The Japan Institute of Heterocyclic Chemistry Publication

HETEROCYCLES

An International Journal for Reviews and Communications in Heterocyclic Chemistry
Web Edition ISSN: 1881-0942

Published online by The Japan Institute of Heterocyclic Chemistry

Scopus Preview   Author search   Sources   Create account   Sign in

Source details

Feedback >   Compare s

Heterocycles

Scopus coverage years: from 1983 to Present

Publisher: Elsevier

ISSN: 0385-5414

Subject area: (Pharmacology, Toxicology and Pharmaceutics: Pharmacology) (Chemistry: Analytical Chemistry) (Chemistry: Organic Chemistry)

Source type: Journal

View all documents >   Set document alert   Save to source list   Source Homepage

CiteScore 2019
1.5

SJR 2019
0.244

SNIP 2019
0.334

Heterocycles

COUNTRY

Japan

Universities and research institutions in Japan

SUBJECT AREA AND CATEGORY

Chemistry
- Analytical Chemistry
- Organic Chemistry

Pharmacology, Toxicology and Pharmaceutics
- Pharmacology

PUBLISHER

Japan Institute of Heterocyclic Chemistry

H-INDEX

63

PUBLICATION TYPE

Journals

ISSN

03855414

COVERAGE

1983-2020

INFORMATION

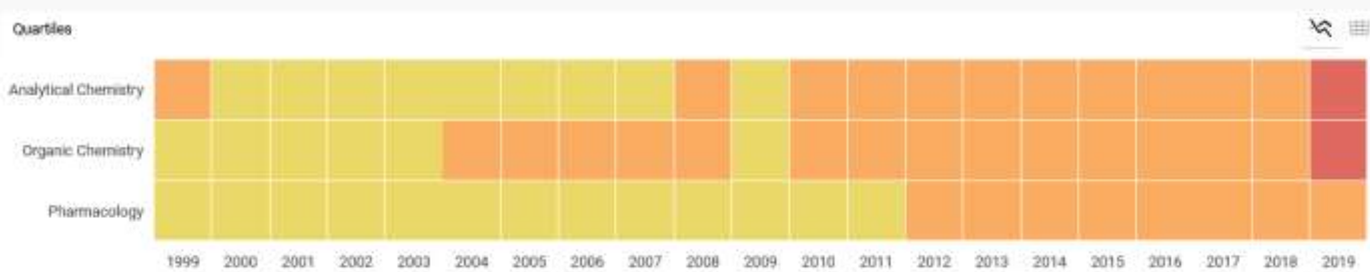
Homepage

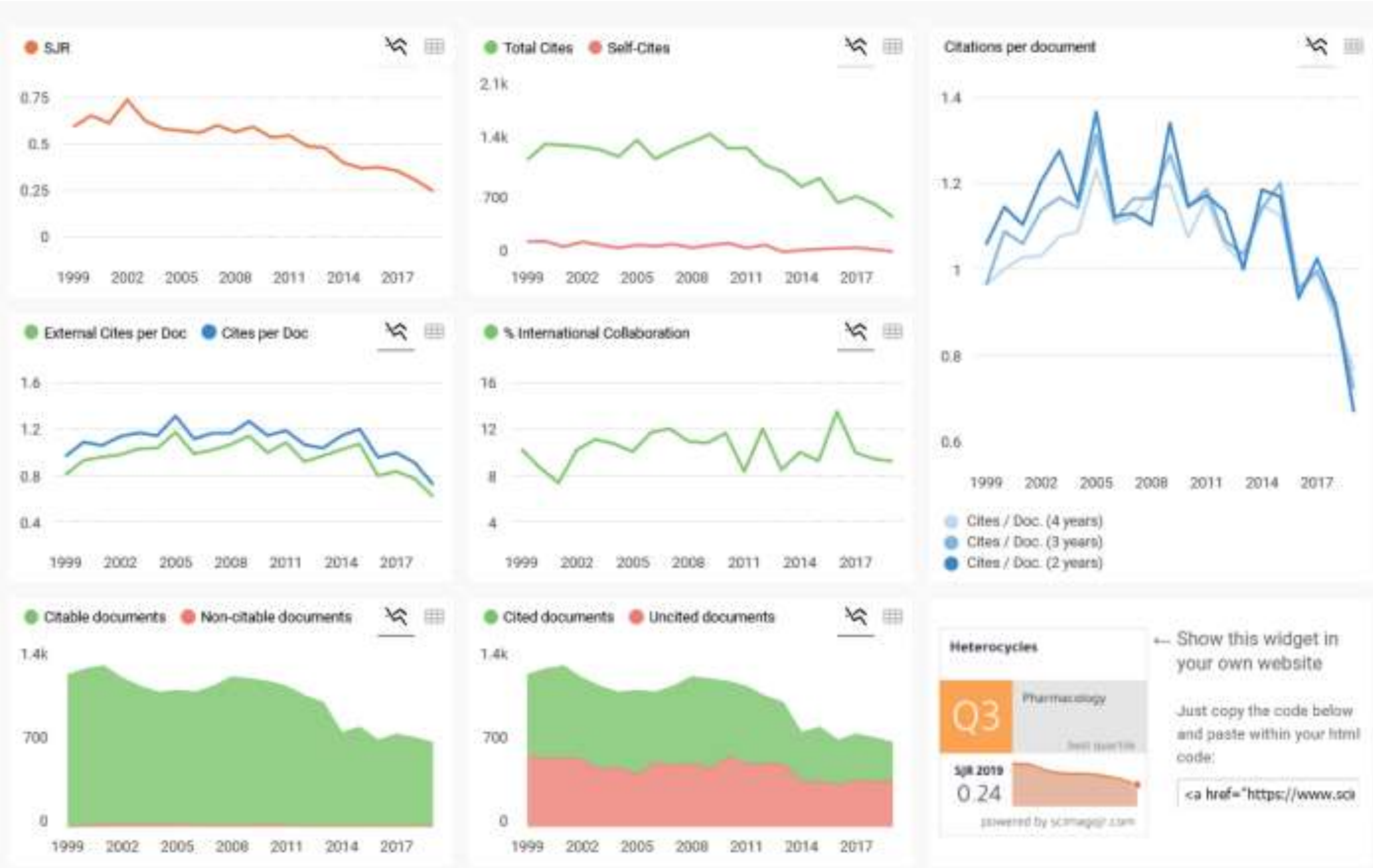
How to publish in this journal

editorial@heterocycles.com

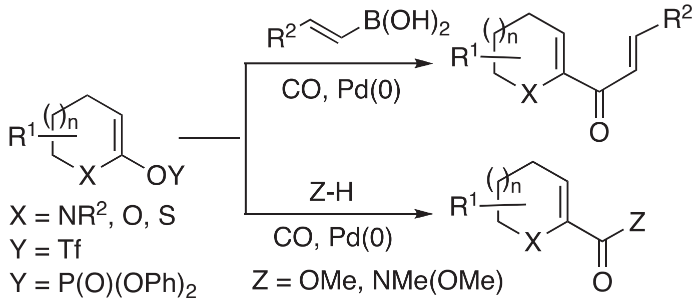
SCOPE

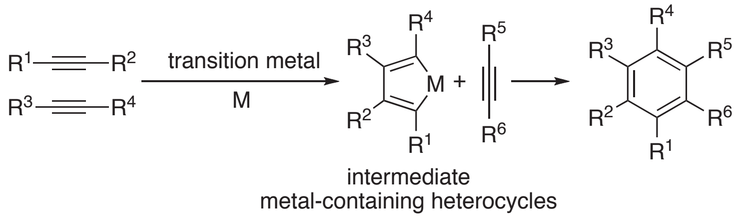
Since its inception in 1973 HETEROCYCLES has provided a platform for the rapid exchange of research in the areas of organic, pharmaceutical, analytical, and medicinal chemistry of heterocyclic compounds in addition to communications, papers, reviews, a special section of the journal presents newly-discovered natural products whose structure has recently been established. Another section is devoted to the total synthesis of previously documented natural products with heterocyclic ring systems. Due to the fact that the journal is able to publish articles within two months of receipt of the manuscripts, researchers in this field can obtain up-to-date information on heterocyclic research by reading Heterocycles regularly. Audience: Organic and Physical Organic Chemists, Biochemists, Pharmacologists and Scientists studying heterocyclic compounds

