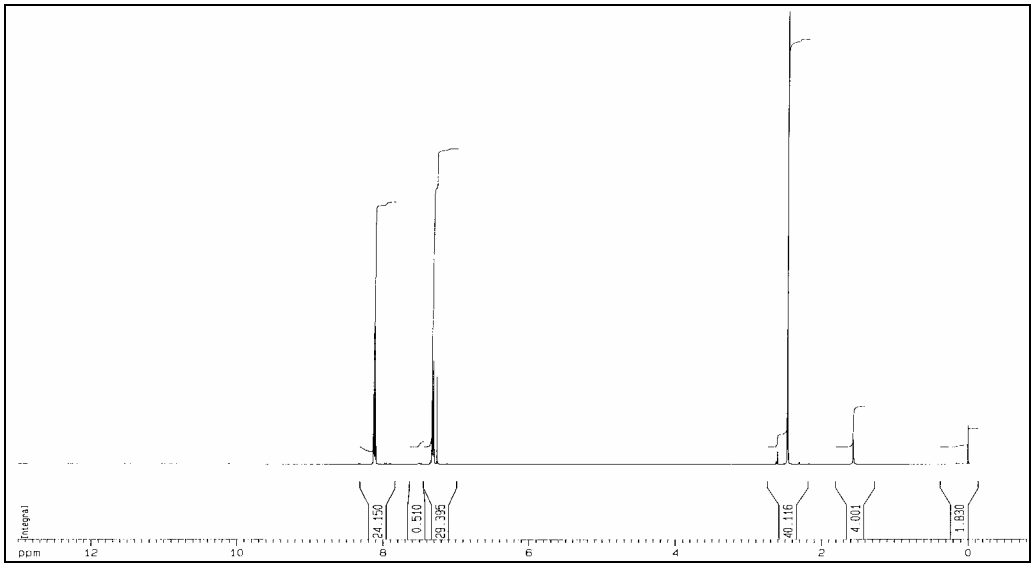
^{13}C NMR spectrum of the crude product (100 MHz, $CDCl_3$)



^{1}H NMR spectrum of the distillate (200 MHz, $CDCl_3$)

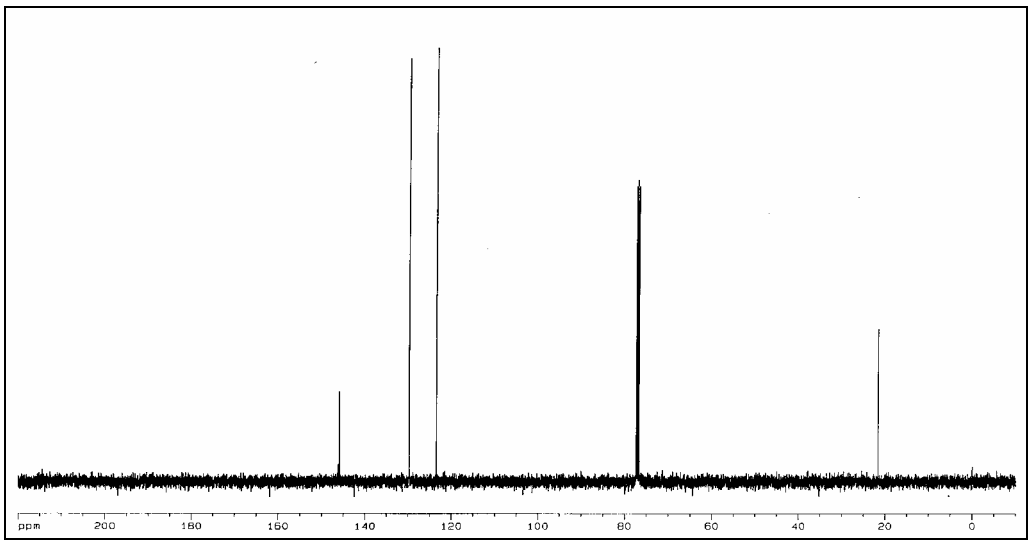


^{1}H NMR spectrum of the pure product 4-nitrotoluene (400 MHz, $CDCl_3$)

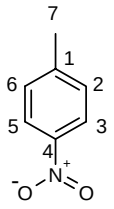


δ (ppm)	Multiplicity	Number of H	Assignment
2.46	s	3	CH_3
7.33	m (AA´)	2	2-H, 6-H
8.11	m (XX´)	2	3-H, 5-H
7.26			Solvent.

