

(+)-Syringaresinol Lignan from New Species *Magnolia Thailandica*

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Abstract: Problem statement: *Magnolia*, an ancient genus, is a large genus of about 210 flowering plant species in the subfamily Magnolioideae of the family Magnoliaceae. Having evolved before bees appeared, the flowers developed to encourage pollination by beetles. Members of this family are rich in a wide variety of biological active compounds including lignans. *Magnolia thailandica*, a new species for Thailand and world, has not been studied chemical composition. The present study described a phytochemical study of twigs of *M. thailandica*. **Approach:** In order to identifying natural product compounds for medicinal use, *M. thailandica* endemic to grow in Thailand was studied. It is shown that this plant is excellent sources of raw material for investigation lignan such as syringaresinol. Thus, the conducted research that we conducted on the above *M. thailandica* consisted of two steps: (1) establishing a methodology for isolation and purification of lignan compound, (2) identification of the compound using UV, MS, IR and a combination of 1D and 2D NMR spectral analysis. **Results:** The constituents of dichloromethane: methanol extract of *M. thailandica* has been investigated. We isolated and identified one bis-tetrahydrofuran-type, syringaresinol lignan derivative. The structure of this compound was elucidated on the basis of spectroscopic evidence. **Conclusion:** Studies on dichloromethane: methanol extract of *M. thailandica* has now resulted the isolation and structural characterization of syringaresinol. However, no phytochemical study has been carried out on this species.

Key words: *Magnolia thailandica*, magnoliaceae, (+)-syringaresinol lignan

INTRODUCTION

The genus *Magnolia* belonging to subfamily Magnolioideae of the family Magnoliaceae comprises about 210 species. It is found in several areas such as Southeast and East parts of Asia and North and Central parts of America. Several *Magnolia* species have been used in a number of traditional medicine in China and Japan (Seo *et al.*, 2008). The studies on phytochemical of genus *Magnolia* afforded lignans (Song *et al.*, 2000), neolignans (Ma *et al.*, 1996), sesquiterpenes (Song *et al.*, 1998), alkaloids (Tsakadze *et al.*, 2005) and isoquinoline (Wu *et al.*, 2010).

M. thailandica was discovered in Thailand and identified as a new species by The Forest Herbarium, Department of National Park, Wildlife and Plant Conservation, Ministry of Natural Resources and

Environment, Thailand. The plant is upto 30 m high and known as 'Champi si mueang thai' in Thai. In this study, the phytochemical investigation of *M. thailandica* was carried out and a known (+)-syringaresinol was isolated establishing by IR, ¹H NMR, ¹³C NMR, 2D NMR and MS spectroscopic data. Previous studies reported that (+)-syringaresinol exhibited various biological activities including antifungal (Kokpol *et al.*, 1993), anti-inflammatory (Cho *et al.*, 2001), antimalarial activities (Zhang *et al.*, 2001) and antileukemic (Badawi *et al.*, 1983).

MATERIALS AND METHODS

General experimental procedure: Column Chromatography (CC): Silica gel 70-7230 mesh; TLC: pre-coated silica gel 60 F₂₅₄ (20×20 cm) thick; E-

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Merck) plates; UV spectra were obtained on a Shimadzu UV-1601 spectrophotometer with EtOH as solvent. Melting point was measured on a Büchi 322 micro melting point apparatus and has to be uncorrected. IR spectra in KBr disk were recorded on Shimadzu 8900 FTIR spectrophotometer. NMR spectroscopic data were obtained on a Bruker AV 500 spectrometer. The chemical shifts were recorded in δ values which were referenced to TMS as the internal standard

Plant material: The combined of twigs of *M. thailandica* were collected in May, 2010 from Petchaboon province and identified by Forest Herbarium, Department of National Park, Wildlife and Plant Conservation, Ministry of Natural Resources and Environment, Bangkok, Thailand, where a voucher specimen has been deposited (BKF.137106).

