

Rigidanthrin, a new dimeric phenanthrene derivative of the orchid *Bulbophyllum rigidum*

P. L. Majumder*, Saswati Bandyopadhyay (née Guha) and Suparna Pal (née Ray)

Department of Chemistry, University College of Science, 92, Acharya Prafulla Chandra Road, Kolkata-700 009, India

E-mail : priyalalm@hotmail.com

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Abstract : Rigidanthrin, a new dimeric phenanthrene derivative, was isolated from the orchid *Bulbophyllum rigidum* which also afforded the known monomeric phenanthrenes nudol and gymnopusin and the simple aromatic compound ethyl 4-hydroxy-3-methoxycinnamate. The structure of rigidanthrin was established as 2,2',7,7'-tetrahydroxy-3,3',4,4'-tetramethoxy-1,1'-biphenanthryl from various spectral and chemical evidence. The structure of rigidanthrin was finally confirmed by regio- as well as regio- and enantio-selective biomimetic synthesis from its monomeric congener nudol (2,7-dihydroxy-3,4-dimethoxyphenanthrene) by oxidative phenol-coupling reaction with phosphomolybdic acid (PMA) on silica gel surface and CuCl(OH).(-)-(S)-proline methyl ester, respectively, in very good yields. The optical purity of (-)-rigidanthrin obtained in the latter case was found to be 95.79%. The co-occurrence of rigidanthrin with its monomer nudol in the same orchid *Bulbophyllum rigidum* provides a strong circumstantial evidence in support of the proposed biogenesis of the naturally occurring biphenanthryl derivatives which are assumed to have been formed from their corresponding monomers by enzymatic oxidative phenol-coupling reaction.

Keywords : *Bulbophyllum rigidum*, orchidaceae, rigidanthrin, dimeric phenanthrene derivative, regioselective biomimetic synthesis, PMA on silica gel surface, enantioselective synthesis, CuCl(OH).(-)-(S)-proline methyl ester.

Introduction

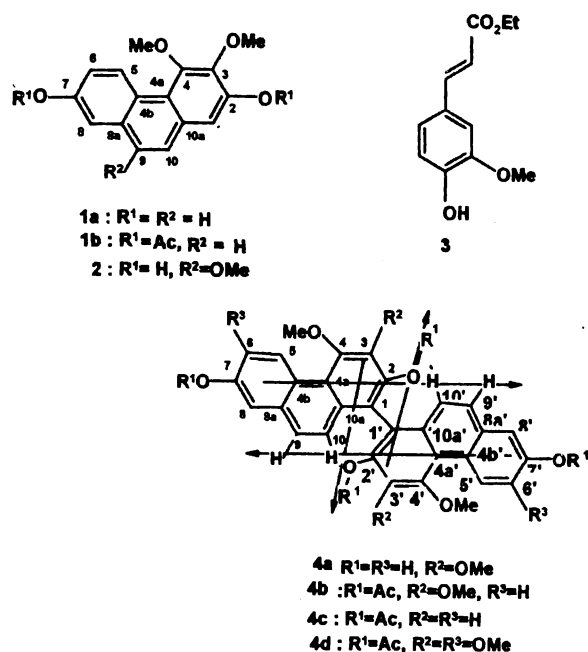
We reported earlier the isolation of a large number of compounds from a series of Indian orchids. These compounds encompass a wide variety of stilbenoids, viz. stilbene¹, bibenzyls², phenanthrenes and 9,10-dihydrophenanthrenes^{3,4} and their dimers⁵⁻⁸, phenanthropyrans and their 9,10-dihydro derivatives⁹⁻¹³, fluorenones¹⁴, and a few other polyphenolics^{15,16}, several triterpenoids¹⁷⁻¹⁹, steroids of biogenetic importance²⁰⁻²² and some simple aromatic compounds²³. As part of this general programme of research, we have chemically investigated yet another Indian orchid *Bulbophyllum rigidum*. This has resulted in the isolation of a new dimeric phenanthrene derivative designated rigidanthrin, besides nudol (**1a**)^{24,25}, gymnopusin (**2**)^{26,27} and ethyl 4-hydroxy-3-methoxycinnamate (**3**)²⁸ of previously known structures. While the known compounds were characterized by comparison with their respective authentic samples, the structure of rigidanthrin was established as 2,2',7,7'-tetrahydroxy-3,3',4,4'-tetramethoxy-1,1'-biphenanthryl (**4a**) from spectral and chemical evidence and was finally confirmed by

regio- as well as regio- and enantio-selective biomimetic synthesis by oxidative phenol-coupling reaction from its monomeric congener (**1a**) with phosphomolybdic acid (PMA) on silica gel surface and CuCl(OH).(-)-(S)-proline methyl ester, respectively, in very high yields.

