

(72)

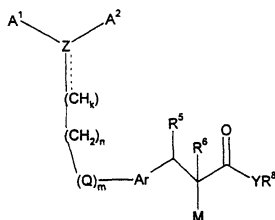
- 2900	1.	.	32
- 3520		27	
- 2830		121	
- 1864	2.	.	18
- 2400			48

(74)

:

(54)

AR) 1 / (PP
(I)



fer ator - Activated Receptors) (PPAR) / (Peroxisome Proli

(CAD) 2 (, 가)
 / ' 4 (deadly quartet)' (, 가)
 (hypolipidaemic fibrate)
 - , 2
 (dyslipidaemia)
 2 가 가
 - 가 (PPAR)
 - 가
 , PPAR PPAR
 PPAR 가
 (specialised proteins)
 , PPAR
 (link), 가
 PPAR (LPL),
 (FATP) -CoA (ACS) , 가
 ,
 PPAR
 PPAR -
 , PPAR HDL
 HDL , apo A - I apo A - II PPAR -
 (hypotriglyceridemic action) PPAR
 , : (I) apo C - 가
 , (II) -CoA
 -CoA , (III) - (IV)
 , (V) VLDL , VLDL
 (hypolipidemic effect)

(
 5,306,726, PCT W091/19702, WO 95/03038, WO 96/04260, WO 94/13650, WO 94/01420, WO 97
 /36579, WO 97/25042, WO 95/17394, WO 99/08501, WO 99/19313 WO 99/16758).

2
 2
 (overt hypertriglyceridaemia)

, R⁵ R⁶ 1 (, R⁵ , , C₁₋₆ - , C₁₋₆ - ,)

, 1 (, R⁵ , , R⁵ R⁶)

, 1 (, R⁵)

, C₂₋₆ - , C₂₋₆ - , R⁶ R⁵ 1 (, R⁶ , C₁₋₆ - , C₁₋₆ - , C₄₋₆ -)

R⁶ R⁵ 1 (, R⁶ , , C₁₋₆ - ,)

6 R⁵ 1 (, R⁶ , C₁₋₆ - , R)

, 1 (, R⁶)

, C₄₋₆ - , C₂₋₆ - , C₂₋₆ - , M OR⁷ , R⁷ , C₁₋₆ - , C₁₋₆ - , C₁₋₆ -)

, C₄₋₆ - , C₂₋₆ - , C₂₋₆ - , M OR⁷ , R⁷ , C₁₋₆ - , C₁₋₆ -)

, M COYR⁸ 1 (, M R⁷ C₁₋₆ - OR⁷)

M COYR⁸ 1 (, M R⁷ OR⁷ ,)

, C₂₋₆ - , 1 (, R⁸ , C₁₋₆ - , C₄₋₆ - , C₂₋₆)

, C₂₋₆ - , 1 (, R⁸ , C₁₋₆ - , C₄₋₆ - , C₂₋₆)

, 1 (, R⁸ C₁₋₆ -)

, 1 (, R⁸ ,)

, C₁₋₆ - , C₁₋₆ - , 1 (, Y , NR¹⁰ , R¹⁰ , R¹⁰)

, 5 6

1 (, Y NR¹⁰ , R¹⁰ , C₁₋₆
 Y가 NR¹⁰ , R⁸ R¹⁰ C₁₋₆ -)
 , 5 6) .

1 (, Y) .

1 (, k 1 2) .

1 (, n m 1) .

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2- -3- {4- [3- -3- (4-)-]- }- ,

2- -3- {4- [3- -3- (4-)- - }- ,

3- {4- [3- (2- -)-3- -]- }-2- - ,

3- {4- [3- (2- -)-3- -]- }-2- - ,

3- {4- [3,3- - (4- -)-]- }-2- - ,

3- {4- [3,3- - (4- -)-]- }-2- - ,

3- {4- [3- -3- (-4-)-]- }-2- - ,

3- {4- [3- -3- (-4-)-]- }-2- - ,

2- -3- {4- [3- -3- (-2-)-]- }- ,

2- -3- {4- [3- -3- (-2-)-]- }- ,

2- -3- {4- [3- -3- (-2-)-]- }- ,

2- -3- {4- [3- -3- (-2-)-]- }- ,

3- [4- (3,3- -)-]-2- - ,

3- [4- (3,3- -)-]-2- - ,

2- -3- {4- [3- -3- (4-)-]- }- ,

2- -3- {4- [3- -3- (4-)-]- }- ,

3- {4- [3- -3- (-4-)-]- }-2- - ,

3- {4- [3- -3- (-4-)-]- }-2- - ,

2- {4- [3,3- - (4- -)-]- }- ,

(E) - (2S) - 2 - 3 - {4 - [3 - (4 - 2 -) - 3 -] - } - ,

(E) - (2S) - 2 - 3 - {4 - [3 - (4 - 2 -) - 3 -] - } - ,

(E) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 - ,

(E) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 - ,

(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 - -

,

(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 - - ,

3 - {4 - [3,3 - (3 - 2 -) -] - } - 2 - - ,

3 - {4 - [3,3 - (4 -) -] - } - 2 - - ,

3 - {4 - [3,3 - (4 -) -] - } - 2 - - ,

2 - 3 - [4 - (3 - 3 - 4 -) -] - ,

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(E,Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 - 2 -] - } - ,

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(E,Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 - 2 -] - } - ,

(E,Z) - (2S) - 2 - 3 - [4 - (3 - 3 - p -) -] - ,

(E,Z) - (2S) - 2 - 3 - [4 - (3 - 3 - p -) -] - ,

(2S) - 3 - [4 - (3,3 -) -] - 2 - - ,

(2S) - 3 - [4 - (3,3 -) -] - 2 - - ,

(Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 -] - } - ,

(Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 -] - } - ,

(E) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 -] - } - ,

(E) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 -] - } - ,

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - - ,

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - - ,

(2S) - 3 - [4 - (3,3 - p -) -] - 2 - - ,

1가

5-6

9-10

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가 가

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C₁₋₆ -

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가 C₃₋₆ - C₁₋₆ - (C₃₋₆ -)C₁₋₆ - , 1 6 , (1

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C₁₋₆ -

C₁₋₆ -

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C₁₋₆ -

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J. Pharm. Sci. 1977,66,2,

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THF,

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" Enantiomers, Racemates and Resoluti

on" (Wiley Interscience, 1981)

Jaques

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nmr

X-

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, " Design

of Prodrugs" , ed. H. Bundgaard, Elsevier, 1985

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(PPAR)

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IGT

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2 /

IGT 2

- 2 2

/

(2), X

(apoptosis)

(PCOS)

가 1

가 1

가 - GHK (PPAR) 가 /

가 가

a) 2

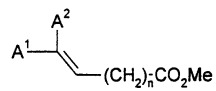
2



(A¹ A²) (Horner Emmons)

3

3

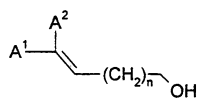


(, A¹ A²) .

3

4

4



(A¹ A²)
CH₂(CH₂)_nCH₂OH.Br BuLi 2

4

(Ph₃P)₃P

4

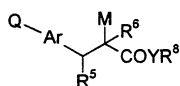
5

(Mitsunobo reaction)

(,) ,

5

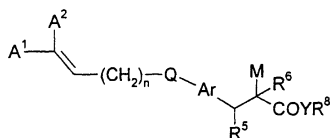
5



(, Q OH, SH , Ar, M, Y , R⁵ - R⁸)

1

(1)



(k=1 , A¹, A², Q, Ar, M, Y, n R⁵ - R⁸) .

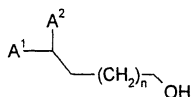
1 , A¹, A², Q, Ar, M, n R⁵ - R⁸ 가)

1(, Y O , k=1

4

6

6



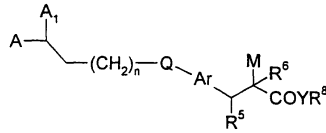
(A¹ A² n) :

6

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(1)



(, k=2 , A¹, A², Q, Ar, M, Y, n R⁵ - R⁸)

1 가 1(, Y O , k=2 , A¹, A², Q, Ar, M, n R⁵ - R⁸)

PPAR PPAR

PPAR (PPAR gene transcription activation assays)
 (reporter protein) HEK293
 GAL4 PPAR (LBD) D
 NA (DBD) PPAR LBD PPAR
 (PPAR ligand dependent transcription factor) (2
 = AF2) GAL4 DBD Gal4 (HEK293)
 Gal4
 , HEK293 GAL4 - DBD - PPAR - LBD
 Gal4 PPAR
 가 , PPAR
 가

: HEK293 DMEM + 10% FCS, 1% PS. Cells 96 -
 80% (confluency) 0.8 g DNA
 (Boehringer - Mannheim) FuGene 가

: PPAR cDNA PCR
 . Amplifie cDNAs pCR2.1 PPAR LBD PCR(PPAR : a
 a 167 - C - term; PPAR : aa 165 - C - term) pMI LBD p
 M1 LBD pM1 GAL4 - DBD
 Gal4 pGL2 (Promega)

: DMSO 가 1:1000 ()
 200µl 1:1000) 24 (Luciferase assay)