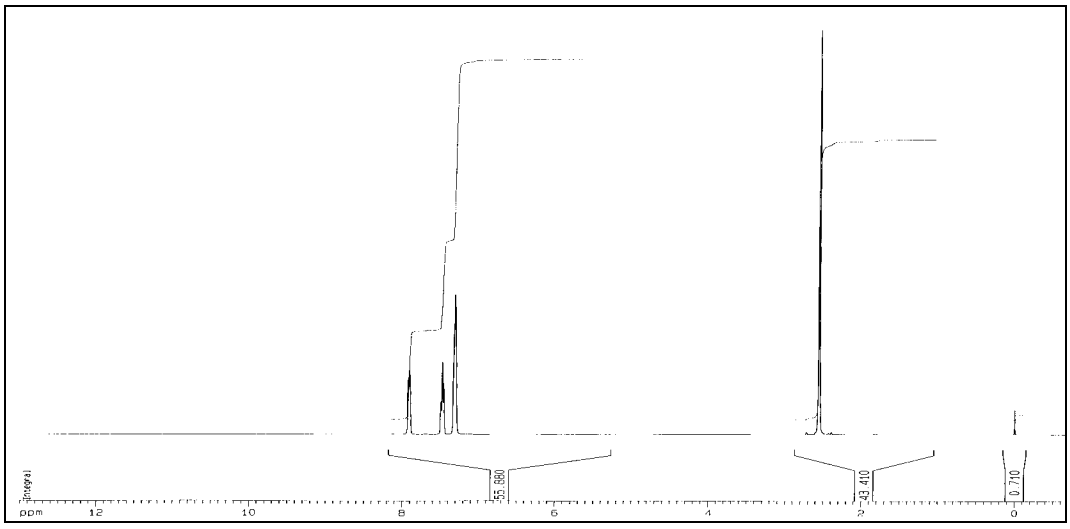
^{13}C NMR spectrum of the pure product 4-nitrotoluene (100 MHz, $CDCl_3$)



δ (ppm)	Assignment
21.57	C-7
123.46	C-3, C-5
129.76	C-2, C-6
145.90	C-1
146.11	C-4

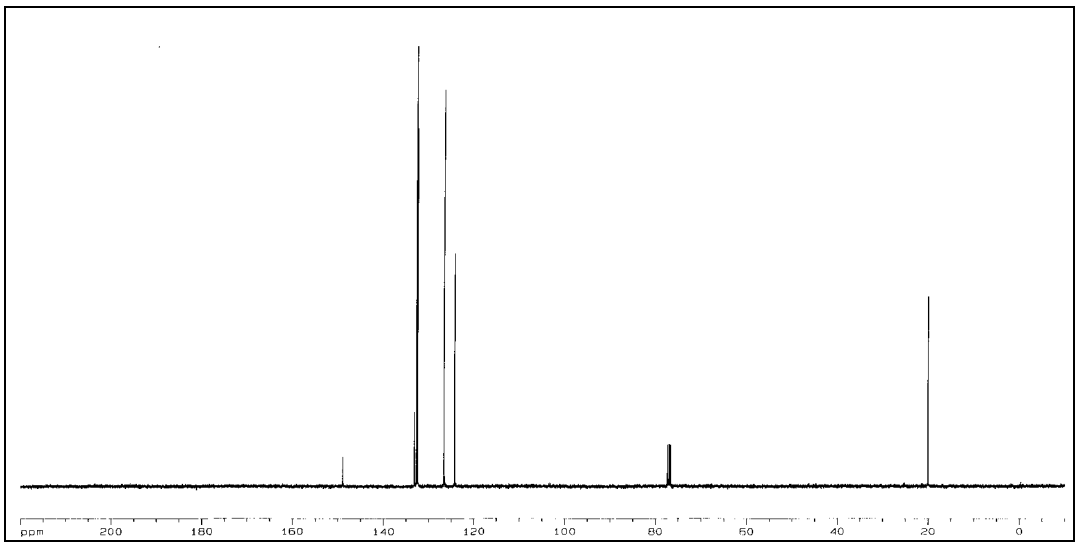


^{1}H NMR spectrum of 2-nitrotoluene (for comparison) (400 MHz, $CDCl_3$)