Extraction and isolation: The twigs of *M. thailandica* (3.0 kg) were dried and milled at room temperature, defatted with hexane and continues extracted with 2:1; CH₂Cl₂: CH₃OH by percolation (Sule *et al.*, 2011). The CH₂Cl₂: CH₃OH extracted (171.64 g) was subjected to silica gel column chromatography with EtOAc: Hexane (1:9, 3:7, 5:5, 10:0) and CH₃OH: EtOAc (1:9, 3:7, 5:5) as elements to give seven fractions (F₁-F₇). Fraction F₄ (3.66 g) was fractionated on a silica gel CC with with EtOAc: Hexane (1:9, 2:8, 4:6, 10:0) to yield six subtractions (A₁-A₆). Syringaresinol (0.38 g) was obtained from A₅ via crystallization by ethanol.

RESULTS

Structure of the (+)-syringaresinol lignan has been deduced by the interpretation of high-resolution NMR data (Table 1) and the details of molecular structure are presented in Fig. 1.

DISCUSSION

(+)-Syringaresinol was obtained as colorless rhombic crystal, m.p. 183-184°C. The molecular formula C₂₂H₂₆O₈ was deduced from EIMS [m/z 418, M⁺]. The UV spectrum showed the absorption bands at 240 nm (log ϵ 4.08) and 271 nm (log ϵ 3.88) which corresponded to the furofuran lignan (Semwal and Sharma, 2011). IR spectrum showed bands at 3340 (hydroxyl), 1610, 1521, 1456 and 1425 (aromatic), 1377 and 1319 (C-O-C linkage). The mass spectrum (Fig. 2) of this compound displayed various stabilized fragment ions at 167 (benzylic carbonation), 181 (acylium carbocation) and 193 (allylic carbocation)

corresponding with the successive lose of aromatic moiety. The ¹H and ¹³C NMR spectral data (Table 1) showed signals characteristic of a 1, 2, 5-trisubstituted humanoid lignin. In addition, The ¹H NMR spectrum clearly indicated the presence of two pairs of equivalent aromatic protons, four aromatic methoxy groups, two singlet signals for phenolic protons and bis-tetrahydrofuran ring (Changzeng and Zhongjian, 1997). The relationship between the dihedral angle and vicinal coupling constant ³J is given theoretically by the Karplus equation: ³J_{ab} = J⁰cos² ϕ -0.28(0°< ϕ <90°) and ³J_{ab} = J¹⁸⁰cos² ϕ -0.28(90°< ϕ <180°). Thus, the relative configuration at H-1 and H-2 could be determined by the ³J_{1,2}, H-C-C-H (12.4 Hz) coupling constant which indicated that the two protons were located opposite side with dihedral angle 180° (Lan *et al.*, 2003). Comparison between the NMR data of (+)-syringaresinol and those previously reported (Wang and Yu, 1998; Das *et al.*, 1999) showed that in the isolated compound, H-2 and H-6 were both axial, i.e., the β -configuration. Moreover, the relative configurations between H-2 (δ 4.76) with H-8a (δ 4.30) and H-1 (δ 3.12) with H-2' (δ 6.61) were also established as cis-configuration by an NOE experiment (Fig. 1).

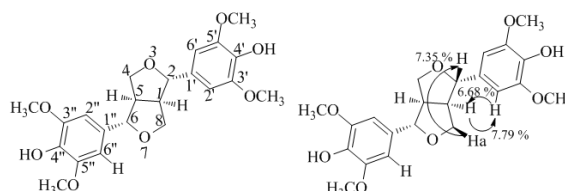


Fig. 1: Structure of (+)-syringaresinol and NOE experiment

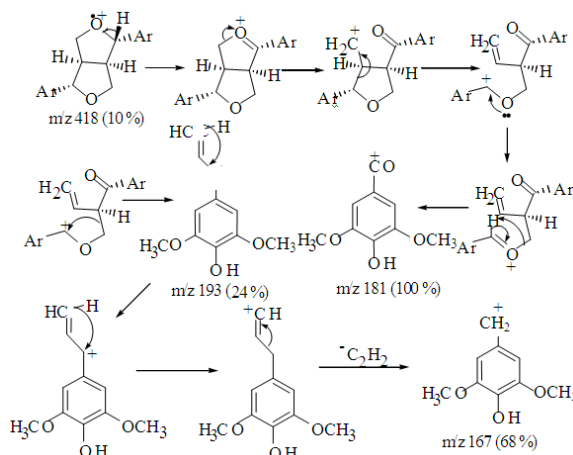


Fig. 2: Mass fragmentation pattern of (+)-syringaresinol

Table 1: ¹³C, ¹H NMR data of (+)-syringaresinol and ¹H-¹³C, ¹H-¹H correlations exhibited in the 2D NMR spectra in CDCl₃

