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SULFUR CONTAINING CINNAMIDES WITH ANTIFUNGAL ACTIVITY FROM *GLYCOSMIS CYANOCARPA*

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Abstract: Bioassay guided analysis of the methanolic leaf extract of *Glycosmis cyanocarpa* (*Rutaceae*) led to the isolation of a new type of sulfur containing cinnamides with antifungal activity: sinharine (cinnamic acid methylsulfidoethylamide) (**2**) and the corresponding N-methyl derivative methylsinharine (**4**). In addition, the dominating furoquinoline kokusaginine (**3**) together with small amounts of skimmianine (**5**) and the carbazole glycozolidol (**1**) were also isolated. A series of quinolone and quinazolone alkaloids were detected as minor components by reversed phase HPLC. The structures of **2** and **4** were elucidated by means of spectroscopic methods (IR, UV, ^{1}H NMR, ^{13}C NMR, MS). Temperature dependent ^{1}H NMR and lanthanide induced shifts (LIS) established the stereochemistry of the two conformers of **4**.

As a result of our screening program on bioactive natural compounds of Sri Lankan *Rutaceae*, we isolated two substances with antifungal activity from the $CHCl_3$ fraction of the methanolic leaf extract of *Glycosmis cyanocarpa*. (Blume) Spreng. var. *simplicifolia* Kurz.[1] They were detected by bioassay-guided TLC analyses[2] on crude extracts using a spore suspension of *Cladosporium cladosporioides*. TLC comparison of both, the original crude extract and the corresponding fractions obtained by medium pressure liquid chromatography (MPLC) with EtOAc/petrol, showed two clearly visible inhibition zones, indicating the presence of fungitoxic compounds. No active zones could be detected in the corresponding extracts from the young stems.

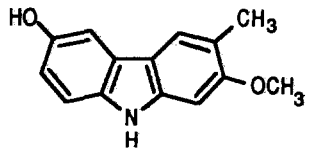
Since both compounds have been shown to belong to the major components of the lipophilic leaf extract, they could easily be isolated by repeated MPLC (Merck, LiChroprep Si 60) with 15%EtOAc in petrol and purified by prep.TLC (silica gel). Based on our experience on alkamides (compare Refs.[3,4])

the UV and IR spectra let expect two closely related cinnamides. However, the interpretation of NMR and MS spectra caused some problems. Whereas the cinnamyl moiety could clearly be confirmed, the amine parts were not comparable with any of the already known derivatives. Regarding the available results, two thioethers have been assumed, which perfectly agree with all spectroscopic data. Elemental analysis as well as high resolution mass spectroscopy undoubtedly supported the presence of sulfur. These compounds, to which we have assigned the trivial names sinharine[5] (2) and methylsinharine (4), represent the first sulfur containing amides.

The accumulation of different amides represents a common chemical character of the family *Rutaceae* [6,7]. Considering the biogenetic origin, the various derivatives are usually grouped by their different acid moieties. Accordingly, cinnamides, benzamides, alkamides and nicotinamides are known from the *Rutaceae* [8]. More rarely, amides derived from other acylating moieties like phenylacetic acid[9] and cyclopropanecarboxylic acid[10] have also been isolated. The different amine parts mostly arise from various amino acids by decarboxylation. Hence, cysteine most likely represents the corresponding precursor of the sulfur containing sinharines (2,4).

Previous investigations within the genus *Glycosmis* have shown that extracts from the leaves, stems and roots are mainly characterised by different classes of alkaloids. Quinolones[12-15], furoquinolines[11,12], acridones[11,12,16], carbazoles[17,18] and quinazolones[9,19,20] are the most widespread structural types[6]. The amide glycomide, isolated from *G. pentaphylla* shows close structural relationships to quinazolones and may be derived from anthranilic acid[9]. Regarding these data, the sulfur containing cinnamides represent a special chemical character which apparently has a very limited distribution.

