



Sintesis Tiga Turunan 4-Nitroindola-3-karboksaldehida

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1412 100 044

Dosen Pembimbing :
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Jurusan Kimia

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Institut Teknologi Sepuluh Nopember Surabaya

Outline

1.

Pendahuluan

2.

Metodologi, Hasil dan Pembahasan

3.

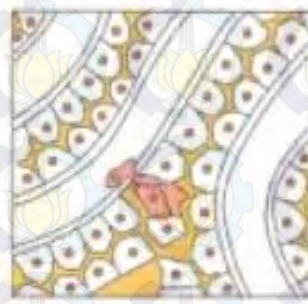
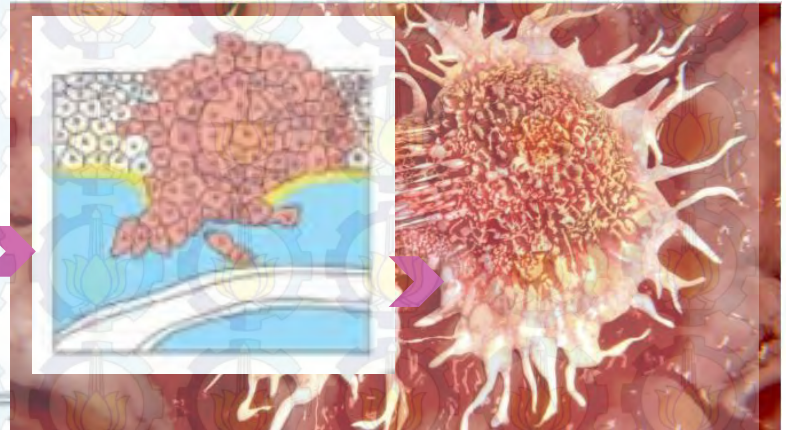
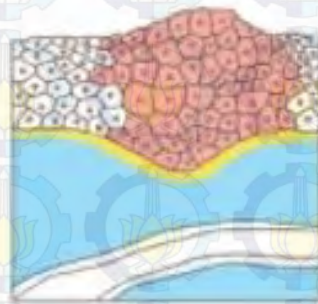
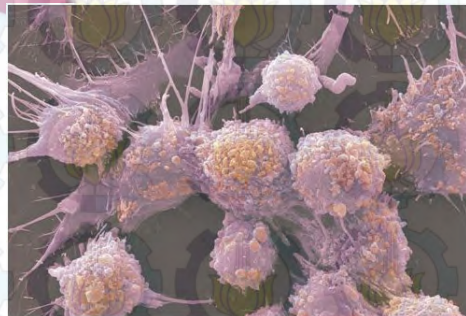
Kesimpulan

The background of the slide features a repeating pattern of a yellow lotus flower inside a light blue gear, arranged in a grid. A horizontal pink bar with a black border is positioned across the middle of the slide, containing the title text.

Pendahuluan

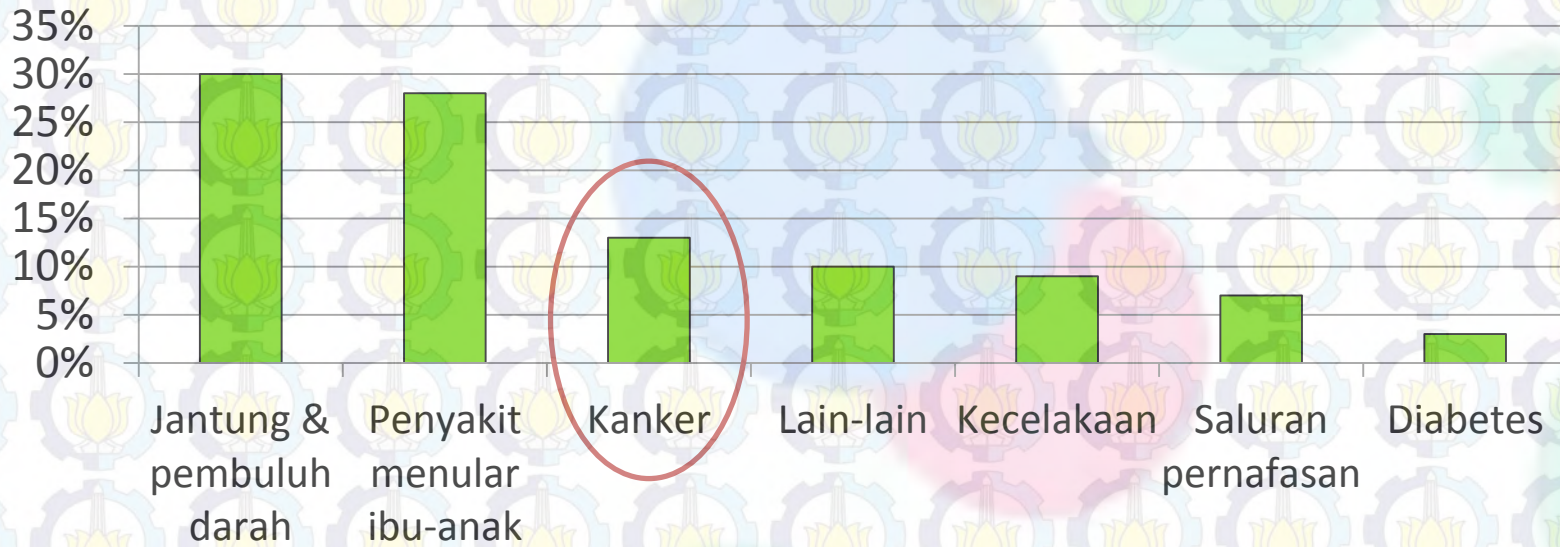
Latar Belakang

Kanker



Latar Belakang

Penyebab Kematian Terbesar di Dunia Tahun 2005



2008

7,6 juta

7,9%

2012

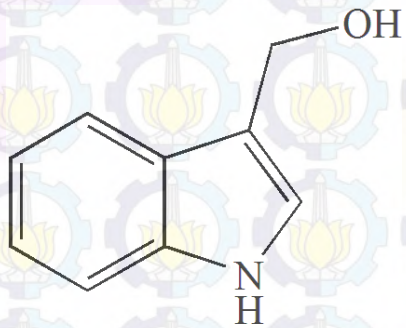
8,2 juta

Latar Belakang



Latar Belakang

Cruciferae (Brassica)

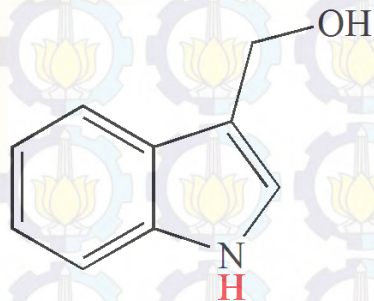


(1)



$IC_{50} = 52 \mu M$
MCF-7

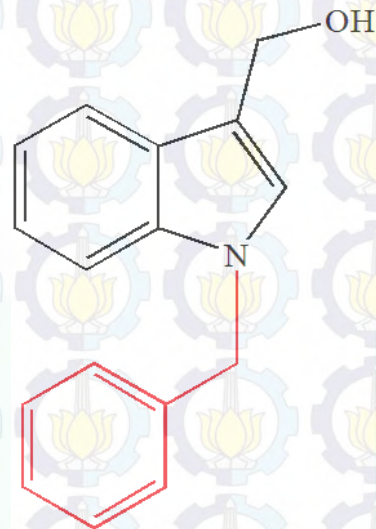
Latar Belakang



(1)

Indola-3-karbinol

$IC_{50} = 52 \mu M$
MCF-7



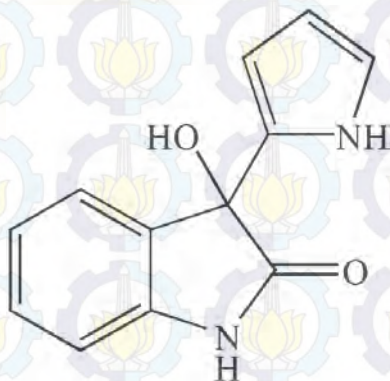
(2)

1-Benzilindola-3-karbinol

$IC_{50} = 0,05 \mu M$
MCF-7



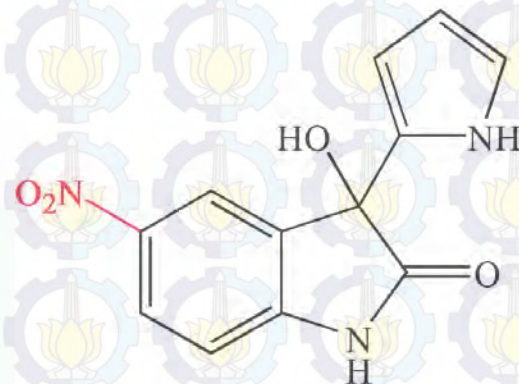
Latar Belakang



(3a)

3-Hidroksi-3-(1*H*-pirol-2-il)indolin-2-ona

$IC_{50} = 10,3 \text{ mM}$
HepG2



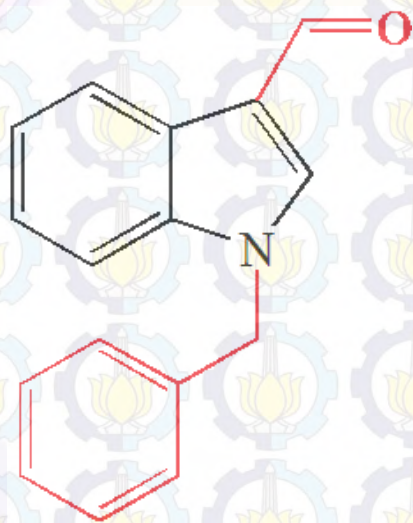
(3b)

3-Hidroksi-5-nitro-3-(1*H*-pirol-2-il)indolin-2-ona

$IC_{50} = 0,5 \text{ mM}$
HepG2

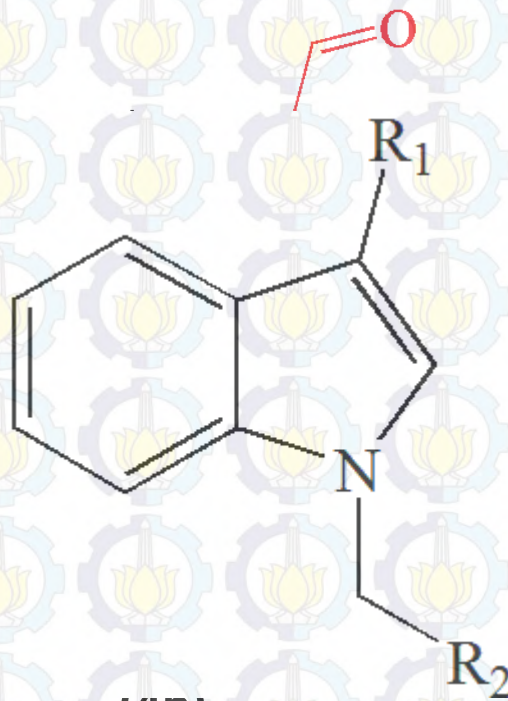


Latar Belakang



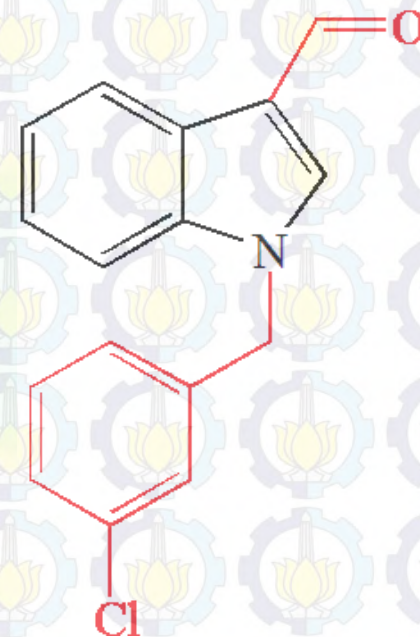
(4a)

$IC_{50} = 0,045 \mu M$
H460



(4b)

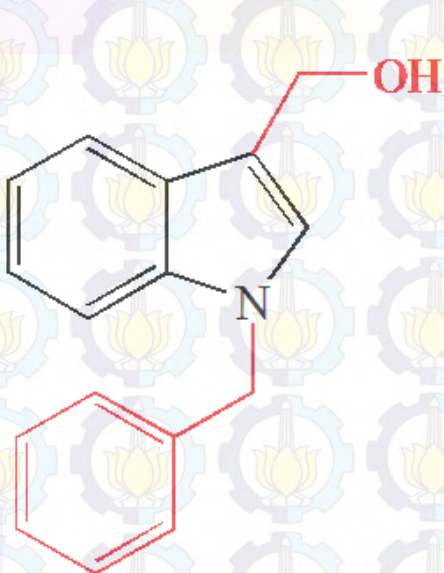
$IC_{50} = 0,250 \mu M$
H460



(4c)

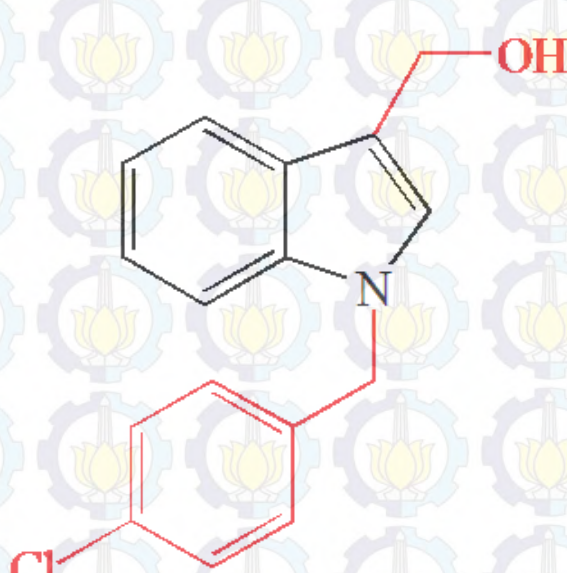
$IC_{50} = 0,037 \mu M$
H460

Latar Belakang



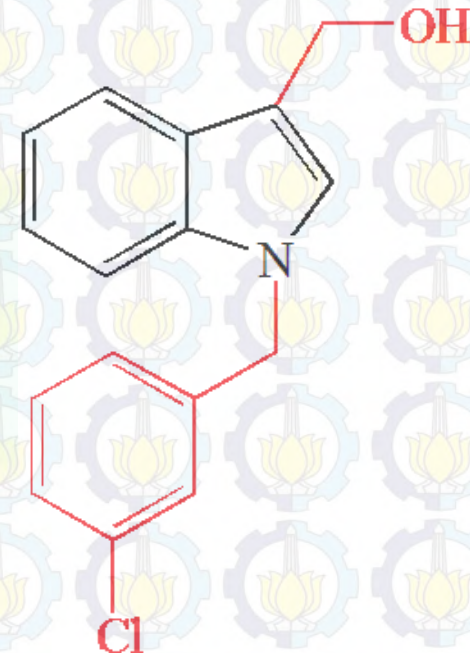
(4d)

$IC_{50} = 0,112 \mu M$
H460



(4e)

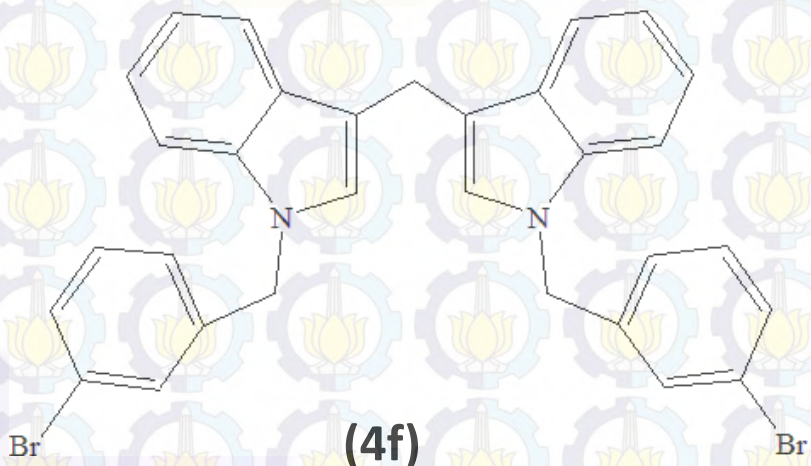
$IC_{50} = 0,100 \mu M$
H460



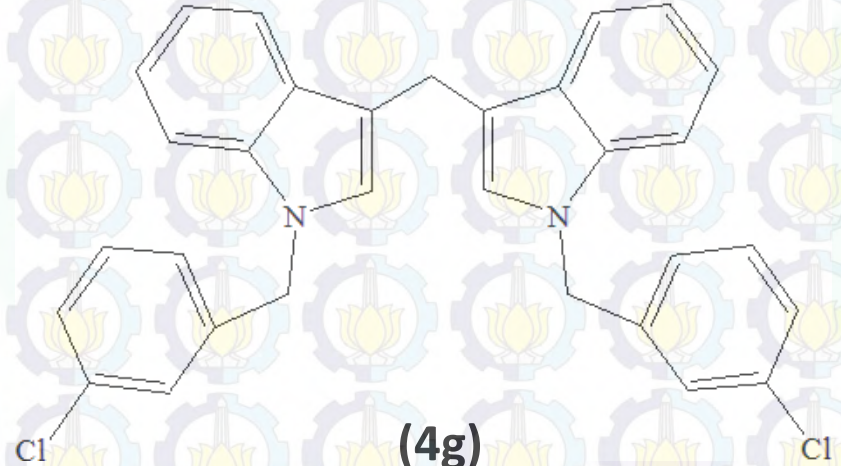
(4f)