Results and discussion

Rigidanthrin (**4a**), amorph., $[\alpha]_D^{30} - 9.5^\circ$ (c, 0.12, MeOH), analyzed for C₃₂H₂₆O₈ which was confirmed by its mass spectrometrically derived molecular weight 538. The appearance of an intense peak at *m/z* 269 in its EI mass spectrum indicated it to be composed of two monomeric halves of the same elemental composition C₁₆H₁₃O₄.

Rigidanthrin (**4a**) showed UV absorptions [λ_{\max} (EtOH) 213, 265, 311 and 350 nm (log ϵ 4.67, 5.02, 4.31 and 4.92)] which strikingly resemble those of phenanthrene derivatives^{24,25}. The phenolic nature of **4a** was indicated by its characteristic colour reactions, alkali-induced bathochromic shifts of its UV maxima [(λ_{\max}) (EtOH - 0.1 M NaOH) 224, 270 and 373 nm (log ϵ 4.56, 4.91 and 4.92)] and by its IR absorption at ν_{\max} 3400 cm⁻¹.



The presence of four phenolic hydroxyl groups in **4a** was confirmed by the formation of its tetraacetyl derivative, $C_{40}H_{34}O_{12}$ ($[M^+]$ at m/z 706), m.p. 159 °C with Ac_2O and pyridine.

The 300 MHz 1H NMR spectrum (d_6 -acetone) of **4a** showed eight sets of signals at δ 4.09, 7.03, 7.21, 7.26, 7.33, 7.87, 8.57 and 9.48 in the integral ratio of 6 : 1 : 1 : 1 : 1 : 1 : 1 : 1. Since **4a** contains a total of 26 protons, each of these signals thus corresponds to double the number of protons given by their respective integral ratio. This, in turn, also implied the symmetrical dimeric formulation of the compound. Thus, the singlet at δ 4.09 in the 1H NMR spectrum of **4a** indicated the presence of two pairs of aromatic methoxyl groups in the compound, while the two two-proton singlets at δ 7.87 and 8.57 (both disappeared on deuterium exchange) corresponded to the presence of four phenolic hydroxyl groups in **4a**. The 1H NMR spectrum of **4a** showed five different sets of aromatic protons at δ 9.48 (d, J 9.0 Hz), 7.21 (dd, J_1 9.0 Hz and J_2 3.0 Hz), 7.26 (d, J 3.0 Hz), 7.33 (d, J 9.0 Hz) and 7.03 (d, J 9.0 Hz), each corresponding to two protons having identical environment.

The signal at δ 9.48 in the spectrum of **4a** is typical of H-4 and H-5 of a phenanthrene derivative^{24,25}. Now, if the above signal of **4a** is assigned to its H-5 and H-5', C-4 and C-4' of the compound must be substituted by methoxyl or hydroxyl function. Again, the appearance of this signal as a clear doublet (J 9.0 Hz) indicated that

