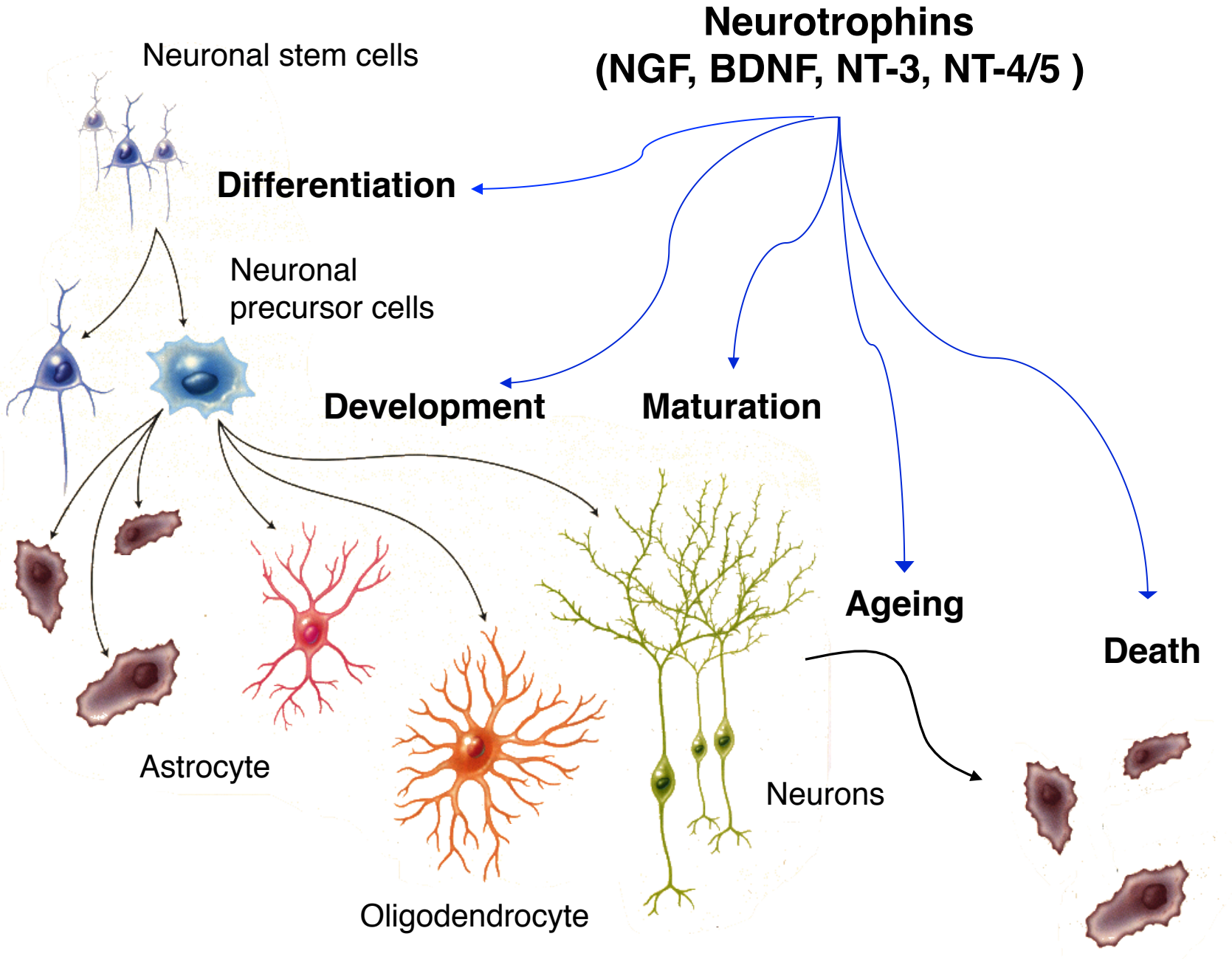
ヒオウギ（*Belamcanda chinensis*）種子の神経栄養因子様活性物質の探索研究

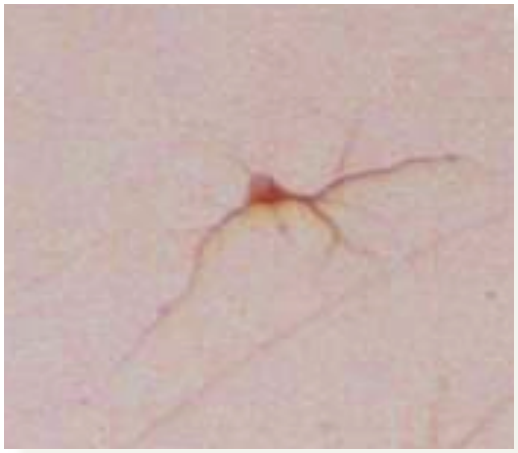
徳島文理大薬
○岩瀬瑠美、原田研一、久保美和、福山愛保

Effects of Neurotrophins

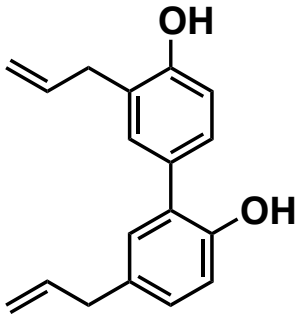


Search for Neurotrophic Mimic Natural Products

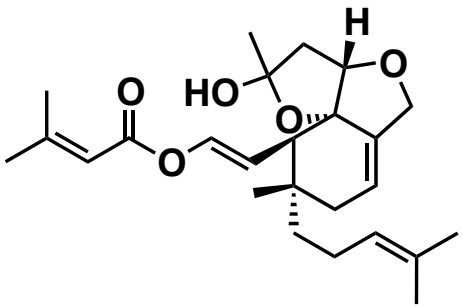
Rat pheochromocytoma cell line (PC12 cells)



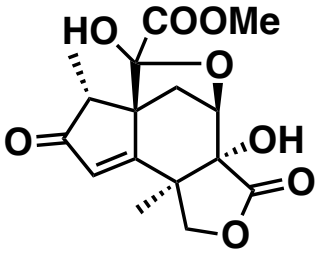
Primary cultured rat neurons (Cortical neurons)