가 : $\approx 100 \mu\text{l}$ PBS incl. 1mM Mg⁺⁺ Ca⁺⁺
(Packard Instruments) LucLite kit
Packard Instruments top - counter SPC

1 가
/

BP (, CART () , NPY (Y) , MC4 (4)
, TNF () , CRF () , CRF
) , MCH (-) , CCK (3) , MSH (-
, 5HT ()
, UCP 2 3 (2 or 3) , TRH()
, DA (,
) , RXR (X) TR

Nordisk A/S) , GLP - 1 (- 1) WO 98/08871(Novo
WO 99/01423(Novo Nordisk A/S Agouron Pharmaceuticals, Inc.)
WO 97/26265 , DPP - IV (- IV) , GLP - 1
, HMG CoA (statins) /
, RXR (-) ATP

ATP -

ACE ()

Remington: The Science and Practice of Pharmacy, 19th Edition, Gennaro, Ed., Mack Publishing Co., Easton, PA, 1995

Remington: The Science and Practice of Pharmacy, 19th Edition, 1995

Remington: The Science and Practice of Pharmacy

:

HPMC approx. 9 mg

*Mywacett 9 - 40 T approx. 0.9 mg

* 가

(domestic animals),
 (nondomestic animals)

100 mg, 70 mg (regimen) 0.1 가 100 mg 0.1 10mg 70mg 가 0.05 0.1 mg

가 0.1 100 mg

0.001 100 mg, 0.01 50 mg 1 가

1 가

(MA), (NMR), (MS), NMR (d) W.
 (ppm), mp Merck 60 (Art 9
 C. Still et al, J. Org. Chem. 1978,43,2923 - 2925 385) 가

:

TLC:

DMSO:

CDCl₃:

DMF: N,N -

min:

h:

1

(E,Z) - 2 - 3 - { 4 - [3 - 3 - (4 -) -] - } -

THF 3 - 3 - (4 -) - - 2 - - 1 - (150mg, 0.6mmol),
 (195mg, 0.73mmol) 2 - 3 - (4 -) - (190mg, 0.79mmol)
 (0.11mL, 0.73mmol) 가 , 1.5 16
 가 ,
 (300mg)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.07 - 1.28 (6H, $2\times\text{CH}_3$), 2.30 - 2.40 (3H, CH_3), 2.90 - 2.93 (2H, CH_2), 3.30 - 3.40 3.51 - 3.61 (2H, OCH_2), 3.90 - 4.0 (1H, CHCO_2), 4.10 - 4.19 (2H, OCH_2), 4.41 - 4.61 (2H, OCH_2), 6.23 - 6.32 (1H, CH), 6.70 - 6.81 (2H,), 7.03 - 7.45 (H,).

$\text{C}_{29}\text{H}_{32}\text{O}_4$ MS 444.6, 444.2

2

(E,Z) - 2 - 3 - { 4 - [3 - 3 - (4 -) -] - } -

(E,Z) - 2 - 3 - { 4 - [3 - 3 - (4 -) -] - } - (1) (8)
 0mg, 0.18mmol) 1N NaOH(0.35mL) (0.35mL) 4 5 16
 가 (1mL) 가 6N HCl
 (48mg)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.07 - 1.20 (3H, CH_3), 2.32 - 2.40 (3H, CH_3), 2.85 - 3.10 (2H, CH_2), 3.30 - 3.45 3.51 - 3.68 (2H, OCH_2), 3.95 - 4.06 (1H, CHCO_2), 4.51-4.61 (2H, OCH_2) 6.21 - 6.41 (1H, CH), 6.72 - 6.82 (2H,), 7.03 - 7.50 (H,).

$\text{C}_{27}\text{H}_{28}\text{O}_4$ MS 416.5, 416.3

3

(E,Z) - 3 - { 4 - [3 - (2 -) - 3 -] - } - 2 - -

3 - (2 -) - 3 - - 2 - - 1 - (370mg, 1.5mmol),
 (0.5mL, 1.6mmol) 2 - 3 - (4 -) - (380mg, 1.6mmol)
 (403mg, 1.6mmol) 가 , 1 1
 (490mg)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.07 - 1.30 (6H, $2\times\text{CH}_3$), 2.90 - 2.95 (2H, CH_2), 3.29 - 3.40 3.52 - 3.63 (2H, OCH_2), 3.90 - 4.0 (1H, CHCO_2), 4.10 - 4.20 (2H, OCH_2), 4.35 - 4.56 4.70 - 4.80 (2H, OCH_2), 6.00 - 6.08 6.42 - 6.53 (1 H, CH), 6.70 - 6.81 (2H,), 7.06 - 7.55 (H,).

C₂₈ H₂₉ ClO₄ MS 465.0, 464.2.

4

(E,Z) - 3 - { 4 - [3 - (2 - -) - 3 - -] - } - 2 - -

(E,Z) - 3 - { 4 - [3 - (2 - -) - 3 - -] - } - 2 - - (3)
 (400mg, 0.86mmol) 2 가 (353mg) .

¹H NMR (CDCl₃, 300 MHz); 1.09 - 1.20 (3H, CH₃), 2.85 - 3.10 (2H, CH₂), 3.30 - 3.42 3.51 - 3.65 (2 H, OCH₂), 3.96 - 4.05 (1H, CHCO₂), 4.35 - 4.50 4.70 - 4.74 (2H, OCH₂) 6.00 - 6.05 6.42 - 6.49 (1 H, CH), 6.71 - 6.82 (2H,), 7.05 - 7.50 (H,).

C₂₆ H₂₅ ClO₄ MS 436.9, 436.2.

5

3 - { 4 - [3,3 - - (4 - -) -] - } - 2 - -

1 3,3 - (4 - -) - - 2 - - 1 - (216mg, 0.8mmol),
 (240mg, 0.9mmol), 2 - - 3 - (4 - -) - - (240mg, 1.0mmol)
 (0.11mL, 0.9mmol) (90mg) .

¹H NMR (CDCl₃, 300 MHz); 1.10 - 1.30 (6H, 2xCH₃), 2.90 - 2.95 (2H, CH₂), 3.29 - 3.39 3.52 - 3.65 (2H, OCH₂), 3.78 (3H, OCH₃), 3.82 (3H, OCH₃), 3.90 - 3.99 (1H, CHCO₂), 4.10 - 4.20 (2H, OCH₂), 4.51 - 4.59 (1 H, OCH₂) 6.12 - 6.19 (1H, CH), 6.70 - 7.45 (H,).

C₃₀ H₃₄ O₆ MS 490.6, 488.3.

6

3 - { 4 - [3,3 - - (4 - -) -] - } - 2 - -

3 - { 4 - [3,3 - - (4 - -) -] - } - 2 - - (5) (80m
 g, 0.16mmol) 2 가 (29mg) .

¹H NMR (CDCl₃, 300 MHz); 1.12 - 1.20 (3H, CH₃), 2.87 - 3.09 (2H, CH₂), 3.32 - 3.49 3.52 - 3.63 (2 H, OCH₂), 3.78 (3H, OCH₃), 3.82 (3H, OCH₃), 3.99 - 4.02 (1H, OCH₂) 6.12 - 6.19 (1H, CH), 6.72 - 7.23 (H,).

C₂₈ H₃₀ O₆ MS 462.5, 462.1

7

(E,Z) - 3 - { 4 - [3 - - 3 - (- 4 -) -] - } - 2 - -

1 3 - - 3 - (- 4 -) - - 2 - - 1 - (250mg, 0.66mmol),
 (195mg, 0.73mmol), 2 - - 3 - (4 - -) - - (190mg, 0.79mmol)
 (0.11mL, 0.79mmol) (180mg) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.10 - 1.32 (6H, $2\times\text{CH}_3$), 2.89 - 2.95 (2H, CH_2), 3.28 - 3.39 (2H, OCH_2), 3.52 - 3.63 (2H, OCH_2), 3.91 - 3.96 (1H, CHCO_2), 4.08 - 4.20 (2H, OCH_2), 4.51 - 4.62 (1H, OCH_2), 6.29 - 6.41 (1H, CH), 6.61 - 6.70 (1H, CH), 6.72 - 7.80 (2H,), 7.08 - 7.18 (2H,), 7.20 - 7.70 (H,).

$\text{C}_{34}\text{H}_{34}\text{O}_4$ MS 506.6, 504.2

8

(E,Z) - 3 - { 4 - [3 - 3 - (- 4 -) -] - } - 2 - -

(E,Z) - 3 - { 4 - [3 - 3 - (- 4 -) -] - } - 2 - - (7)
(70mg, 0.13mmol) 2 가 (25mg) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.02 - 1.23 (3H, CH_3), 2.83 - 3.12 (2H, CH_2), 3.32 - 3.50 (2H, OCH_2), 3.52 - 3.63 (2H, OCH_2), 3.96 - 4.07 (1H, CHCO_2), 4.51 - 4.70 (1H, OCH_2), 6.39 - 6.41 (1H, CH), 6.72 - 7.82 (2H,), 7.01 - 7.65 (H,).