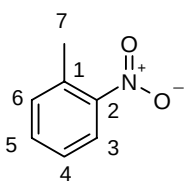


δ (ppm)	Multiplicity	Number of H	Assignment
2.55 - 2.56	d	3	CH_3
7.30 - 7.33	m	2	4-H, 6-H
7.45 - 7.50	m	1	5-H
7.90 - 7.93	m	1	3-H

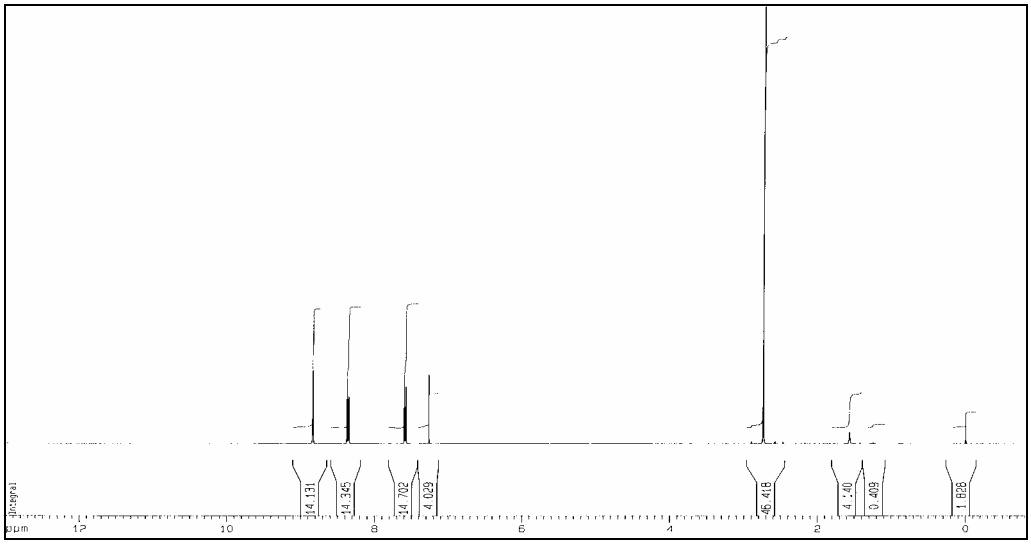
^{13}C NMR spectrum of 2-nitrotoluene (for comparison) (100 MHz, $CDCl_3$)



δ (ppm)	Assignment
20.05	CH_3
124.29	C-3
126.64	C-4
132.51	C-6
132.80	C-5
133.21	C-1
148.29	C-NO_2