$IC_{50} = 0,019 \mu M$
H460

Latar Belakang

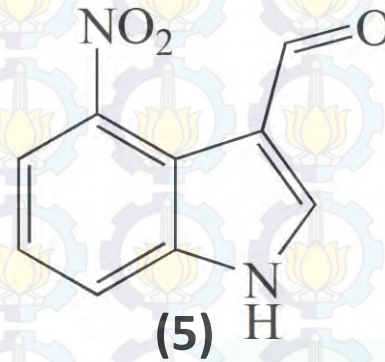


$IC_{50} = >31,6 \mu M$
H460

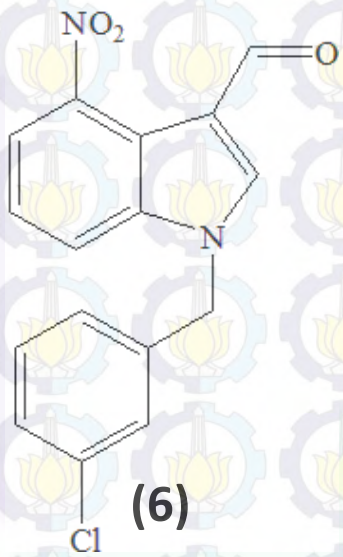


$IC_{50} = >31,6 \mu M$
H460

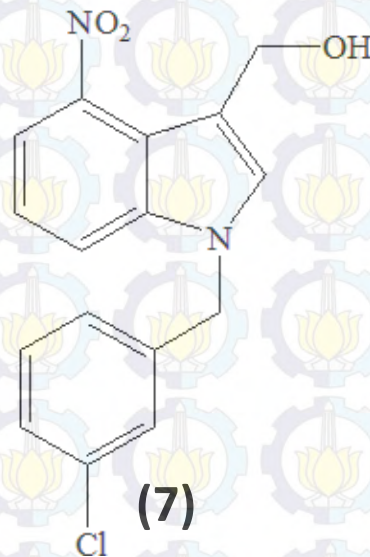
Latar Belakang



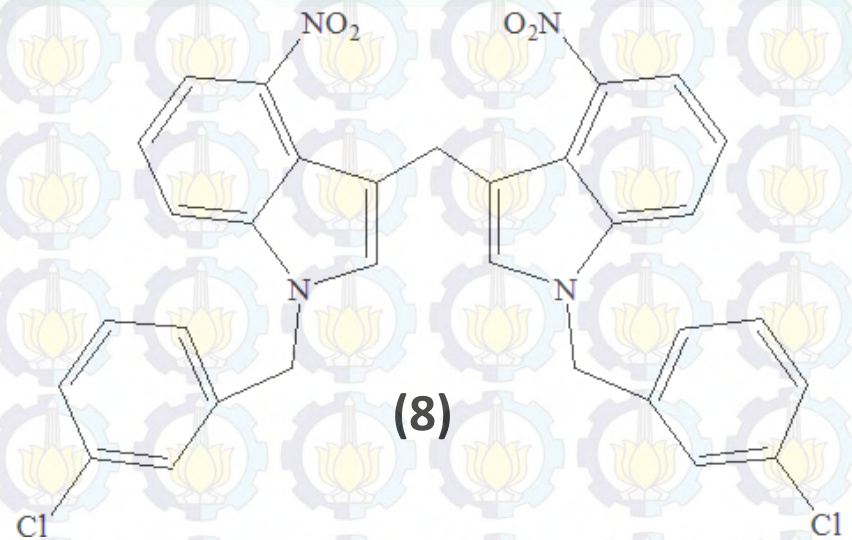
4-Nitroindola-3-karboksaldehida



1-(3-Klorobenzil)-4-nitroindola-3-karbaldehida

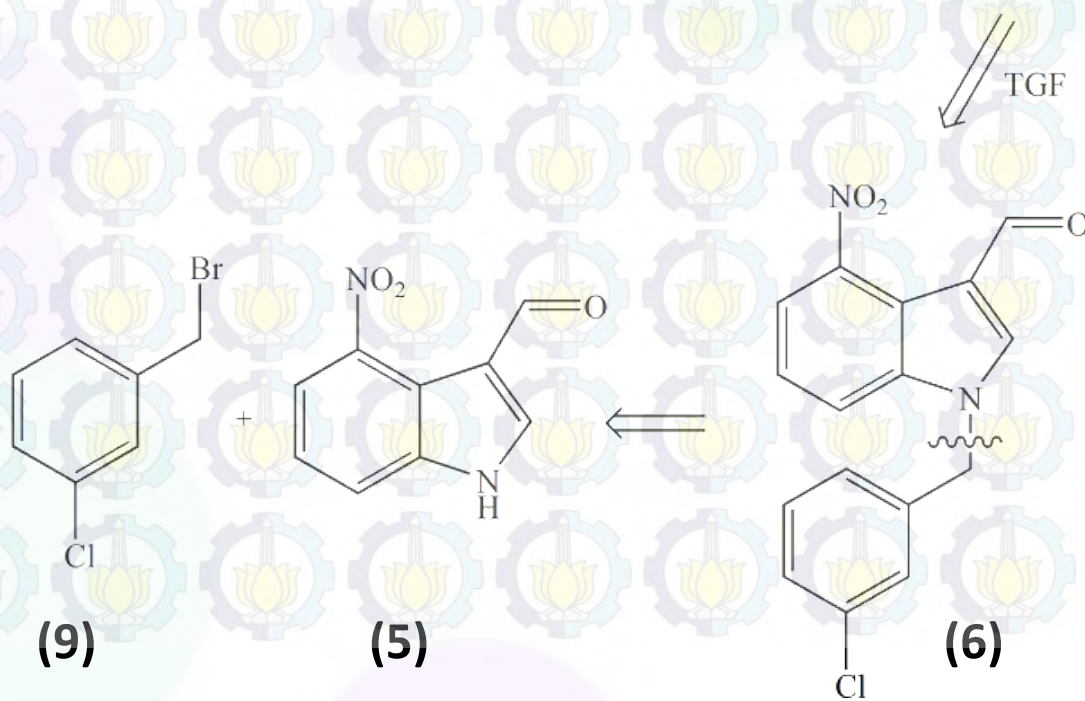
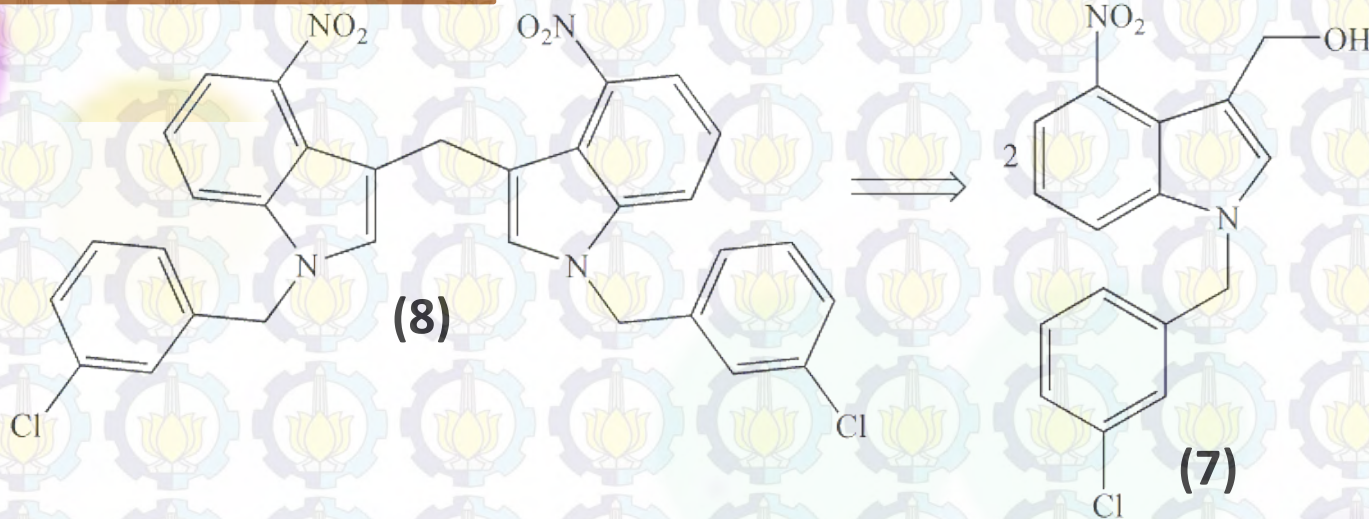


[1-(3-Klorobenzil)-4-nitroindola-3-il]metanol

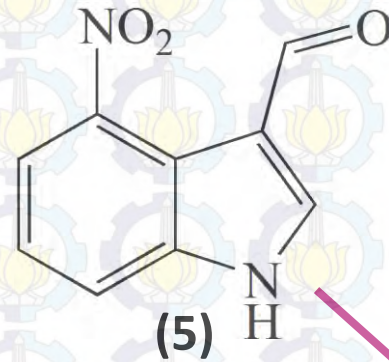


Bis(1-(3-klorobenzil)-4-nitroindola-3-il)metana

Latar Belakang



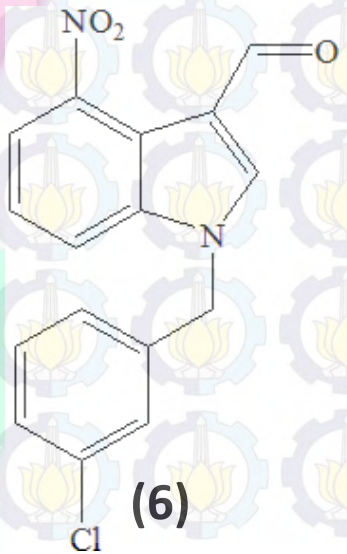
Permasalahan



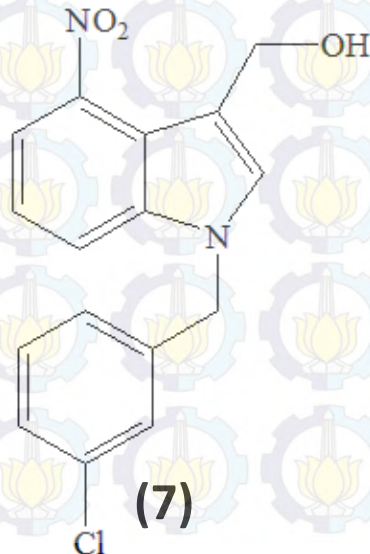
?

?

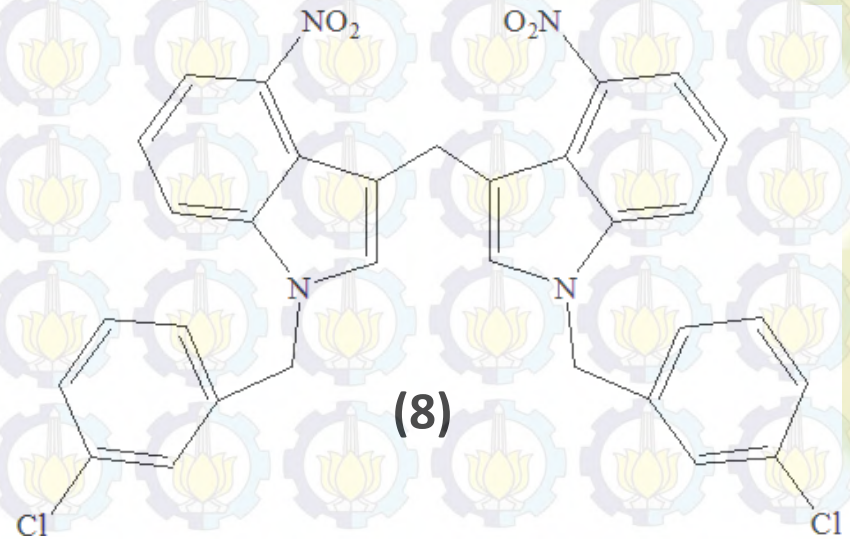
?



(6)

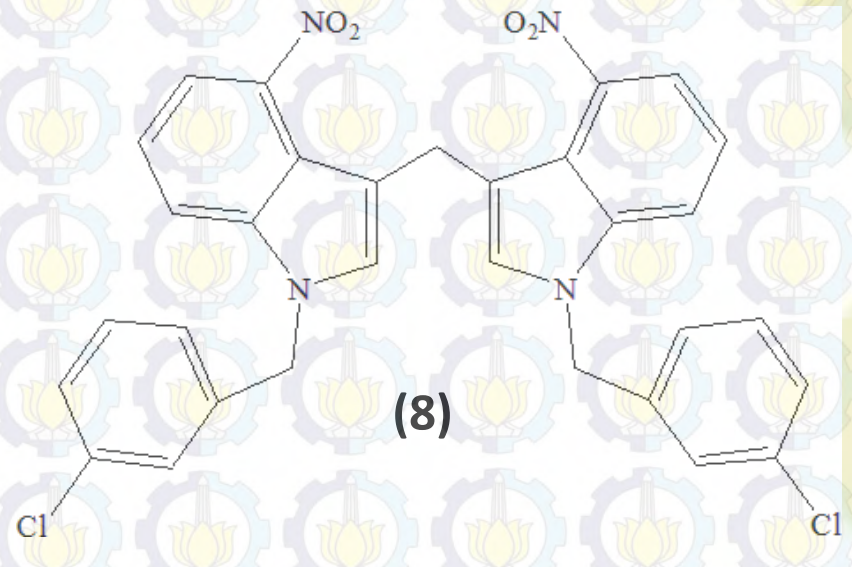
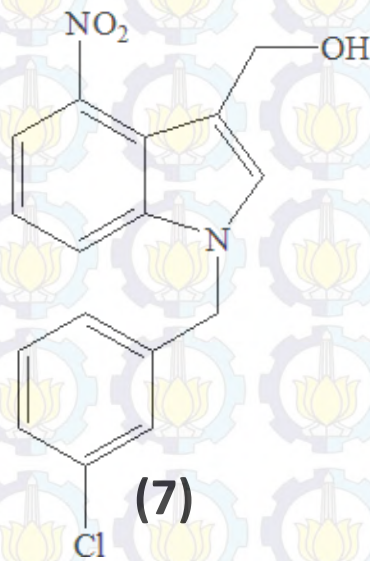
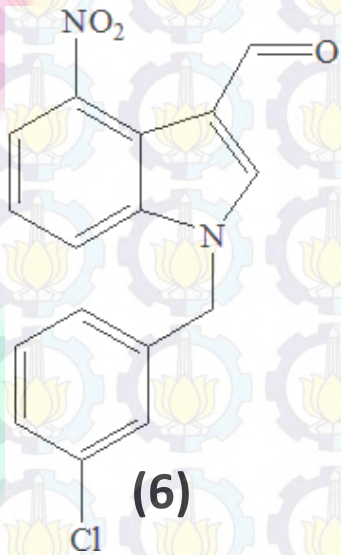
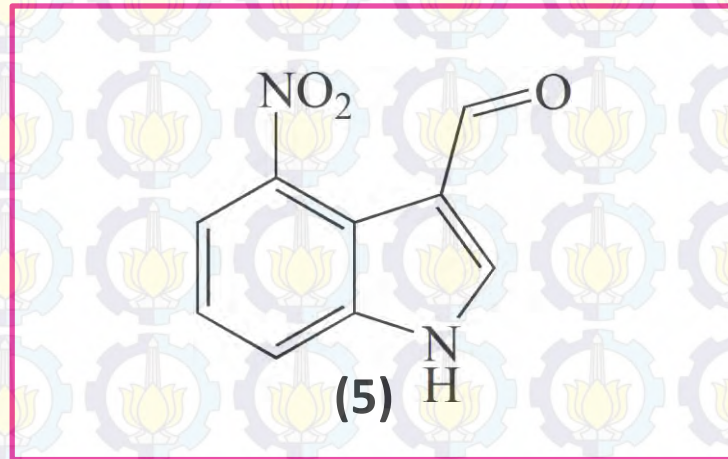


(7)



(8)

Tujuan



Tahapan Penelitian

T.1

Sintesis 1-(3-Klorobenzil)-4-nitroindola-3-karbaldehida (6)

T.2

Sintesis [1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7)

T.3

Sintesis Bis(1-(3-klorobenzil)-4-nitroindola-3-il)metana(8)

The background of the slide features a repeating pattern of stylized lotus flowers in yellow and light blue, each enclosed within a light blue gear-like border. The pattern is arranged in a grid across the entire slide. A horizontal pink bar with a black border is positioned in the center, containing the main text.