$\text{C}_{32}\text{H}_{30}\text{O}_4$ MS 478.6, 478.2

9

(E,Z) - 2 - 3 - { 4 - [3 - 3 - (- 2 -) -] - } -

3 3 - 3 - (- 2 -) - - 2 - - 1 - (320mg, 1.5mmol),
(0.4mL, 1.6mmol), 2 - 3 - (4 - -) - (380mg, 1.6mmol)
(403mg, 1.6mmol) (290mg) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.08 - 1.32 (6H, $2\times\text{CH}_3$), 2.90 - 2.99 (2H, CH_2), 3.28 - 3.39 (2H, OCH_2), 3.52 - 3.63 (2H, OCH_2), 3.91 - 3.99 (1H, CHCO_2), 4.08 - 4.21 (2H, OCH_2), 4.42 - 4.50 (2H, OCH_2), 4.72 - 4.80 (1H, OCH_2), 6.19 - 6.25 (1H, CH), 6.32 - 6.39 (1H, CH), 6.62 - 7.48 (H,).

$\text{C}_{26}\text{H}_{28}\text{O}_4\text{S}$ MS 436.6, 436.1.

10

(E,Z) - 2 - 3 - { 4 - [3 - 3 - (- 2 -) -] - } -

(E,Z) - 2 - 3 - { 4 - [3 - 3 - (- 2 -) -] - } - (9)
(200mg, 0.45mmol) 2 가 (94mg) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.12 - 1.31 (3H, CH_3), 2.88 - 3.10 (2H, CH_2), 3.28 - 3.48 (2H, OCH_2), 3.52 - 3.58 (2H, OCH_2), 3.96 - 4.03 (1H, CHCO_2), 4.42 - 4.48 (2H, OCH_2), 4.76 - 4.80 (1H, OCH_2), 6.19 - 6.22 (1H, CH), 6.65 - 7.48 (H,).

$\text{C}_{24}\text{H}_{24}\text{O}_4\text{S}$ MS 408.5, 408.2.

11

2 - 3 - { 4 - [3 - 3 - (- 2 -) -] - } -

3 (0.42mL, 1.6mmol), 2- (403mg, 1.6mmol) 3- (320mg, 1.5mmol), -3- (380mg, 1.6mmol) -2- (650mg) -1- (380mg, 1.6mmol)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.10 - 1.30 (6H, $2\times\text{CH}_3$), 2.90 - 2.95 (2H, CH_2), 3.28 - 3.39 3.51 - 3.62 (2H, OCH_2), 3.90 - 3.95 (1H, CHCO_2), 4.05 - 4.20 (2H, OCH_2), 4.53 - 4.59 (1H, OCH_2) 6.72 - 6.78 (1 H, C H), 6.95 - 7.60 (H,), 8.58 - 8.61 (1 H,).

$\text{C}_{27}\text{H}_{29}\text{O}_4\text{N}$ MS 431.5, 431.3.

12

2- (110mg) 3- (110mg) -3- (110mg) -2- (110mg) -1- (110mg)

2- (110mg) 3- (110mg) -3- (110mg) -2- (110mg) -1- (110mg) (11) (210mg, 0.48mmol) 가 (110mg)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.10 - 1.18 (3H, CH_3), 2.82 - 3.04 (2H, CH_2), 3.28 - 3.39 3.51 - 3.62 (2 H, OCH_2), 3.92 - 3.97 (1H, CHCO_2), 4.53 - 4.65 (1H, OCH_2) 6.70 - 6.78 (1H, CH), 6.88 - 7.62 (H,), 8.58 - 8.62 (1H,).

$\text{C}_{25}\text{H}_{25}\text{O}_4\text{N}$ MS 403.5, 403.2.

13

3- (110mg) 4- (110mg) -3- (110mg) -2- (110mg) -1- (110mg)

1 (110mg, 0.5mmol), (145mg, 0.55mmol), 2- (140mg, 0.6mmol) -3- (120mg) (0.09mL, 0.55mmol)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.10 - 1.29 (6H, $2\times\text{CH}_3$), 2.44 - 2.55 (2H, CH_2), 2.90 - 2.95 (2H, CH_2), 3.28 - 3.39 3.51 - 3.62 (2H, OCH_2), 3.80 - 3.89 (2H, CH_2), 3.90 - 3.95 (1H, CHCO_2), 4.10 - 4.28 (3H, CH OCH_2), 6.70 - 6.77 (2H,), 7.05 - 7.35 (H,).

$\text{C}_{28}\text{H}_{32}\text{O}_4$ MS , 432.6, 432.3.

14

3- (110mg) 4- (110mg) -3- (110mg) -2- (110mg) -1- (110mg)

3- (110mg) 4- (110mg) -3- (110mg) -2- (110mg) -1- (110mg) (13) (110mg, 0.25mmol) 가 (55mg) ..

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.10 - 1.19 (3H, CH_3), 2.42 - 2.55 (2H, CH_2), 2.87 - 3.08 (2H, CH_2), 3.30 - 3.47 3.51 - 3.62 (2H, OCH_2), 3.80 - 3.89 (2H, CH_2), 3.98 - 4.03 (1H, CHCO_2), 4.10 - 4.25 (1H, CH), 6.70 - 6.77 (2H,), 7.05 - 7.35 (H,).

$\text{C}_{26}\text{H}_{28}\text{O}_4$ MS , 404.5 404.3.

15

2- -3- {4- [3- -3- (4-) -]- } -

3- -3- (4-) - 2- -1- (210mg, 0.88mmol), (0.25mL, 1.0mmol), 2-
-3- (4- -) - (240mg, 1.0mmol) (250m
g, 1.0mmol) 3 (160mg) .

¹H NMR (CDCl₃, 300 MHz); 1.07 - 1.28 (6H, 2xCH₃), 2.29 (3H, CH₃), 2.42 - 2.49 (2H, CH₂), 2.89 - 2.93 (2H, CH₂), 3.25 - 3.40 3.51 - 3.61 (2H, OCH₂), 3.88 - 3.85 (2H, CH₂), 3.90 - 4.00 (1H, CHCO₂), 4.10 - 4.19 (3H, CH OCH₂), 6.69 - 6.73 (2H,), 7.03 - 7.29 (H,).

C₂₉ H₃₄ O₄ MS 446.6, 446.3.

16

2- -3- {4- [3- -3- (4-) -]- } -

2- -3- {4- [3- -3- (4-) -]- } - (15) (130mg,
0.30mmol) 2 가 (55mg) .

¹H NMR (CDCl₃, 300 MHz); 1.11 - 1.21 (3H, CH₃), 2.29 (3H, CH₃), 2.42 - 2.53 (2H, CH₂), 2.83 - 3.12 (2H, CH₂), 3.38 - 3.50 3.51 - 3.63 (2H, OCH₂), 3.80 - 3.88 (2H, CH₂), 3.99 - 4.05 (1H, CHCO₂), 4.12 - 4.22 (1H, CH), 6.69 - 6.73 (2H,), 7.03 - 7.29 (H,).

C₂₇ H₃₀ O₄ MS 418.5, 418.3.

17

3- {4- [3- -3- (-4-) -]- } - 2- -

1 3- -4- -3- - -1- (145mg, 0.5mmol), (145m
g, 0.55mmol), 2- -3- (4- -) - (140mg, 0.6 mmol)
(0.09mL, 0.55mmol) (230mg) .

¹H NMR (CDCl₃, 300 MHz); 1.07 - 1.28 (6H, 2xCH₃), 2.48 - 2.55 (2H, CH₂), 2.89 - 2.93 (2H, CH₂), 3.25 - 3.40 3.51 - 3.63 (2H, OCH₂), 3.88 - 4.00 (3H, CH₂ CHCO₂), 4.10 - 4.19 (2H, OCH₂), 4.20 - 4.30 (1H, CH), 6.67 - 6.71 (2H,), 7.05 - 7.55 (H,).

C₃₄ H₃₆ O₄ MS 508.7, 508.3.

18

3- {4- [3- -3- (-4-) -]- } - 2- -

3- {4- [3- -3- (-4-) -]- } - 2- - (17) (200m
g, 0.39mmol) 2 가 (70mg) .

¹H NMR (CDCl₃, 300 MHz); 1.07 - 1.20 (3H, CH₃), 2.49 - 2.61 (2H, CH₂), 2.88 - 3.09 (2H, CH₂), 3.32 - 3.48 3.51 - 3.66 (2H, OCH₂), 3.88 - 3.92 (2H, CH₂) 3.95 - 4.05 (1H, CHCO₂), 4.20 - 4.30 (1 H, CH), 6.67 - 6.79 (2H,), 7.05 - 7.55 (H,).

C₃₂ H₃₂ O₄ MS 480.6, 480.3.

19

2 - { 4 - [3,3 - (4 - -) -] - } -

, 3,3 - (4 - -) - - 2 - - 1 - (500mg, 1.95 mmol), (42
4mg, 2.1 mmol) 2 - (4 - -) - (464mg, 1.95 mmol) (50 mL)
(ADDP) (530mg, 2.1mmol) 0 가
. 10 , 16 (10 mL) 가
- ADDP / (4:1)
150 mg (16%)

¹H NMR (CDCl₃, 300 MHz); 3.15 (2H, PhCH₂), 3.63 (1H, CH), 3.70 (6H, 2xCO₂CH₃), 3.80 (3H, PhOC
H₃), 3.83 (3H, PhOCH₃), 4.55 (1H, OCH₂), 6.15 (1H, CH), 6.70 - 7.20 (H,).