C-6 and C-6' of **4a** must be unsubstituted. In the light of the well-documented observation^{29,30} that H-5 of a 4-hydroxyphenanthrene derivative is shifted upfield by 0.5–0.6 ppm on acetylation, the downfield shift of H-5 and H-5' of rigidanthrin tetraacetate (**4b**) by 0.25 ppm compared to that of the corresponding proton of **4a**, implied that C-4 and C-4' of the compound must contain a methoxyl rather than a hydroxyl function. The signal at δ 7.21 (dd, J_1 9.0 Hz and J_2 3.0 Hz) of **4a** could then be assigned to H-6 and H-6', which was split by H-5 and H-5' (J_1 9.0 Hz) and also by H-8 and H-8' (J_2 3.0 Hz), resonating at δ 7.26 (d, J 3.0 Hz). That the protons at C-6 and C-8 and C-6' and C-8' are flanked by hydroxyl at C-7 and C-7' in **4a** was supported by the downfield shifts of these protons by 0.23–0.33 ppm in the 1H NMR spectrum of its tetraacetyl derivative **4b**. Further supportive evidence for the structure of rigidanthrin including the site of dimerization was provided by a comparison of the 1H NMR spectra of the compound and its tetraacetyl derivative **4b** with those of nudol (**1a**) and its diacetate **1b**, respectively. The 1H NMR spectrum of **4a** and its tetraacetyl derivative **4b** exhibited striking resemblance with those of nudol (**1a**) and its diacetate **1b** except that (i) the signal corresponding to H-1 of **1a** at δ 7.33 and that at δ 7.55 of its diacetate **1b**, both appearing as sharp singlets, were absent in the 1H NMR spectra of **4a** and **4b**, (ii) the signals corresponding to H-9 and H-10 of nudol (**1a**) at δ 7.77 and 7.55, respectively and that of its diacetate **1b** at δ 7.90 (2H, s) were shifted upfield in the spectra of **4a** (δ 7.33 and 7.03) and its tetraacetyl derivative **4b** (δ 7.39 and 7.02) and (iii) the protons of two of the acetate methyls of **4b** exhibited substantial upfield shift [δ 1.94 (6H, s)] compared to those of its other two acetate methyls [δ 2.37 (6H, s)] and that at δ 2.38 and 2.45 (each 3H, s) in **1b**.

The above observations are intelligible only in terms of a 1,1'-dimeric formulation **4a** for rigidanthrin and **4b** for its tetraacetyl derivative. The observed differences in the chemical shifts of some of the protons of **4a** and **4b** from those of the corresponding protons of nudol (**1a**) and its diacetate **1b**, respectively may be explained in the light of the most preferred conformations of **4a** and **4b**. Construction of the Dreiding models of **4a** and **4b** shows that in the most preferred conformations of the compounds, the two monomeric units remain almost perpendicular to each other. In this conformation, H-10 and H-10' and H-9 and H-9' of **4a** and **4b** fall in the shielding zones of the neighbouring aromatic rings of the compounds. Accord-

ingly, these protons of **4a** and **4b** were shifted upfield [**4a**: δ 7.03 (H-10, H-10') and 7.33 (H-9, H-9'); **4b**: δ 7.02 (H-10, H-10') and 7.36 (H-9, H-9')] compared to H-10 and H-9 of nudol (**1a**) and its diacetate **1b**, which appeared at the normal regions [**1a**: δ 7.63 (2H, ABq, J 8.0 Hz); **1b**: δ 7.90 (2H, s)]. The greater shielding of H-10 and H-10' of **4a** and **4b** than those of their H-9 and H-9' may be attributed to the greater proximity of H-10 and H-10' than H-9 and H-9' to the shielding zones of the neighbouring aromatic rings as shown in structural diagrams of **4a** ($R^1 = H$) and **4b** ($R^1 = Ac$). This also affirmed the site of dimerization in **4a** and **4b** to be at 1,1' position.

Again, in the light of the reported observations⁵⁻⁸ that protons of methyl, methoxyl and acetoxyl groups *ortho* to the site of dimerization in similar biaryls⁵⁻⁸, which fall in the shielding zones of the neighbouring aromatic rings resonate at higher fields than such protons at other parts of the molecules, the appearance of the protons of the two acetate methyls of **4b** at much higher field (δ 1.94) compared to those of the other two acetate methyls appearing at the normal region (δ 2.37) required the high field acetate methyls to be associated with the acetoxyl functions at C-2 and C-2' of **4b** ($R^1 = Ac$), the other two acetoxyl functions being already placed at C-7 and C-7'. This, in turn, affirmed the placement of two hydroxyl functions at C-2 and C-2' in **4a**, the other two hydroxyl groups being at C-7 and C-7'. The four methoxyl groups of **4a** were thus placed at C-3, C-3' and C-4, C-4'. The energy barrier for rotation around the 1,1'-bond of **4a** seems to be high enough to make it optically active.