Carbon	δ ¹³ C (DEPT)	Proton	*δ ¹ H (J Hz)	HMBC correlation	COSY correlation
1	54.29 (CH)	1	3.12 (m)	C-1, C-2, C-8, C-1ϕ	H-2, H-8a, H-8b
2	86.01 (CH)	2	4.76 (d, 12.4, 8.16)	C-1, C-8, C-1', C-2', C-6'	H-1, H-8a, H-8b
3	-	-	-	-	-
4	71.75 (CH ₂)	4a	4.30 (m)	C-5, C-6	H-4b, H-5, H-6
		4b	3.94 (d, 12.4, 8.16)	C-5, C-6	H-4a, H-5, H-6
5	54.29 (CH)	5	3.12 (m)	C-5, C-4, C-6, C-1"	H-4a, H-4b, H-6
6	86.01 (CH)	6	4.76 (d, 12.4, 8.16)	C-4, C-5, C-1", C-2", C-6"	H-4a, H-4b, H-5
7	-	-	-	-	-
8	71.75 (CH ₂)	8a	4.30 (m)	C-1, C-2	H-8b, H-1, H-2
		8b	3.94 (d, 12.4, 8.16)	C-1, C-2	H-8a, H-1, H-2
1'	132.04	-	-	-	-
2'	102.69 (CH)	2'	6.61 (s)	C-2, C-1', C-2', C-3', C-4'	-
3'	147.13	-	-	-	-
4'	134.29	-	-	-	-
5'	147.13	-	-	-	-
6'	102.69 (CH)	6'	6.61 (s)	C-2, C-1', C-4', C-5', C-6'	-
1"	132.04	-	-	-	-
2"	102.69 (CH)	2"	6.61 (s)	C-6, C-1", C-2", C-3", C-4"	-
3"	147.13	-	-	-	-
4"	134.29	-	-	-	-
5"	147.13	-	-	-	-
6"	102.69 (CH)	6"	6.61 (s)	C-6, C-1", C-4", C-5", C-6"	-
3'-OCH ₃	56.33 (CH ₃)	3'-OCH ₃	3.92 (s, obsc.)	C-2', C-3'	-
4'-OH	-	4'-OH	5.57 (s)	C-3', C-4', C-5'	-
5'-OCH ₃	56.33 (CH ₃)	5'-OCH ₃	3.92 (s, obsc.)	C-5', C-6'	-
3"-OCH ₃	56.33 (CH ₃)	3"-OCH ₃	3.92 (s, obsc.)	C-2", C-3"	-
4"-OH	-	4"-OH	5.57 (s)	C-3", C-4", C-5"	-
5"-OCH ₃	56.33 (CH ₃)	5"-OCH ₃	3.92 (s, obsc.)	C-5", C-6"	-

*δ in ppm from TMS [coupling constants (J) in Hz are given in parentheses], obsc. = obscure

The complete assignments were based on the result of COSY, HMQC and HMBC experiments were used to determine the bis-tetrahydrofuran ring (Table 1). HMBC correlations were observed between H-1 (δ 3.12) with C-1, C-2, C-8 and C-1' of aromatic part; H-2 (δ 4.76) with C-1, C-8, C-1' and C-2', C-6' of aromatic; H-8a (δ 4.30) and H-8b (3.94) with C-1 and C-2, respectively. Thus, this compound was identified as (+)-syringaresinol which is being reported for the first time from *M. thailandica*, the natural product source, to the best of our knowledge.

CONCLUSION

Lignan represents a vast reservoir of aromatic materials, mainly untapped because of the difficulties associated with release of shikimate metabolites. The monomer coniferyl alcohol can react to the dimer of lignan containing a heterogeneous series of intermolecular bondings, as seen in the furan rings of pinoresinol which it was related to the (+)-syringaresinol derivative.

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