As shown in the HPLC profile (Fig.1), the original crude extract of the leaves is clearly characterised by the dominating peaks of sinharines (2,4) accompanied by large amounts of kokusaginine (4,6,7-trimethoxyfuroquinoline) (3). The carbazole glycozolidol (1)[17] and the furoquinoline skimmianine (5) could only be identified as minor constituents. Based on the typical UV spectra obtained by on-line photodiode array detection, the other peaks represent a series of quinolones (6,7,11,12) and quinazolones (8,9,10,13), respectively.



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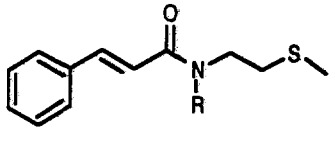
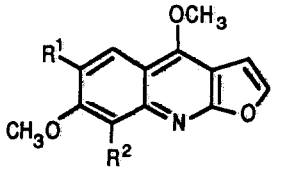


2 R = H

4 R = CH_3



3 R^1 = OCH_3, R^2 = H

5 R^1 = H, R^2 = OCH_3

Structure Elucidation

Unambiguous assignment of structures 2 and 4 followed from NMR and MS spectroscopy. The ^{1}H NMR spectrum of sinharine (2) showed a monosubstituted benzene and the typical olefinic AB system of cinnamic acid derivatives (dublets at 7.62 and 5.54 ppm). In the upfield region a very broad signal of 1H (5.34 ppm) with still recognizable triplet structure, a quartet of 2H (actually a dt, 3.59 ppm) and a triplet of 2H (2.85ppm) indicated an element -NH-CH_2-CH_2- with no further coupling possibilities at both ends of the chain. A sharp singlet at 2.30 ppm completed the spectrum. Assuming an amide functionality (already indicated by the UV and IR spectra) the structure Ar-CH=CH-CO-NH-CH_2-CH_2-*X*-CH_3 followed, with -*X*- either -CO- (the first working hypothesis) or -S-.

Although HPLC examination of isolated 4 indicated a pure compound, the ^{1}H NMR spectrum was puzzling in the first moment. There were too many resonances in ratios deviating slightly from integer numbers. The aromatic part was broad and an uninterpretable multiplet. All other resonances

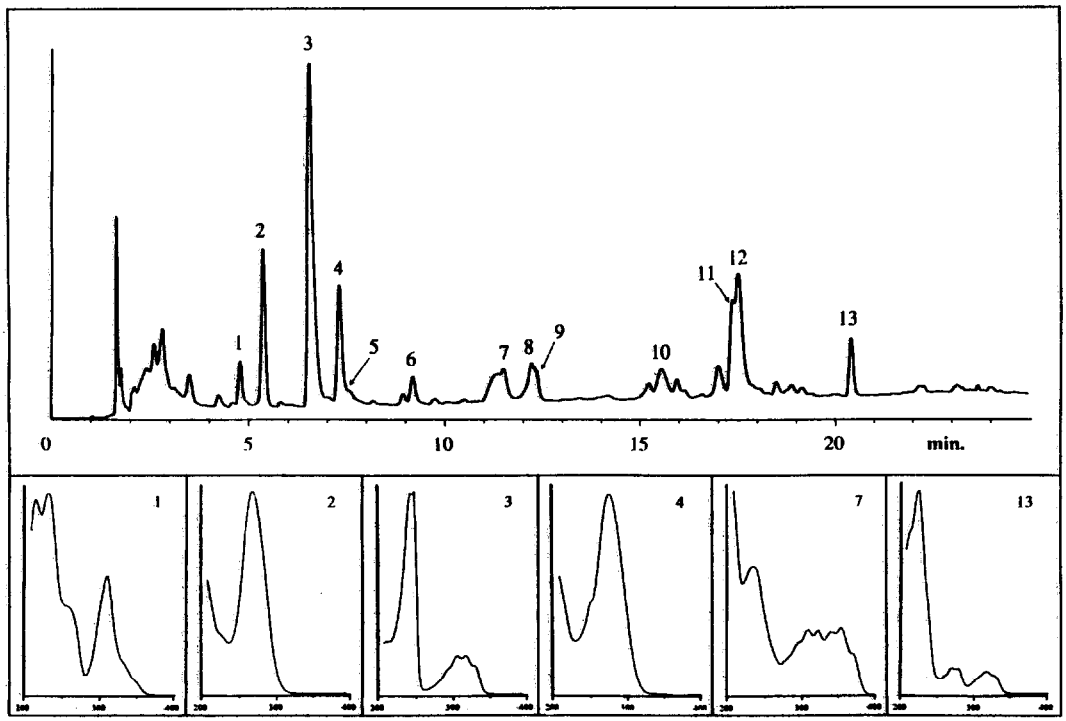
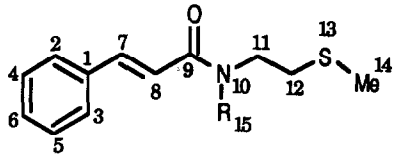