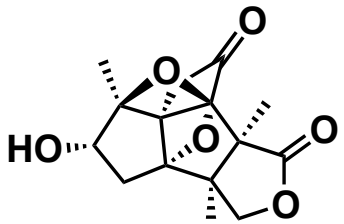
honokiol



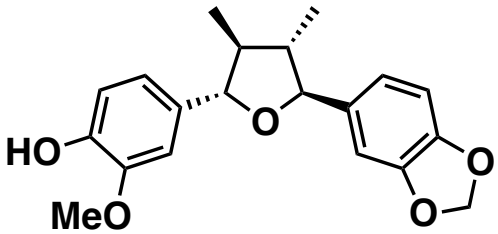
neovibsanin



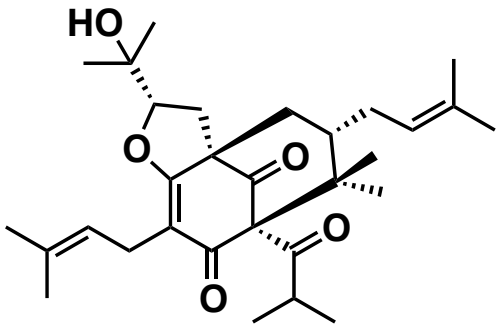
jiadifenin



merrilactone A



talaumidin



garsubellin A

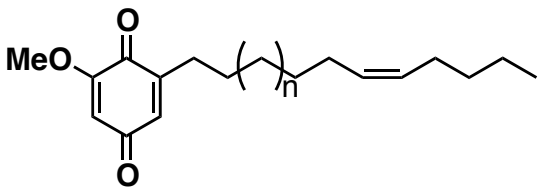
Neurotrophic Compounds Library

ヒオウギ
(*Belamcanda chinensis*)
アヤメ科ヒオウギ属

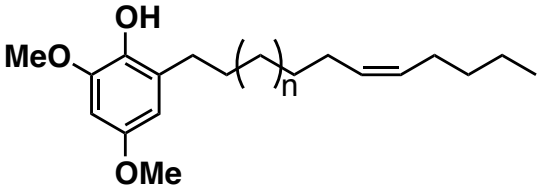
野山の草地や海岸に自生する多年草で，日本の本州から南西諸島までと、朝鮮半島、中国に分布している。根茎は「射干」と呼ばれ解熱、解毒剤として用いられ、他にも風邪や喘息，頭痛などに効能があるとされている。

DNA解析によりアヤメ属に編入され学名が*Belamcanda chinensis* から*Iris domestica*になった。

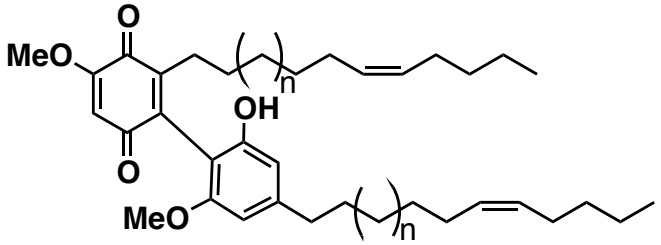
Compounds isolated from *Belamcanda chinensis*



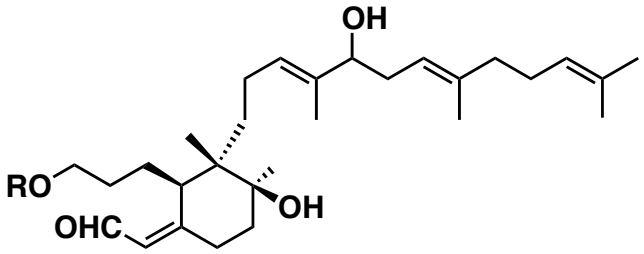
Ardisianone A: n = 5[1)]



Belamcandol A: n = 5[2)]

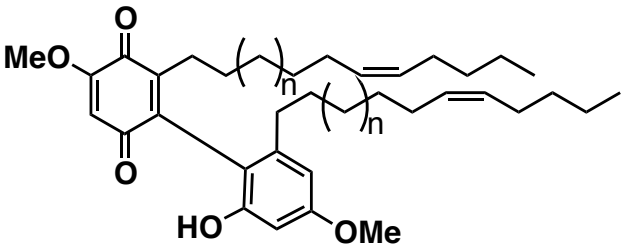


Belamcandaquinone A (抗アレルギー作用): n = 5[3)]

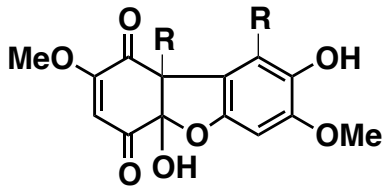


R = -$CO(CH_2)_{12}CH_3$

3-*O*-Tetradecanoyl-16-*O*-hydroxyisoiridogermanal[4)]

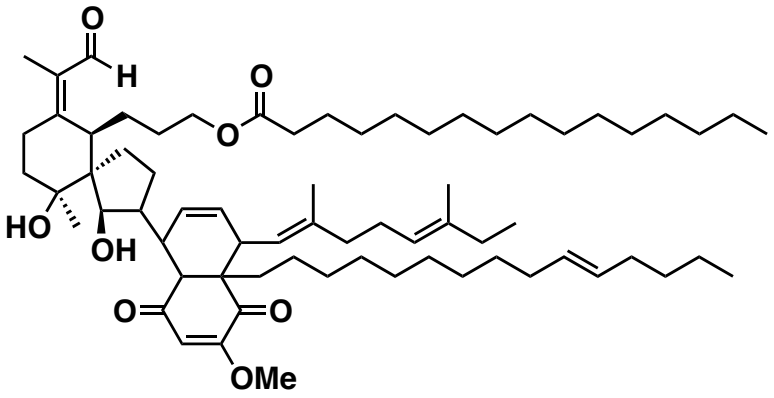


Belamcandaquinone B: n = 5[3)]

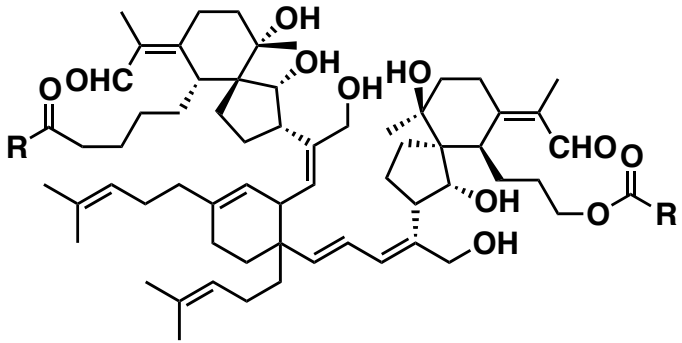


R = -$(CH_2)_{10}CH{=}CH(CH_2)_3CH_3$

Belamcandone C[5)]