Metodologi, Hasil dan Pembahasan

4-Nitroindola-3-
karboksaldehida (5)
(0,20 g; 1,05 mmol)

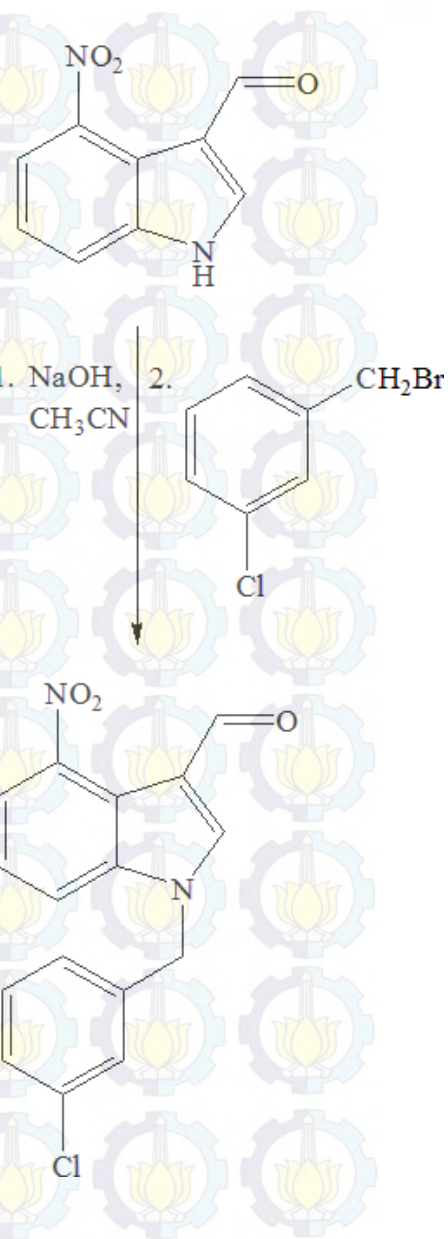
Natrium hidroksida
(0,084 g; 2,10 mmol)

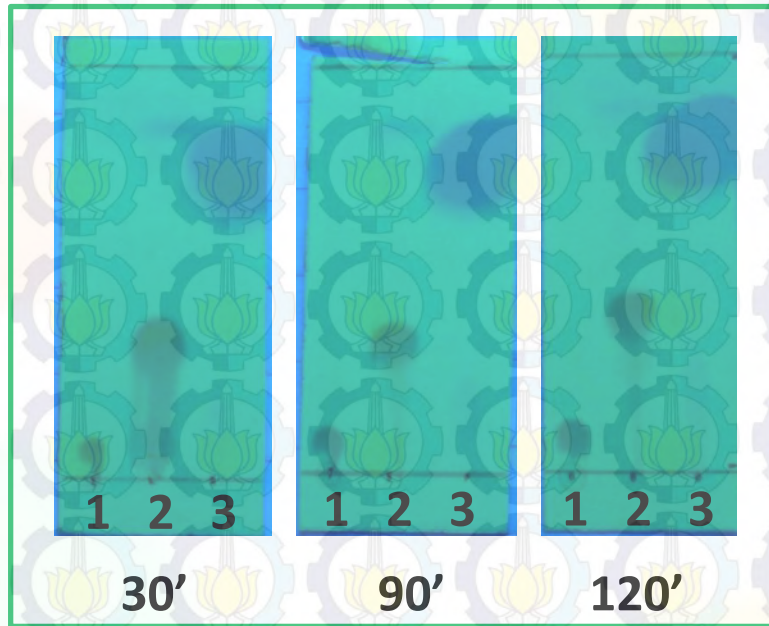
- dilarutkan dalam asetonitril (15 mL)
- diaduk pada suhu kamar selama 60 menit

Hasil reaksi 1

3-Klorobenzil bromida (9)
(144,43 μ L; 1,10 mmol)

- diaduk lebih lanjut pada suhu kamar selama 120 menit (jalannya reaksi dipantau dengan KLT)





Keterangan :
1 = 4-nitroindola-3-karboksaldehida (5)
2 = hasil reaksi
3 = 3-klorobenzil bromida (9)

Eluen :
n-heksana ; etil asetat (5:2)

T.1

4-Nitroindola-3-karboksaldehida (5)
(0,20 g; 1,05 mmol)

Natrium hidroksida
(0,084 g; 2,10 mmol)

- dilarutkan dalam asetonitril (15 mL)
- diaduk pada suhu kamar selama 60 menit

Hasil reaksi 1

3-Klorobenzil bromida (9)
(144,43 μ L; 1,10 mmol)

- diaduk lebih lanjut pada suhu kamar selama 120 menit (jalannya reaksi dipantau dengan KLT)

Hasil reaksi 2

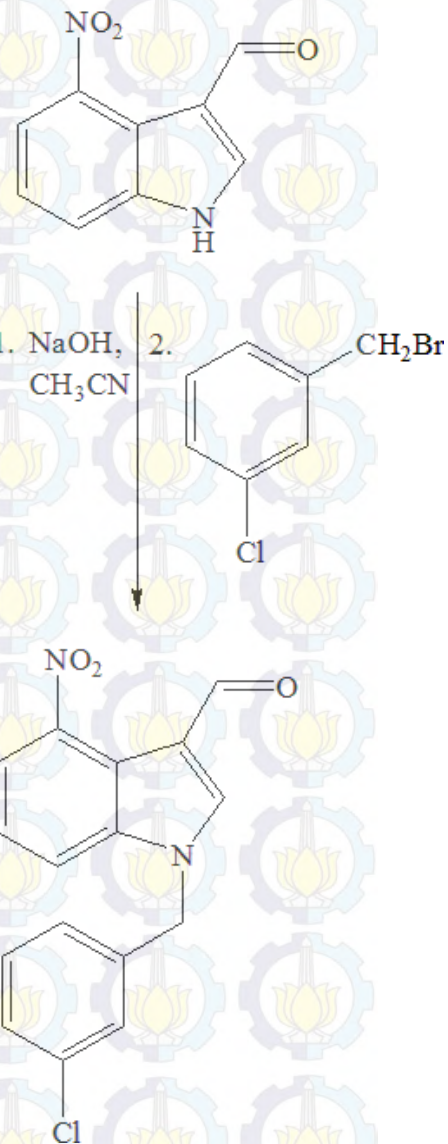
- ditambah dengan akuades dingin (15 mL)
- diekstrak dengan diklorometana (3x15 mL)

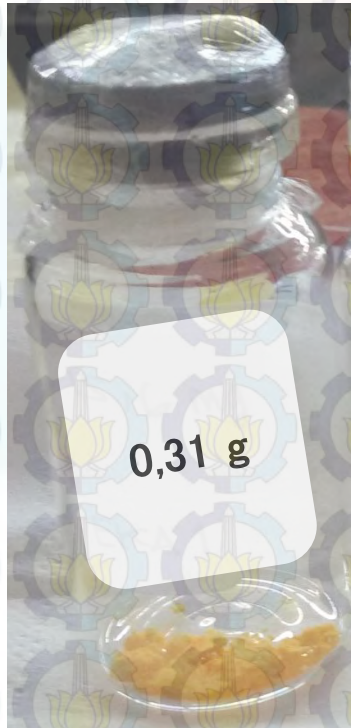
Fasa organik

Fasa air

- dikeringkan dengan MgSO_4 anhidrat
- diuapkan dengan *rotary evaporator*

1-(3-Klorobenzil)-4-nitroindola-3-karbaldhida (6)*





0,31 g

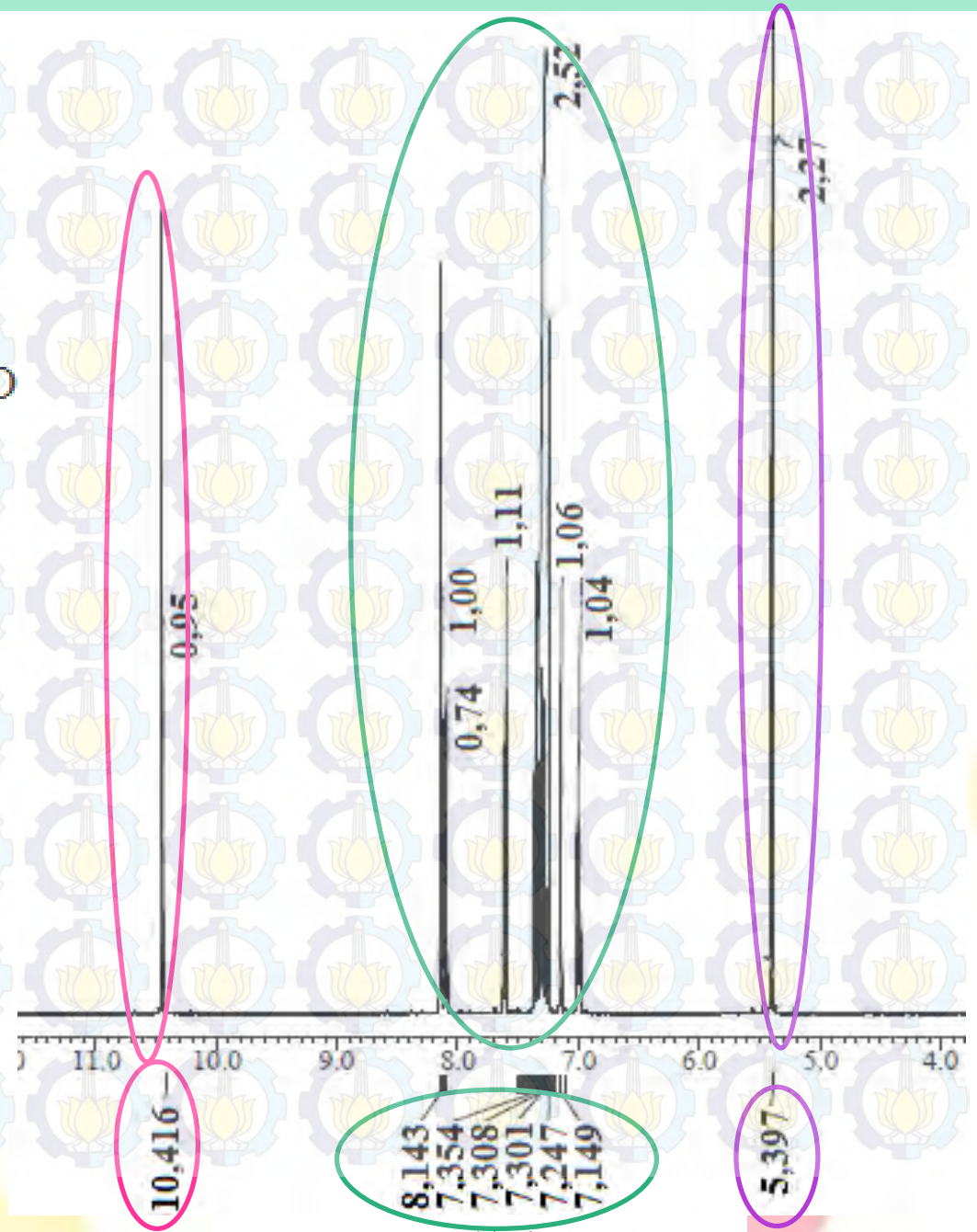
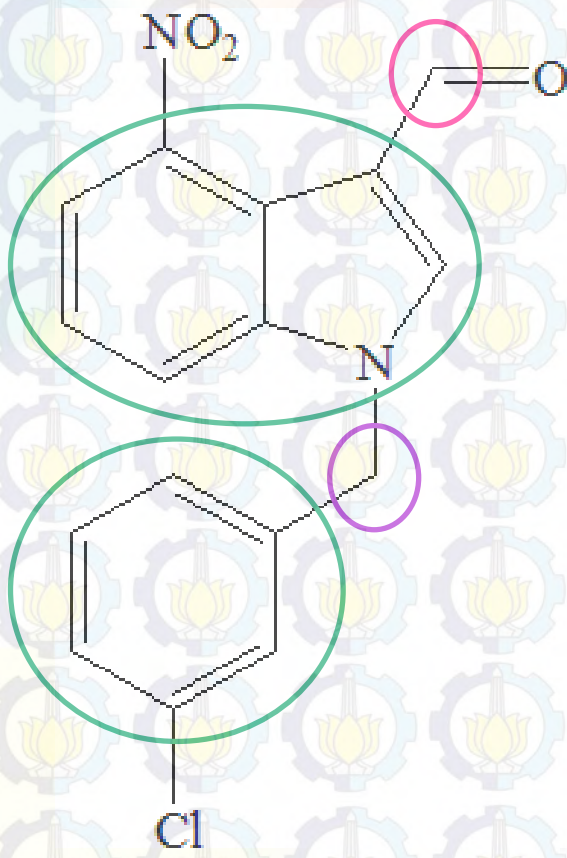


Keterangan eluen :

- a = *n*-heksana : kloroform (5:3)
- b = *n*-heksana : etil asetat (5:2)
- c = *n*-heksana : etil asetat (5:4)