20

(E) - (2S) - 2 - - 3 - { 4 - [3 - (4 - - 2 - -) - 3 - -] - } -

3 (E) - 3 - (4 - - 2 - -) - 3 - - 2 - - 1 - (475mg, 1.7
2mmol), (0.63ml, 2.58mmol), (2S) - 2 - - 3 - (4 - -) -
(451mg, 1.89mmol) (650mg, 2.58mmol) (450mg, 53
%)

¹H NMR (CDCl₃, 300 MHz); 1.16 (3H, t), 1.21 (3H, t), 2.93 (2H, d), 3.26 - 3.40 (1H, m), 3.52 - 3.64
(1H, m), 3.94 (1H, t), 4.14 (2H, q), 4.58 (2H, d), 6.36 (1H, t), 6.47 (1H, dd), 6.63 (1H, d), 6.77 (2H, d
m), 7.12 (2H, dm), 7.16 - 7.31 (4H, m), 7.31 - 7.50 (4H, m), 7.58 (2H, dm).

21

(E) - (2S) - 2 - - 3 - { 4 - [3 - (4 - - 2 - -) - 3 - -] - } -

(E) - (2S) - 2 - - 3 - { 4 - [3 - (4 - - 2 - -) - 3 - -] - } -
(20) (440mg, 0.89mmol) 2 가 (408mg, 97%)

¹H NMR (CDCl₃, 300 MHz); 1.17 (3H, t), 2.93 (1H, dd), 3.07 (1H, dd), 3.39 - 3.52 (1H, m), 3.52 - 3.6
4 (1H, m), 4.04 (1H, dd), 4.58 (2H, d), 6.36 (1H, t), 6.48 (1H, m), 6.63 (1H, d), 6.79 (2H, dm), 7.12 (2
2H, dm), 7.16 - 7.32 (4H, m), 7.32 - 7.50 (4H, m), 7.59 (2H, dm), COOH.

LCMS (): 491 (M+Na), 259 (100%).

22

(E) - (2S) - 3 - [4 - (3 - - 4 - - 3 - -) -] - 2 - -

3 (E) - 3 - - 4 - - 3 - - - 2 - - 1 - (1.0g, 3.49mmol),
(1.3ml, 5.24mmol), (2S) - 2 - - 3 - (4 - -) - (0.92g,
3.84 mmol) (1.32g, 5.24 mmol) (1.47g, 83%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.16 (3H, t), 1.21 (3H, t), 2.95 (2H, d), 3.28 - 3.40 (1H, m), 3.533.65 (1H, m), 3.95 (1H, t), 4.15 (2H, q), 4.57 (2H, d), 6.39 (1H, t), 6.78 (2H, dm), 7.12 (2H, dm), 7.20 - 7.48 (10H, m), 7.48 - 7.62 (4H, m).

23

(E) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 -

(E) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 - (2
2) (1.38g, 2.72mmol) 2 가 (1.25mg, 96%) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.17 (3H, t), 2.95 (1H, dd), 3.06 (1 H, dd), 3.37 - 3.52 (1H, m), 3.52 - 3.64 (1H, m), 4.03 (1H, dd), 4.59 (2H, d), 6.38 (1H, t), 6.78 (2H, m), 7.12 (2H, dm), 7.20 - 7.49 (10H, m), 7.49 - 7.62 (4H, m), COOH.

24

(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 -

(E,Z) - 3 - 4 - 3 - - 2 - - 1 - (601 mg, 2.1 mmol), (606mg, 2.31mmo
l), (2S) - 2 - 3 - (4 -) - (601mg, 2.52mmol)
(402mg, 2.31mmol) 1 (400mg, 38%) .

$^1\text{H NMR}$ (CDCl_3 , 200 MHz); 1.10 - 1.30 (6H, m), 2.94 (2H, d), 3.25 - 3.45 (1H, m), 3.50 - 3.65 (1H, m), 3.96 (1H, t), 4.16 (2H, dd), 4.55 - 4.68 (2H, d), 6.30 - 6.44 (1H, m), 6.73 - 6.84 (2H, m), 7.14 (2H, dm), 7.20 - 7.70 (14H, m).

25

(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 -

(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 - (2
24) (400mg, 0.79mmol) 2 (250mg, 66%) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.05 - 1.20 (3H, m), 2.94 (1H, dd), 3.01 (1H, dd), 3.30 - 3.43 (1H, m), 3.50 - 3.68 (1H, m), 4.00 (1 H, dd), 4.50 - 4.68 (2H, m), 6.27 - 6.40 (1H, m), 6.72 - 6.84 (2H, m), 7.12 (2H, dm), 7.18 - 7.65 (14H, m), 9.85 (1H, br s).

26

3 - {4 - [3,3 - (3 - - 2 -) -] - } - 2 -

3 3,3 - (3 - 2 -) - - 2 - - 1 - (1.0mg, 3.99mmol),
(0.91g, 4.5mmol), 2 - 3 - (4 -) - (1.07g, 4.5mmol)
(1.14g, 4.5mmol) (680mg, 36%) .

$^1\text{H NMR}$ (CDCl_3 , 200 MHz); 1.15 (3H, t), 1.23 (3H, t), 2.00 (3H, s), 2.08 (3H, s), 2.93 (2H, d), 3.28 - 3.40 (1H, m), 3.50 - 3.64 (1H, m), 3.94 (1H, t), 4.14 (2H, dd), 4.58 (2H, d), 6.24 (1H, t), 6.70 - 6.81 (3H, m), 6.88 (1H, d), 7.04 - 7.15 (3H, m), 7.21 - 7.30 (1H, m).

27

3 - { 4 - [3,3 - (4 -) -] - } - 2 -

1 (0.39g, 1.50mmol), 2 - (0.26g, 1.51mmol) 3,3 - (4 -) - - 2 - - 1 - (0.50g, 1.36mmol), (0.39g, 1.63mmol) (450mg, 56%)

¹H NMR (CDCl₃, 300 MHz); 1.15 (3H, t), 1.22 (3H, t), 2.94 (2H, d), 3.28 - 3.42 (1H, m), 3.53-3.65 (1 H, m), 3.96 (1H, t), 4.16 (2H, q), 4.52 (2H, d), 6.32 (1H, t), 6.75 (2H, dm), 7.01 - 7.20 (6H, m), 7.43 (2H, dm), 7.52 (2H, dm).

MS (EI): 586/588/590 (M⁺), 513/515/517,349/351/353 (100%).

28

3 - { 4 - [3,3 - (4 -) -] - } - 2 -

3 - { 4 - [3,3 - (4 -) -] - } - 2 - (27) (150 mg, 0.25mmol) 2 가 (135mg, 96%)

¹H NMR (CDCl₃, 300 MHz); 1.17 (3H, t), 2.94 (1H, dd), 3.06 (1H, dd), 3.40 - 3.52 (1 H, m), 3.52 - 3.66 (1H, m), 4.04 (1 H, dd), 4.51 (2H, d), 6.30 (1H, t), 6.76 (2H, dm), 7.00 - 7.20 (6H, m), 7.42 (2H, dm), 7.52 (2H, dm), COOH.

MS (EI): 558/560/562 (M⁺), 349/351/353,270/272 (100%), 191.

29

2 - - 3 - [4 - (3 - - 3 - - 4 - -) -] -

1 (0.68g, 2.61mmol), 2 - (0.46g, 2.63mmol) 3 - - 3 - - 4 - - - 2 - - 1 - (0.50 g, 2.37mmol), (0.68g, 2.84mmol) (435mg, 43%)

¹H NMR (CDCl₃, 200 MHz); 1.16 (3H, t), 1.21 (3H, t), 2.94 (2H, d), 3.25 - 3.43 (1H, m), 3.50 - 3.70 (1H, m), 3.98 (1H, t), 4.17 (2H, q), 4.52 (2H, d), 6.41 (1H, t), 6.76 (2H, dm), 7.05 - 7.40 (9H, m), 8.66 (2H, dm).

MS (EI): 431 (M⁺), 194 (100%).

Mp. 84 - 87

30

2 - - 3 - [4 - (3 - - 3 - - 4 - -) -] -

2 - - 3 - [4 - (3 - - 3 - - 4 - -) -] - (29) (200mg, 0.46mmol) 2 가 (50mg, 27%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.16 (3H, t), 2.98 (1H, dd), 3.06 (1H, dd), 3.33 - 3.49 (1H, m), 3.60 - 3.75 (1H, m), 4.03 (1H, dd), 4.52 (2H, d), 6.46 (1H, t), 6.78 (2H, dm), 7.09 - 7.40 (9H, m), 8.63 (2H, dm), 9.23 (1H, br s).