Iristectorone E[4)]

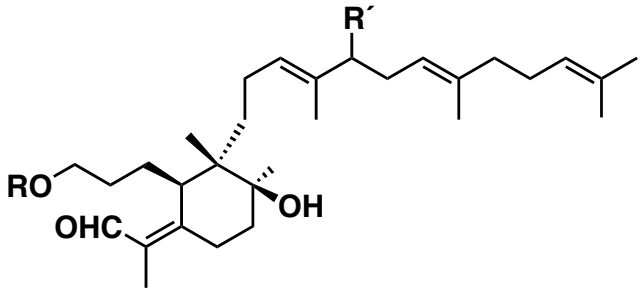


R = -$(CH_2)_{12}CH_3$

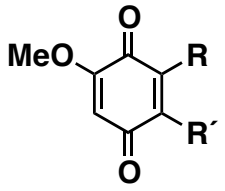
Dibelamcandal A[6)]

1) Y. Fukuyama, Y. Kiriyama, J. Okino, M. Kodama, H. Iwaki, S. Hosozawa, K.Matsui. *Chem. Pharm. Bull,* 41, 561-565, (1993).
2) Y. Fukuyama, J. Okino, and M. Kodama. *Chem. Pharm. Bull,* 39, 1877, (1991).
3) Y. Fukuyama, Y. Kiriyama, J. Okino, M. Kodama. *Tetrahedron Lett.,* 34, 7633-7636, (1993).
4) K. Seki, T. Tomihari, K. Haga, R. Kaneko. *Phytochemistry,* 37, 807-815, (1994).
5) K. Seki, K. Haga, R. Kaneko. *Phytochemistry,* 38, 703-709, (1995).
6) Z. Song, X. Xu, W.Deng, S. Peng, L. Ding, and H. Xu. *Org Lett,* 13, 462-465, (2011).

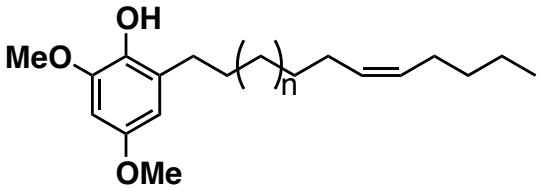
Compounds isolated from *Belamcanda chinensis* in the present study



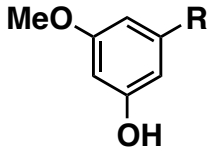
1: R = -$CO(CH_2)_{14}CH_3$, R´ = -H
2: R = -$CO(CH_2)_{16}CH_3$, R´ = -H
4: R = -$CO(CH_2)_9CH{=}CH(CH_2)_3CH_3$, R´ = -H
5: 3-*O*-Tetradecanoyl-16-*O*-hydroxyisoiridogermanal[4)]
: R = -$CO(CH_2)_{12}CH_3$, R´ = -OH



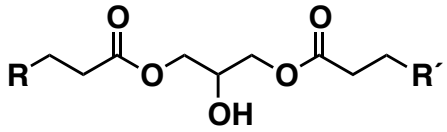
3: R = -$(CH_2)_4CH{=}CH(CH_2)_{10}CH_3$, R´ = -H
6: Ardisianone A[1)]
: R = -$(CH_2)_9CH{=}CH(CH_2)_3CH_3$, R´= -H
7: R = -$(CH_2)_9CH{=}CH(CH_2)_3CH_3$, R´= -OH



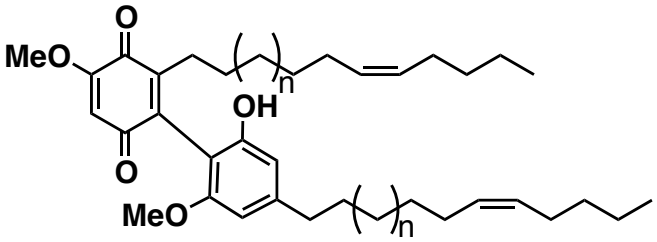
8: Belamcandol A : n = 5[2)]



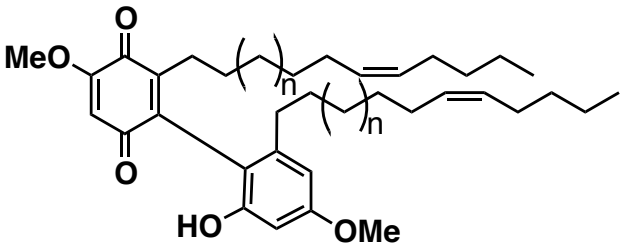
9: 3-heptadecyl-5-methoxy-phenol[5)]
: R = -$(CH_2)_{16}CH_3$
10: Belamcandol B[2)]
: R = -$(CH_2)_9CH{=}CH(CH_2)_3CH_3$



11: R = -$(CH_2)_{12}CH_3$, R´ = -$(CH_2)_5CH{=}CH(CH_2)_4CH_3$



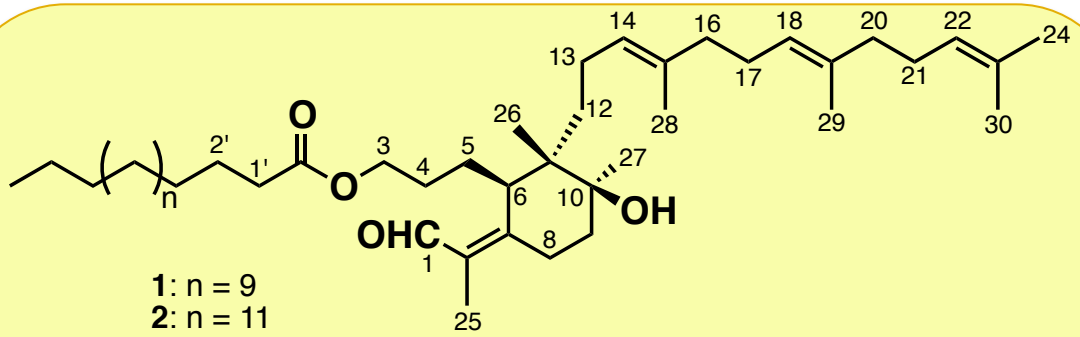
12: Belamcandaquinone A (抗アレルギー作用) : n = 5[3)]



13: Belamcandaquinone B : n = 5[3)]

1) Y. Fukuyama, Y. Kiriyama, J. Okino, M. Kodama, H. Iwaki, S. Hosozawa, K.Matsui. *Chem. Pharm. Bull,* 41, 561-565, (1993).
2) Y. Fukuyama, J. Okino, and M. Kodama. *Chem. Pharm. Bull,* 39, 1877, (1991).
3) Y. Fukuyama, Y. Kiriyama, J. Okino, M. Kodama. *Tetrahedron Lett.,* 34, 7633-7636, (1993).
4) K. Seki, T. Tomihari, K. Haga, R. Kaneko. *Phytochemistry,* 37, 807-815, (1994).
5) G. Feresin, A. Tapia, M. Sortino, S. Zacchino, A. Rojas de Arias, G. Yaluff, J. Rodriguez, C. Theoduloz, G. Schmeda-Hirschmann. *J. Ethnopharm.,* 88, 241-247, (2003).