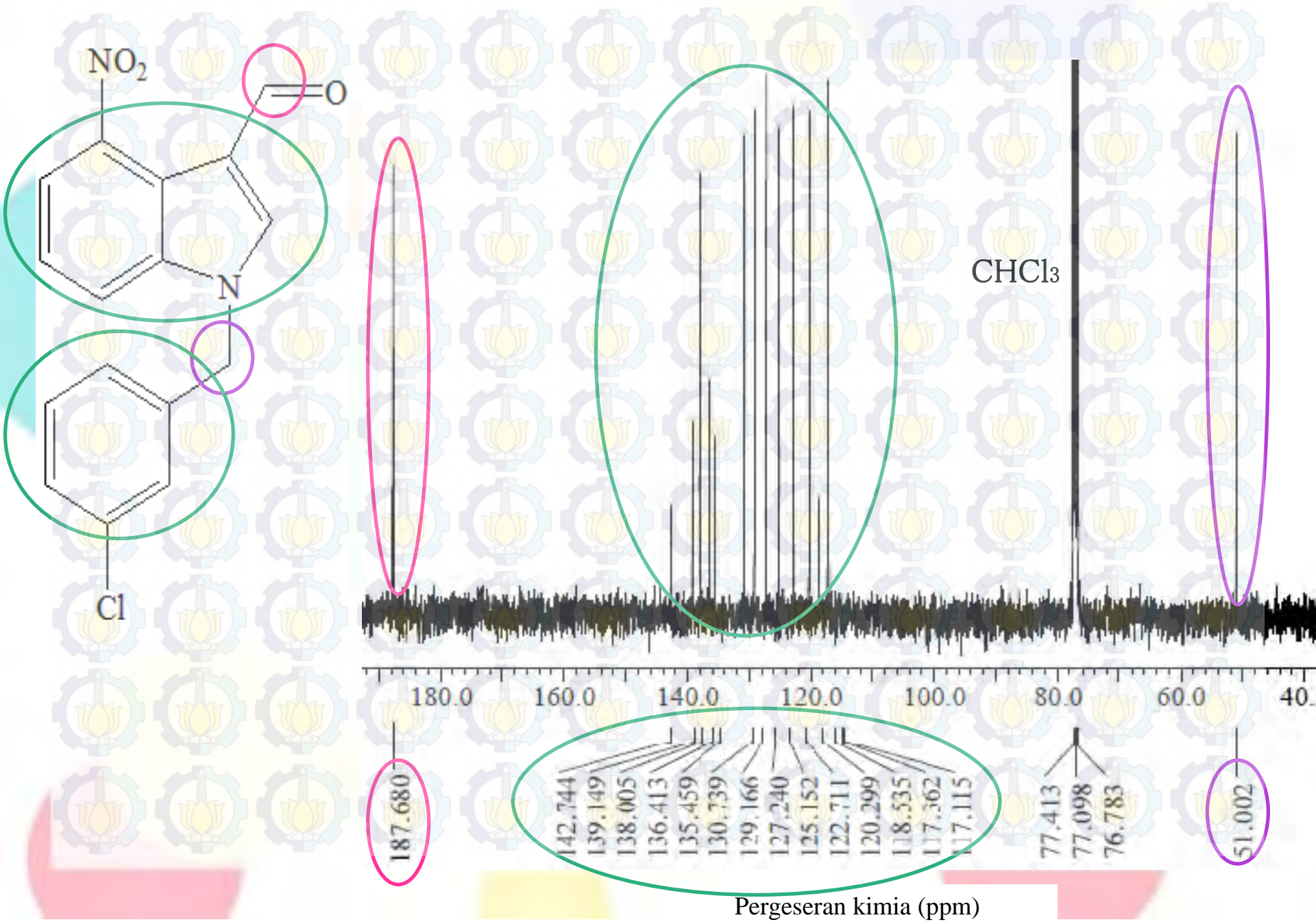
Titik Leleh : 177° C

Spektrum ¹H-NMR 1-(3-Klorobenzil)-4-nitroindola-3-karbalehida (6) hasil sintesis

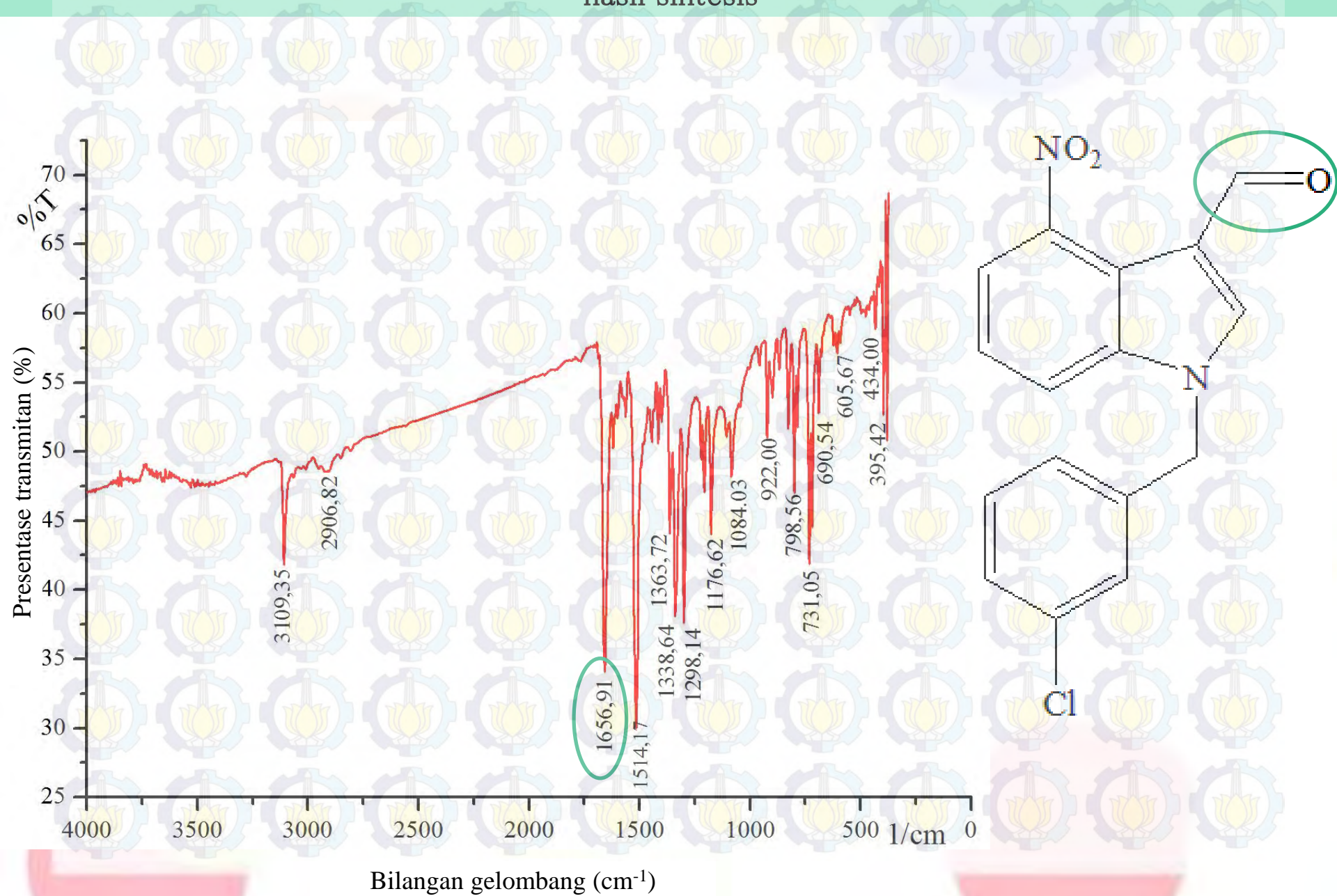


Pergeseran kimia (ppm)

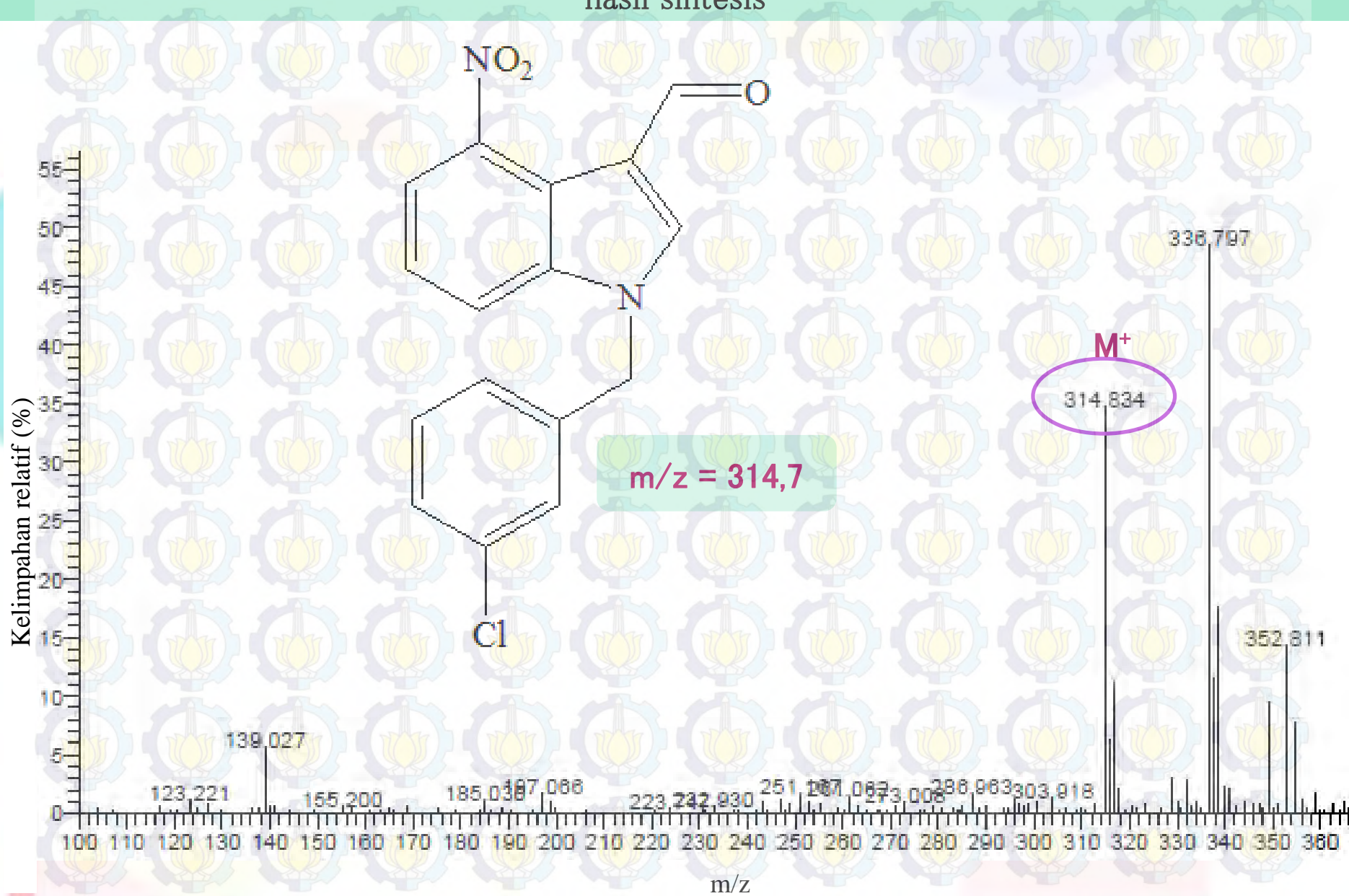
Spektrum ^{13}C -NMR 1-(3-Klorobenzil)-4-nitroindola-3-karbalehida (6) hasil sintesis



Spektrum infra merah 1-(3-Klorobenzil)-4-nitroindola-3-karbaldehida (6) hasil sintesis



Spektrum massa (APCI)1-(3-Klorobenzil)-4-nitroindola-3-karbalehida (6) hasil sintesis

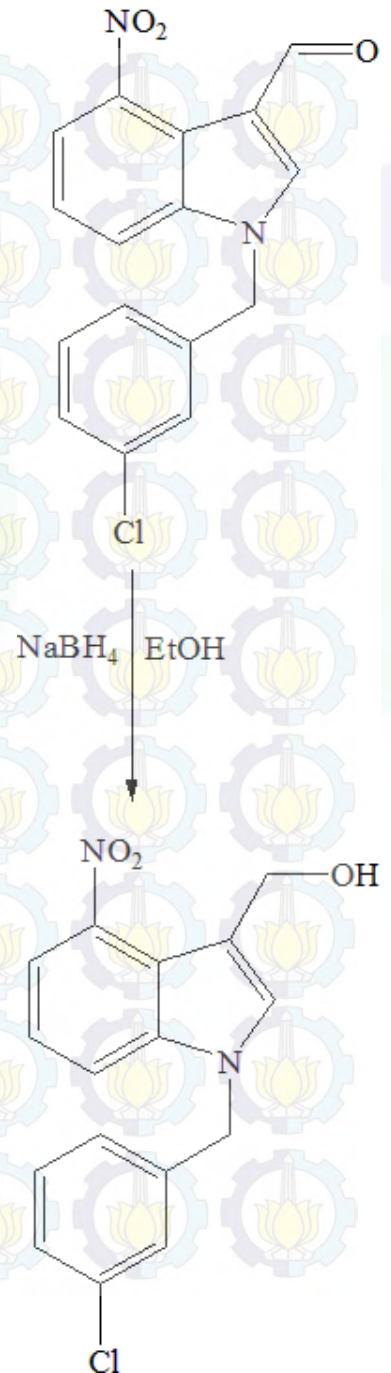


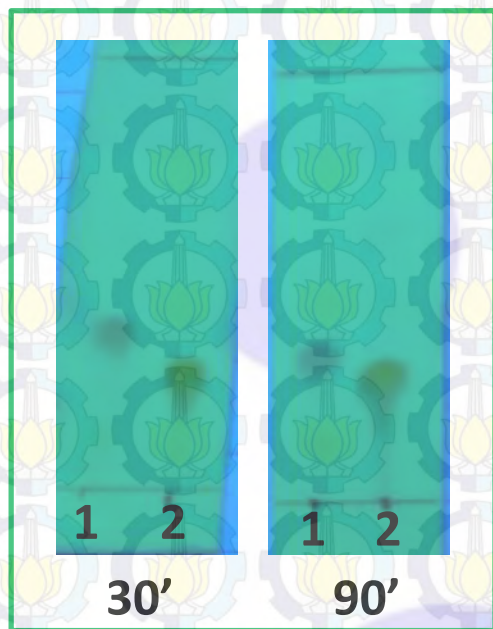
T.2

1-(3-Klorobenzil)-4-nitroindola-
3-karbalehida (**6**)
(0,030 g; 0,95 mmol)

Natrium borohidrida
(0,018 g; 4,73 mmol)

- dilarutkan dalam etanol (20 mL)
- diaduk pada suhu kamar selama 90 menit
(jalannya reaksi dipantau dengan KLT)





Keterangan :
1 = 1-(3-klorobenzil)-4-nitroindola-3-karbaldehida (6)
2 = hasil reaksi

Eluen :
n-heksana ; etil asetat (5:2)

T.2

1-(3-Klorobenzil)-4-nitroindola-3-karbalehida (6)
(0,030 g; 0,95 mmol)

Natrium borohidrida
(0,018 g; 4,73 mmol)

- dilarutkan dalam etanol (20 mL)
- diaduk pada suhu kamar selama 90 menit (jalannya reaksi dipantau dengan KLT)

Hasil reaksi

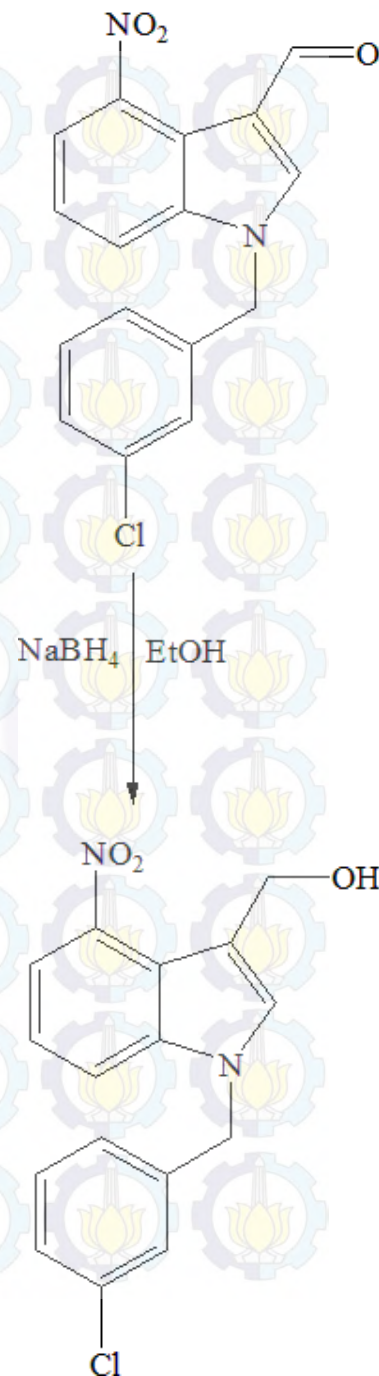
- ditambah aseton (1,04 mL; 14,19 mmol)
- diuapkan pelarutnya sehingga hampir kering
- ditambah larutan natrium hidroksida 10% (7,6 mL)
- diuapkan pelarutnya dengan *rotary evaporator*
- disaring

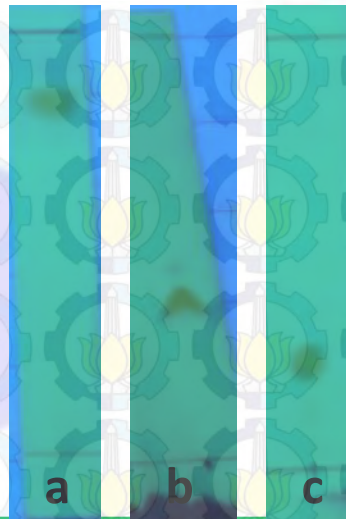
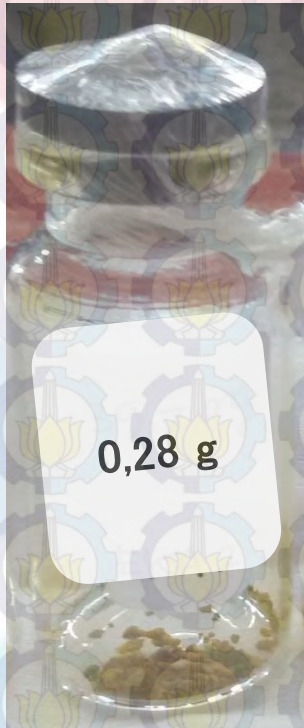
Endapan