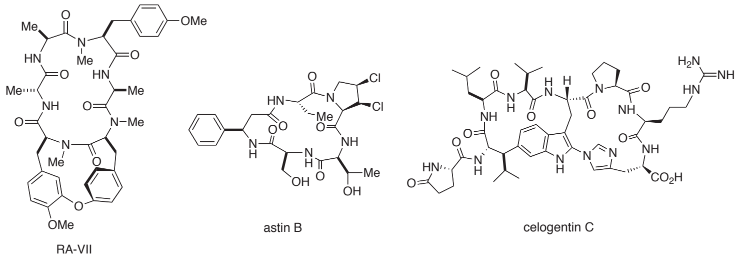



SJR
Total Cites
Self-Cites
Citations per document
External Cites per Doc
Cites per Doc
% International Collaboration
Cites / Doc. (4 years)
Cites / Doc. (3 years)
Cites / Doc. (2 years)
Citable documents
Non-citable documents
Cited documents
Uncited documents
Heterocycles
Q3
Pharmacology
SJR 2019
0.24
Show this widget in your own website
Just copy the code below and paste within your html code:
<a href="https://www.sci

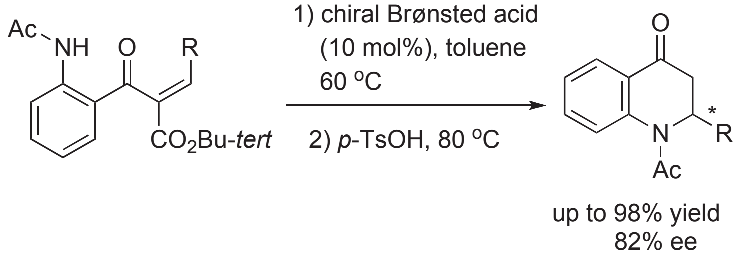
■ REVIEWS

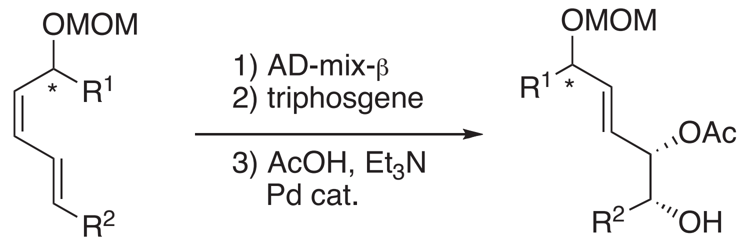


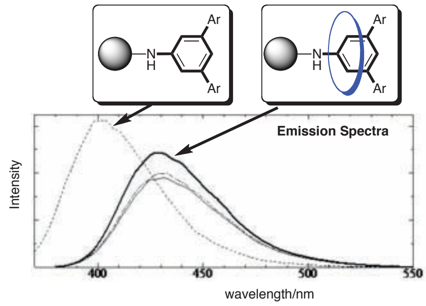


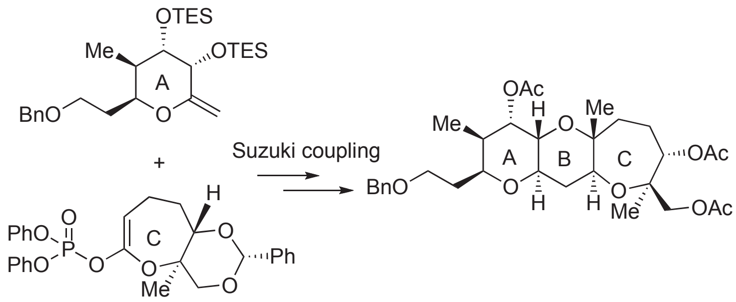


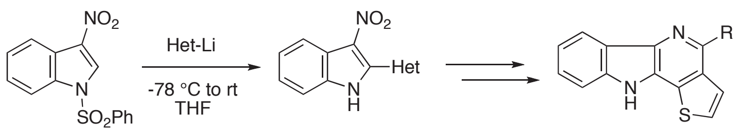
■ COMMUNICATIONS

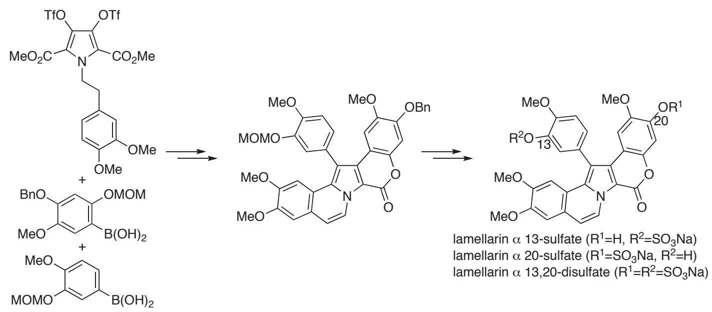


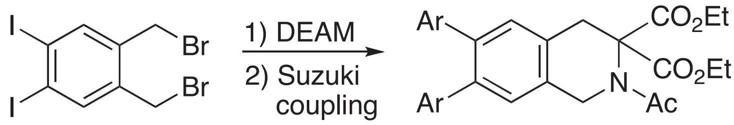

OMOM
R1
R2
1) AD-mix-β
2) triphosgene
3) AcOH, Et3N
Pd cat.
OMOM
R1
OAc
R2
OH

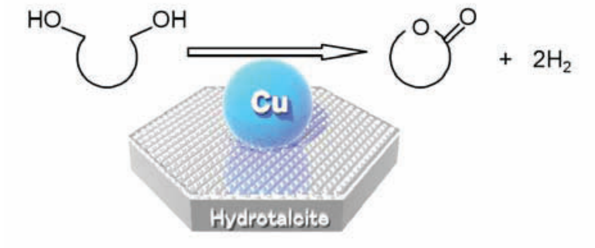

Ar
Ar
Emission Spectra
Intensity
400
450
500
550
wavelength/nm

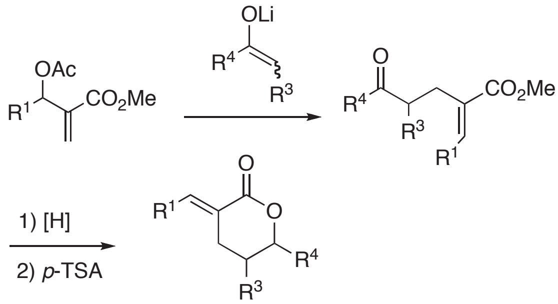

OTES
OTES
Me
BnO
Suzuki coupling
PhO
PhO
Ph
OAc
OAc
OAc

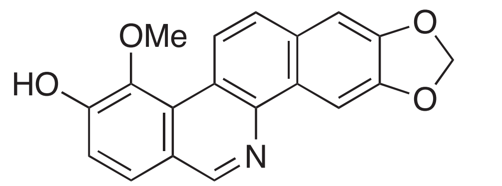

NO2
SO2Ph
Het-Li
-78 °C to rt
THF
NO2
Het
R


TfO
OTf
MeO2C
CO2Me
OMe
BnO
OMOM
B(OH)2
MOMO
B(OH)2
lamellarin α 13-sulfate (R1=H, R2=SO3Na)
lamellarin α 20-sulfate (R1=SO3Na, R2=H)
lamellarin α 13,20-disulfate (R1=R2=SO3Na)