^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 2

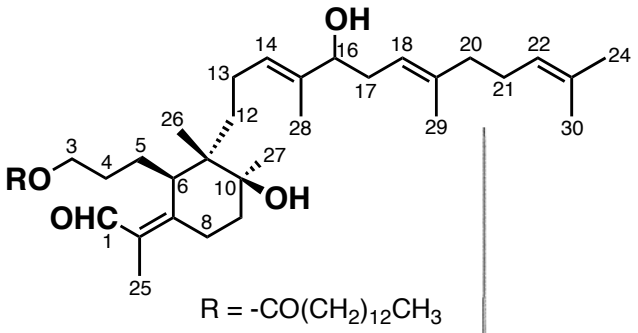


Physical data of Compound 1

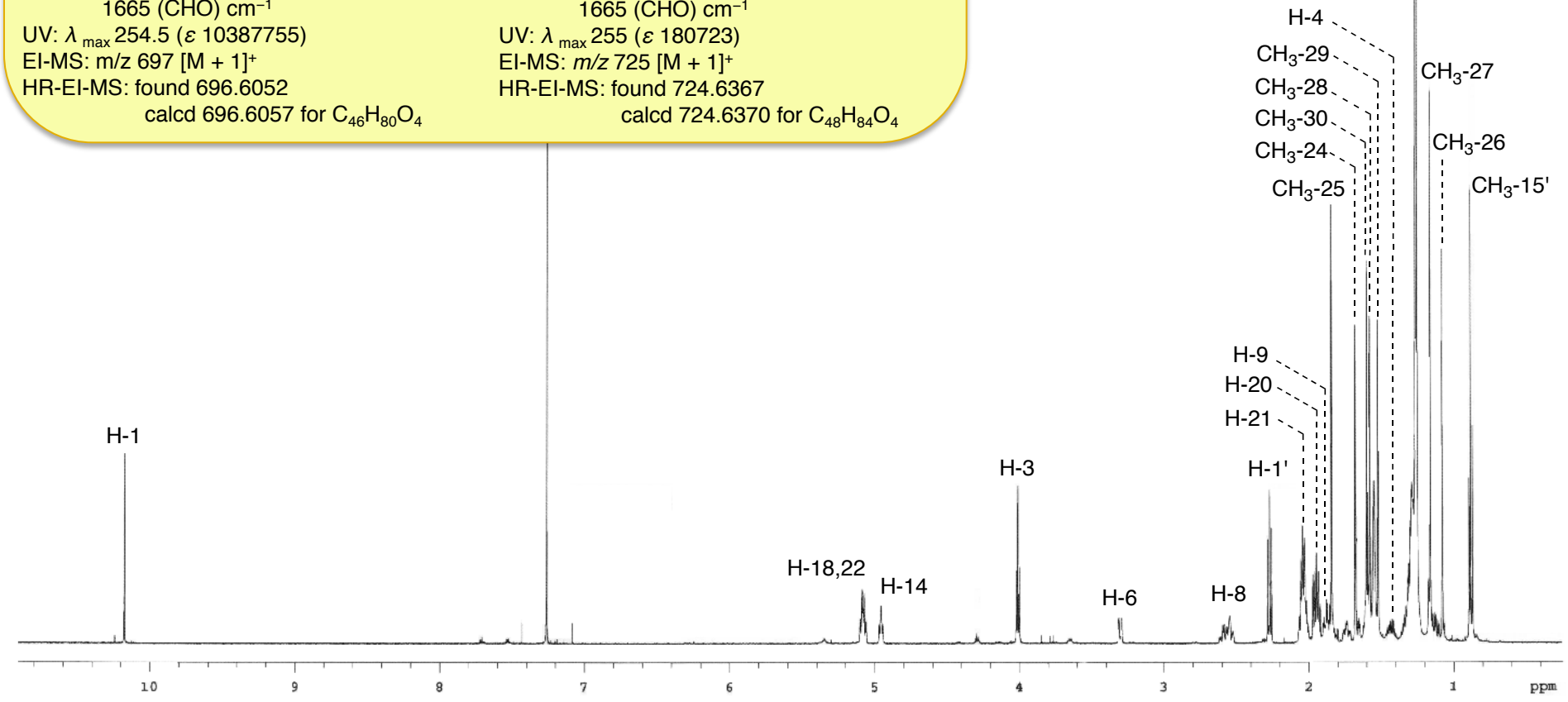
$[\alpha]_D^{26}$ = -1.43 (*c* 0.0125, $CHCl_3$) nm
IR: ν_{max} 3514 (OH), 1730 (C=O), 1665 (CHO) cm^{-1}
UV: λ_{max} 254.5 (ε 10387755)
EI-MS: m/z 697 $[M + 1]^+$
HR-EI-MS: found 696.6052
calcd 696.6057 for $C_{46}H_{80}O_4$