- dicuci dengan akuades
- dikeringkan dalam desikator

[1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7)*

Fasa air



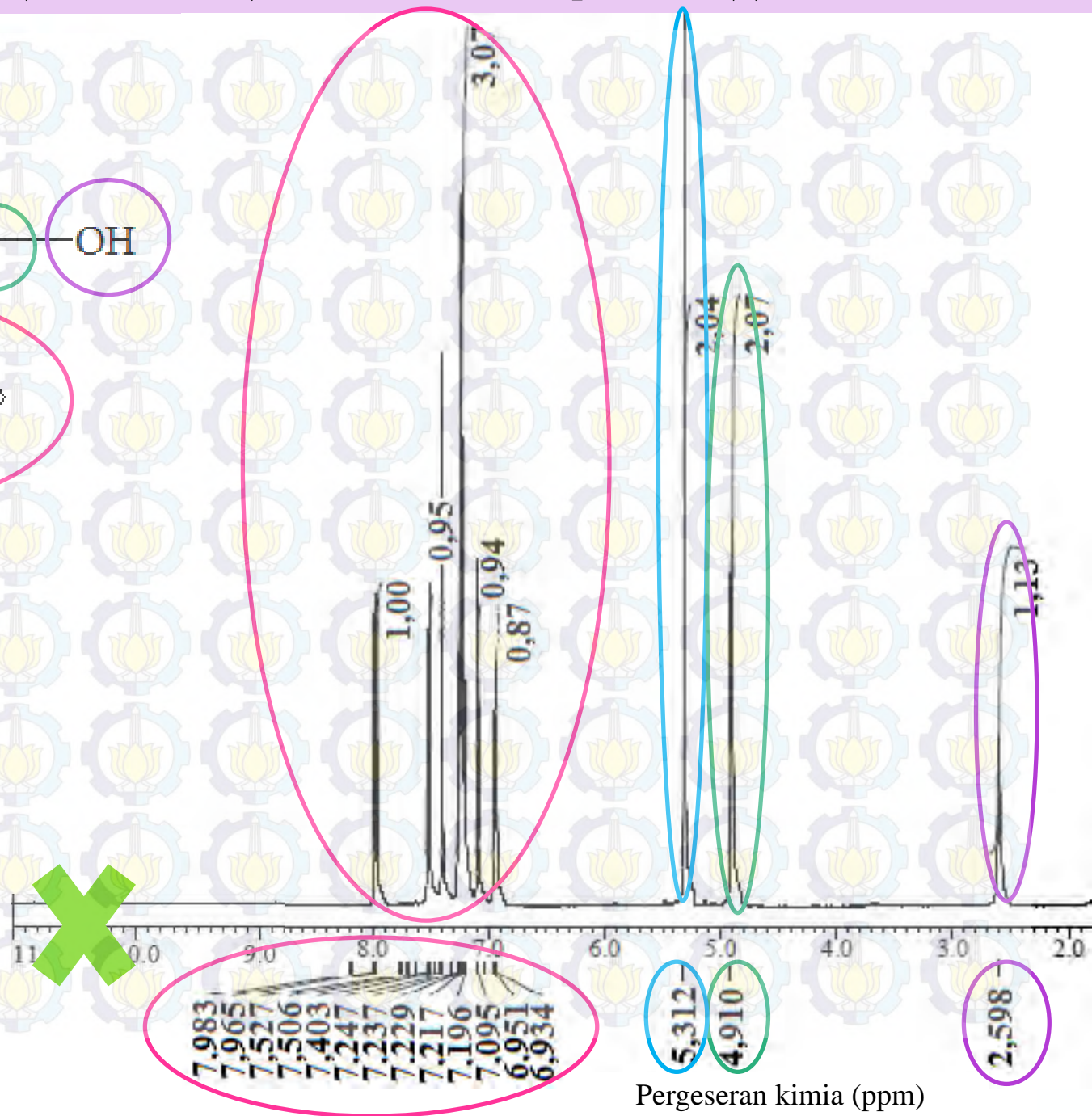
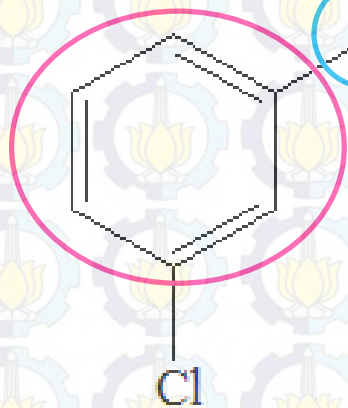
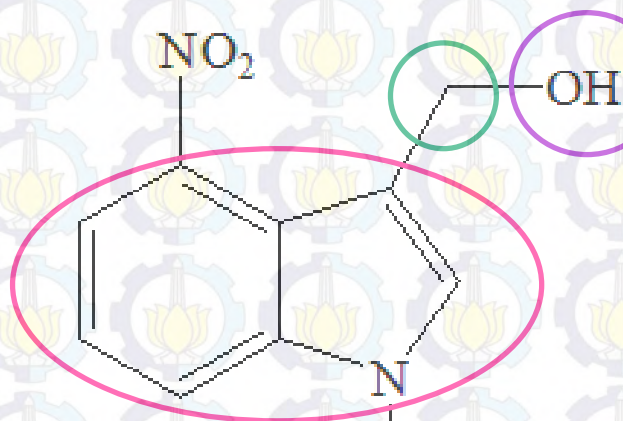


Keterangan eluen :

- a = *n*-heksana : kloroform (1:4)
- b = *n*-heksana : diklorometana (1:4)
- c = *n*-heksana : etil asetat (1:4)

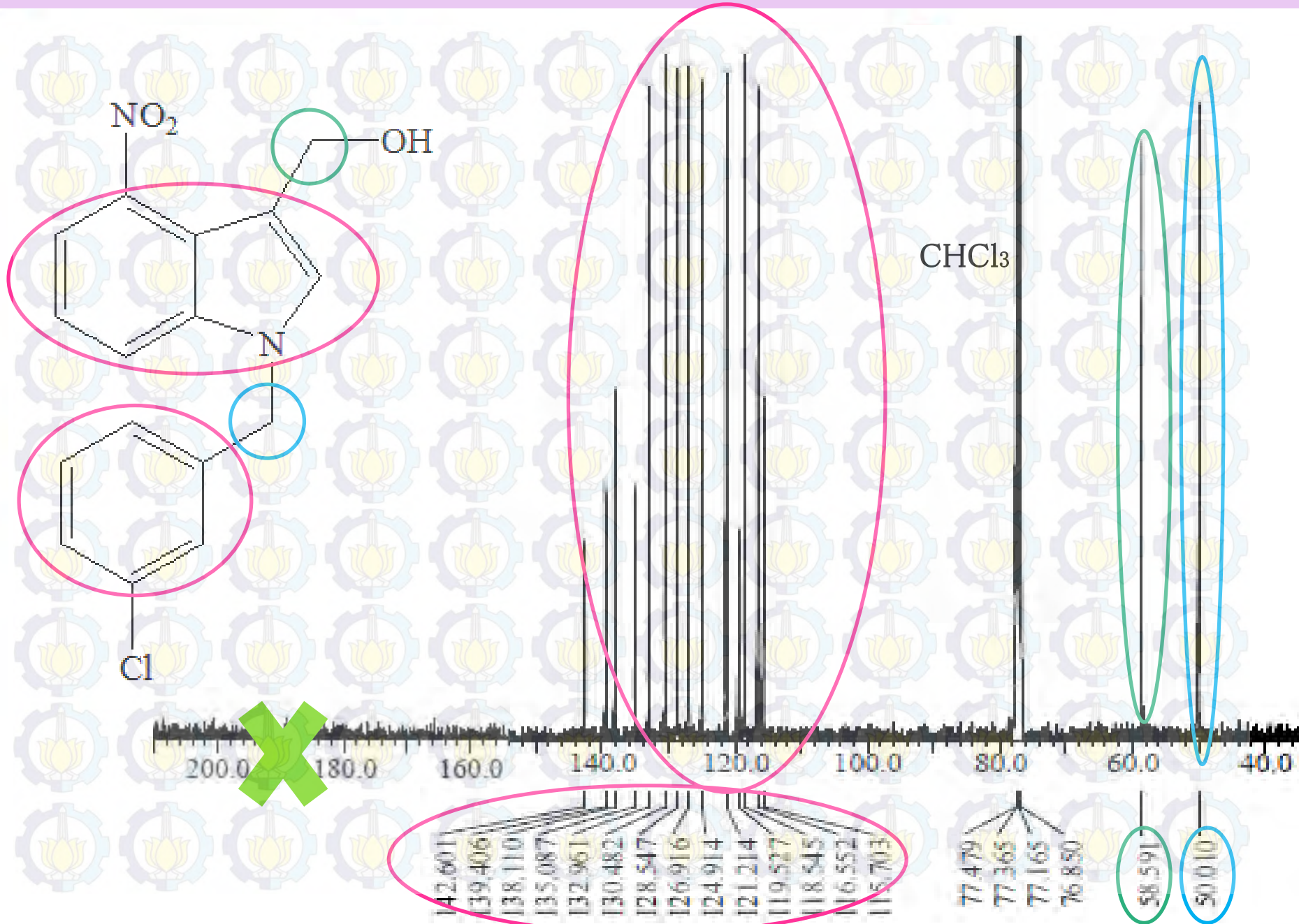
Titik Leleh : 112–113° C

Spektrum $^1\text{H-NMR}$ [1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7) hasil sintesis



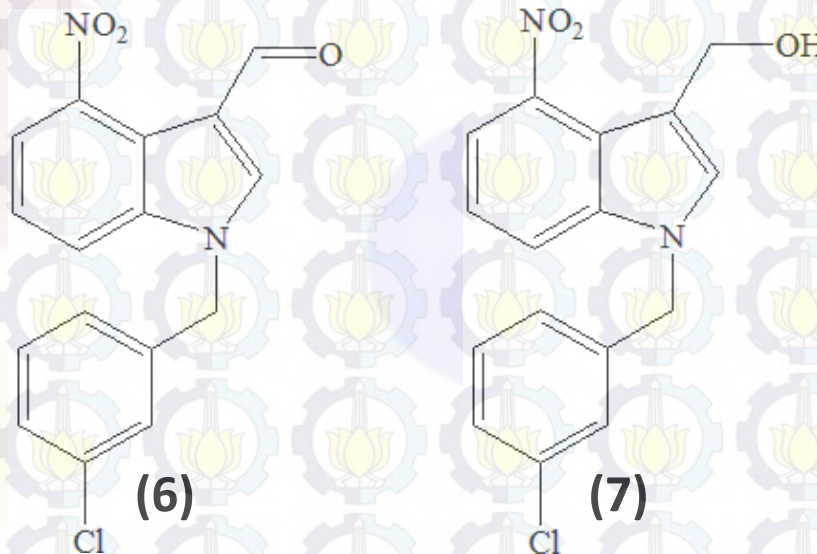
Pergeseran kimia (ppm)

Spektrum ^{13}C -NMR [1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7) hasil sintesis



Pergeseran kimia (ppm)

Perbandingan data $^1\text{H-NMR}$ turunan
4-nitroindola-3-karboksaldehida (6-7) (dalam ppm)

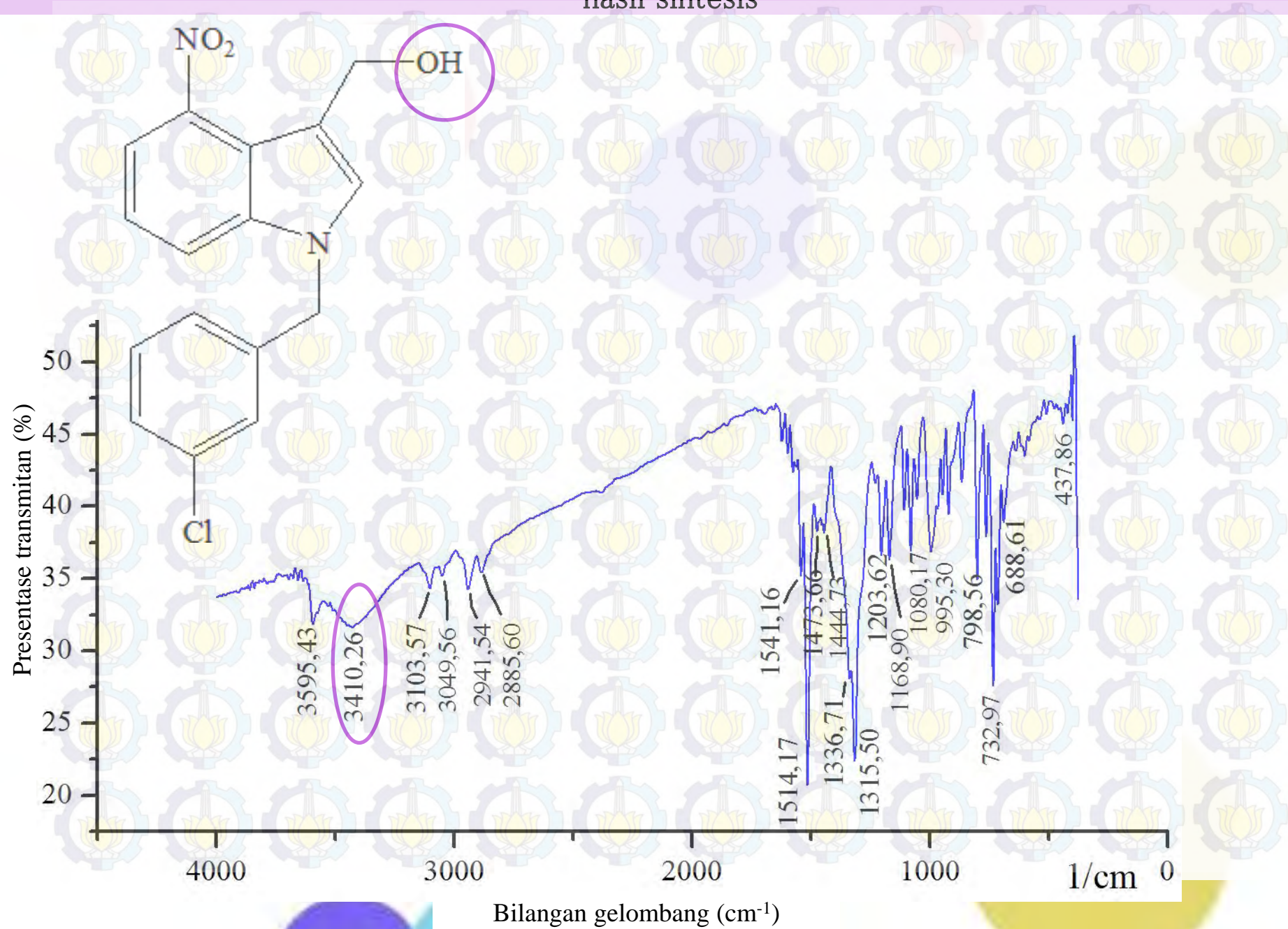


| Proton | Hasil Sintesis (6) | Hasil Sintesis (7) |
|-------------------------|---------------------|---------------------|
| <u>OH</u> | — | 2,60 (s,1H) |
| <u>CH₂OH</u> | — | 4,90 (s,2H) |
| <u>CH₂Ar</u> | 5,40 (s,2H) | 5,38 (s,2H) |
| <u>ArH</u> | 6,99–8,14 (m,8H) | 6,93–7,98 (m,8H) |
| <u>CHO</u> | 10,42 (s,1H) | — |