31

(E,Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 - 2 - -] - } -

1 (289mg, 1.10mmol), (2S) - 2 - 3 - (4 - -) - (271mg, 1.10mmol),
1.0mmol) (188mg, 1.08mmol) (80mg, 17%) (238mg, 1.0mmol)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.10 - 1.28 (6H, m), 2.88 - 2.98 (2H, m), 3.25 - 3.43 (1H, m), 3.473.69 (1H, m), 3.77 - 3.90 (3H, m), 3.95 (1H, tm), 4.16 (2H, q), 4.45 - 4.78 (2H, m), 6.10 - 6.48 (1H, m), 6.70 - 7.50 (11H, m).

32

(E,Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 - 2 - -] - } -

(E,Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 - 2 - -] - } -
(31) (75mg, 0.16mmol) 2 가 (40mg, 57%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.17 (3H, t), 2.83 - 3.13 (2H, m), 3.27 - 3.50 (1H, m), 3.50 - 3.70 (1H, m), 3.77 - 3.88 (3H, m), 3.97 - 4.09 (1H, m), 4.43 - 4.28 (2H, m), 6.10 - 6.30 (1H, m), 6.70 - 7.40 (11H, m), COOH.

MS (EI): 438 (M+), 229 (100%).

33

(E,Z) - (2S) - 2 - 3 - [4 - (3 - 3 - p - -) -] -

1 (E,Z) - 3 - 3 - - 2 - - 1 - (841 mg, 3.75mmol),
(1.03g, 3.93mmol), (2S) - 2 - 3 - (4 - -) - (851mg, 3.57mmol)
(656mg, 3.94mmol) (0.64g, 40%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.14 (3H, t), 1.22 (3H, t), 2.30 - 2.42 (3H, m), 2.93 (2H, d), 3.263.40 (1H, m), 3.51 - 3.66 (1H, m), 3.94 (1H, t), 4.16 (2H, q), 4.49 - 4.63 (2H, m), 6.20 - 6.33 (1H, m), 6.76 (2H, dm), 7.00 - 7.45 (11H, m).

MS (EI): 444 (M+), 207 (100%).

34

(E,Z) - (2S) - 2 - 3 - [4 - (3 - 3 - p - -) -] -

(E,Z) - (2S) - 2 - 3 - [4 - (3 - 3 - p - -) -] - (33)
(0.55g, 1.24mmol) 2 가 (0.50g, 97%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.17 (3H, t), 2.24 - 2.41 (3H, m), 2.93 (1H, dd), 3.04 (1H, dd), 3.37 - 3.64 (2H, m), 4.03 (1H, dd), 4.50 - 4.63 (2H, m), 6.20 - 6.32 (1H, m), 6.78 (2H, dm), 7.007.43 (11H, m), COOH.

MS (EI): 416 (M+), 207 (100%).

35

(2S) - 3 - [4 - (3,3 -) -] - 2 - -

3 3,3 - - - 2 - - 1 - (210mg, 1.0mmol), (303mg, 1.50mmol), (2S) - 2 - - 3 - (4 - -) - (250mg, 1.05mmol)
(378mg, 1.50mmol) (290mg, 67%) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.14 (3H, t), 1.21 (3H, t), 2.92 (2H, d), 3.28 - 3.40 (1H, m), 3.523.65 (1H, m), 3.94 (1H, t), 4.14 (2H, q), 4.56 (2H, d), 6.31 (1H, t), 6.75 (2H, dm), 7.10 (2H, dm), 7.16 - 7.44 (10H, m).

36

(2S) - 3 - [4 - (3,3 -) -] - 2 - -

(2S) - 3 - [4 - (3,3 -) -] - 2 - - (35) (215mg, 0.50mmol)
mol) 2 가 (180mg, 90%) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.17 (3H, t), 2.93 (1H, dd), 3.04 (1H, dd), 3.38 - 3.50 (1H, m), 3.50 - 3.63 (1H, m), 4.03 (1H, dd), 4.58 (2H, d), 6.31 (1H, t), 6.77 (2H, dm), 7.11 (2H, dm), 7.17 - 7.43 (10H, m), COOH.

37

(Z) - (2S) - 2 - - 3 - {4 - [3 - (4 -) - 3 - -] - } -

1 (Z) - 3 - (4 -) - 3 - - - 2 - - 1 - (200mg, 0.88mmol),
(242mg, 0.92mmol), (2S) - 2 - - 3 - (4 - -) - (200mg, 0.84mmol)
(160mg, 0.92mmol) (275mg, 73%) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.15 (3H, t), 1.21 (3H, t), 2.93 (2H, d), 3.27 - 3.40 (1H, m), 3.51 - 3.65 (1H, m), 3.96 (1H, t), 4.14 (2H, q), 4.54 (2H, d), 6.33 (1H, t), 6.76 (2H, dm), 6.95 - 7.40 (11H, m).

MS (EI): 448 (M+), 375,211 (100%).

38

(Z) - (2S) - 2 - - 3 - {4 - [3 - (4 -) - 3 - -] - } -

(Z) - (2S) - 2 - - 3 - {4 - [3 - (4 -) - 3 - -] - } - (37) (200mg, 0.45mmol) 2 가 (158mg, 86%) .

$^1\text{H NMR}$ (CDCl_3 , 200 MHz); 1.15 (3H, t), 2.84 - 3.14 (2H, m), 3.35 - 3.68 (2H, m), 4.04 (1H, dd), 4.54 (2H, d), 6.32 (1H, t), 6.77 (2H, dm), 7.00 - 7.40 (11H, m), COOH.

MS (EI): 420 (M+), 368,317,211 (100%).

39

(E) - (2S) - 2 - 3 - { 4 - [3 - (4 -) - 3 -] - } -

1 (E) - 3 - (4 -) - 3 - - 2 - - 1 - (200mg, 0.88mmol),
(242mg, 0.92mmol), (2S) - 2 - 3 - (4 -) - (200mg, 0.84mmol)
(160mg, 0.92mmol) (320mg, 85%)

¹H NMR (CDCl₃, 300 MHz); 1.15 (3H, t), 1.21 (3H, t), 2.93 (2H, d), 3.24 - 3.43 (1H, m), 3.50 - 3.67 (1H, m), 3.96 (1H, t), 4.16 (2H, q), 4.54 (2H, d), 6.25 (1H, t), 6.75 (2H, dm), 6.90 - 7.03 (2H, m), 7.03 - 7.30 (6H, m), 7.30 - 7.45 (3H, m).

MS (EI): 448 (M+), 375,211 (100%).

40

(E) - (2S) - 2 - 3 - { 4 - [3 - (4 -) - 3 -] - } -

(E) - (2S) - 2 - 3 - { 4 - [3 - (4 -) - 3 -] - } - ((39) (225mg, 0.50mmol) 2 가 (245mg, 95%))

¹H NMR (CDCl₃, 300 MHz); 1.17 (3H, t), 2.83 - 3.14 (2H, m), 3.34 - 3.68 (2H, m), 4.02 (1H, dd), 4.53 (2H, d), 6.24 (1H, t), 6.78 (2H, dm), 6.89 - 7.05 (2H, m), 7.05 - 7.49 (9H, m), COOH.

MS (EI): 420 (M+), 317,211 (100%).

41

(2S) - 3 - { 4 - [3,3 - (4 -) -] - } - 2 - -

1 3,3 - (4 -) - - 2 - - 1 - (1.62g, 5.99mmol),
(2.88g, 10.98mmol), (2S) - 2 - 3 - (4 -) - (1.19g, 4.99mmol)
(1.92g, 11.04mmol) (0.434g, 17%)

¹H NMR (CDCl₃, 300 MHz); 1.15 (3H, t), 1.21 (3H, t), 2.93 (2H, d), 3.27 - 3.41 (1H, m), 3.53 - 3.65 (1H, m), 3.80 (3H, s), 3.84 (3H, s), 3.95 (1H, t), 4.15 (2H, q), 4.56 (2H, d), 6.17 (1H, t), 6.71 - 6.87 (4H, m), 6.92 (2H, dm), 7.05 - 7.25 (6H, m).

42

(2S) - 3 - { 4 - [3,3 - (4 -) -] - } - 2 - -

(2S) - 3 - { 4 - [3,3 - (4 -) -] - } - 2 - - (41)
(225mg, 0.495mmol) 2 가 (150mg, 71%)

¹H NMR (CDCl₃, 300 MHz); 1.17 (3H, t), 2.95 (1H, dd), 3.04 (1H, dd), 3.38 - 3.50 (1H, m), 3.52 - 3.66 (1H, m), 3.80 (3H, s), 3.83 (3H, s), 4.03 (1H, dd), 4.57 (2H, d), 6.17 (1H, t), 6.71 - 6.85 (4H, m), 6.92 (2H, dm), 7.05 - 7.25 (6H, m), COOH.

43

(2S) - 3 - [4 - (3,3 - p -) -] - 2 - -
 3, 3 - - (4 -) - - 2 - - 1 - (1.0 g, 4.20 mmol),
 1.27 g, 6.30 mmol), (2S) - 2 - - 3 - (4 - -) - (1.10g, 4.62mmol)
 (1.59g, 6.30mmol) (0.76g, 39%)

¹H NMR (CDCl₃, 300 MHz); 1.13 (3H, t), 1.21 (3H, t), 2.33 (3H, s), 2.38 (3H, s), 2.93 (2H, d), 3.26 - 3.41 (1H, m), 3.52 - 3.66 (1 H, m), 3.95 (1H, t), 4.15 (2H, q), 4.56 (2H, d), 6.27 (1 H, t), 6.75 (2H, d m), 7.00 - 7.21 (10H,m).