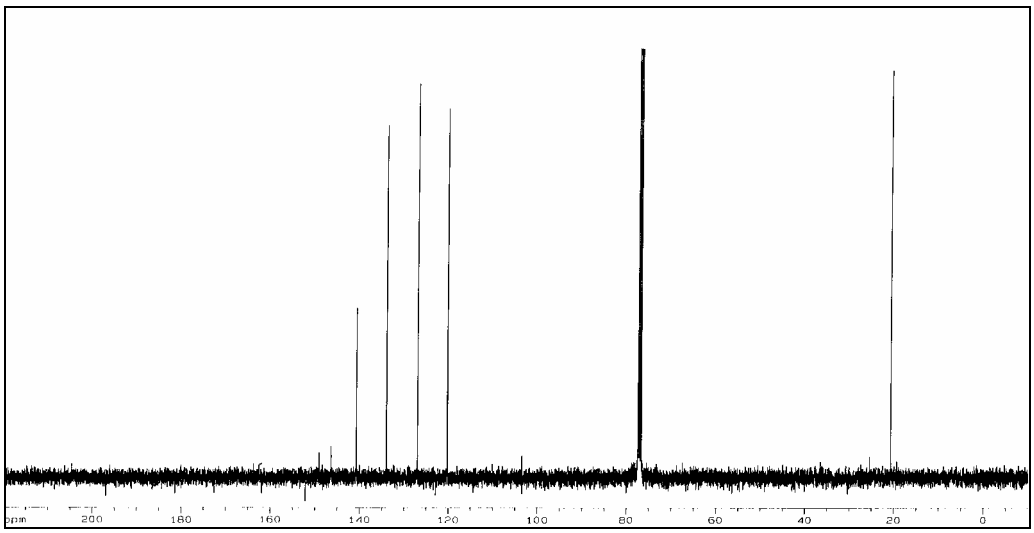


^{1}H NMR spectrum of the pure product 2,4-dinitrotoluene (400 MHz, $CDCl_3$)

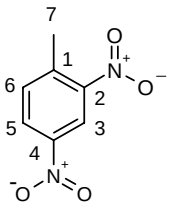


δ (ppm)	Multiplicity	Number of H	Assignment
2.74	s	3	CH_3
7.58 – 7.60	d	1	5-H
8.35 – 8.36	dd	1	6-H
8.83 – 8.84	d	1	3-H

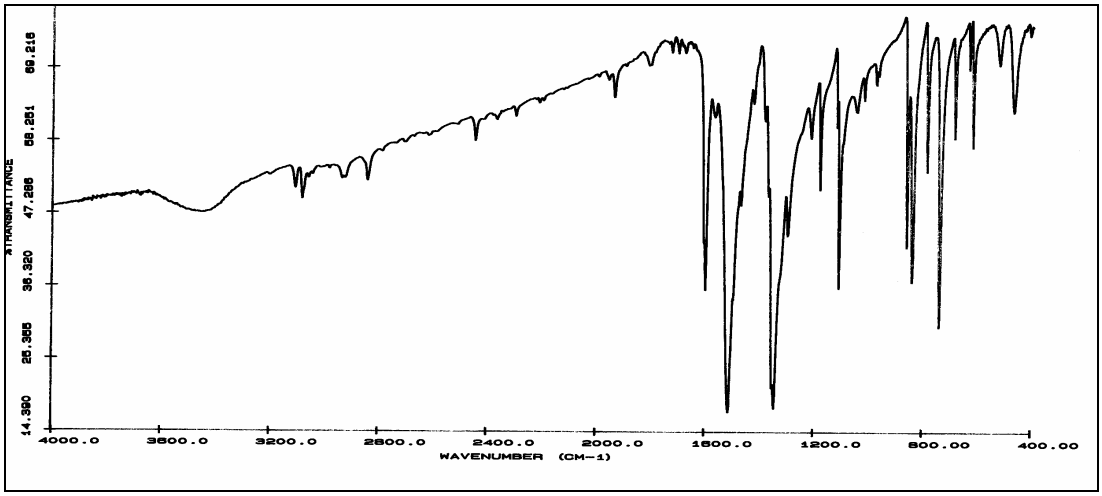
^{13}C NMR spectrum of the pure product 2,4-dinitrotoluene (100 MHz, $CDCl_3$)