Fig.1. HPLC chromatogram (Hewlett-Packard 1090 M) of the chloroform soluble fraction of the methanol leaf extract of *Glycosmis cyanocarpa* together with characteristic UV spectra (diode array detection) of selected compounds: **1** glycozolidol, **2** sinharine, **3** kokusaginine, **4** methylsinharine, **7** quinolone type, **13** quinazolone type.

Table 1. NMR data (Bruker AM 400 WB) for sinharine (2) and methylsinharine (4)

	^{1}H NMR ($CDCl_3$)		^{13}C NMR		^{1}H NMR (C_6D_6)		$Eu(fod)_3$ LIS[e]	
	2	4[a]	2[b]	4[c]	2		4	
No.			(CD_3OD)	($CDCl_3$)	280 K[d]	350 K	exp.	calc.
1	–	–	140.5	[h]	–	–	–	–
2,3	7.20 (d)	7.15 –	129.5[g]	125.0[i] 125.8	~7.10[j] 6.79 (d)	6.98 (br.d)	**a**: 0.86 **b**: 0.57	0.77 0.65
4,5	7.32 (t)	7.30 (m)[f]	129.8[g]	126.3 128.0	ca.7.0 –	7.09 (t)	**a**: 0.29 **b**: 0.29	0.20 0.24
6	7.23 (d)		127.3	128.3	7.15 (m)	7.03 (t)	**a**: 0.14 **b**: 0.14	0.15 0.19
7	5.54 (d)	**a**: 5.78 (d) **b**: 6.07 (d)	143.5	143.7 144.4	5.83 (d) 5.69 (d)	5.87 (d)	**a**: 4.66 **b**: 3.43	4.73 3.20
8	7.62 (d)	**a**: 7.58 (d) **b**: 7.71 (d)	116.7	111.9 112.1	8.03 (d) 7.94 (d)	7.80 (d)	**a**: 2.95 **b**: 1.94	3.50 2.28
9	–	–	167.3	[h]	–	–	–	–
11	3.59 (ps.q)	**a**: 3.58 (m) **b**: 3.63 (m)	42.1	51.3 50.0	3.52 (t) 2.94 (t)	3.34 (br.t)	**a**: 2.57 **b**: 2.26	2.43 2.32
12	2.85 (t)	**a**: 2.87 (t) **b**: 2.87 (t)	36.6	34.9 33.5	2.75 (t) 2.31 (t)	2.62 (br.t)	**a**: 1.86 **b**: 1.23	1.89 1.10
14	2.30 (s)	**a**: 2.23 (br.s) **b**: 2.35 (br.s)	14.3	14.3 14.5	1.58 (s) 1.60 (s)	1.73 (s)	**a**: 0.54 **b**: 0.17	– –
15	5.34 (br.t)	**a**: 2.98 (br.s) **b**: 2.96 (br.s)	–	29.8 29.8	2.76 (s) 2.18 (s)	2.56 (br.s)	**a**: 4.58 **b**: 1.60	4.12 1.56