MS (EI): 458 (M+), 385,221 (100%).

44

(2S) - 3 - [4 - (3,3 - p -) -] - 2 - -
 (2S) - 3 - [4 - (3,3 - p -) -] - 2 - - (43) (0.76g, 1.66mmol)
 2 가 (0.696g, 98%)

¹H NMR (CDCl₃, 300 MHz); 1.16 (3H, t), 2.33 (3H, s), 2.38 (3H, s), 2.94 (1 H, dd), 3.05 (1H, dd), 3.39 - 3.51 (1H, m), 3.51 - 3.65 (1H, m), 4.03 (1H, dd), 4.57 (2H, d), 6.23 (1H, t), 6.77 (2H, dm), 7.00 - 7.22 (10H, m), COOH.

MS (EI): 430 (M+), 327,221 (100%).

45

(Z) - (2S) - 3 - [4 - (3 - 4 - - 3 - -) -] - 2 - -
 1 (Z) - 3 - - 4 - - 3 - - - 2 - - 1 - (171mg, 0.60mmol),
 (142mg, 0.63mmol), (2S) - 2 - - 3 - (4 - -) - (149mg, 0.63 mmol)
 (95mg, 0.55mmol) (160mg, 53%)

¹H NMR (CDCl₃, 300 MHz); 1.16 (3H, t), 1.21 (3H, t), 2.93 (2H, d), 3.28 - 3.40 (1H, m), 3.52 - 3.65 (1H, m), 3.95 (1 H, t), 4.14 (2H, q), 4.63 (2H, d), 6.33 (1H, t), 6.78 (2H, dm), 7.12 (2H, dm), 7.20 - 7.50 (10H, m), 7.55 - 7.68 (4H, m).

46

(Z) - (2S) - 3 - [4 - (3 - 4 - - 3 - -) -] - 2 - -
 (Z) - (2S) - 3 - [4 - (3 - 4 - - 3 - -) -] - 2 - - (4
 5) (0.36g, 0.71mmol) 2 가 0.6
 (0.345g, 86%)

¹H NMR (CDCl₃, 300 MHz); 1.17 (3H, t), 1.26 (1.8H, t,), 2.04 (1.8H, s,), 2.95 (1H, dd), 3.06 (1H, dd), 3.38 - 3.52 (1H, m), 3.52 - 3.64 (1H, m), 4.03 (1H, dd), 4.12 (1.2H, q,), 4.63 (2H, d), 6.32 (1H, t), 6.80 (2H, dm), 7.11 (2H, dm), 7.20 - 7.50 (10H, m), 7.54 - 7.68 (4H, m), COOH.

MS (EI): 478 (M+), 375,269 (100%).

47

(Z) - (2S) - 3 - {4 - [3 - (4 -) - 3 - -] - } - 2 - -

1 (144mg, 0.55mmol), 3 - (4 -) - 3 - - - 2 - - 1 - (145mg, 0.50mmol),
(2S) - 2 - - 3 - (4 - -) - (119 mg, 0.50 mm
ol) (96mg, 0.55mmol) (110mg, 43%) .

¹H NMR (CDCl₃, 300 MHz); 1.17 (3H, t), 1.21 (3H, t), 2.94 (2H, d), 3.29 - 3.41 (1H, m), 3.53 - 3.65 (1H, m), 3.96 (1H, t), 4.15 (2H, q), 4.53 (2H, d), 6.32 (1H, t), 6.75 (2H, dm), 7.05 - 7.18 (4H, m), 7.18 - 7.38 (5H, m), 7.52 (2H, dm).

MS (EI): 508/510 (M+) 435/437,393/395,271/273,192 (100%).

C₂₈ H₂₉ BrO₄ + 0.1 H₂O : = 65.78% C, 5.76% H, 65.79 C, 5.91% H.

48

(Z) - (2S) - 3 - {4 - [3 - (4 -) - 3 - -] - } - 2 - -

(Z) - (2S) - 3 - {4 - [3 - (4 -) - 3 - -] - } - 2 - - ((47) (90mg, 0.18mmol) 2 가 (60mg, 71%) .

¹H NMR (CDCl₃, 300 MHz); 1.17 (3H, t), 2.96 (1 H, dd), 3.05 (1H, dd), 3.39 - 3.51 (1H, m), 3.51 - 3.64 (1H, m), 4.03 (1H, dd), 4.52 (2H, d), 6.32 (1H, t), 6.75 (2H, dm), 7.02 - 7.18 (4H, m), 7.18 - 7.40 (5 H, m), 7.51 (2H, dm), COOH.

LCMS (): 503/505 (M+Na), 498/500 (M+NH₄), 271/273 (100%).

49

(2S) - 3 - [4 - (3,3 - - - 4 - -) -] - 2 - -

3 (303mg, 1.5mmol), 3,3 - - - 4 - - - 2 - - 1 - (363 mg, 1.0mmol),
(2S) - 2 - - 3 - (4 - -) - (262mg, 1.1mmol)
(378mg, 1.5mmol) 0.8 (44
5mg, 76%) .

¹H NMR (CDCl₃, 300 MHz); 1.16 (3H, t), 1.21 (3H, t), 1.25 (2.4H, t,), 2.04 (2.4H, s,), 2.93 (2H, d), 3.28 - 3.40 (1 H, m), 3.51 - 3.65 (1H, m), 3.96 (1H, t), 4.07 - 4.20 ({2H, q} {1.6H, q, }), 4.54 (2H, d), 6.40 (1H, t), 6.80 (2H, dm), 7.03 (2H, dm), 7.27 - 7.70 (18H, m).

50

(2S) - 3 - [4 - (3,3 - - - 4 - -) -] - 2 - -

(2S) - 3 - [4 - (3,3 - - - 4 - -) -] - 2 - - ((49) (5
60mg, 0.96mmol) 2 가 (450mg, 84%) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.13 (3H, t), 2.93 (1H, dd), 3.05 (1H, dd), 3.35 - 3.50 (1H, m), 3.50 - 3.64 (1H, m), 4.02 (1H, dd), 4.62 (2H, d), 6.39 (1H, t), 6.80 (2H, dm), 7.02 (2H, dm), 7.27 - 7.72 (18H, m), COOH.

51

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - -

3 (2.52g, 10.0mmol), 3,3 - (4 -) - - 2 - - 1 - (2.60g, 7.0mmol),
(2S) - 2 - - 3 - (4 - -) - (1.50g, 6.3mmol)
(2.02g, 10.0mmol) (2.8g, 75%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.16 (3H, t), 1.21 (3H, t), 2.93 (2H, d), 3.27 - 3.40 (1H, m), 3.53 - 3.65 (1H, m), 3.94 (1H, t), 4.15 (2H, q), 4.51 (2H, d), 6.31 (1H, t), 6.75 (2H, dm), 7.01 - 7.19 (6H, m), 7.42 (2H, dm), 7.52 (2H, dm).

52

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - -

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - - (51)
(2.8g, 4.76mmol) 2 가 0.25
(2.3 g, 83%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.15 (3H, t), 1.25 (0.75H, t), , 2.04 (0.75H, s),
, 2.93 (1H, dd), 3.04 (1H, dd), 3.37 - 3.49 (1H, m), 3.52 - 3.68 (1H, m), 4.02 (1H, dd), 4.12 (0.5H, q,
, 4.50 (2H, d), 6.30 (1H, t), 6.74 (2H, dm), 7.00 - 7.19 (6H, m), 7.49 (2H, dm), 7.50 (2H, dm), COOH.

53

(Z) - (2S) - 2 - - 3 - {4 - [3 - (4 - - 2 - -) - 3 - -] - } -

3 (300mg, 1.09 mmol), (Z) - 3 - (4 - - 2 - -) - 3 - - - 2 - - 1 - (0.40ml, 1.64mmol), (2S) - 2 - - 3 - (4 - -) -
(286mg, 1.20mmol) (413mg, 1.64mmol) (260mg, 4 8%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.15 (3H, t), 1.21 (3H, t), 2.93 (2H, d), 3.28 - 3.40 (1H, m), 3.52 - 3.65 (1H, m), 3.94 (1H, t), 4.14 (2H, q), 4.60 (2H, d), 6.30 (1H, t), 6.49 (1H, dd), 6.69 (1H, d), 6.77 (2H, d m), 7.11 (2H, dm), 7.18 - 7.32 (7H, m), 7.49 (1H, d), 7.69 (2H, dm).

LCMS (): 519 (M+Na), 514 (M+NH₄), 259 (100%).