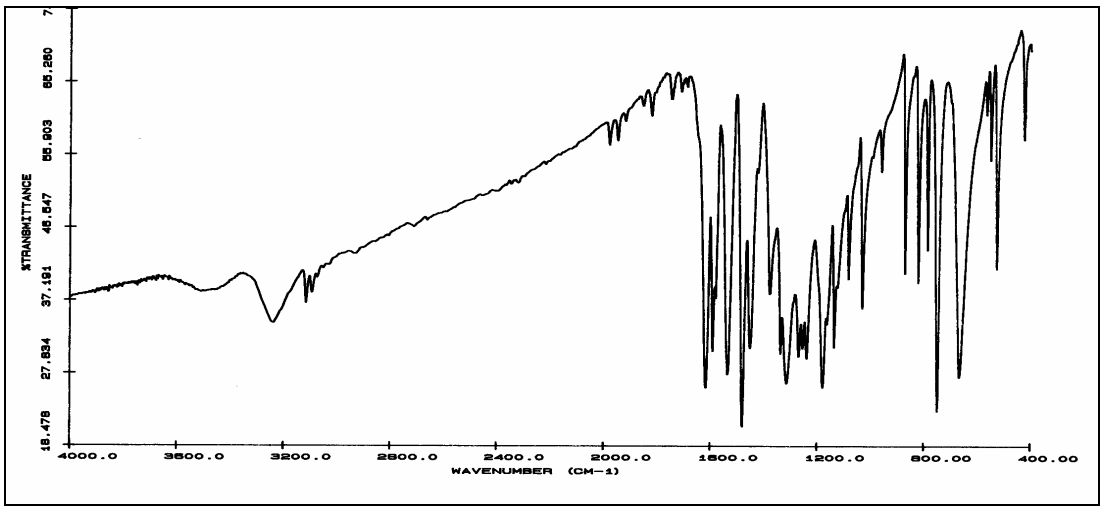
δ (ppm)	Assignment
20.69	CH_3
120.22	C-3
126.97	C-5
133.98	C-6
140.69	C-1
146.40	C-4
149.04	C-2



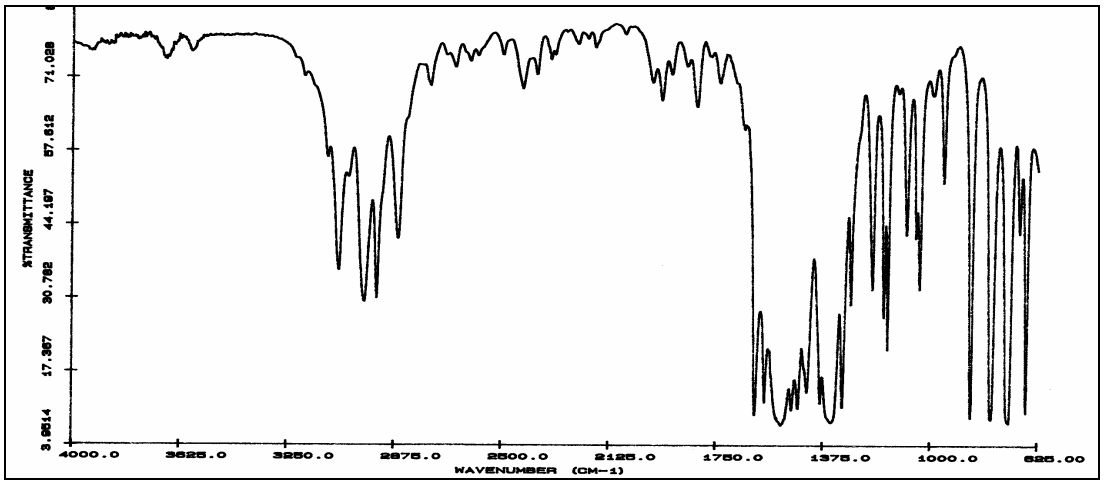
IR spectrum of the pure product 4-nitrotoluene (KBr)



IR spectrum of the pure product 2,4-dinitrotoluene (KBr)



IR spectrum of 2-nitrotoluene (for comparison) (Film)