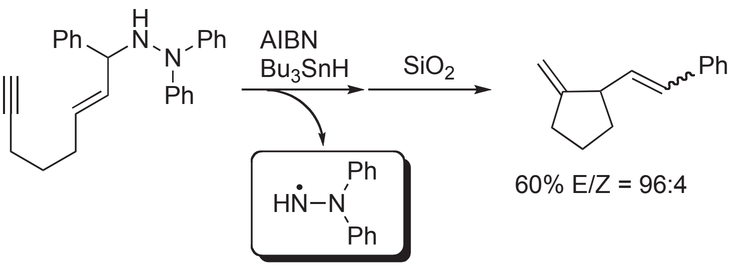


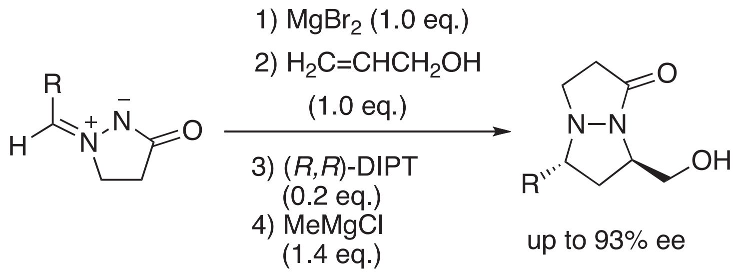


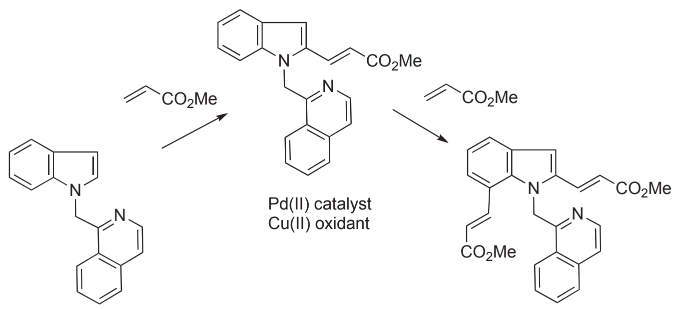


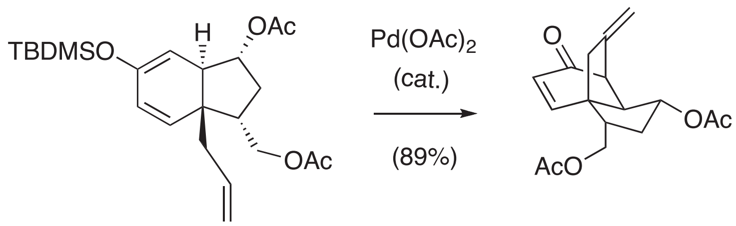


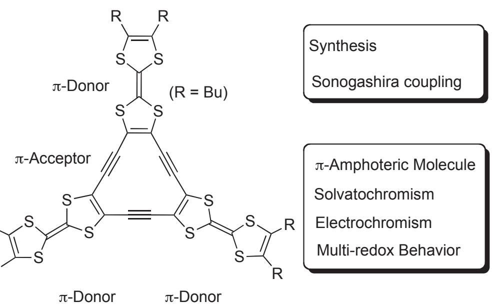
zanthoxyline (reported structure)

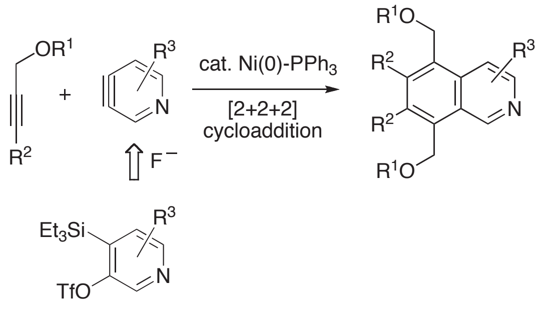



1) $MgBr_2$ (1.0 eq.)
2) H_2C=$CHCH_2OH$ (1.0 eq.)
3) (*R,R*)-DIPT (0.2 eq.)
4) MeMgCl (1.4 eq.)
up to 93% ee

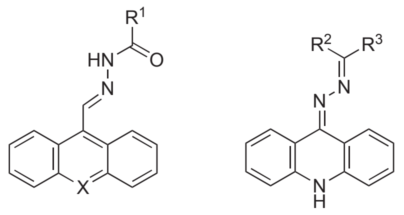

Pd(II) catalyst
Cu(II) oxidant


$Pd(OAc)_2$ (cat.)
(89%)


π-Donor
(R = Bu)
π-Acceptor
π-Donor
π-Donor
Synthesis
Sonogashira coupling
π-Amphoteric Molecule
Solvatochromism
Electrochromism
Multi-redox Behavior


cat. Ni(0)-PPh_3
[2+2+2] cycloaddition

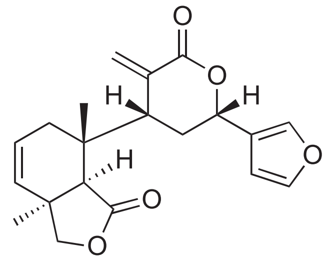
■ **PAPERS**



X = N, CH
R^1 = Me, C_6H_2, 3-Py, 4-Py, 9-oxoacridin-4-yl

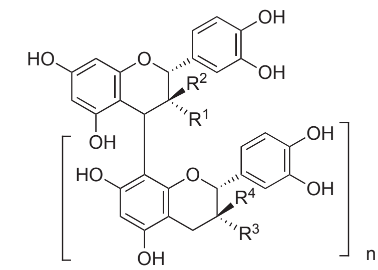
R^2 = H, Me
R^3 = Me, Ph, 4-BrC_6H_4, 4-$MeOC_6H_4$, 2,4,6-triMeC_6H_2, 2,4,6-tri$MeOC_6H_2$

Acridine Carbohydrazide Hydrazone Fluorescence DFT



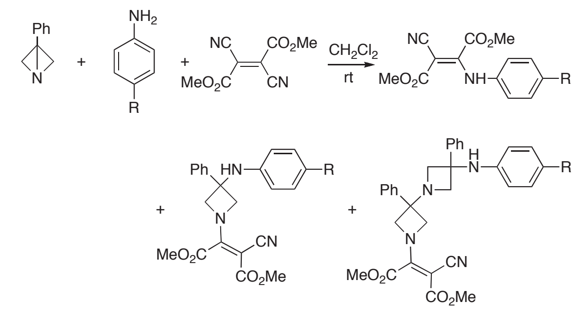
clutiolide

Clutiolide Diterpene Ireland-Claisen Rearrangement Chelation Control Diels-Alder Reaction

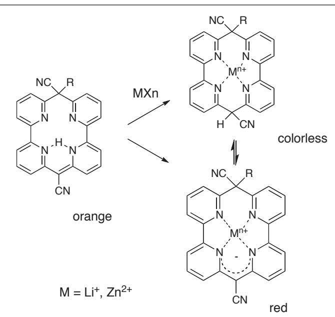


$R^1 = R^2 = R^3 = R^4$: H, OH or *O*-Galloyl, n = 0 - 4

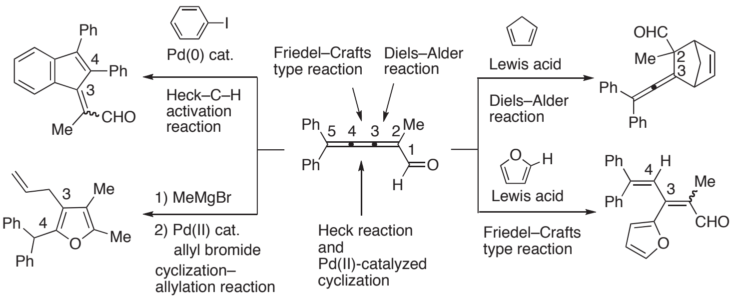
Condensed Tannin Antioxidant Tea Catechin Polyphenol Artificial Procyanidin Oligomer