54

(Z) - (2S) - 2 - - 3 - {4 - [3 - (4 - - 2 - -) - 3 - -] - } -

(Z) - (2S) - 2 - - 3 - {4 - [3 - (4 - - 2 - -) - 3 - -] - } -
(53) (240mg, 0.483mmol) 2 가 (170mg, 75%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.15 (3H, t), 2.93 (1H, dd), 3.05 (1H, dd), 3.33 - 3.49 (1H, m), 3.50 - 3.65 (1H, m), 4.01 (1H, dd), 4.60 (2H, d), 6.30 (1H, t), 6.49 (1H, dd), 6.68 (1H, d), 6.78 (2H, dm), 7.11 (2H, dm), 7.15 - 7.36 (7H, m), 7.49 (1H, d), 7.68 (2H, dm), COOH.

LCMS (): 491 (M+Na), 486 (M+NH₄), 259 (100%).

55

(E) - (2S) - 3 - {4 - [3 - (4 -) - 3 - -] - } - 2 - -

3 (E) - 3 - (4 -) - 3 - - - 2 - - 1 - (289mg, 1.0mmol),
 (0.37ml, 1.5mmol), (2S) - 2 - - 3 - (4 - -) - (26
 2mg, 1.10mmol) (378mg, 1.5mmol) (460mg, 90%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.15 (3H, t), 1.21 (3H, t), 2.92 (2H, d), 3.26 - 3.40 (1H, m), 3.51 - 3.65 (1H, m), 3.94 (1H, t), 4.15 (2H, q), 4.54 (2H, d), 6.29 (1H, t), 6.74 (2H, dm), 7.03 - 7.45 (11H, m).

LCMS (): 531/533 (M+Na), 271/273 (100%).

56

(E) - (2S) - 3 - {4 - [3 - (4 -) - 3 - -] - } - 2 - -

(E) - (2S) - 3 - {4 - [3 - (4 -) - 3 - -] - } - 2 - - ((55) (382mg, 0.75mmol) 2 가 (350mg, 97%) .

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.16 (3H, t), 2.93 (1H, dd), 3.05 (1H, dd), 3.38 - 3.50 (1H, m), 3.50 - 3.63 (1H, m), 4.03 (1H, dd), 4.53 (2H, d), 6.30 (1H, t), 6.75 (2H, dm), 7.03 - 7.45 (11H, m), COOH.

LCMS (): 503/505 (M+Na), 498/500 (M+NH₄), 271/273 (100%).

57

(2S) - 3 - {4 - (3,3 - - (4 - - 2 - -) -] - } - 2 - -

3 3,3 - - (4 - - 2 - -) - - 2 - - 1 - (460mg, 1.34mmol),
 (0.50ml, 2.0mmol), (2S) - 2 - - 3 - (4 - -) - (320mg, 1.34mmol) (504mg, 2.0mmol) (541mg, 72%)

$^1\text{H NMR}$ (CDCl_3 , 300 MHz); 1.16 (3H, t), 1.21 (3H, t), 2.93 (2H, d), 3.28 - 3.40 (1H, m), 3.51 - 3.64 (1H, m), 3.94 (1H, t), 4.14 (2H, q), 4.59 (2H, d), 6.35 (1H, t), 6.40 - 6.51 (2H, m), 6.62 (1H, d), 6.69 (1H, d), 6.77 (2H, dm), 7.13 (2H, dm), 7.20 - 7.33 (4H, m), 7.44 (1H, d), 7.48 (1H, d), 7.58 (2H, dm), 7.70 (2H, m).

58

(2S) - 3 - {4 - (3,3 - - (4 - - 2 - -) -] - } - 2 - -

(2S) - 3 - { 4 - (3,3 - - (4 - - 2 - -) -] - } - 2 - - (57) (530mg, 0.95mmol) 2 가 (400mg, 79%) .

¹H NMR (CDCl₃, 300 MHz); 1.17 (3H, t), 2.95 (1H, dd), 3.07 (1H, dd), 3.40 - 3.52 (1H, m), 3.52 - 3.63 (1H, m), 4.05 (1H, dd), 4.60 (2H, d), 6.35 (1H, t), 6.44 - 6.51 (2H, m), 6.64 (1H, d), 6.70 (1H, d), 6.79 (2H, dm), 7.12 (2H, dm), 7.20 - 7.34 (4H, m), 7.47 (1H, d), 7.50 (1H, d), 7.59 (2H, dm), 7.70 (2H, d m), COOH.

59

(E,Z) - (2S) - 3 - [4 - (3 - - 4 - - 3 - p - -) -] - 2 - - 3 (E,Z) - 3 - - 4 - - 3 - p - - 2 - - 1 - (300mg, 1.0mmol), (0.37ml, 1.5mmol), (2S) - 2 - - 3 - (4 - -) - (26 2mg, 1.10mmol) (378mg, 1.50mmol) (390mg, 76%)

¹H NMR (CDCl₃, 300 MHz); 1.10 - 1.25 (6H, m), 2.30 - 2.42 (3H, m), 2.92 (2H, d), 3.27 - 3.40 (1H, m), 3.50 - 3.65 (1H, m), 3.94 (1H, tm), 4.13 (2H, qm), 4.57 - 4.64 (2H, m), 6.23 - 6.38 (1H, m), 6.79 (2H, dm), 7.03 - 7.67 (15H, dm).

LCMS (): 543 (M+Na), 538 (M+NH₄), 283 (100%).

60

(E,Z) - (2S) - 3 - [4 - (3 - - 4 - - 3 - p - -) -] - 2 - - (E,Z) - (2S) - 3 - [4 - (3 - - 4 - - 3 - p - -) -] - 2 - - (59) (370mg, 0.71mmol) 2 가 (310mg, 89%) .

¹H NMR (CDCl₃, 300 MHz); 1.10 - 1.22 (3H, m), 2.30 - 2.44 (3H, m), 2.93 (1 H, dd), 3.04 (1H, dd), 3.37 - 3.63 (2H, m), 3.98 - 4.07 (1H, m), 4.54 - 4.65 (2H, m), 6.25 - 6.38 (1H, m), 6.79 (2H, dm), 7.02 - 7.67 (15H, m), COOH.

LCMS (): 515 (M+Na), 283 (100%).

61

(E,Z) - (2R) - 3 - [4 - (3 - - 4 - - 3 - -) -] - 2 - - (0.25g, 1.81mmol) (20ml) 4 - (3 - - 1 - - - 1 -) - (0.35g, 1.00mmol) (2R) - 2 - - 3 - (4 - -) - (0.215g, 0.90mmol) 가 , 18 60 가 . 15% (0.40g, 87%)

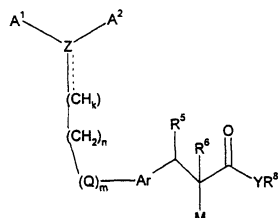
¹H NMR (CDCl₃, 300 MHz); 1.09 - 1.32 (6H, m), 2.93 (2H, d), 3.27 - 3.41 (1H, m), 3.51 - 3.67 (1H, m), 3.96 (1H, t), 4.18 - 4.20 (2H, m), 4.52 - 4.68 (2H, m), 6.28 - 6.41 (1H, m), 6.72 - 6.83 (2H, m), 7.12 (2H, dm), 7.18 - 7.69 (14H, m).

(57)

1.

1 가 , , .

(1)



, A¹ A² , , , , , C₁₋₁₂ - , (C₃
 -6 -)C₁₋₆ - , C₄₋₁₂ - , C₂₋₁₂ - , C₂₋₁₂ - , C₁₋₁₂ - , , , ,
 , C₁₋₁₂ - , , , C₁₋₁₂ - - , C₁₋₆ - , , , , ,
 , C₁₋₁₂ - , C₁₋₁₂ - , , , , , , C₁
 -12 - C₁₋₁₂ - , C₁₋₁₂ - , C₁₋₁₂ - , C₁₋₁₂ - , C₁₋₁₂ - , C₁₋₁₂ - , C₁₋
 12 - , C₁₋₁₂ - , , , -COR¹, -SO
 2R² (, R¹ R² , , , , C₁₋₆ - , C₁₋₆ - ,
) , , , 5-6 9-10 ;

Z C, CR³ (, R³ , , , C₁₋₁₂ - , C₄₋₁₂ - , C₂₋₁₂ - , C₂₋₁₂ -
 , C₁₋₁₂ - , , , , , C₁₋₁₂ -
 , C₁₋₁₂ - C₁₋₁₂ - , C₁₋₁₂ - , C₁₋₁₂ - , C₁₋₁₂ - , -COR⁴,
 -SO₂R¹¹ (, R⁴ R¹¹ , , , , C₁₋₆ - C₁₋₆ - ,
) ;

Q O, S, NR¹² (, R¹² , , , C₁₋₁₂ - , C₄₋₁₂ - , C₂₋₁₂ - , C₂₋₁₂ -
 , , , , , , C₁₋₁₂ - , C₁₋₁₂ - ,
 C₁₋₁₂ - , , , , , C₁₋₁₂ - , C₁₋₁₂ - , C₁₋₁₂ - ,
 , C₁₋₆ C₁₋₁₂ - , C₁₋₁₂ - , -COR¹³, -SO₂R¹⁴ (, R¹³ R¹⁴ , ,
 , C₁₋₆ C₁₋₆ , , , , ,
) ;

..... 2 ;

Ar , , 2가 , C₁₋₆- , , , C₁₋₆- ;

6.