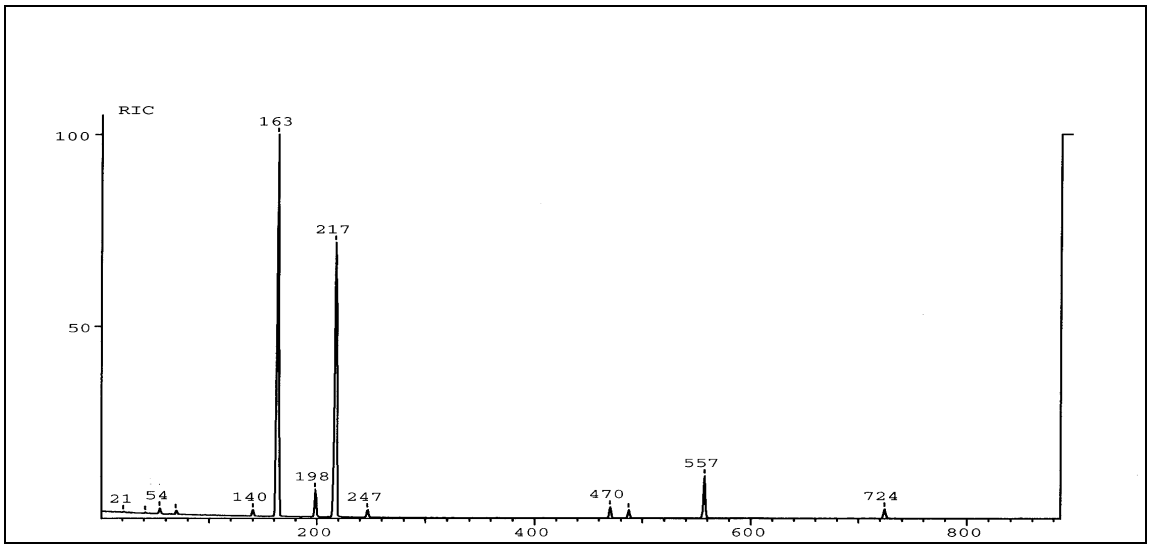


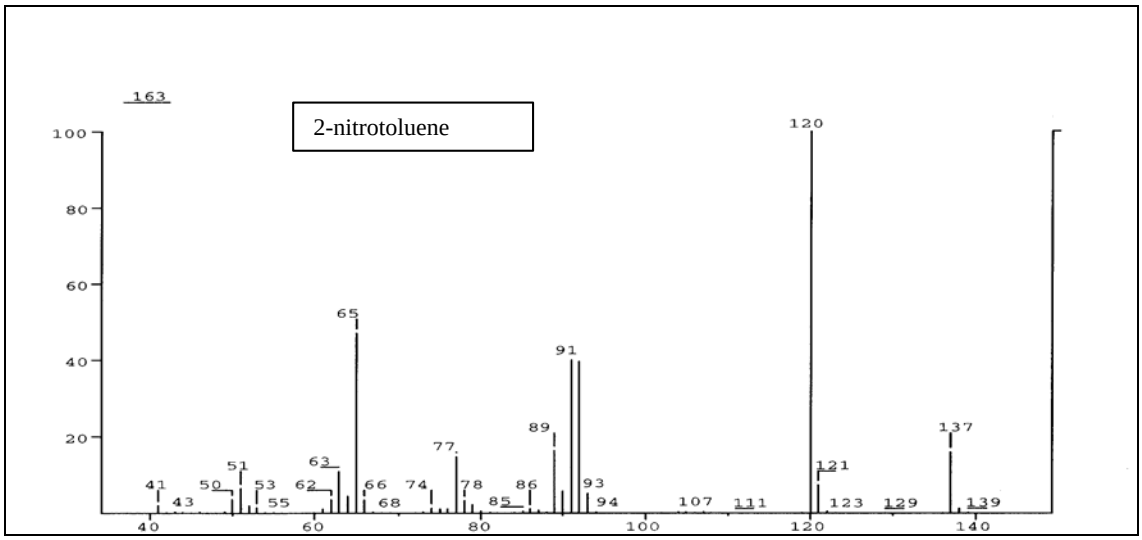
(cm-1)	Assignment
3100	C-H- valence, arene
1600	C=C- valence, arene
1520, 1340	N=O- valence, asymm. and symm.