Physical data of Compound 2

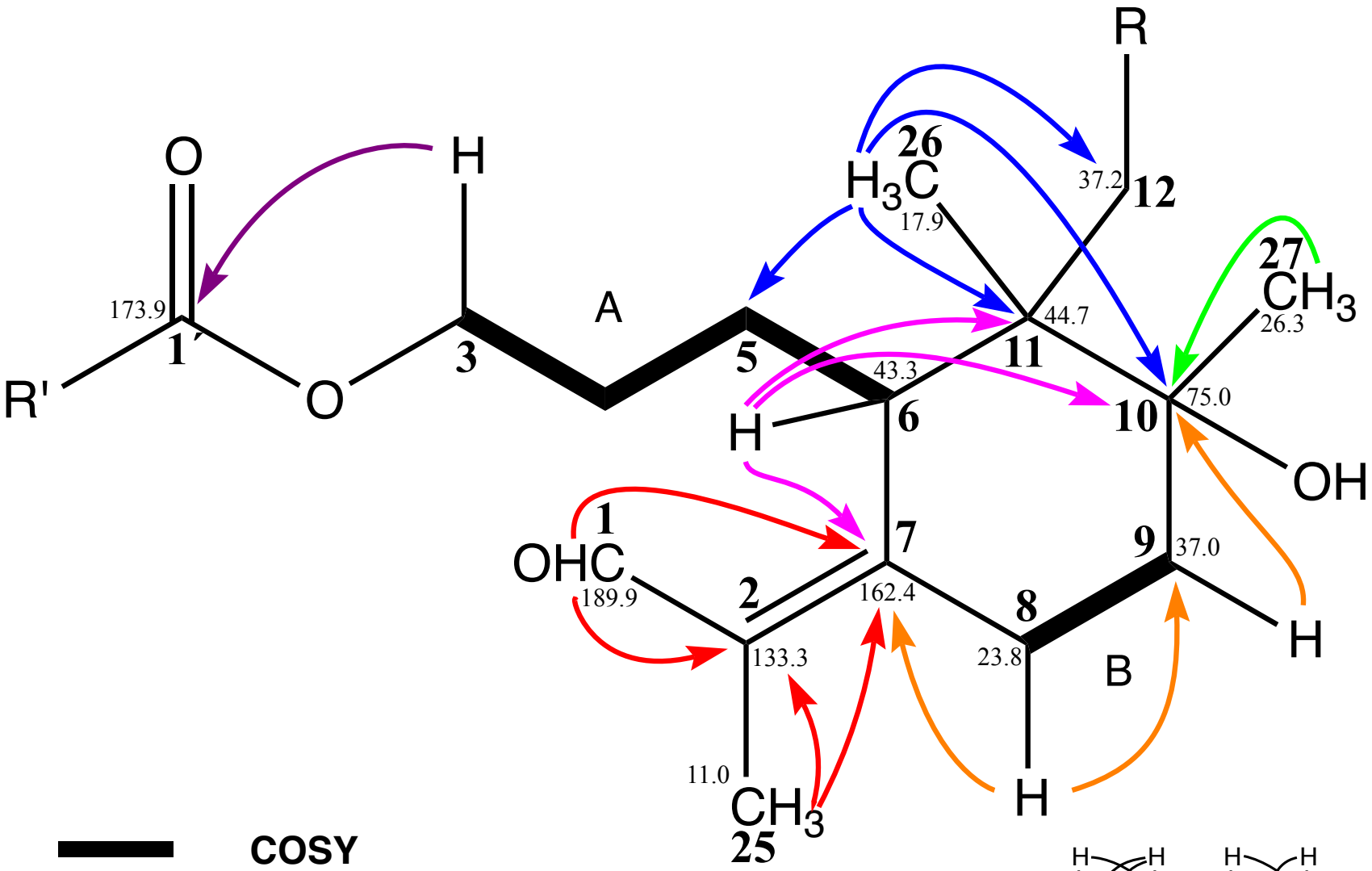
$[\alpha]_D^{26}$ = -2.35 (*c* 0.0105, $CHCl_3$)
IR: ν_{max} 3524 (OH), 1730 (C=O), 1665 (CHO) cm^{-1}
UV: λ_{max} 255 (ε 180723)
EI-MS: *m/z* 725 $[M + 1]^+$
HR-EI-MS: found 724.6367
calcd 724.6370 for $C_{48}H_{84}O_4$



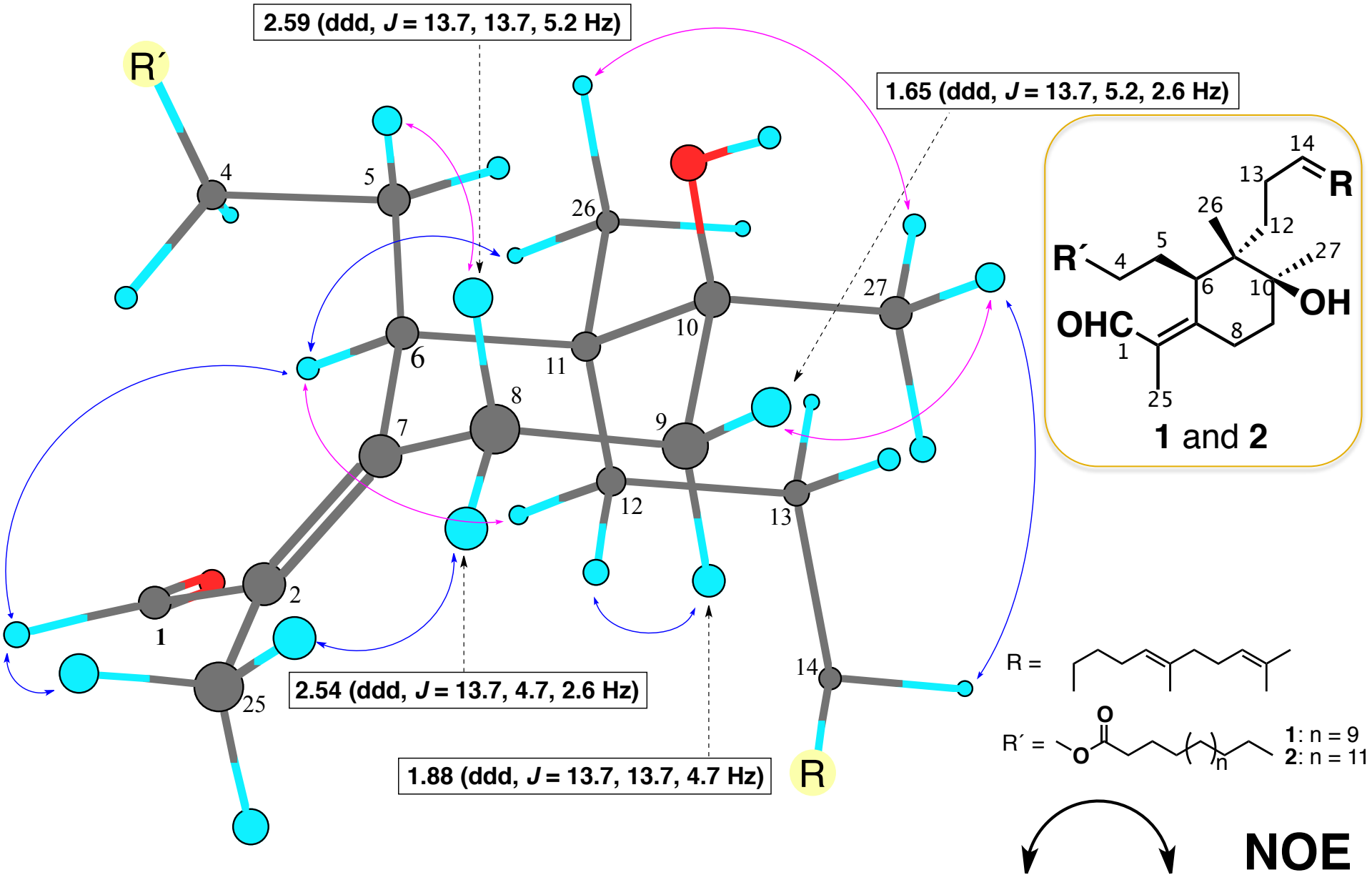
5: 3-*O*-Tetradecanoyl-16-*O*-hydroxyisoiridogermanal[3)]