2 R = H[15]

4 R = Me[15]

Coupling constants: $J_{7,8}$= 14.5 Hz (2 and 4); $J_{11,12}$= 7 Hz (2); $J_{11,12}$= 7.5 Hz (4); $J_{NH,11}$= 7 Hz (2). [a] The protons 7-15 can be clearly assigned to conformers **a** or **b** (ratio **a**:**b** = 0.54 : 0.46); [b] recorded in deuteromethanol due to better solubility ; [c] for the C atoms 7-15 the first value corresponds to the relatively stronger signal (presumably conformer **a**); [d] in deuterobenzene no assignments to conformers **a** or **b** are possible because **a**:**b**=1:1 in this solvent; [e] LIS values in ppm for the 1:1 complex (for details see text and Exp.); [f] multiplet with a br.t, 2H, at 7.29, 2H v.br. at 7.23 and 1H v. br. at 7.16 ppm (due to the conformer mixture no assignments are possible); [g] interchangeable; [h] quaternary carbons not detectable; [i] no assignments; j actually hidden under the m at 7.0-7.15 ppm, but necessary supplement to the corresponding signal at 6.79 of the other conformer.

were similar to sinharine (2) but occurred twice with the only exception of a triplet for *X*-CH_2-. In contrast to the other lines it was very sharp and occurred only once. Additionally two somewhat broadened singlets (one larger at 2.98 and one smaller at 2.96 ppm) appeared as new signals when compared with 2. The new resonances were obviously due to an N-CH_3 group instead of the absent N-H. The ratio of the apparently two sets of resonances was 54:46 %. In principle two explanations were possible for the experimental data: either a mixture of two components or one compound with two conformers. Since most lines were unusually broad for a proton spectrum and HPLC indicated a pure sample, the latter was presumed. Rotation about the C-N amide bond may be restricted in the tertiary amide 4 but not in the secondary amide 2. Recording a series of proton spectra at different temperatures proved this unambiguously.

To reach at least a temperature of 75°C, the temperature dependent spectra for methylsinharine (4) were measured in benzene-d_6. Surprisingly enough the ^{1}H NMR spectrum at room temperature (300 K) in benzene was rather different from that in $CDCl_3$. In benzene some of the resonances were already in the fast exchange range, e.g. the low field olefinic proton at 7.92 ppm (coalescence at 300 K) or the *X*-CH_3 singlet at 1.63 ppm (coalescence at 285 K). The others were all very broad and still occurring twice. Some of the corresponding resonances for the conformers were rather wide apart (e.g. N-CH_2, and N-CH_3 with $\Delta\delta$ =120 Hz; see Exp. Part). The coalescence temperature for these resonances with large $\Delta\delta$ was at ca. 320 K. All coalescence data agree with a ΔG^* of 62 ± 1 kJ/mol for the conformer interconversion which is due to hindered rotation about the C-N amide bond (from the differences in the room temperature spectra one can conclude that in $CDCl_3$ as solvent the barrier must be slightly higher).

The J-modulated ^{13}C NMR spectra of 2 and 4 were consistent with the structures outlined above. The rather clear spectrum for sinharine (2) showed all necessary carbon atoms as sharp lines, including the small quaternary amide >C=O resonance at 167.3 ppm. Of special interest was the -CH_3 resonance at 14.3 ppm. This chemical shift is not compatible with a -CO-CH_3 group but agrees well with -S-CH_3. The ^{13}C NMR spectrum of methylsinharine (4) showed generally rather broad lines due to the conformer exchange. Because of the broadness of lines and the limited amount of material, the quaternary carbon atom resonances were too weak for detection. All observable lines were twice with the exception of two accidental coincidences: one in the aromatic C-H region (128.3 ppm) and the other one for the N-CH_3 resonance at 29.8 ppm. The two broad lines at 14.3 and 14.5 ppm were again assigned to -S-CH_3.