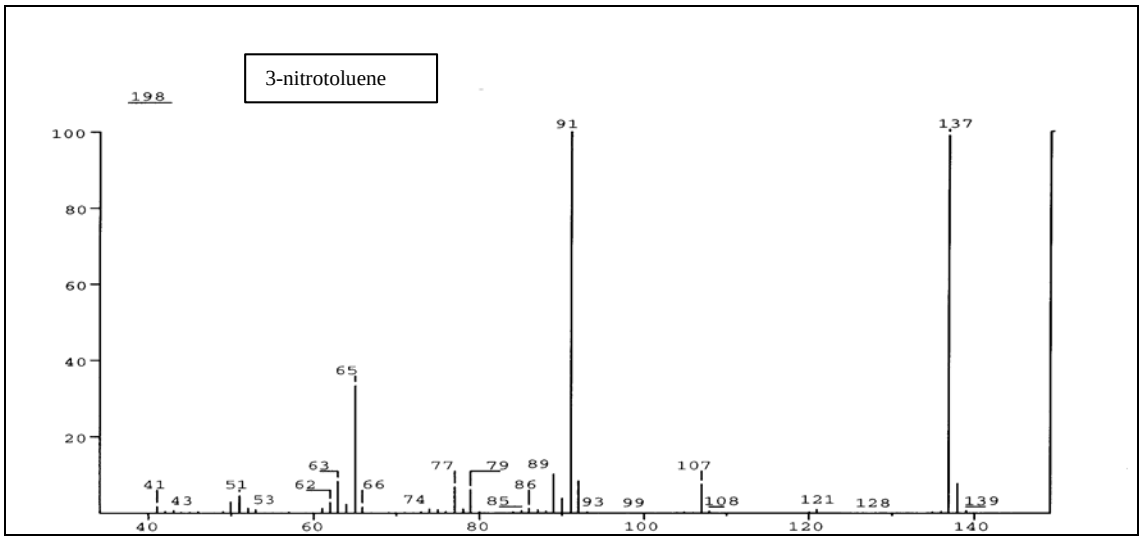
GC/MS of the crude product

GC conditions:

column:	ZB-1, L=30 m
inlet:	splitinjection 1 : 20
oven:	70 – 300 °C, 6 °C/min






3-nitrotoluene
198
91
137
65
63
77
79
89
107
41
51
62
66
74
86
43
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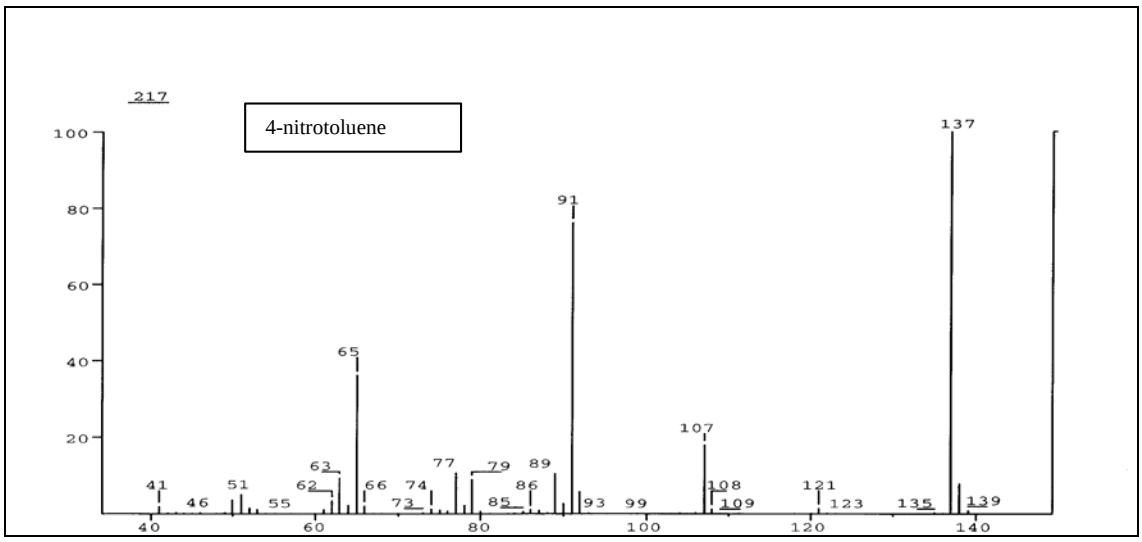
80
60
40
20
40
60
80
100
120
140