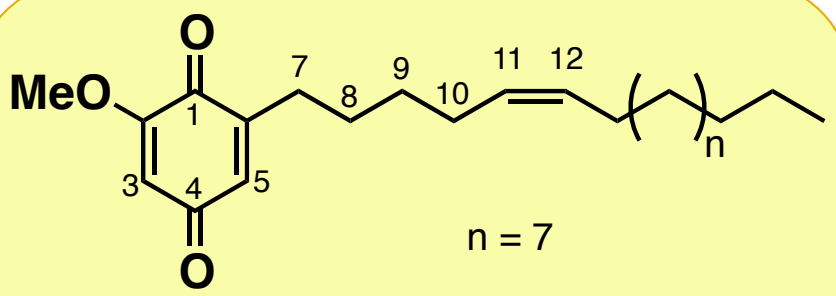
HMBC correlations of 1 and 2



NOESY correlations of 1 and 2

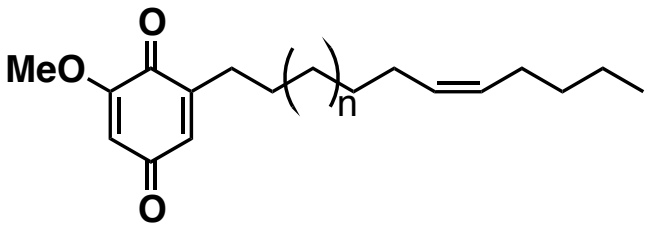


^{1}H NMR spectrum (600 MHz, $CDCl_3$) of 3



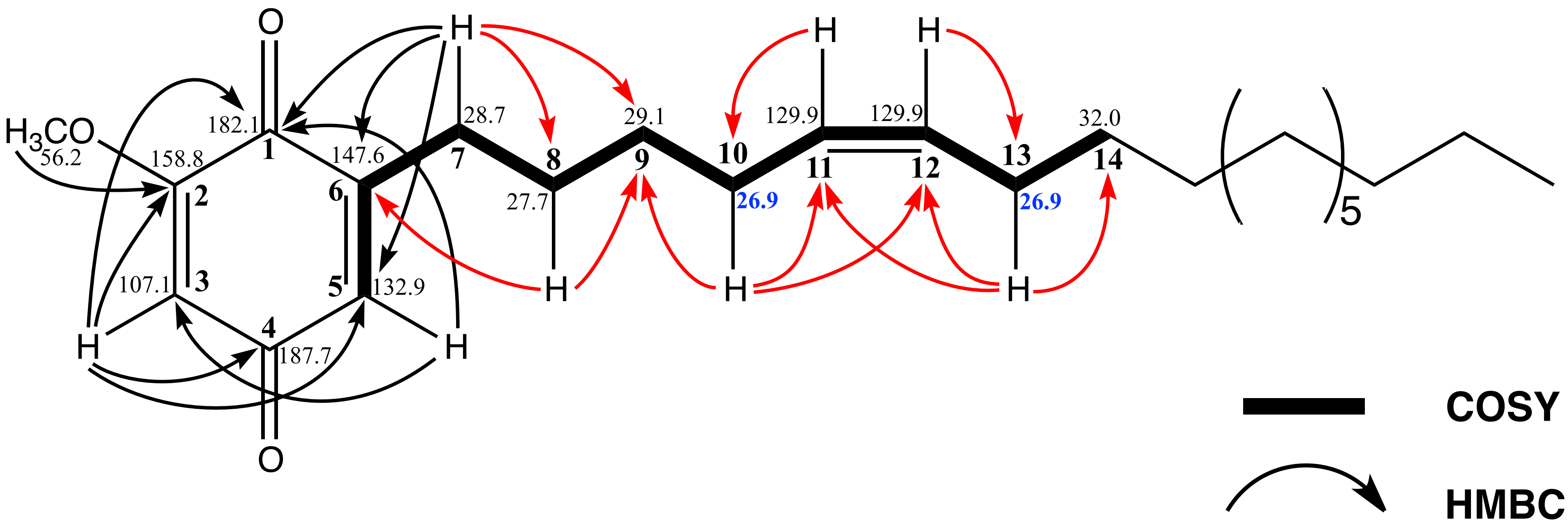
n = 7

IR: ν_{max} 1679 (C=O), 1600 (C=C) cm^{-1}
UV: λ_{max} 240 (ε 680079), 275 (ε 779258),
280 (ε 793426) nm
EI-MS: *m/z* 374 $[M]^+$
HR-EI-MS: found 374.2820
calcd 374.2821 for $C_{24}H_{38}O_3$