The molecular ion peaks of the EI-mass spectra were compatible with molecular formulas $C_{12}H_{15}NOS$ (M^+=221 with 9% rel.int.) for sinharine (2) and $C_{13}H_{17}NOS$ (M^+=235, 79% rel.int.) for methylsinharine (4); in the case of 4 this could be confirmed by high resolution MS (calcd.

m/z=235.1031, found 235.103) and a perfect match of experimental and simulated isotope pattern. The fragmentation pattern was consistent with the proposed structure. For **2** the fragments M – SCH_3 (m/z= 174, 38% rel.int.) and M – CH_2SCH_3 (m/z= 160, 25%) were characteristic, for the N-CH_3 derivative **4** the peaks for M – CH_3 (m/z= 220, 6% rel.int.), M – 2x CH_3 (m/z= 205, 10% rel.int.), M – SCH_3 (m/z= 188, 20% rel.int.), and M – CH_2SCH_3 (m/z= 174, 48% rel.int.) agreed well with the expected fragmentation.

For further confirmation of the unusual sulfur content of this type of natural constituent, some of the scarce material of compound **2** (needed for more detailed studies on its fungitoxic properties) was used for elemental analysis giving good agreement between calculated and found sulfur values (S calcd.14.49%, found 14.20%).

Conformational Analysis of 4

The conformers of **4** were identified by measurements of lanthanide induced shifts (^{1}H NMR LIS) and computational simulation of the data (e.g., see Refs.[21-23]). Geometries for possible rotamers were obtained using a model building program (force field program PCMODEL[24] run on an Apple Macintosh). These geometries showed a planar O=C—N—C arrangement (torsional angle O–C9–N10–C11 practically 180° for **4a** and 0° for **4b**, compare Fig.2), but a significant torsion about the C8–C9 bond (torsional angle C7–C8–C9–O ca. 45° out of the planar arrangement). The latter

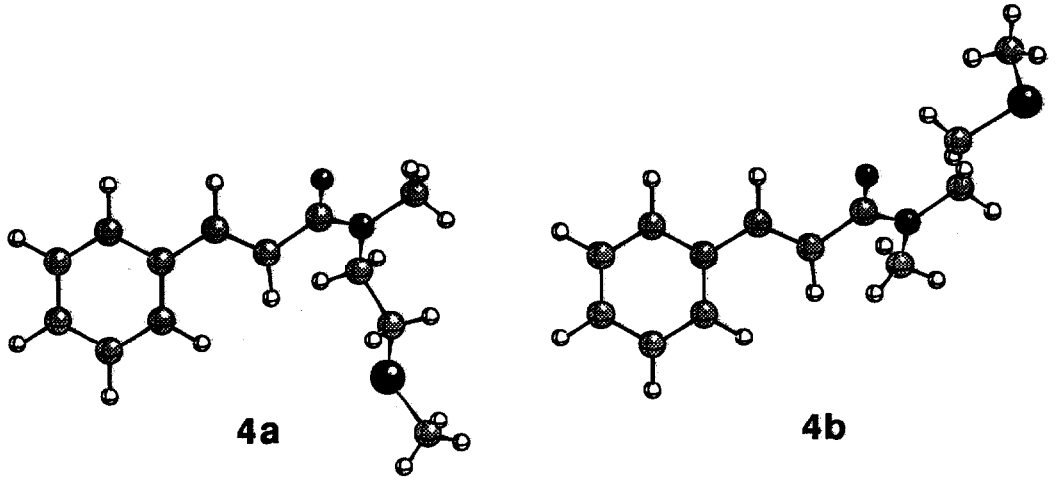


Fig.2. "Ball & Stick" model[28] for the conformers of methylsinharine: **4a** (54% population in $CDCl_3$) and **4b** (46% population in $CDCl_3$).