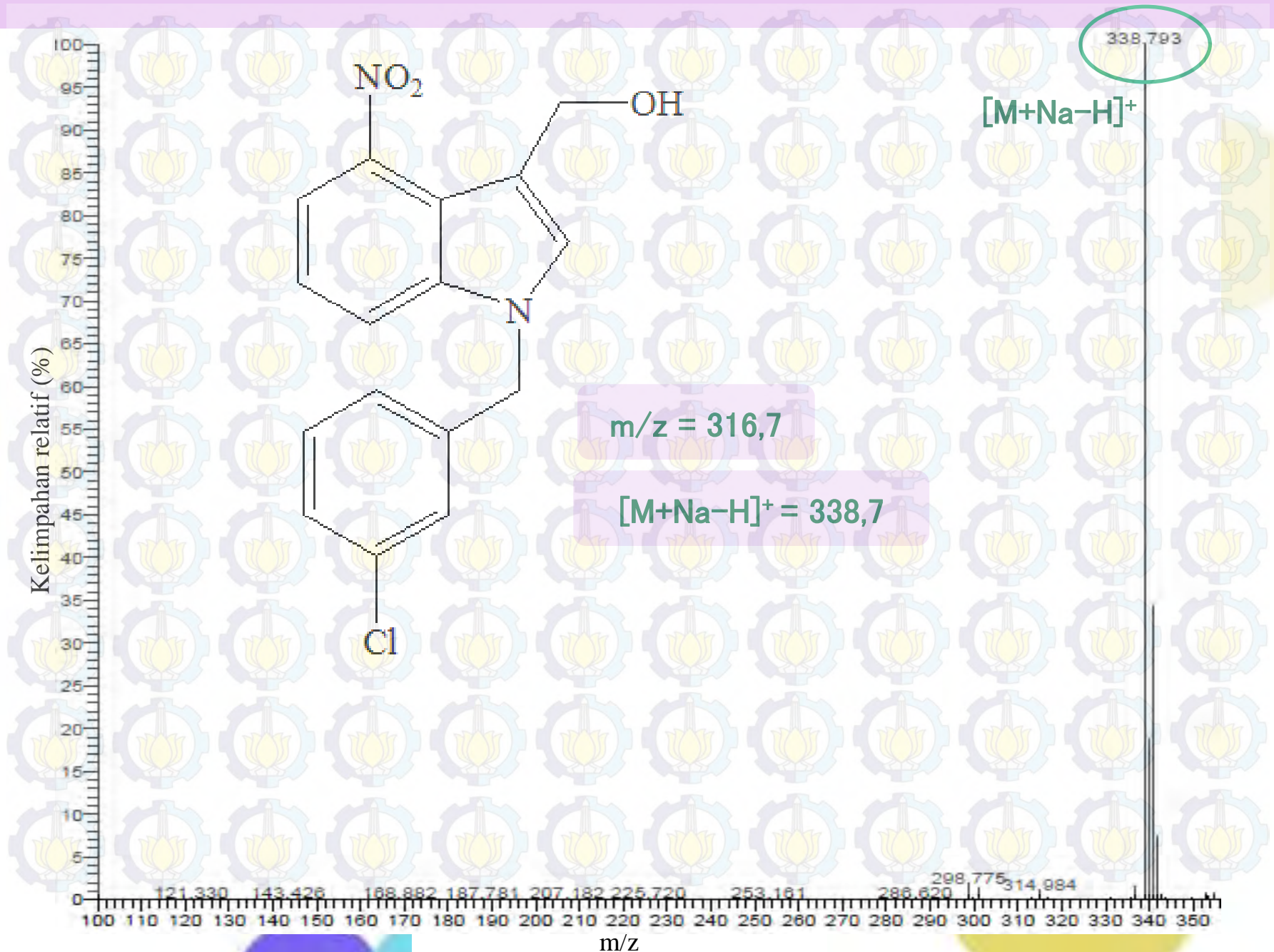
Perbandingan data ^{13}C -NMR turunan
4-nitroindola-3-karboksaldehida (6-7) (dalam ppm)

| Karbon | Hasil Sintesis (6) | Hasil Sintesis (7) |
|---|---|-----------------------|
| $\underline{\text{C}}\text{H}_2\text{OH}$ | – | 58,59 |
| $\underline{\text{C}}\text{H}_2\text{Ar}$ | 51,00 | 50,01 |
| $\text{Ar}\underline{\text{C}}$ | 117,36 | 115,70 |
| | 118,54 | 119,53 |
| | 135,46 | 135,09 |
| | 136,41 | 138,11 |
| | 139,15 | 139,41 |
| | 142,74 | 142,60 |
| | $\text{Ar}\underline{\text{C}}\text{H}$ | 117,12 |
| 120,30 | | 118,55 |
| 122,71 | | 121,21 |
| 125,15 | | 124,91 |
| 127,24 | | 126,92 |
| 129,17 | | 128,55 |
| 130,74 | | 130,48 |
| 138,01 | | 132,96 |
| $\underline{\text{C}}\text{HO}$ | 187,68 | – |

Spektrum infra merah [1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7) hasil sintesis



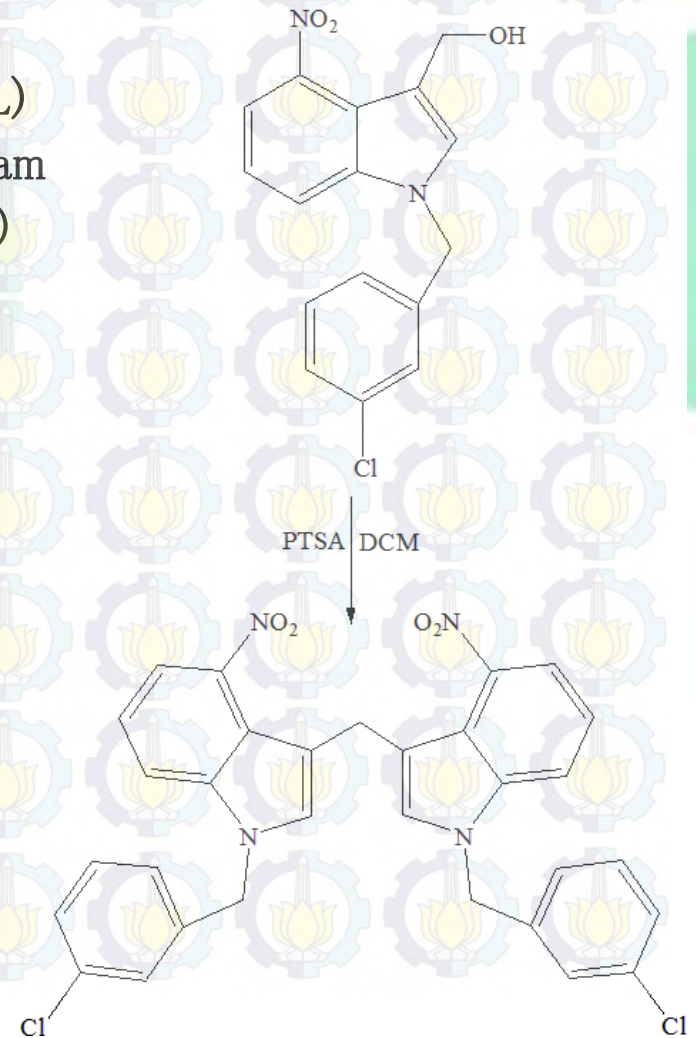
Spektrum massa (APCI) [1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7) hasil sintesis

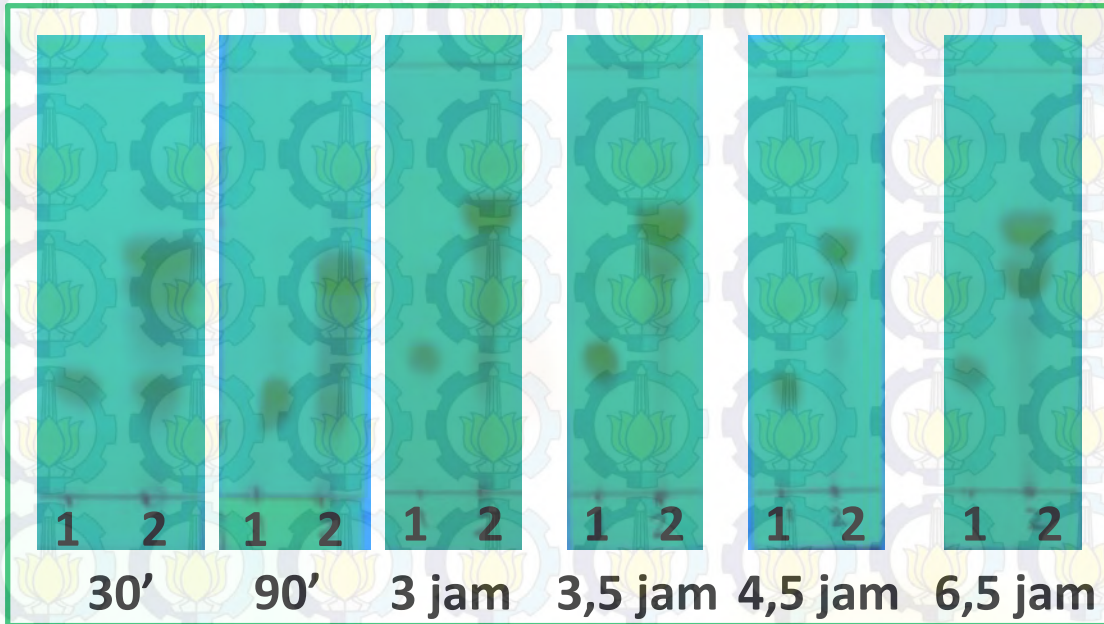


[1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7)
(0,10 g; 0,17 mmol)

PTSA (21)
(0,05 g; 0,26 mmol)

- dilarutkan dalam diklorometana (7 mL)
- diaduk pada suhu kamar selama 6,5 jam
(jalannya reaksi dipantau dengan KLT)





Keterangan :

1 = [1-(3-klorobenzil)-4-nitroindola-3-il]
 metanol (7)
 2 = hasil reaksi

Eluen :

n-heksana ; etil asetat (5:2)

[1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7)
(0,10 g; 0,17 mmol)

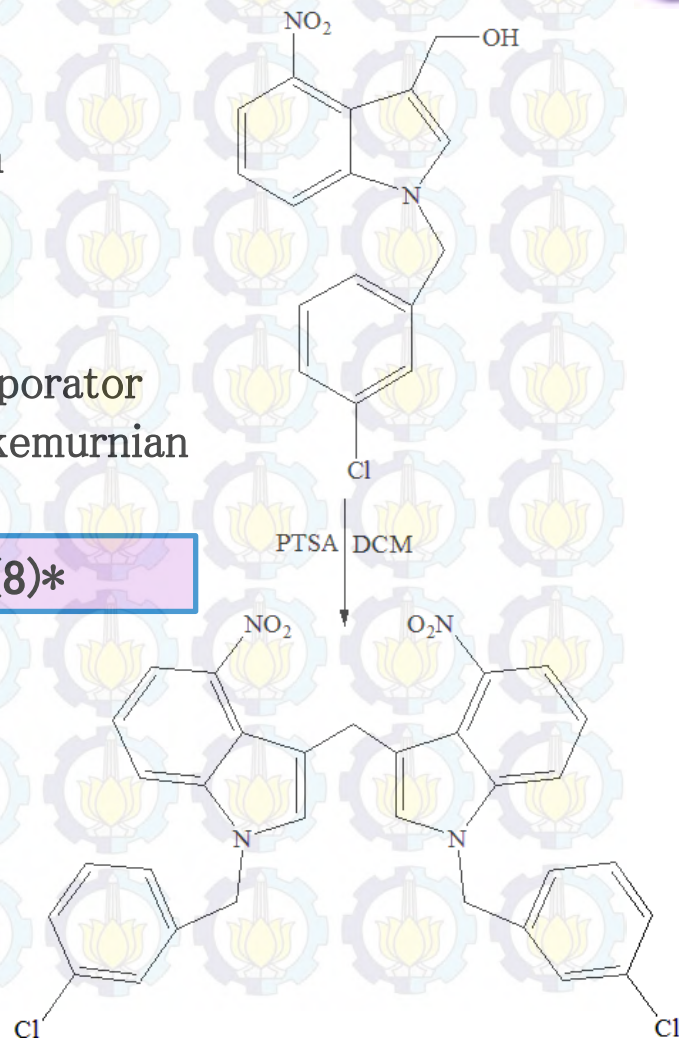
PTSA (21)
(0,05 g; 0,26 mmol)

- dilarutkan dalam diklorometana (7 mL)
- diaduk pada suhu kamar selama 6,5 jam
(jalannya reaksi dipantau dengan KLT)

Hasil reaksi

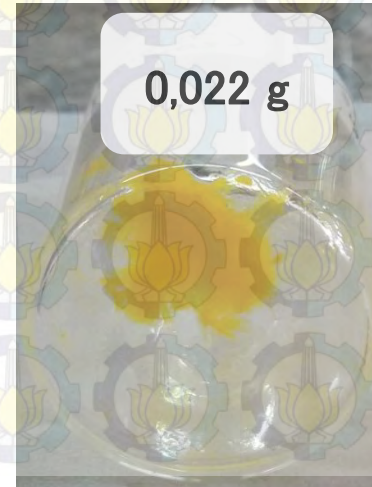
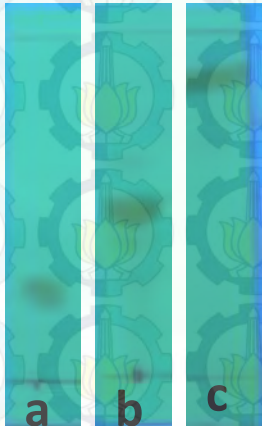
- diuapkan pelarutnya dengan rotary evaporator
- dimurnikan dengan KLT preparatif, uji kemurnian dengan KLT dan uji titik leleh

Bis(1-(3-klorobenzil)-4-nitroindola-3-il]metana (8)*





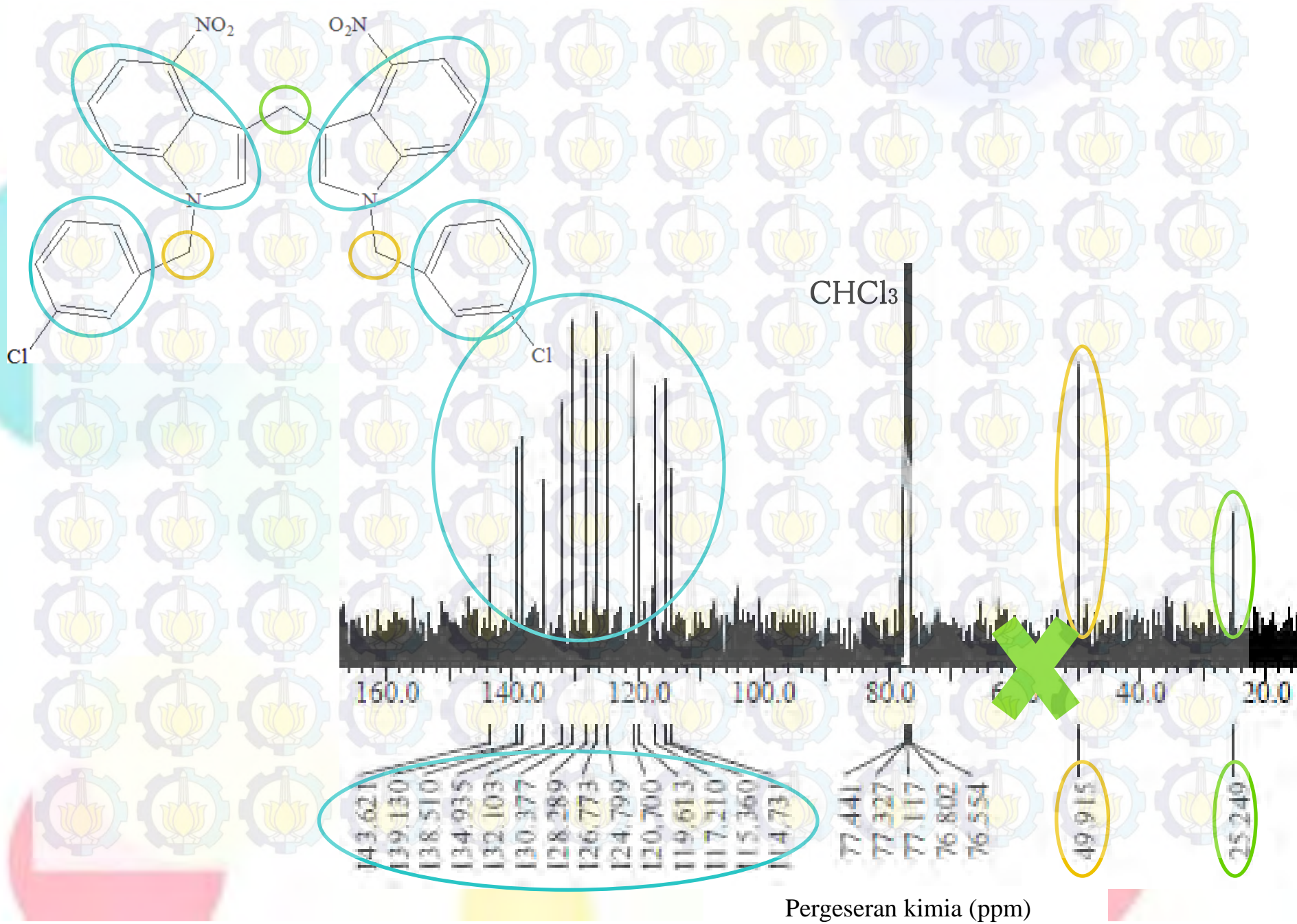
Eluen :
n-heksana ; etil asetat (5:2)