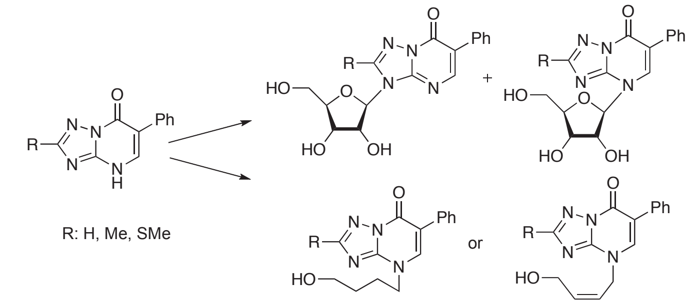


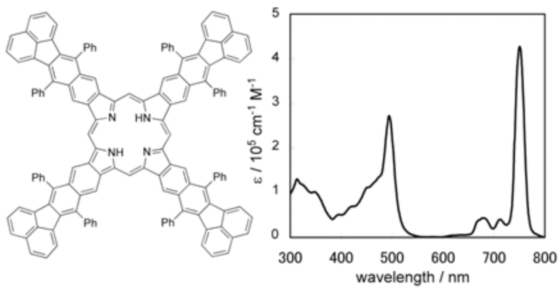
1-Azabicyclo[1.1.0]butane 2,3-Dicyanofumarate Zwitterionic Intermediate Three-Component Reaction Addition Reaction

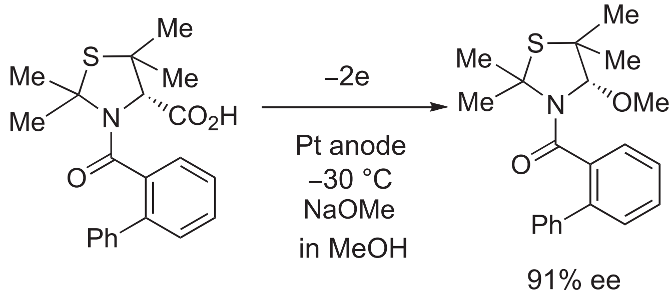


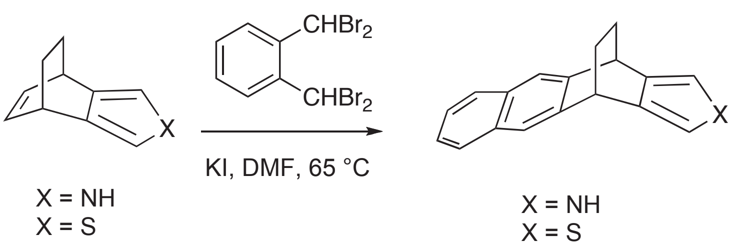
Tetraazamacrocycle Lithium Complex Unsymmetrical Structure Strained Molecule Anion Control


Pd(0) cat.
Heck–C–H activation reaction
1) MeMgBr
2) Pd(II) cat. allyl bromide
cyclization–allylation reaction
Friedel–Crafts type reaction
Diels–Alder reaction
Heck reaction and Pd(II)-catalyzed cyclization
Lewis acid
Diels–Alder reaction
Lewis acid
Friedel–Crafts type reaction


R: H, Me, SMe
or

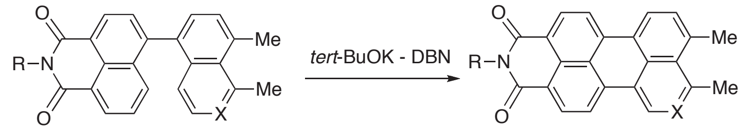

ε / 10⁵ cm⁻¹ M⁻¹
wavelength / nm


–2e
Pt anode
–30 °C
NaOMe
in MeOH
91% ee


KI, DMF, 65 °C
X = NH
X = S
X = NH
X = S

1197 Synthesis and Properties of Dicarboximide Derivatives of Perylene and Azaperylene

Yukinori Nagao,* Tatsurou Yoshida, Koji Arimitsu, and Kozo Kozawa

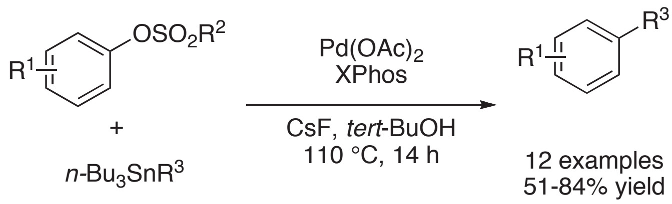


X = C, N
R = n-C_6H_{13}, cyclohexyl

Coupling Reaction Ring Closure Reaction Absorption Spectrum Fluorescence Spectrum

1215 Stille Cross-Coupling Reactions of Aryl Mesylates and Tosylates Using a Biarylphosphine Based Catalyst System

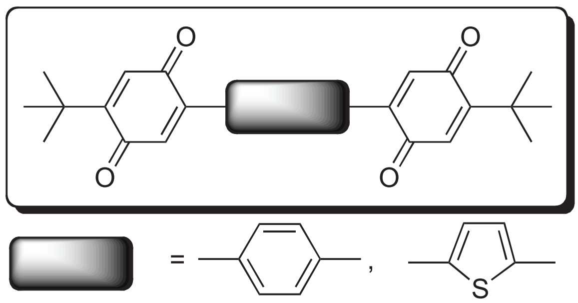
John R. Naber, Brett P. Fors, Xiaoxing Wu, Jonathon T. Gunn, and Stephen L. Buchwald*



Aryl Mesylate Palladium Catalysis C-C Bond Formation Stille Reaction Aryl Tosylate

1227 Quinone Dimers Connected by 1,4-Phenylene and 2,5-Thienylene Moieties as a π Linker

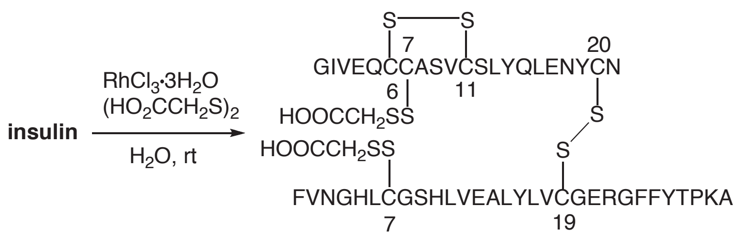
Naoto Hayashi,* Teru Sakakibara, Takahiro Ohnuma, Junro Yoshino, and Hiroyuki Higuchi



π Linker Quinone Electronic Absorption Spectra π-Conjugation System Cyclic Voltammetry

1239 $RhCl_3$-Catalyzed Disulfide Exchange Reaction of Insulin and Dithiodiglycolic Acid

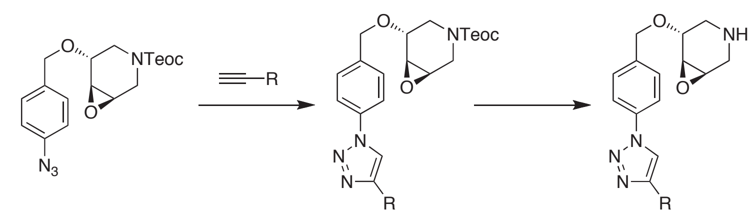
Mieko Arisawa, Manabu Kuwajima, Atsushi Suwa, and Masahiko Yamaguchi*



Rhodium Chloride Disulfide Exchange Reaction Catalysis A7/B7 Disulfide Insulin

1249 Synthesis and Evaluation of Novel 3,4-Epoxypiperidines as Efficient DNA Alkylating Agents

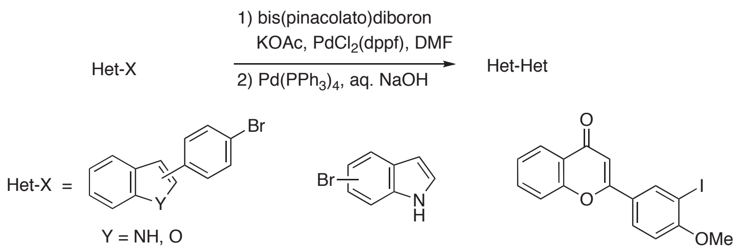
Yuji Kawada, Tetsuya Kodama, Kazuyuki Miyashita, Takeshi Imanishi, and Satoshi Obika*