torsion is necessary to avoid an unfavourable nonbonded interaction between 8-H / 11-methylene in **4a** and 8-H / 15-Me in **4b**. Two sets of LIS data corresponding to two conformers were obtained from the ^{1}H NMR spectra upon addition of Eu(fod)$_3$ as shift reagent. These data sets could be simulated well by the two conformers shown in Fig. 2. Taking the force field geometries, only one variation in the geometrical parameters was allowed, namely the rotation about the C8–C9 bond which was optimized in the LIS simulation procedure; the LIS results gave a torsional angle of 40°, which agrees very well with the force field derived value of 45°. It is interesting to note that conformer **4a** shows a stronger complexation towards Eu(fod)$_3$ in comparison to **4b**: the complex formation constants differ by a factor of ca. 1.5 (compare the LIS values in Table 1). This may be due to the steric requirements of the bulky shift reagent allowing a better approach to the carbonyl group of **4a** with a methyl group cisoid towards -C=O, compared to the long CH_2-CH_2-S-CH_3 - chain of **4b** already interfering with the coordinating fod ligands (for this reason the S-methyl values were not included in the LIS simulation). **4a** is the conformer favoured slightly in $CDCl_3$ solution (54% population for **4a**, 46% for **4b**); however, in C_6D_6 the ratio is practically 50:50%. Note that the energy barrier of rotation about the C9-N bond is also somewhat lower in benzene; both findings – equal population and easier interconversion in C_6D_6 – may be attributed to an aromatic solvent effect.

EXPERIMENTAL

Plant material – Twigs and young stems from *Glycosmis cyanocarpa* (Blume) Spreng. var. *simplicifolia* Kurz. were collected in Sinharaja Forest, Ratnapura District, Sri Lanka (10.2.1991) and voucher specimens were deposited at the herbarium of the Department of Botany, University of Peradeniya.

Extraction – Fresh leaves (75 g), were coarsly chopped in the field and directly preserved with MeOH in a polyethylene square bottle. After shipping back to Vienna the methanolic extract was filtered, concentrated and partitioned with $CHCl_3$. The chloroform fraction was evaporated to dryness (300 mg) and dissolved in 15% EtOAc in petrol for prep. MPLC. A small sample was dissolved in MeOH for reversed phase HPLC (Fig. 1).

Chromatography and Isolation – MPLC with 15%, 30% and 70% (v/v) EtOAc in petrol (400 x 38 mm homemade column packed with Merck LiChroprep Si 60, 25-40 µm, ca. 6000 theoretical plates, UV detection, 254 nm, ISCO UA-5); prep. TLC (Merck silica gel 60 F_{254}) with EtOAc : petrol 6 : 4; HPLC Spherisorb ODS II (5 mm), 250 x 4 mm i. d. with a 50 mm precolumn (Forschungszentrum Seibersdorf GmbH, Austria), mobile phase: gradient of 60-100% MeOH in H_2O, flow rate: 1ml/min, detection: 210-250 nm (diode array).

MPLC with 15% EtOAc afforded 30mg crude methylsinharine (4), whereas 25mg sinharine (2), 35mg kokusaginine (3, ^{1}H NMR s.Ref.[25]), and 10 mg skimmianine (5) were eluated with 30% EtOAc as crude products; in the case of 3 and 5 the pure compounds were obtained by crystallisation from Et_2O-petrol (20 mg 3 and 3mg 5), while the two cinnamides were purified by repeated MPLC and preparative TLC affording 10 mg 2 and 15 mg 4; from the crude MPLC fraction of 4 the carbazole derivative 1 could also be isolated in pure state (2 mg).

Glycozolidol (1). The ^{1}H NMR spectrum of 1 in DMSO-d_6 is described in Ref.[17]. However, since we observed somewhat different chemical shifts we reassured the identity of our compound 1 by additional NOE experiments to exclude any other possible isomers. ^{1}H NMR (DMSO-d_6): 10.59 (s, 1H, 6-OH), 8.76 (s, 1H, N9-H), 7.66 (s, 4-H), 7.24 (d, 2.4 Hz, 5-H, irradiation gave a NOE enhancement for 4-H), 7.17 (d, 8.5 Hz, 8-H), 6.86 (s, 1-H), 6.73 (dd, 8.5 and 2.4 Hz, 7-H), 3.84 (s, 2-OMe, irradiation gave a NOE enhancement for 1-H), 2.24 (s, 3-Me); ^{1}H NMR ($CDCl_3$): 7.74 (s, 1H, N9-H), 7.70 (s, 4-H), 7.37 (d, 2.4 Hz, 5-H), 7.23 (d, 8.5 Hz, 8-H), 6.86 (dd, 8.5 and 2.4 Hz, 7-H), 6.83 (s, 1-H), 3.91 (s, 2-OMe), 2.35 (s, 3-Me).