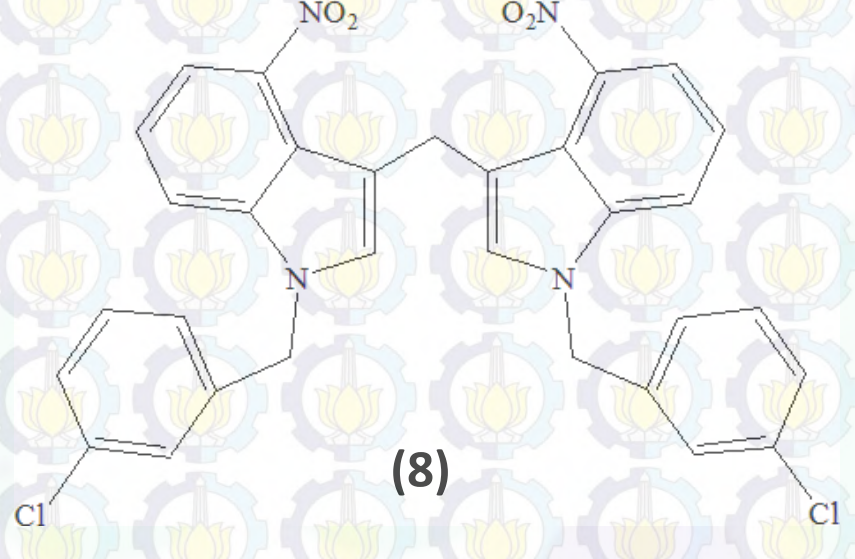
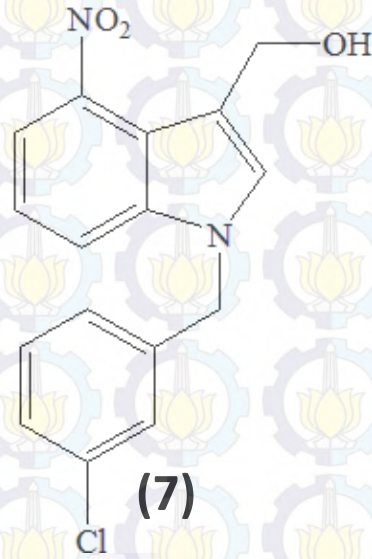
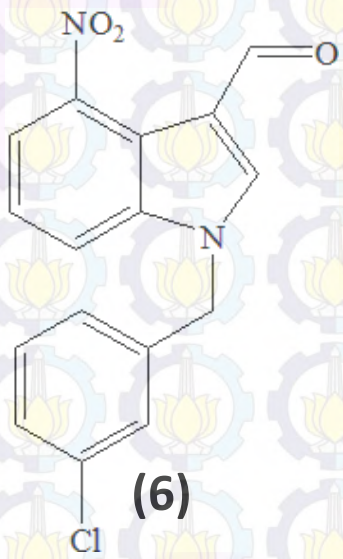
Keterangan eluen :
a = *n*-heksana : kloroform (4:2)
b = *n*-heksana : etil asetat (5:2)
c = *n*-heksana : diklorometana (1:2)

Titik Leleh : 165–166° C

Spektrum ^{13}C -NMR Bis(1-(3-klorobenzil)-4-nitroindola-3-il)metana (8) hasil sintesis



Perbandingan data $^1\text{H-NMR}$ turunan
4-nitroindola-3-karboksaldehida (6-8) (dalam ppm)

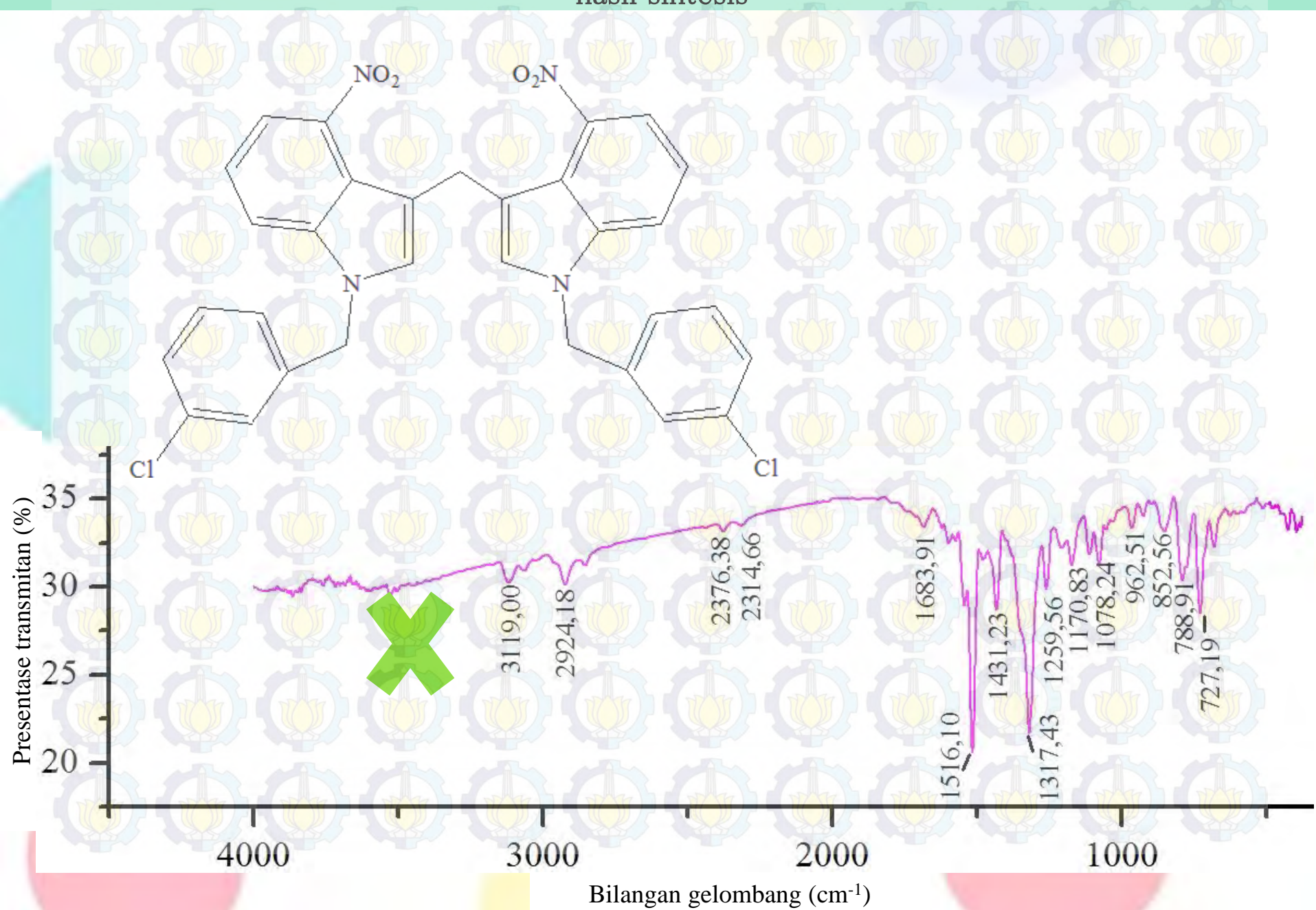


| Proton | Hasil Sintesis (6) | Hasil Sintesis (7) | Hasil Sintesis (8) |
|--------------------------|---------------------|---------------------|---------------------|
| OH | — | 2,60 (s,1H) | — |
| CH_2OH | — | 4,90 (s,2H) | — |
| ArCH_2Ar | — | — | 4,46 (s,2H) |
| CH_2Ar | 5,40 (s,2H) | 5,38 (s,2H) | 5,24 (s,2H) |
| ArH | 6,99–8,14 (m,8H) | 6,93–7,98 (m,8H) | 6,87–7,67 (m,8H) |
| CHO | 10,42 (s,1H) | — | — |

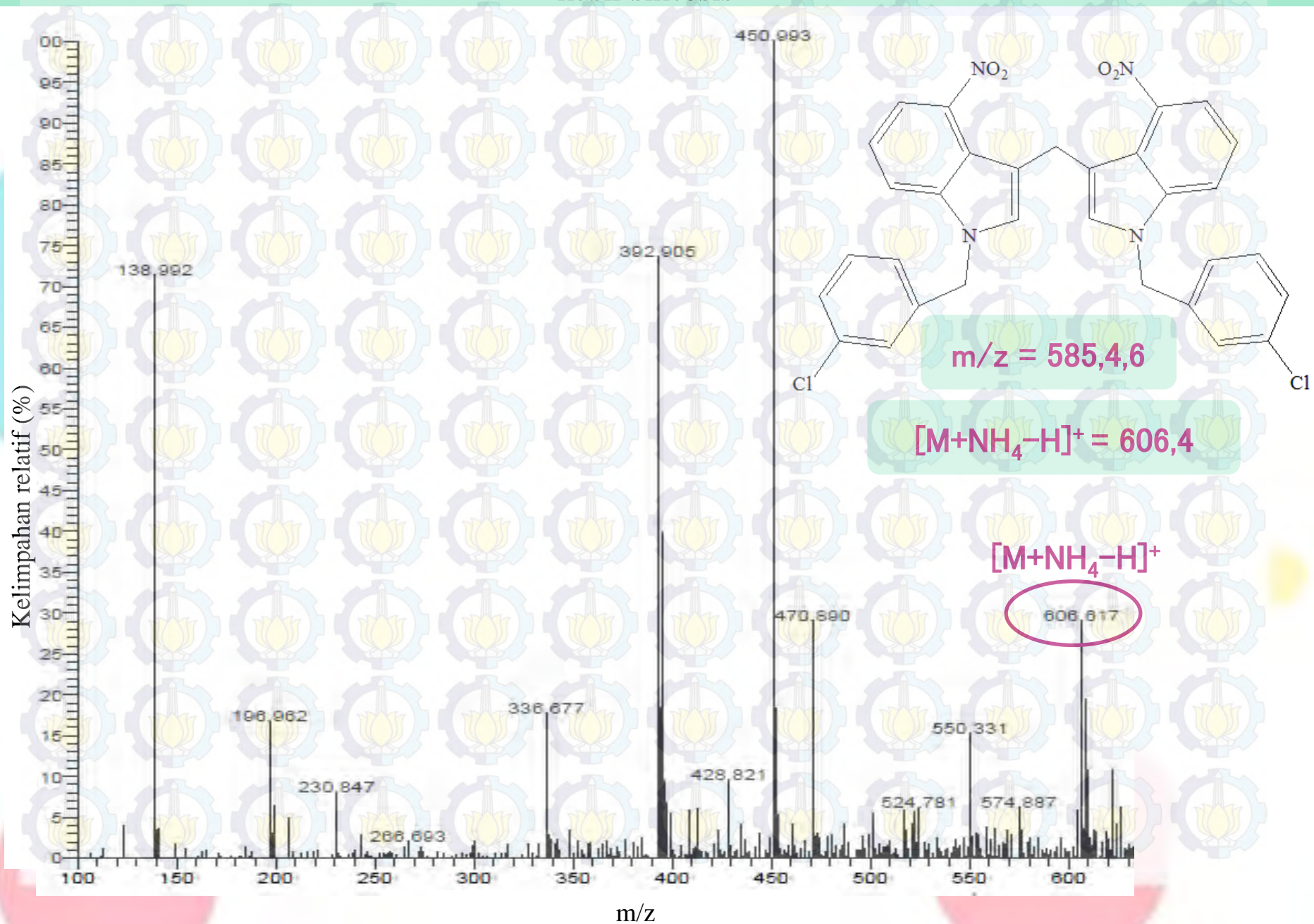
Perbandingan data ^{13}C -NMR turunan
4-nitroindola-3-karboksaldehida (6-8) (dalam ppm)

| Karbon | Hasil Sintesis (6) | Hasil Sintesis (7) | Hasil Sintesis (8) |
|------------------------------|-----------------------|-----------------------|-----------------------|
| Ar <u>CH</u> ₂ Ar | - | - | 25,25 |
| <u>CH</u> ₂ OH | - | 58,59 | - |
| <u>CH</u> ₂ Ar | 51,00 | 50,01 | 49,92 |
| Ar <u>C</u> | 117,36 | 115,70 | 114,73 |
| | 118,54 | 119,53 | 119,61 |
| | 135,46 | 135,09 | 134,94 |
| | 136,41 | 138,11 | 138,51 |
| | 139,15 | 139,41 | 139,13 |
| | 142,74 | 142,60 | 143,63 |
| Ar <u>CH</u> | 117,12 | 116,55 | 115,36 |
| | 120,30 | 118,55 | 117,20 |
| | 122,71 | 121,21 | 120,70 |
| | 125,15 | 124,91 | 124,81 |
| | 127,24 | 126,92 | 126,77 |
| | 129,17 | 128,55 | 128,29 |
| | 130,74 | 130,48 | 130,38 |
| | 138,01 | 132,96 | 132,10 |
| <u>CHO</u> | 187,68 | - | - |

Spektrum infra merah Bis(1-(3-klorobenzil)-4-nitroindola-3-il)metana (8) hasil sintesis



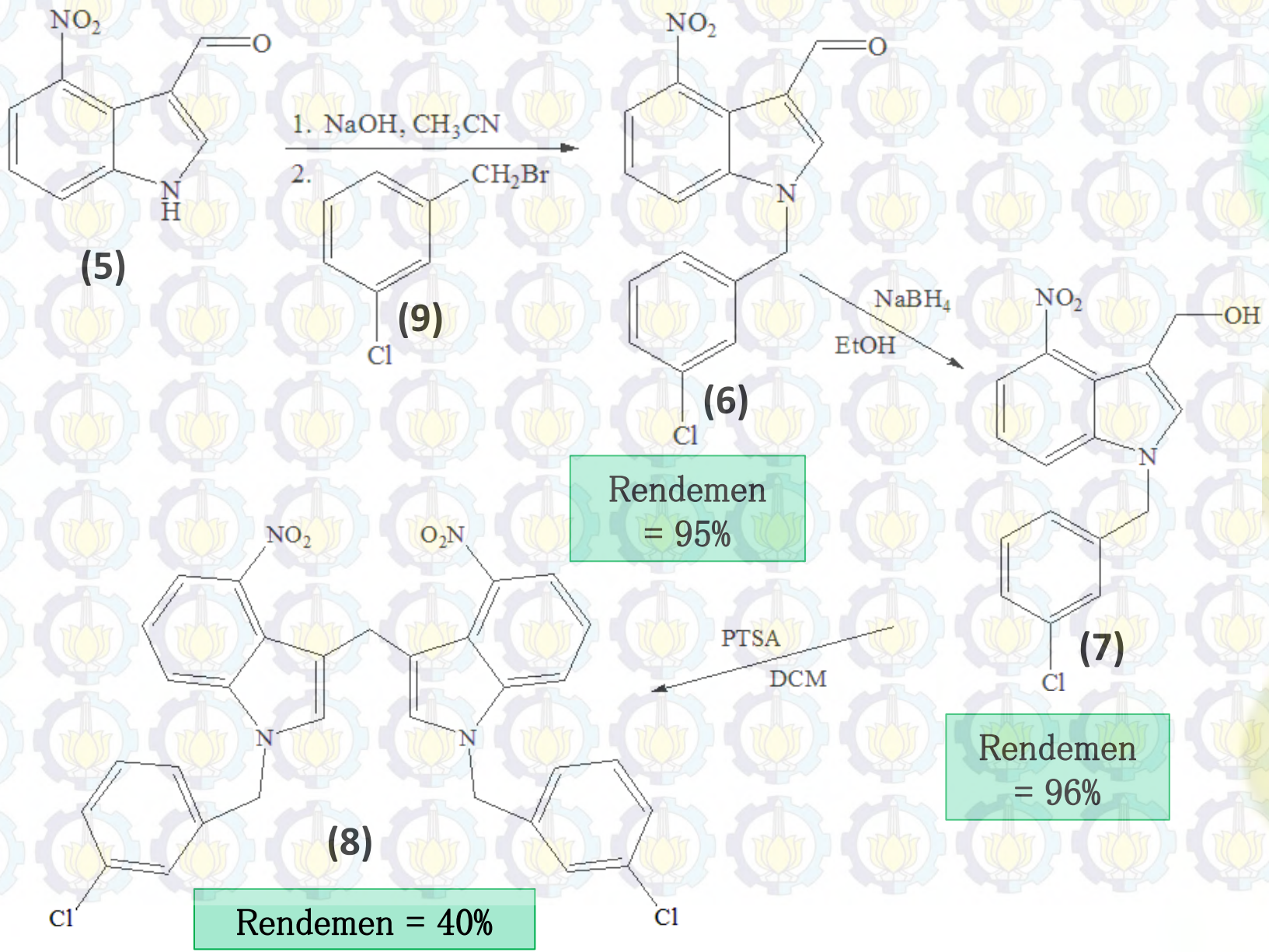
Spektrum massa (APCI) Bis(1-(3-klorobenzil)-4-nitroindola-3-il)metana (8) hasil sintesis