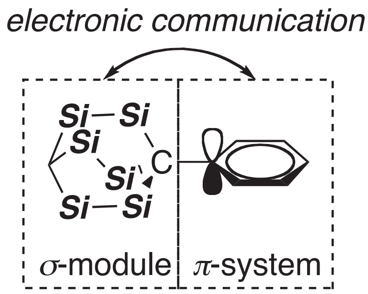


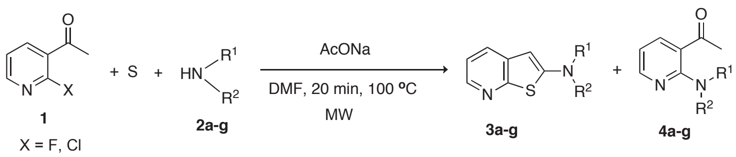
Teoc = 2-trimethylsilylethoxycarbonyl

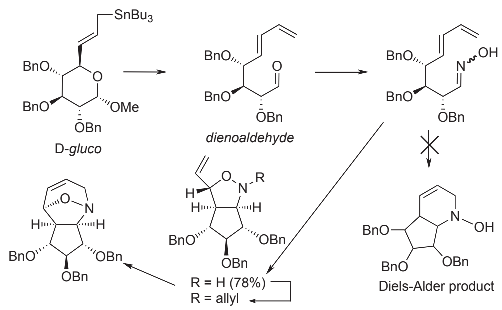
DNA alkylating agents

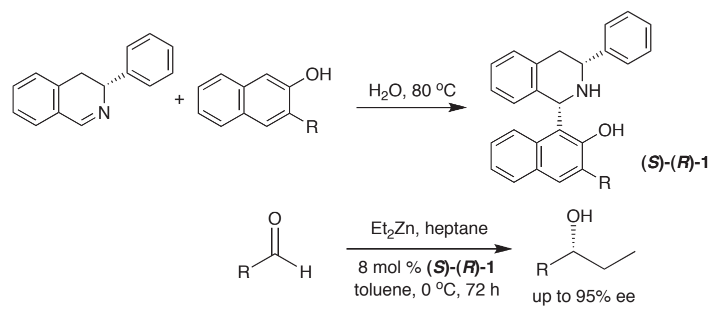
DNA Alkylating Agent Epoxypiperidine Huisgen Reaction Anticancer Azinomycin

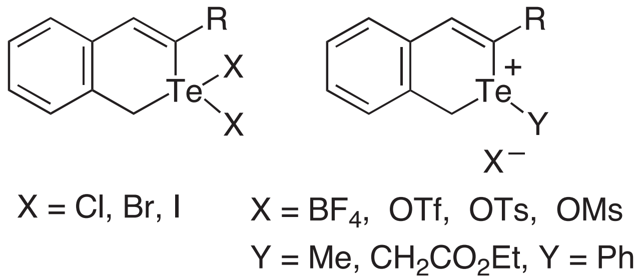

1) bis(pinacolato)diboron
KOAc, $PdCl_2$(dppf), DMF
2) $Pd(PPh_3)_4$, aq. NaOH
Het-X
Het-Het
Het-X =
Br
Y
Y = NH, O
N
H
O
I
OMe

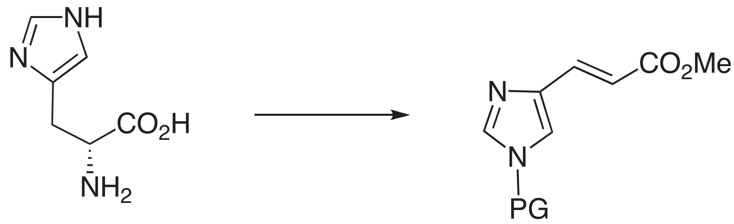

electronic communication
Si
Si
Si
Si
Si
Si
C
σ-module
π-system

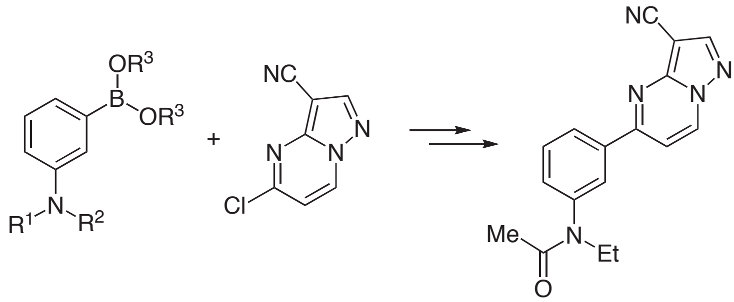

O
N
X
1
X = F, Cl
+ S +
HN
R^1
R^2
2a-g
AcONa
DMF, 20 min, 100 ºC
MW
S
3a-g
+
4a-g

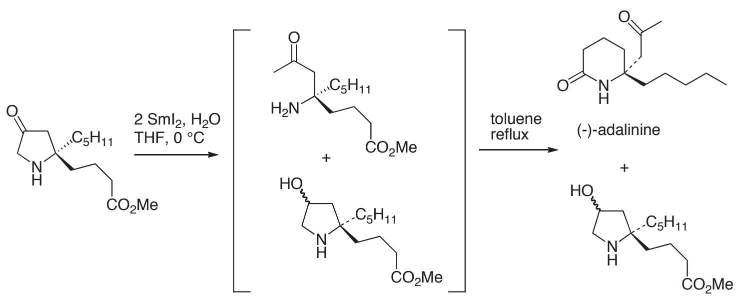

$SnBu_3$
BnO
OMe
OBn
D-*gluco*
dienoaldehyde
OH
Diels-Alder product
R = H (78%)
R = allyl

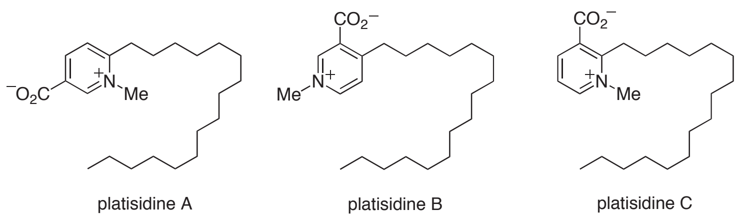

N
+
OH
R
H_2O, 80 °C
NH
(*S*)-(*R*)-1
Et_2Zn, heptane
8 mol % (*S*)-(*R*)-1
toluene, 0 °C, 72 h
up to 95% ee