4-nitrotoluene
217
137
91
65
107
63
77
79
89
41
51
62
66
74
86
46
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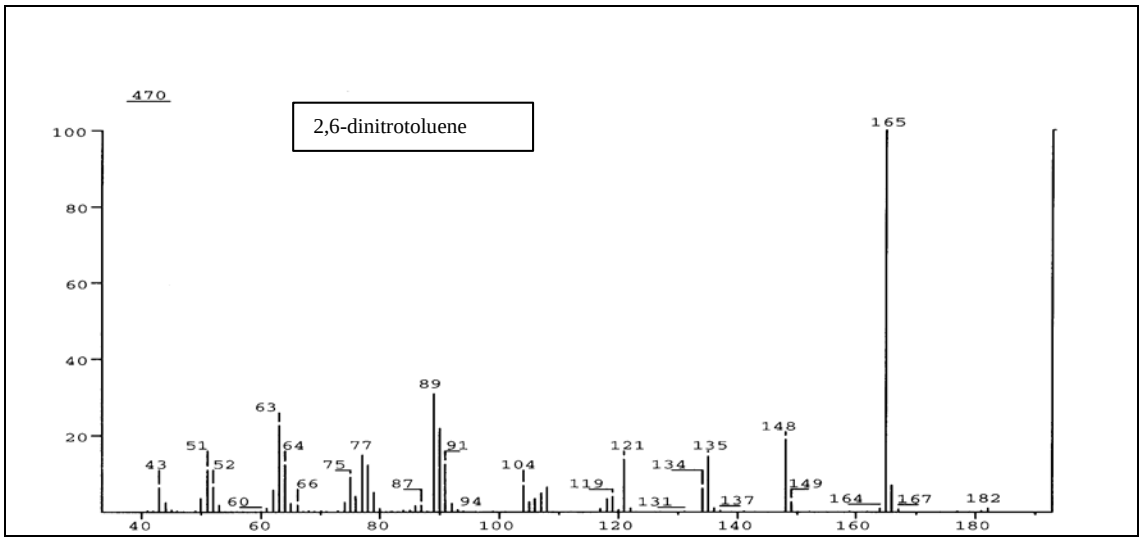
80
100
120
140


2,6-dinitrotoluene
470
165
89
63
148
51
64
77
91
121
135
43
52
75
104
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87
119
149
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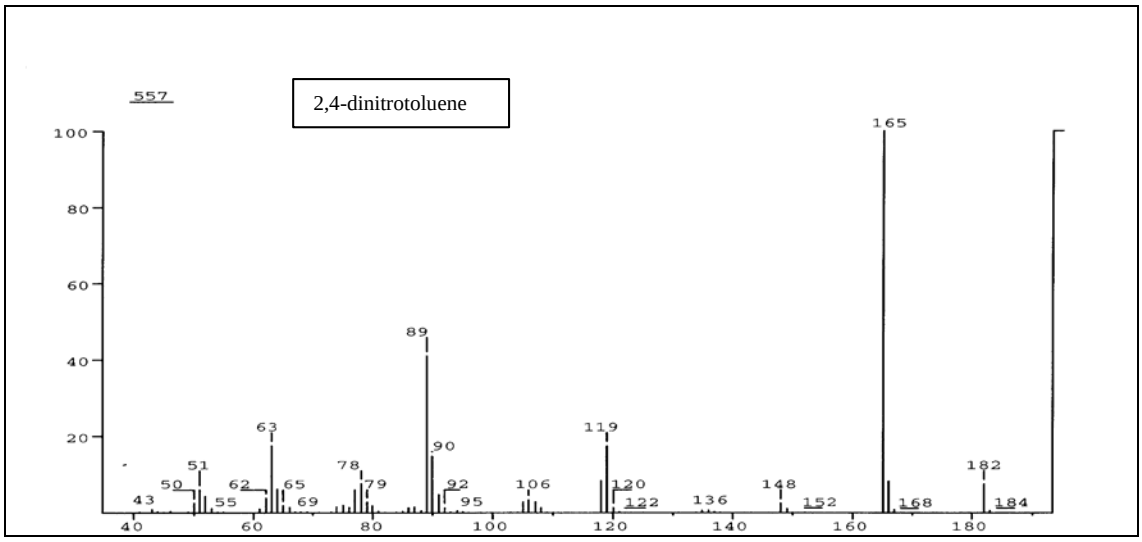
557
2,4-dinitrotoluene
100
80
60
40
20
165
89
63
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90
51
78
182
50
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79
92
106
120
148
43
55
69
95
122
136
152
168
184
40
60
80
100
120
140
160
180