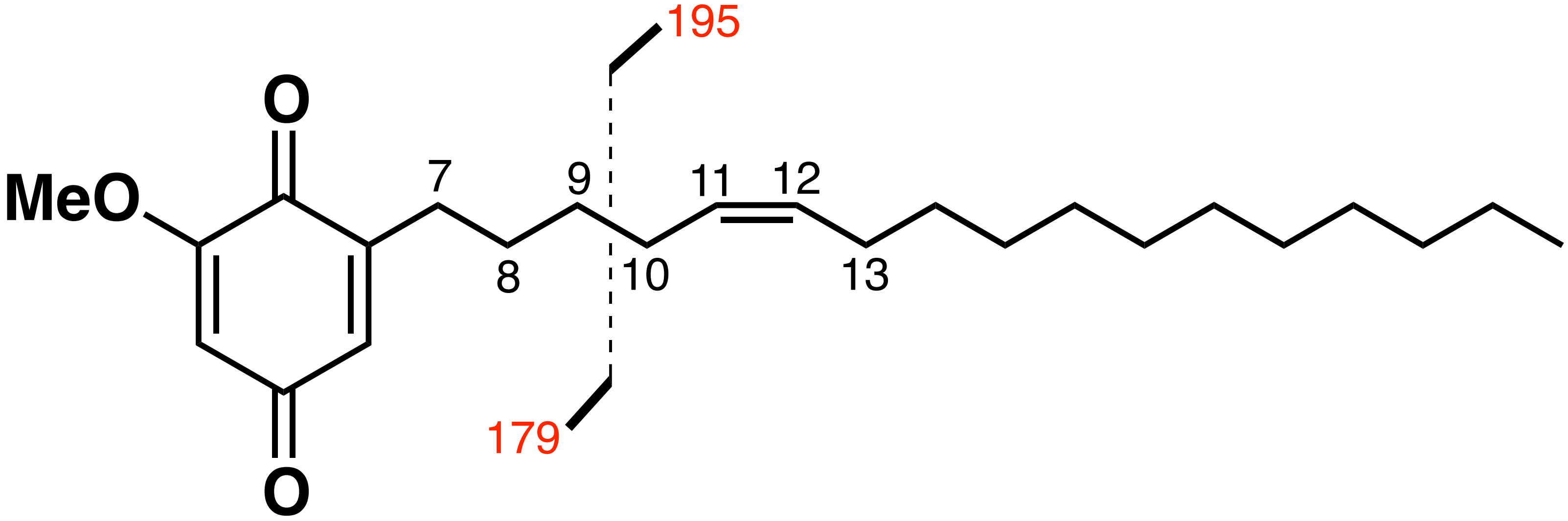


6: Ardisianone A: n = 5[1)]

HMBC correlations of 3

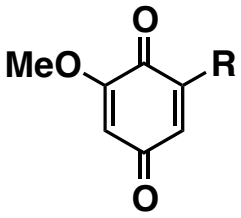


EI-MS spectrum of 3

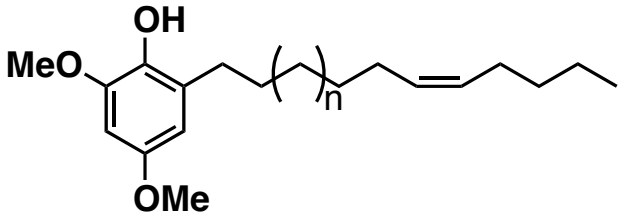


m/z 374 [M$^+$]

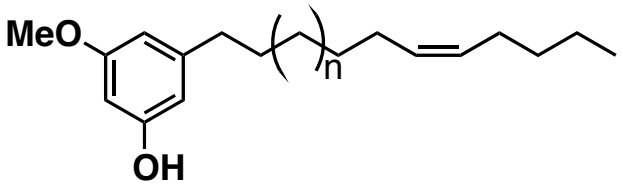
Screening results of compounds from *Belamcanda* chinensis by PC12 cells



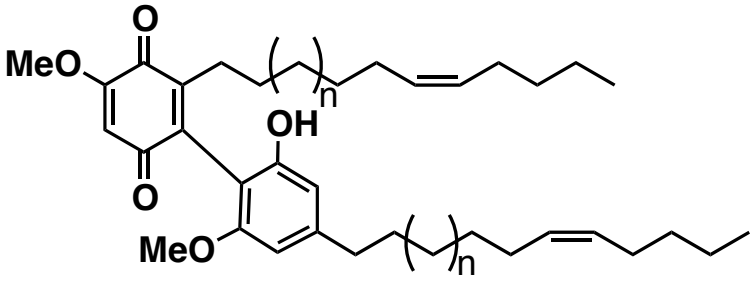
3: R = -$(CH_2)_4CH{=}CH(CH_2)_{10}CH_3$
6: Ardisianone A
: R = -$(CH_2)_9CH{=}CH(CH_2)_3CH_3$



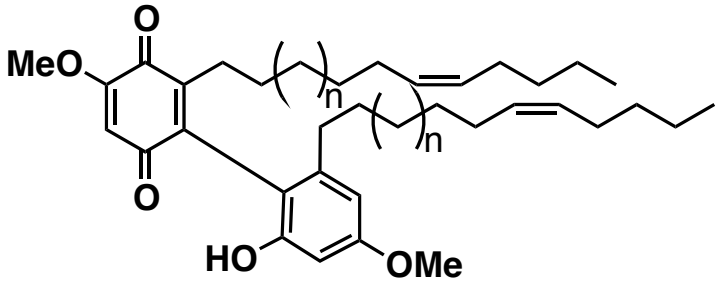
8: Belamcandol A: n = 5



10: Belamcandol B: n = 5

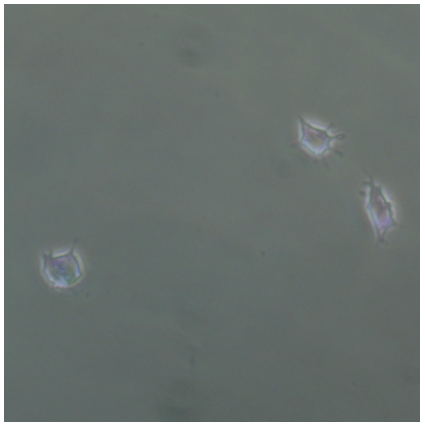


12: Belamcandaquinone A: n = 5

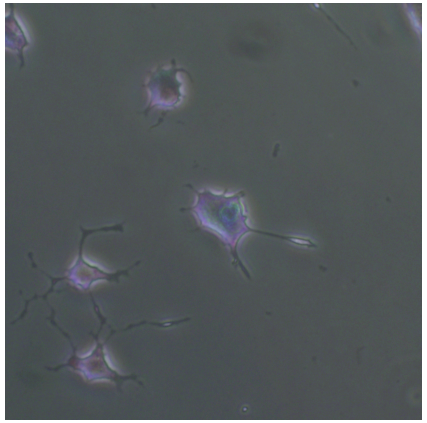


13: Belamcandaquinone B: n = 5

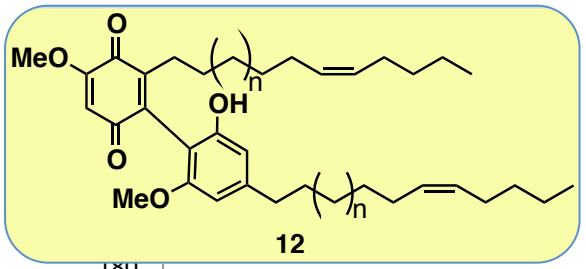
Neurite outgrowth of PC12 cells promoted by 12