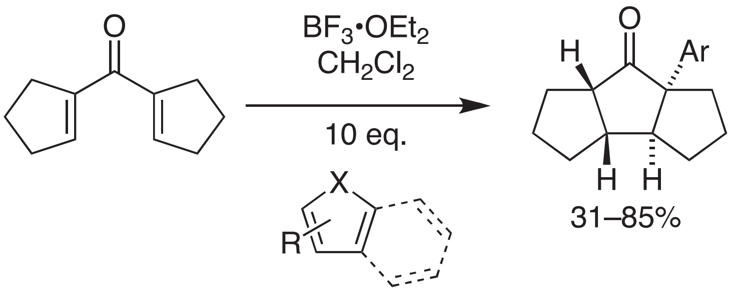

X = Cl, Br, I
X = BF4, OTf, OTs, OMs
Y = Me, CH2CO2Et, Y = Ph

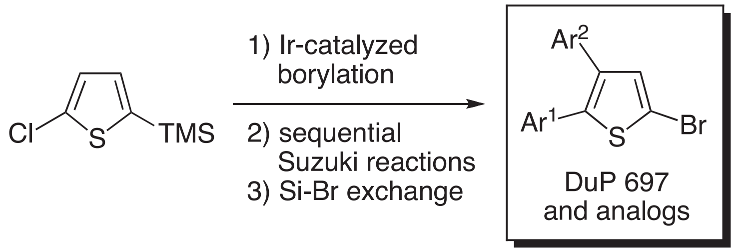




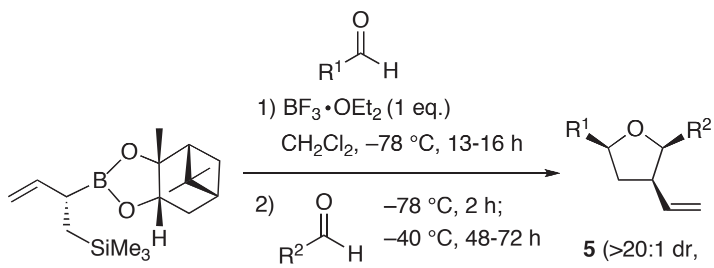

2 SmI2, H2O
THF, 0 °C
toluene
reflux
(-)-adalinine


platisidine A
platisidine B
platisidine C



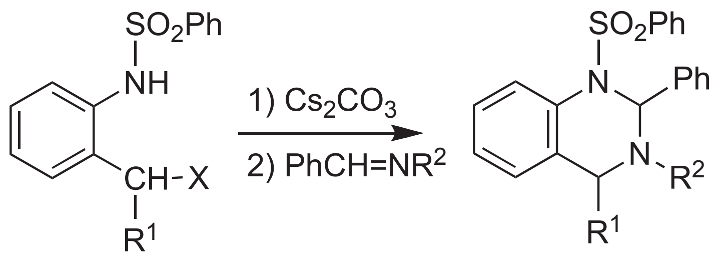


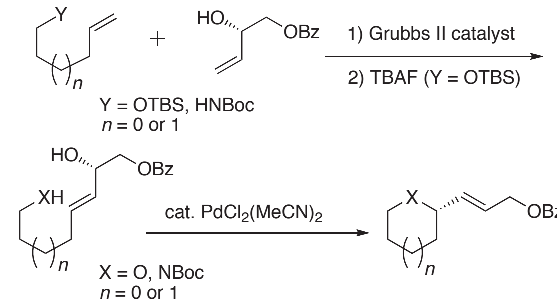
■ **NOTES**

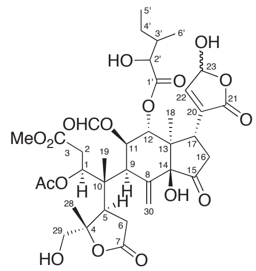


1

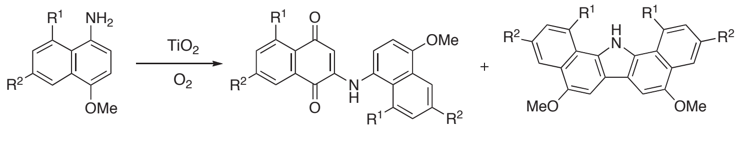
5 (>20:1 dr, >91% ee)

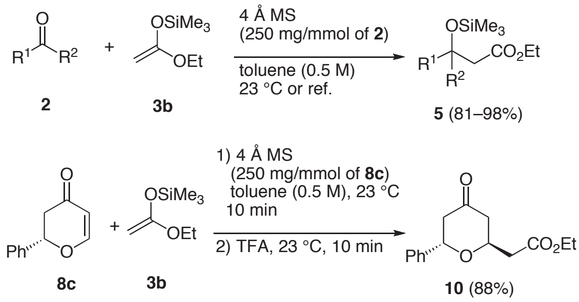






gaudichaudysolin A (**1**)





■ **INDEXES**

Contributors To This Issue

HETEROCYCLES, Vol. 80, No. 2, 2010, pp. 1471 - 1477. © The Japan Institute of Heterocyclic Chemistry
Received, 4th August, 2009, Accepted, 18th September, 2009, Published online, 24th September, 2009
DOI: 10.3987/COM-09-S(S)106

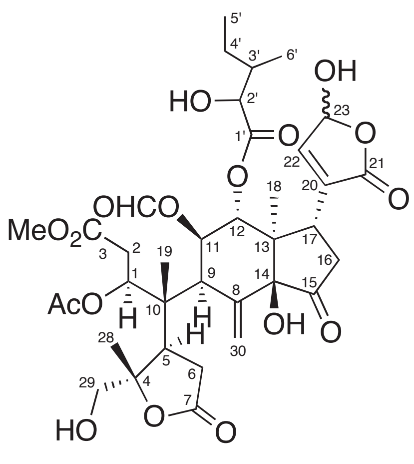
GAUDICHAUDYSOLIN A, A NEW LIMONOID FROM THE BARK OF *DYSOXYLUM GAUDICHAUDIANUM*

Yuta Nagakura,[a] Reiko Yamanaka,[a] Yusuke Hirasawa,[a] Takahiro Hosoya,[a] Abdul Rahman,[b] Idha Kusumawati,[b] Noor Cholies Zaini,[b] and Hiroshi Morita[a,]*

[a]Faculty of Pharmaceutical Sciences, Hoshi University, Shinagawa-ku, Tokyo 142-8501, Japan; [b]Faculty of Pharmacy, Airlangga University, Jalan Dharmawangsa Dalam, Surabaya 60286, Indonesia

Abstract – A new limonoid, gaudichaudysolin A (**1**) was isolated from the bark of *Dysoxylum gaudichaudianum* (Meliaceae) and the structure was elucidated by spectroscopic analysis.

Limonoids, highly oxidative unique secondary metabolites obtained from Meliaceae are produced by a unique biosynthetic route through tetranortriterpenoid nucleus,[1,2] and are known to show various biological activities such as insecticidal, insect antifeedant, antibacterial, antifungal, antimalarial, anticancer, and antiviral activities.[3] Recently, we have isolated new limonoids, ceramicines A – D[4] with an unique tetranortriterpenoid skeleton from *Chisocheton ceramicus* and walsogyne A[5] with a ring C–*seco* limonoid from *Walsura chrysogyne*. They showed an antiplasmodial and cytotoxic activities.[4,5]



gaudichaudysolin A (**1**)

[†]Dedicated to Professor Emeritus Akira Suzuki, Hokkaido University, on the occasion of his 80[th] birthday.

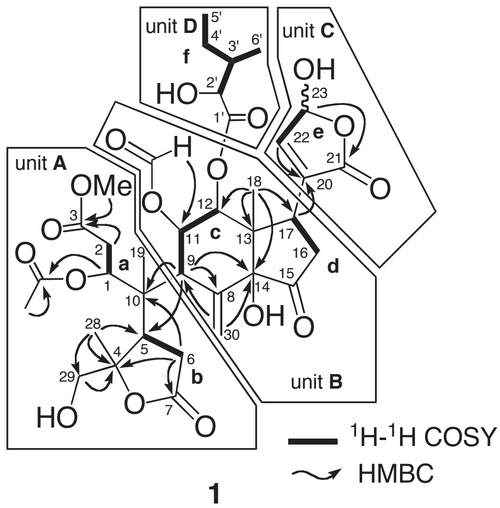
In continuation of our research on limonoids containing in the plants belonging to Meliaceae family, we have isolated a new limonoid, gaudichaudysolin A (**1**) from the bark of *Dysoxylum gaudichaudianum*. Herein we report the structure elucidation of gaudichaudysolin A (**1**) by spectroscopic methods.

The bark of *D. gaudichaudianum* was extracted with MeOH, and the MeOH extract was in turn partitioned between EtOAc and H_2O. EtOAc-soluble materials were subjected to a silica gel column (hexane/EtOAc, 1:0→1:1; $CHCl_3$/MeOH, 1:0→0:1) and the fractions eluted by hexane/EtOAc (1:1) were subjected to a silica gel column (Toluene/EtOAc, 1:0→5:5; $CHCl_3$/MeOH, 1:0→5:5; $CHCl_3$/MeOH/H_2O, 5:5:1) followed by C_{18} HPLC (40% CH_3CN/0.1%TFA) to afford gaudichaudysolin A (**1**, 0.00002 %).