Kesimpulan

Kesimpulan



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Penguji

Ibu Lidia

UNAIR (Analisis NMR)

Bapak Kaliawan

POLINEMA (Analisis LCMS APCI)

Mas Erfan

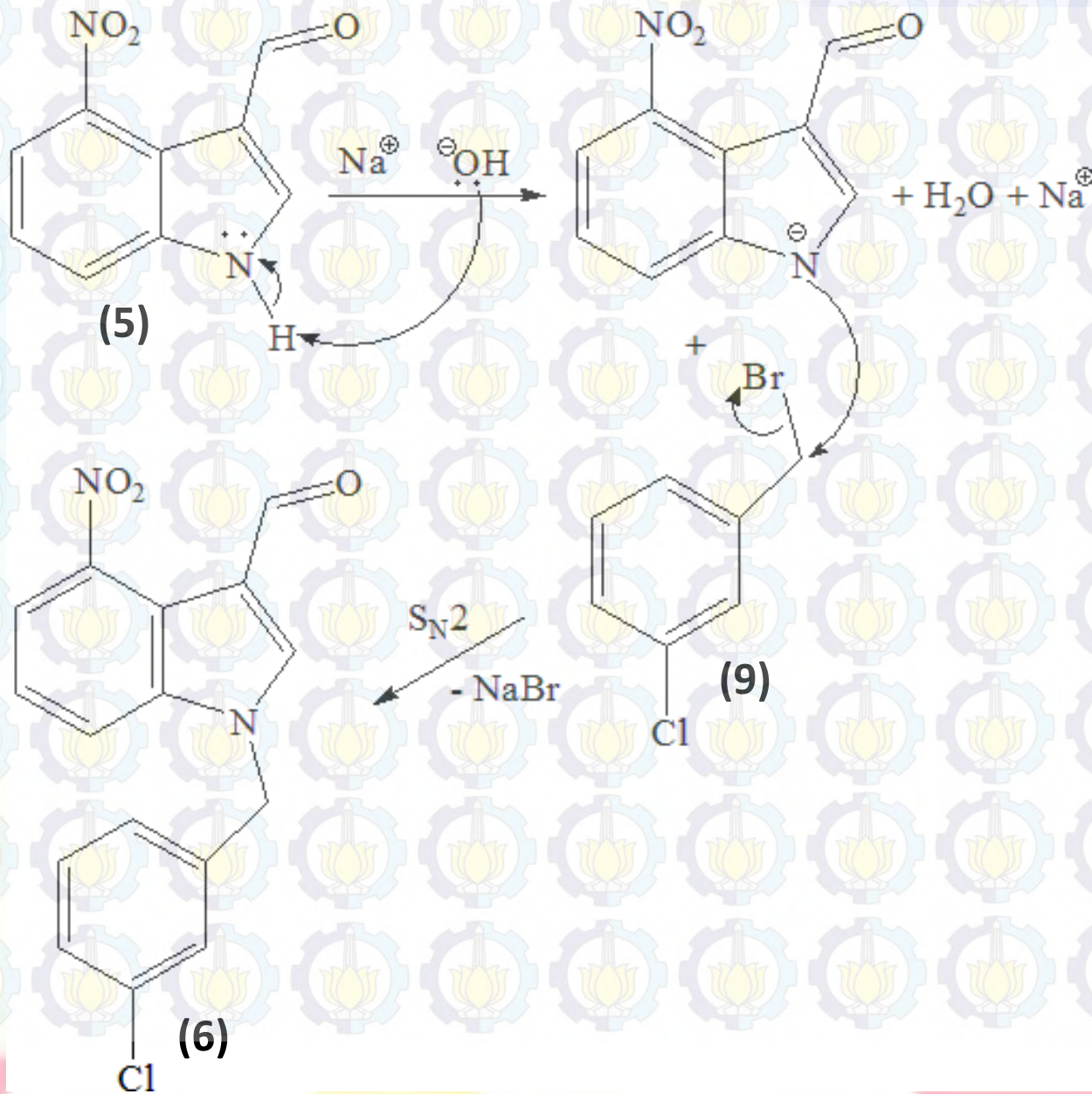
ITS (Analisis FTIR)

DP2M DIKTI

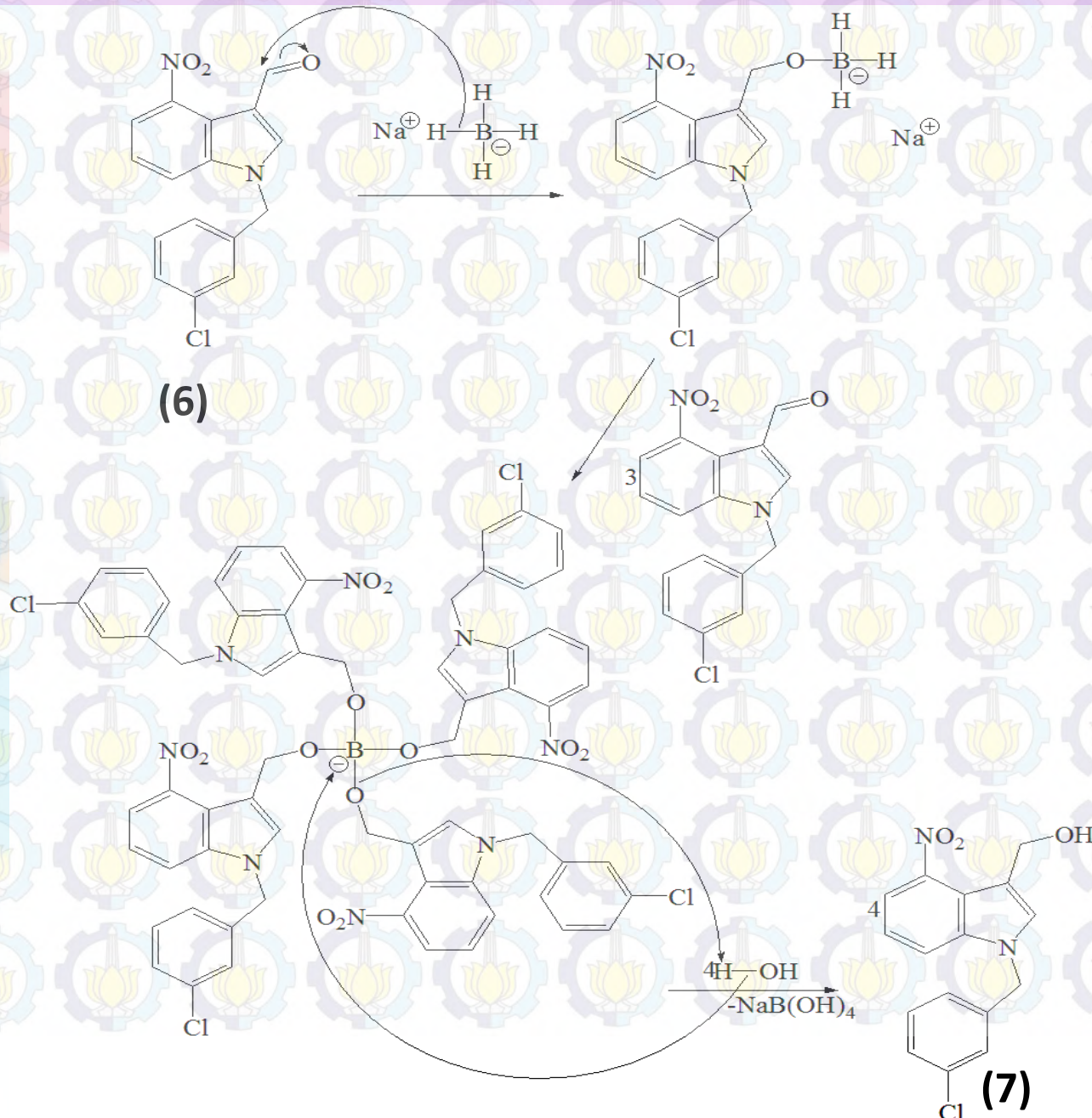
Hibah Penelitian

Mekanisme reaksi pembentukan

1-(3-Klorobenzil)-4-nitroindola-3-karbalehida (6) hasil sintesis

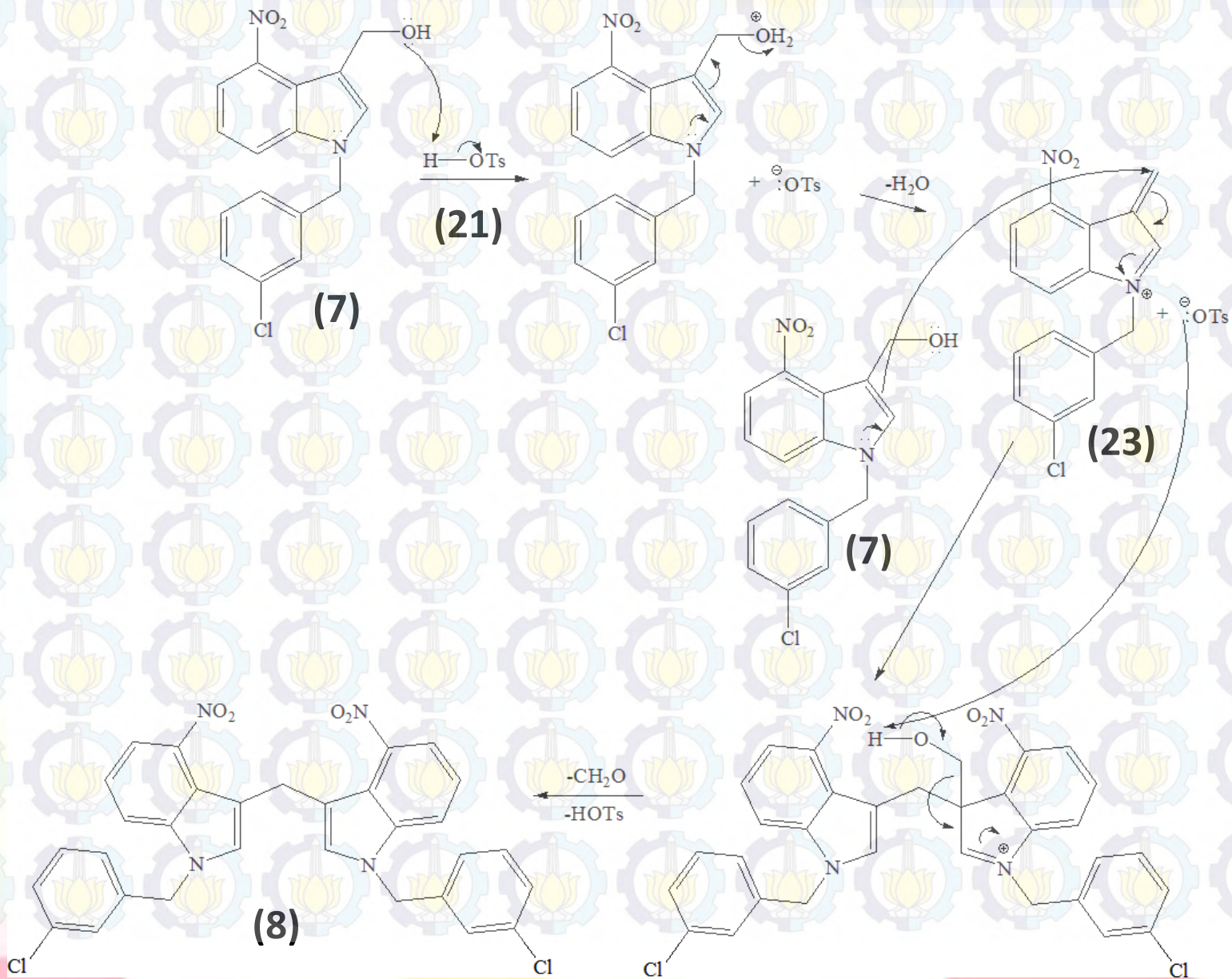


Mekanisme reaksi pembentukan [1-(3-Klorobenzil)-4-nitroindola-3-il]metanol (7) hasil sintesis

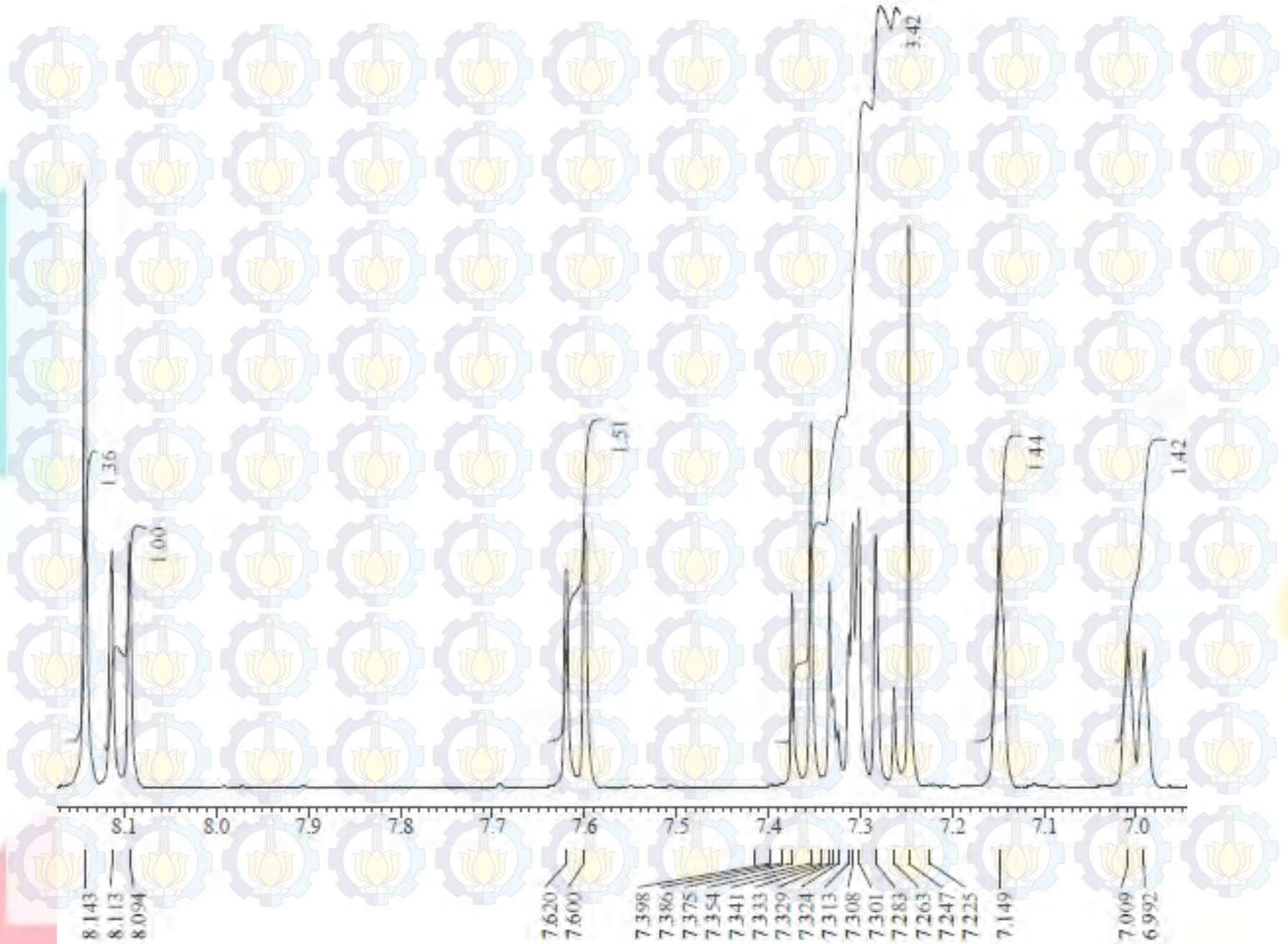


Mekanisme reaksi pembentukan

Bis(1-(3-klorobenzil)-4-nitroindola-3-il)metana (8) hasil sintesis



Spektrum $^1\text{H-NMR}$ 1-(3-Klorobenzil)-4-nitroindola-3-karbalehida (6) hasil sintesis



Pergeseran kimia (ppm)