Sinharine (2). Colourless crystals, m.p. 74-75°C; UV (Et_2O, λ/nm): 263, 230 sh; IR (CCl_4, ν /cm^{-1}): 3459 m, 3335 m(br.), 3091 vw, 3070 w, 3033 w, 2930 m, 2860 w, 1673 s, 1583 s, 1499 s, 1455 w, 1437 w, 1366 w, 1325 m, 1312 w, 1250 m, 1178 m, 1084 w, 1031 w, 981 w, 943 s, 869 w, 700 s; MS (70 eV): m/z (rel.int.) 221 (9, M$^+$), 174 (38, M – SMe), 160 (25, M – CH_2-S-Me), 130 (16), 111 (20), 104 (21), 102 (28), 101 (100), 97 (32), 85 (43), 71 (67), 57 (94); $C_{12}H_{15}NOS$ requires S 14.49%, found 14.20% (Mikroanalytisches Labor, Institute of Physical Chemistry, University of Vienna); ^{1}H and ^{13}C NMR see Table 1.

Methylsinharine (4). Colourless oil. UV (Et_2O, λ/nm): 269; IR (CCl_4, ν/cm^{-1}): 3091 vw, 3069 w, 3032 w, 2930 m, 2865 w, 1645 s, 1568 s, 1476 w,1455 w, 1429 w, 1398 m, 1361 w, 1323 w, 1277 m, 1244 w, 1169 m, 1156 w, 1118 m, 1077 w, 1031 w, 968 w, 944 s, 880 w, 863 w, 700 s, 620 w; MS (70 eV): m/z (rel.int.) 235 (79, M$^+$), 220 (6, M – Me), 205 (10, M – 2xMe), 188 (20, M – SMe), 174 (48, M – CH_2-S-Me), 144 (100), 116 (44), 101 (98), 91 (54), 73 (89), 57 (83); $C_{13}H_{17}NOS$ high resolution MS requires m/z (M$^+$) 235.1031, found 235.103; ^{1}H and ^{13}C NMR see Table 1.

Lanthanide Induced Shifts. For the determination of ^{1}H LIS values increasing amounts of Eu(fod)$_3$ were added to a solution of 4 mg of compound 4 in $CDCl_3$. The LIS for the concentration ratio R_o: S_o = 1:1 ("1:1 complex") were obtained by extrapolation of 4 different reagent concentrations in the range of R_o : S_o = 0.0 – 0.35 : 1. The accuracy of the values suffer from severe line broadening

upon addition of shift reagent. The reason for this effect is the dynamic equilibrium between the two conformers **4a** and **4b**: an increase of the frequency difference between corresponding resonances of the conformers results in strong line broadening (an additional explanation could be a change in the conversion barrier in the complex species). For the LIS calculations the "one site model" [26,27] for ketones was used. The optimal lanthanide ion position in the complexes was found at polar coordinates[21,22] of d= 2.9 Å, $\phi = 0°$ (equal for both conformers of **4**) and $\rho = 0°$ (**4a**) or 10° (**4b**). The R factor (corresponding to the average deviation between experimental and calculated values) were 8.9% for **4a** and 9.4% for **4b**. This indicates a fit which is not perfect but still reliable. The results (experimental and calculated LIS values) are listed in Table 1.