Gaudichaudysolin A {**1**, $[\alpha]_D^{23}$ -126 (*c* 0.2, MeOH)} was obtained as a colorless solid and was revealed to have the molecular formula $C_{36}H_{48}O_{17}$, by HRESITOFMS [*m/z* 775.2780 $(M+Na)^+$, Δ -0.9 mmu]. IR absorptions implied the presence of hydroxyl (3425 cm^{-1}) and carbonyl (1755 and 1680 cm^{-1}) groups. UV spectrum (230 nm) indicated the presence of an unsaturated carbonyl group. ^1H and ^{13}C NMR data (Table 1) revealed thirty six carbon resonances due to seven carbonyls, two sp^2 quaternary carbons, three sp^3 quaternary carbons, one sp^2 methine, ten sp^3 methines, one sp^2 methylene, five sp^3 methylenes, and seven methyl groups. Among them, eight sp^3 carbons (δ_C 67.3, 70.0, 72.0, 75.2, 76.3, 81.4, 93.1, and 98.8) and seven sp^2 carbons (δ_C 163.5, 172.1, 172.9, 173.2, 173.3, 177.8, and 208.0) were ascribed to those bearing an oxygen atom.

Six partial structures **a** (C-1 to C-2), **b** (C-5 to C-6), **c** (C-9 and C-11 to C-12), **d** (C-16 to C-17), **e** (C-22 to C-23), and **f** (C-2´ to C-6´) were deduced from ^1H-^1H COSY analysis of **1** in CD_3OD (Figure 1). Unit **A** composed of the partial structures **a** and **b** was assigned as shown in Figure 1 with a γ-lactone ring by using HMBC and NOESY correlations as follows. HMBC correlations of H_3-28 (δ_H 1.58) to C-4 (δ_C 93.1), C-5 (δ_C 43.8), and C-29 (δ_C 67.3), H_2-6 (δ_H 2.80) to C-4 and C-7 (δ_C 177.8), and H_2-29 (δ_H 3.72 and 3.78) to C-4 revealed the presence of a γ-lactone ring[6] with a hydroxymethyl and a methyl groups at C-4. Acetoxy group at C-1 and a methyl carboxylate at C-2 were assigned by the HMBC correlations as shown in Figure 1. Connection between the partial structures **a** and **b** through C-10 (δ_C 49.6), was deduced by an HMBC correlation of H_2-6 to C-10 and the NOESY correlations as shown in Figure 2. Unit **B** composed of the partial structures **c** and **d** was assigned as an octahydroinden-1-one ring system with a methyl, an exo-methylene, a hydroxyl, and two ester functions as follows. These functions can be connected by the HMBC correlations of H_3-18 (δ_H 1.02) to C-12 (δ_C 75.2), C-13 (δ_C 51.5), C-14 (δ_C 81.4), and C-17 (δ_C 36.8), H-9 (δ_H 3.29) to C-8 (δ_C 142.0) and C-14, and H_2-30 (δ_H 5.75 and 5.84) to C-9 and C-14. This ring system and functions were also supported by the comparison of the ^1H and ^{13}C NMR chemical shifts [C-14 (δ_C 81.4), C-15 (δ_C 208.0), and C-16 (δ_C 40.8)] with those [C-14 (δ_C 79.5), C-15 (δ_C 209.3), and C-16 (δ_C 42.0)] of rohituka 14[7] isolated from the seeds of *Aphanamixis polystacha*. The presence of a formate at C-11 was indicated by an HMBC correlation of an aldehyde proton to C-11 (δ_C

72.0). Connection between the units **A** and **B** was indicated by HMBC correlations of H-9 to C-5 and C-10. Unit **C** composed of the partial structure **e**, which was attached at C-17 in the unit **B**, was assigned as an α-substituted γ-lactone ring system with a hydroxyl at γ position by HMBC correlations of H-17 (δ_H 3.86) and H-22 (δ_H 7.19) to C-20 (δ_C 136.5), H-23 (δ_H 6.10) to C-21 (δ_C 172.9), and IR absorption at 1755 cm^{-1}. Unit **D** composed of the partial structure **f** was assigned as a 2-hydroxy-3-methylpentanoic acid by the ^1H-^1H COSY correlation in Figure 1 and the comparison of NMR data in turrapubesin D,[8] which might be attached at the hydroxy group at C-12 (δ_C 75.2). Thus, the gross structure of **1** was assigned as A,B-*seco*-tetranorlimonoid skeletal system with a γ-butanolide at C-17.



1

Figure 1. Selected 2D NMR correlations for **1**

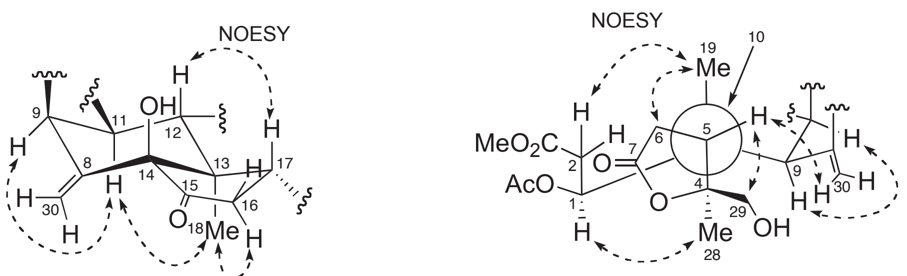


Figure 2. Selected NOESY correlations in unit **B** and rotation model of C-5/C-10 bond in unit **A** for **1**

The relative stereochemistry with selected NOESY correlations in unit B and rotation model of C-5/C-10 bond in unit A for **1** were elucidated by NOESY correlations as shown in Figure 2. Configurations of C-9, C-11, C-12, C-13, and C-17 in the unit **B** were elucidated by NOESY correlations of H_3-18/H-11 and H-16a, H-12/H-17, and H-9/H-11. As you can see the rotation model of C-5/C-10 bond, NOESY correlations of H_3-19/H-2 and H_2-6, H_3-28/H-1, and H-5/H_2-29 and H-30 indicated connectivity of C-5/C-10 bond and the relative stereochemistry in the unit **A** as shown in Figure 2. Thus, the relative configuration of **1** was assigned to be shown in computer-generated 3D drawing in Figure 3 except for

C-2' and C-3' in the 2-hydroxy-3-methylpentanoic acid.

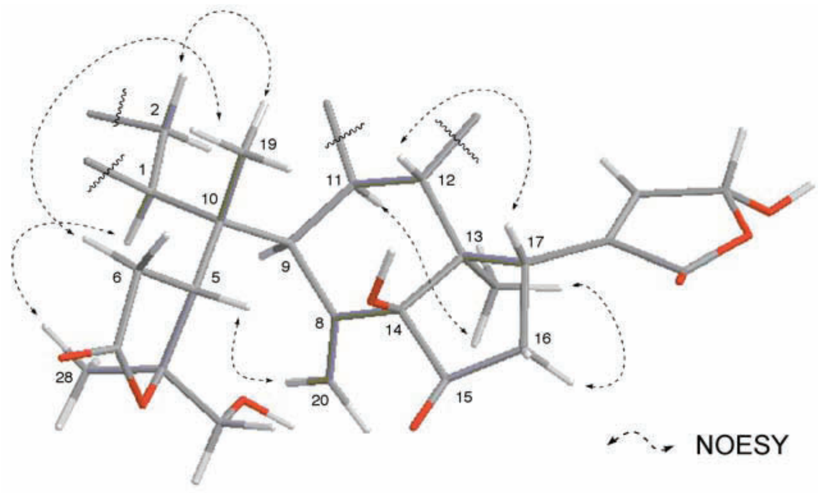


Figure 3. Selected NOESY correlations and relative configurations for **1**

From the bark of *Dysoxylum gaudichaudianum*, a series of dysoxylins A – D with a tetranortriterpenoid nucleus have already been isolated.[9] Biogenetically, gaudichaudysolin A (**1**) may be derived by a unique oxidative route through this tetranortriterpenoid nucleus. Gaudichaudysolin A (**1**) was evaluated *in vitro* for cytotoxicity against five human cancer cell lines, HL60 (human blood premyelocytic leukemia), RPMI8226 (multiple myeloma), NCI-H226 (non-small cell lung carcinoma), HCT116 (human colon cancer), and MCF7 (human breast adenocarcinoma) cells, using MTT assay, but showed no inhibitory activity against five tested cell lines (IC_{50} >50 μM).