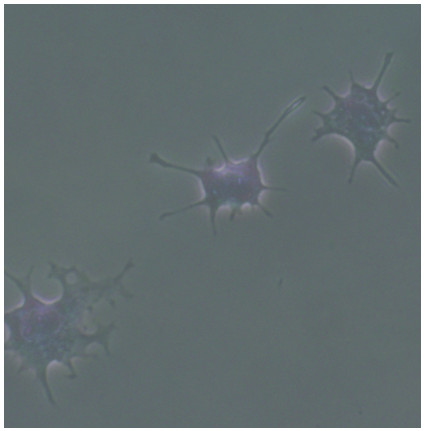
Control (0.5% EtOH)



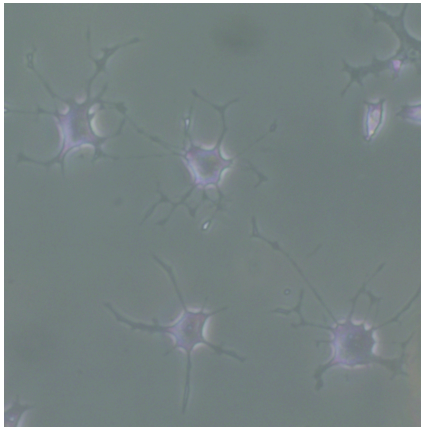
NGF (2 ng/mL)



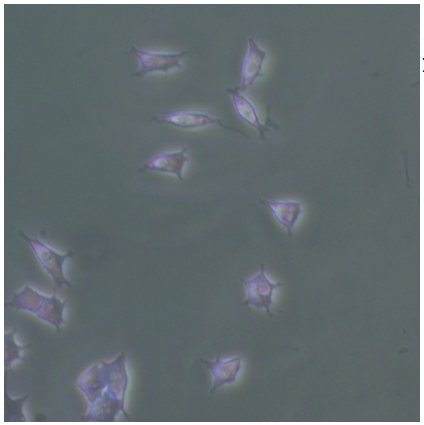
12



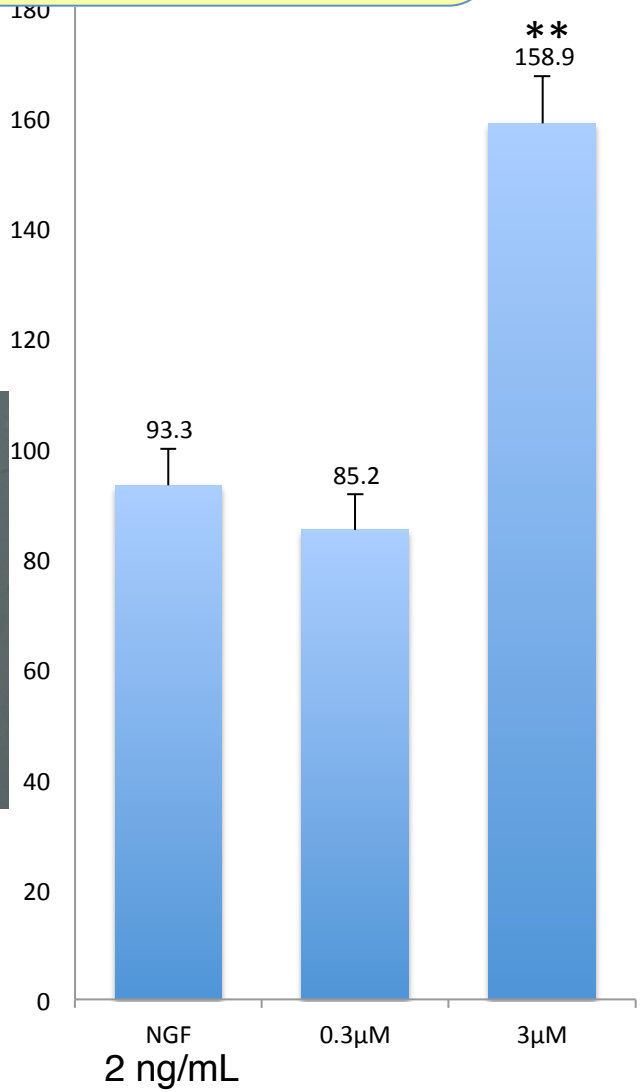
12 (30 µmol/L)



12 (3 µmol/L)

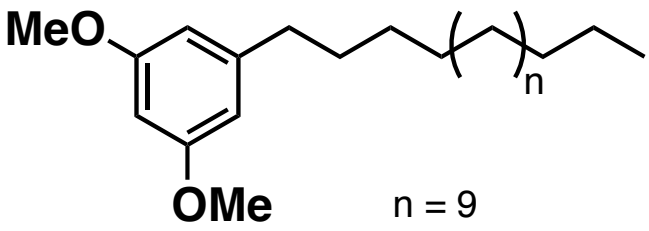


12 (0.3 µmol/L)

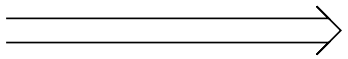


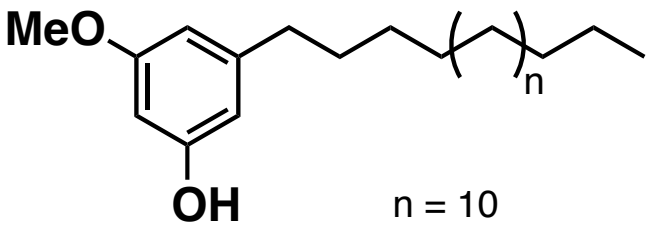
PC12 cells were cultured in 24-well plate in DMEM/10%HS+5%FBS for 1day at the density of 2000 cells/cm^2 then medium change to DMEM/2%HS+ 1%FBS with control (0.5% EtOH), NGF 2 ng/mL, NGF 2 ng/mL + samples 10µM. after 96 hr, PC12 cells were fixed and stained with methylene blue, then were quantified for the neurite length. At least 100 cells were selected for calculating the neurite length. Data were expressed a mean as ± SE. *, *P*<0.01; compared with NGF by Dunnett's t-test.

訂正



4





9