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REFERENCES

1. Stone, B.C. *A Revised Handbook to the Flora of Ceylon* (Dassanayake, M.D.; Fosberg, F.R. eds.) **1985**, Vol. 5, pp 406-476, Amerind Publishing Co., New Delhi.
2. Homans, A.L.; Fuchs, A. *J. Chromatog.* **1970**, *51*, 327-329.
3. Greger, H. *Pl.Syst.Evol.* **1985**, *150* , 1-13.
4. Greger, H.; Hofer, O.; Werner, A. *Phytochemistry* **1987**, *26*, 2235-2242.
5. named after Sinharaja, the last patch of undisturbed lowland evergreen Rain Forest of Sri Lanka.
6. Mester, I. *Chemistry and Chemical Taxonomy of the Rutales* (Waterman, P.G.; Grundon, M.F. eds.) **1983**, pp. 31- 96, Academic Press, London.
7. Hegnauer, R. *Chemistry and Chemical Taxonomy of the Rutales* (Waterman, P.G.; Grundon, M.F. eds.) **1983**, pp. 401-439 Academic Press, London.
8. Hegnauer, R. *Chemotaxonomie der Pflanzen* **1990**, Vol.9, Birkhäuser Verlag, Basel.
9. Sarkar, M.; Chakraborty, D.P. *Phytochemistry* **1977**, *16* , 2007-2008.
10. Dadson, B.A.; Minta, A. *J.Chem.Soc.Perkin Trans.I.* **1976**, 146-147.
11. Bowen, I.A.; Perera, K.P.W.C.; Lewis, J.R. *Phytochemistry* **1980**, *19*, 1566-1568.
12. Rastogi, K.; Kapil, R.S.; Popli, S.P. *Phytochemistry* **1980**, *19* , 945-948.
13. Bhattacharyya, P.; Chowdhury, B.K. *Phytochemistry* **1985**, *24* , 634-635.

14. Das, B.P; Chowdhury, D.N. *Chem.Ind.* **1978**, 272-273.
15. Kumar, P.; Das, B.P.; Sinha, S.K.P. *Chem.Ind.* **1986**, 669-670.
16. Govindachari, T.R.; Pai, B.R.; Subramaniam, P.S. *Tetrahedron* **1966**, *22*, 3245-3252.
17. a) Bhattacharyya, P.; Chakrabartty, P.K.; Chowdhury, B.K. *Phytochemistry* **1985**, *24* , 882-883. b) Kumar, V.; Reisch, J.; Wickramasinghe, A. *Aust.J.Chem.* **1989**, *42* , 1375-1379.
18. a) Chakraborty, D.P. *Progress in the Chemistry of Organic Natural Products* (Herz, W.; Grisebach, H.; Kirby, G.W. eds.) **1977**, Vol. 34, pp. 299-371 Springer, Wien, New York. b) Bhattacharyya, P.; Chakraborty, D.P. *Progress in the Chemistry of Organic Natural Products* (Herz, W.; Kirby, G.W.; Steglich, W.; Tamm, Ch. eds.) **1987**, Vol. 52, pp. 159-209 Springer, Wien, New York. c) Chakraborty, D.P.; Shymali, R. *Progress in the Chemistry of Organic Natural Products* (Herz, W.; Kirby, G.W.; Steglich, W.; Tamm, Ch. eds.) **1991**, Vol. 57, pp. 71-152 Springer, Wien, New York.
19. Sarkar, M.; Chakraborty, D.P. *Phytochemistry* **1979**, *18*, 694-695.
20. Johne, S. *Progress in the Chemistry of Organic Natural Products* (Herz, W.; Grisebach, H.; Kirby, G.W.; Tamm, Ch. eds.) **1984**, Vol. 46, pp. 159-229 Springer, Wien, New York.
21. Willcott III, M.R.; Lenkinski, R.E.; Davis, R.E. *J.Amer.Chem.Soc.* **1972**, *94*, 1742-1744.
22. Davis, R.E.; Willcott III, M.R. *J.Amer.Chem.Soc.* **1972**, *94*, 1744-1745.
23. Hofer, O. in: *Topics in Stereochemistry* (Allinger, N.L.; Eliel, E.L. eds.) **1976**, Vol.9, pp. 111-197.
24. Molecular Modeling Software PCMODEL **1990** Serena Software, Bloomington, IN.
25. Ulubelen, A. *Phytochemistry* **1984**, *23*, 2123-2124.
26. Hofer, O.; Greger, H.; Robien, W.; Werner, A. *Tetrahedron* **1986**, *42*, 2707-2716.
27. Greger, H.; Hofer, O. *Phytochemistry* **1989**, *28*, 2363-2368.
28. Müller, N.; Falk, A. **1989** Ball & Stick Program for Apple Macintosh.