EXPERIMENTAL

General Experimental Procedures. ^1H and 2D NMR spectra were recorded on a Bruker AV600 spectrometer and chemical shifts were reported using residual CD_3OD (δ_H 3.31 and δ_C 49.0) as internal standards. HSQC experiments were optimized for $^1J_{CH}$=145 Hz and HMBC experiments for $^nJ_{CH}$=8Hz. Mass spectra were recorded on a Micromass LCT spectrometer.

Plant Material. The bark of *D. gaudichaudianum* was collected at Alas Purwo, Indonesia in 2007. A voucher specimen is deposited at the Purwodadi Botanical Garden, Indonesia.

Extraction and Isolation. The bark of *D. gaudichaudianum* (1370 g) was extracted with MeOH, and the MeOH extract was partitioned between EtOAc and H_2O. Water-soluble materials were extracted with BuOH. EtOAc-soluble materials were subjected to a silica gel column (hexane/EtOAc, 1:0→1:1; $CHCl_3$/MeOH, 1:0→0:1) and the fractions eluted by hexane/EtOAc (1:1) were subjected to a silica gel column (toluene/EtOAc, 1:0→5:5; $CHCl_3$/MeOH, 1:0→5:5, $CHCl_3$/MeOH/H_2O 5:5:1) followed by C_{18} HPLC (40% CH_3CN/0.1%TFA) to afford gaudichaudysolin A (**1**, 1.3 mg, 0.00002 %).

Table 1. ^{1}H and ^{13}C NMR Data [δ_H (J, Hz) and δ_C] of Gaudichaudysolin A (**1**) in CD_3OD at 300K

Position	δ_H	δ_c
1	5.70 (1H, m)	70.0
2a	2.70(1H, dd,15.0,11.4)	36.0
2b	3.05 (1H, d, 14.4)	
3		173.2
4		93.1
5	3.16 (1H, m)	43.8
6	2.80 (2H, d, 10.2)	35.7
7		177.8
8		142.0
9	3.29 (1H, m)	55.4
10		49.6
11	5.38 (1H, t, 10.2)	72.0
12	5.97 (1H, d, 10.8)	75.2
13		51.5
14		81.4
15		208.0
16a	2.51 (1H, m)	40.8
16b	2.86 (1H, m)	
17	3.86 (1H, m)	36.8
18	1.02 (3H, s)	13.0
19	1.44 (3H, s)	20.0
20		136.5
21		172.9
22	7.19 (1H, br s)	148.6
23	6.10 (1H, br s)	98.8
28	1.58 (3H, s)	20.0
29a	3.72 (1H, d, 13.2)	67.3
29b	3.78 (1H, d, 13.2)	
30a	5.52 (1H, br s)	123.3
30b	5.84 (1H, br s)	
1-OAc	2.04 (3H, s)	21.1
		172.1
3-OMe	3.65 (3H, s)	52.4
11-OCHO	8.15	163.5
1’		173.3
2’	3.86 (1H, m)	76.3
3’	1.62 (1H, m)	39.3
4’a	1.28 (1H, m)	24.4
4’b	1.20 (1H, m)	
5’	0.86 (3H, s)	11.9
6’	0.93 (3H, s)	15.9

Gaudichaudysolin A (1): a colorless amorphous solid; $[\alpha]_D^{23}$ -126 (*c* 0.2, MeOH); IR (KBr) ν_{max} 3425, 1755, 1680, 1630, 1585, 1440, 1390, 1200, 1135, 1075, 840, and 801 cm^{-1}; UV (MeOH) λ_{max} 230 (ε 9000); ^1H and ^{13}C NMR data (Table 1); ESIMS *m/z* 775 $(M+Na)^+$; HRESITOFMS *m/z* 775.2780 [$(M+Na)^+$, calcd for $C_{36}H_{48}O_{17}$, 775.2789].

Cytotoxic Activity. Each cell line [HL60 (human blood premyelocytic leukemia), RPMI8226 (multiple myeloma), NCI-H226 (non-small cell lung carcinoma), HCT116 (human colon cancer), and MCF7 (human breast adenocarcinoma) cells] was seeded onto 96-well microtiter plates at 1×10^4 cells per well for HL60 and RPMI8226 and 5×10^3 cells per well for NCI-H226, HCT116, and MCF7, respectively. Cells were preincubated for 24 h at 37°C in humidified atmosphere of 5% CO_2. Different concentrations of each compound (10 μL) were added to the cultures, and then the cells were incubated at 37°C for 48 h. On the third day, 15 μL MTT solution (5 mg/mL) was added into each well of the cultured medium. After further 2 h of incubation, 100 μL of 10% SDS-0.01N HCl solution was added to each well and the formazan crystals in each well were dissolved by stirring with a pipette. The optical density measurements were made using a micropipette reader (Benchmark Plus microplate spectrometer, BIO-RAD) equipped with a two wavelengths system (550 and 700 nm). In each experiment, three replicate of wells were prepared for each sample. The ratio of the living cells was determined based on the difference of the absorbance between those of samples and controls. These differences are expressed in percentage and cytotoxic activity was indicated as an IC_{50} value.

ACKNOWLEDGMENTS

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan, and grants from the Research Foundation for pharmaceutical Sciences and The Open Research Center Project.

REFERENCES

1. (a) D. A. H. Taylor, In Progress in the Chemistry of Organic Natural Products; ed. by W. Herz, H. Grisebach, and G. W. Kirby; Springer, New York, 1984; Vol. 45; (b) D. A. Mulholland, B. Parel, and P. H. Coombes, *Curr. Org. Chem.*, 2000, **4**, 1011.
2. (a) S. Yin, X. N. Wang, C. Q. Fan, S. G. Liao, and J. M. Yue, *Org. Lett.,* 2007, **9**, 2353; (b) C. R. Zhang, S. P. Yang, S. G. Liao, C. Q. Fan, Y. Wu, and J. M. Yue, *Org. Lett.,* 2007, **9**, 3383; (c) Y. T. Di, H. P. He, H. Y. Liu, P. Yi, Z. Zhang, Y. L. Ren, J. S. Wang, Q. Y. Sun, F. M. Yang, X. Fang, S. L. Li, H. J. Zhu, and X. J. Hao, *J. Nat. Prod.,* 2007, **70**, 1352.
3. (a) H. Zhang, X. Wang, F. Chen, X. M. Androulakis, and M. J. Wargovich, *Phytotherapy Res.,*

2007, **21**, 731; (b) A. Roy and S. Saraf, *Biol. Pharm. Bull.,* 2006, **29**, 191; (c) D. H. Bray, D. C. Warhurst, J. D. Connolly, M. J. O'Neill, and J. D. Phillipson, *Phytotherapy Res.,* 1990, **4**, 29.

4. K. Mohamad, Y. Hirasawa, M. Litaudon, K. Awang, A. H. A. Hadi, K. Takeya, W. Ekasari, A. Widyawaruyanti, N. C. Zaini, and H. Morita, *Bioorg. Med. Chem.,* 2009, **17**, 727.
5. K. Mohamad, Y. Hirasawa, C. S. Lim, K. Awang, A. H. A. Hadi, K. Takeya, and H. Morita, *Tetrahedron Lett.,* 2008, **49**, 4276.
6. L. K. MacLachlan and D. A. H. Taylor, *Phytochemistry*, 1982, **21**, 2426.
7. D. A. Mulholland and N. Naidoo, *Phytochemistry*, 1999, **51**, 927.
8. X. N. Wang, S. Yin, C. Q. Fan, L. P. Lin, J. Ding, and J. M. Yue, *Tetrahedron,* 2007, **63**, 8234.
9. J. L. Chen, M. R. Kernan, S. D. Jolad, C. A. Stoddart, M. Bogan, and R. Cooper, *J. Nat. Prod.,* 2007, **70**, 312.