1 5 , Z 2 , Z CR³ , R³
 , , , C₁₋₁₂ - , C₄₋₁₂ - , C₂₋₁₂ - , C₂₋₁₂ - , C₁₋₁₂ - ,
 , , , C₁₋₁₂ - , C₁₋₁₂ - C₁₋
¹² - R¹¹ , C₁₋₁₂ , C₁₋₁₂ - , C₁₋₁₂ - , -COR⁴ , -SO₂R¹¹ , ,R
 , , , C₁₋₆ - C₁₋₆ - , C₁₋₆ - ,

7.

1 6 , Z 2 , Z CR³ , R³
 , , , C₁₋₆ - , C₄₋₆ - , C₂₋₆ - , C₂₋₆ - , C₁₋₆ - ,
 , , , C₁₋₆ - , C₁₋₆ - , C₁₋₆ - , -COR⁴ , -SO₂R¹¹ , , R⁴ R¹¹
 C₁₋₆ - , C₁₋₆ - , C₁₋₆ - C₁₋₆ - ,

8.

1 7 , Z 2 , Z CR³ , R³
 , , , C₁₋₆ - , C₄₋₆ - , C₂₋₆ - , C₂₋₆ - , C₁₋₆ - ,
 , , , C₁₋₆ - , C₁₋₆ - , C₁₋₆ - , C₁₋₆ - , C₁₋₆ - , C₁₋₆ - ,
¹⁻⁶ - C

9.

1 8 , Z 2 , Z CR³ , R³

10.

1 9 , Q O S, NR¹² , , R¹² , , C₁₋₆ -
 , C₄₋₆ - , C₂₋₆ - , C₂₋₆ - , , , ,
 , C₁₋₆ - , C₁₋₆ - , C₁₋₆ - , , , , C₁₋
⁶ - C₁₋₆ - , C₁₋₆ - , C₁₋₆ - , C₁₋₆ - , -COR¹³ , -SO₂R¹⁴
 , , R¹³ R¹⁴ , , C₁₋₆ - C₁₋₆ - ,

11.

1 10 , Q O S, NR¹² , , R¹² , , C₁₋₆ -

12.

1 11 , Q O S

13.

1 12 , Q O .

14.

1 13 , 2 .

15.

1 14 , Ar , C₁₋₆ - C₁₋₆ - , 2가 .

16.

1 15 , Ar .

17.

1 16 , Ar .

18.

1 17 , R⁵ , , C₁₋₆ - , C₁₋₆ - , C₄₋₆ - , C₂₋₆ - R⁵ R⁶ , C₂₋₆ - .

19.

1 18 , R⁵ , , C₁₋₆ - , C₁₋₆ - , R⁵ R⁶ .

20.

1 19 , R⁵ , , R⁵ R⁶ .

21.

1 20 , R⁵ .

22.

1 21 , R⁶ , C₁₋₆ - , C₁₋₆ - , C₄₋₆ - , C₂₋₆ - , C₂₋₆ - R⁶ R⁵ , .

32.

1 31 , R⁸ C₁₋₆ - .

33.

1 32 , R⁸ .

34.

1 33 , Y , NR¹⁰ , R¹⁰ , C₁₋₆ - ,
 , C₁₋₆ - , Y가 NR¹⁰ , R⁸ R¹⁰ C₁₋
 6 - , 5 6 .

35.

1 34 , Y NR¹⁰ , R¹⁰ , C₁₋₆ - ,
 , Y가 NR¹⁰ , R⁸ R¹⁰ C₁₋₆ - , 5 6 .

36.

1 35 , Y .

37.

1 36 , k 1 2 .

38.

1 37 , n m 1 .

39.

1 ,
 2 - - 3 - { 4 - [3 - - 3 - (4 -) -] - } - ,
 2 - - 3 - { 4 - [3 - - 3 - (4 -) - - } - ,
 3 - { 4 - [3 - (2 - -) - 3 - -] - } - 2 - - ,
 3 - { 4 - [3 - (2 - -) - 3 - -] - } - 2 - - ,
 3 - { 4 - [3, 3 - - (4 - -) -] - } - 2 - - ,
 3 - { 4 - [3, 3 - - (4 - -) -] - } - 2 - - ,
 3 - { 4 - [3 - - 3 - (- 4 -) -] - } - 2 - - ,

$3 - \{4 - [3 - 3 - (4 -) -] - \} - 2 -$,
 $2 - 3 - \{4 - [3 - 3 - (2 -) -] - \} -$,
 $2 - 3 - \{4 - [3 - 3 - (2 -) -] - \} -$,
 $2 - 3 - \{4 - [3 - 3 - (2 -) -] - \} -$,
 $2 - 3 - \{4 - [3 - 3 - (2 -) -] - \} -$,
 $3 - [4 - (3,3 - -) -] - 2 -$ - ,
 $3 - [4 - (3,3 - -) -] - 2 -$ - ,
 $2 - 3 - \{4 - [3 - 3 - (4 -) -] - \} -$,
 $2 - 3 - \{4 - [3 - 3 - (4 -) -] - \} -$,
 $3 - \{4 - [3 - 3 - (4 -) -] - \} - 2 -$ - ,
 $3 - \{4 - [3 - 3 - (4 -) -] - \} - 2 -$ - ,
 $2 - \{4 - [3,3 - - (4 - -) -] - \} -$,
 $(E) - (2S) - 2 - 3 - \{4 - [3 - (4 - 2 - -) - 3 - -] - \} -$,
 $(E) - (2S) - 2 - 3 - \{4 - [3 - (4 - 2 - -) - 3 - -] - \} -$,
 $(E) - (2S) - 3 - [4 - (3 - 4 - 3 - -) -] - 2 -$ - ,
 $(E) - (2S) - 3 - [4 - (3 - 4 - 3 - -) -] - 2 -$ - ,
 $(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 - -) -] - 2 -$ - ,
 $(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 - -) -] - 2 -$ - ,
 $3 - \{4 - [3,3 - - (3 - - 2 -) -] - \} - 2 -$ - ,
 $3 - \{4 - [3,3 - - (4 - -) -] - \} - 2 -$ - ,
 $3 - \{4 - [3,3 - - (4 - -) -] - \} - 2 -$ - ,
 $2 - 3 - [4 - (3 - 3 - 4 - -) -] -$,
 $2 - 3 - [4 - (3 - 3 - 4 - -) -] -$,
 $(E,Z) - (2S) - 2 - 3 - \{4 - [3 - (4 -) - 3 - 2 - -] - \} -$,

(E,Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 - 2 -] - } - ,

(E,Z) - (2S) - 2 - 3 - [4 - (3 - 3 - p -) -] - ,

(E,Z) - (2S) - 2 - 3 - [4 - (3 - 3 - p -) -] - ,

(2S) - 3 - [4 - (3,3 -) -] - 2 - - ,

(2S) - 3 - [4 - (3,3 -) -] - 2 - - ,

(Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 -] - } - ,

(Z) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 -] - } - ,

(E) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 -] - } - ,

(E) - (2S) - 2 - 3 - {4 - [3 - (4 -) - 3 -] - } - ,

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - - ,

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - - ,

(2S) - 3 - [4 - (3,3 - p -) -] - 2 - - ,

(2S) - 3 - [4 - (3,3 - p -) -] - 2 - - ,

(Z) - (2S) - 3 - [4 - (3 - 4 - 3 -) -] - 2 - - ,

(Z) - (2S) - 3 - {4 - [3 - (4 -) - 3 -] - } - 2 - - ,

(Z) - (2S) - 3 - {4 - [3 - (4 -) - 3 -] - } - 2 - - ,

(2S) - 3 - [4 - (3,3 - 4 -) -] - 2 - - ,

(2S) - 3 - [4 - (3,3 - 4 -) -] - 2 - - ,

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - - ,

(2S) - 3 - {4 - [3,3 - (4 -) -] - } - 2 - - ,

(Z) - (2S) - 2 - 3 - {4 - [3 - (4 - 2 -) - 3 -] - } - ,

(Z) - (2S) - 2 - 3 - {4 - [3 - (4 - 2 -) - 3 -] - } - ,

(E) - (2S) - 3 - {4 - [3 - (4 -) - 3 -] - } - 2 - - ,

(E) - (2S) - 3 - {4 - [3 - (4 -) - 3 -] - } - 2 - - ,

(2S) - 3 - {4 - (3,3 - (4 - 2 -) -] - } - 2 - - ,

(2S) - 3 - { 4 - (3,3 - (4 - 2 -) -] - } - 2 - ,

(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 - p -) -] - 2 - ,

(E,Z) - (2S) - 3 - [4 - (3 - 4 - 3 - p -) -] - 2 - ,

(E,Z) - (2R) - 3 - [4 - (3 - 4 - 3 -) -] - 2 - ;

가

40.

가
가

41.

40 , 0.05 100 mg, 0.1 50 mg
가

42.

가
가

(PPAR)

/

43.

가
가

, / /

44.

40 43 , , , , ,

45.

가 , 40 44

46.

가 , 40 44

(PPAR)

/

47.

가 , 40 44 /

48.

45 , 46 47 , 0.05 100mg, 0.1 가 50 mg .

49.

가

50.

, - (PPAR) / 가

51.

/ 가 / .