Further evidence in support of the structure of rigidanthrin (**4a**) was provided by the ^{13}C NMR spectral data of its more soluble tetraacetyl derivative (**4b**) [Table 1]. The degree of protonation of each carbon atom was determined by DEPT experiments and the assignments of the carbon chemical shifts of **4b** were made by comparison of the δ values with of those of **1b** and other structurally related compounds like **4c**⁶ and **4d**³¹. The ^{13}C NMR spectrum of **4b** showed 20 carbon resonances which corresponded to just half the number of carbon atoms present in its molecule. This further affirmed the symmetrical dimeric formulation of **4b** and hence of the parent rigidanthrin (**4a**). The carbon chemical shifts of **4b** are virtually identical with those of nudol diacetate (**1b**) except that the protonated C-1 resonance (δ 117.1) of the latter is replaced by a relatively lowfield quaternary carbon signal at δ_c 121.9 in the former and that

C-10 of **1b** is shifted upfield by 2.0 ppm in **4b**. Such downfield shifts of C-1 and C-1' and upfield shifts of C-10 and C-10' of structurally similar phenanthrene dimers compared to the corresponding carbon atoms of their respective monomers are typical of 1,1'-biphenanthryl derivatives^{5-9,31}. Rigidanthrin (**4a**) is thus the symmetrical 1,1'-dimer of nudol (**1a**). The above contention was further confirmed by the virtually identical δ_c values of C-4b (C-4b'), C-5 (C-5'), C-6 (C-6'), C-7 (C-7'), C-8 (C-8'), C-8a (C-8a') and C-9 (C-9') of **4b** and the corresponding carbon atoms of cirrhopetalanthrin tetraacetate (**4c**)⁶ possessing acetoxyl functions at C-7 and C-7'. Again, the essentially identical δ_c values of C-1 (C-1'), C-2 (C-2'), C-3 (C-3'), C-4 (C-4'), C-4a (C-4a'), C-10 (C-10') and C-10a (C-10a') of **4b** and those of the corresponding carbon atoms of **4d**³¹ confirmed the presence of four methoxyl groups at C-3, C-3', C-4 and C-4' and two of the four acetoxyl functions at C-2 and C-2' in **4b**, the other two acetoxyl functions of **4b** being already placed at C-7 and C-7'. The placement of the four methoxyl groups at C-3, C-3', C-4 and C-4' was also supported by the relatively downfield shifts of the methoxyl carbon resonances (δ_c 61.0 and 60.0) of **4b**, which are typical of the methoxyl functions having no *ortho* hydrogen atom. The structure of rigidanthrin is thus established as 2,2',7,7'-tetrahydroxy-3,3',4,4'-tetramethoxy-1,1'-biphenanthryl (**4a**).

More compelling evidence in support of the structure **4a** for rigidanthrin was provided by the 2D NMR spectral analysis (HMQC and HMBC with J_{C-H} parameters set to 160 Hz and 7 Hz, respectively) of its tetraacetyl derivative **4b**. The chemical shifts of all the protonated carbon atoms of **4b** were confirmed by the 1-bond 1H - ^{13}C correlations observed in the HMQC spectrum of the compound, while the long range (3-bond and in a few cases 2-bond) 1H - ^{13}C correlations exhibited by the HMBC spectrum of **4b** further confirmed the assignments of its protonated as well as nonprotonated carbon atoms. In the HMBC spectrum the strongest correlations are those between 3-bonds, while 2-bond correlations are also sometimes observed in compounds containing oxygenated functions like methoxyl and hydroxyl/acetoxyl groups attached to the aromatic ring, which probably alter the electron distribution in favour of such couplings^{6,27}. Thus, the most downfield protons at δ 9.72 (2H, d, J 9.36 Hz) assigned to H-5 (H-5') of **4b** showed three strong 3-bond correlations with carbon resonances at δ_c 123.2, 149.0 and 133.8 attributed to its C-4a, (C-4a'), C-7 (C-7') and C-8a (C-8a'), respectively. The protons at δ 7.42 (2H,

Table 1. ^{13}C NMR spectral data of **4b**, **1b**, **4c** and **4d**

C	Chemical shifts* (δ_{ppm})			
	4b^a	1b^a	4c^a	4d^a
1 (1')	121.9	117.1	119.2	122.6
2 (2')	145.2	144.9	147.8	144.7
3 (3')	142.5	143.2	104.1	142.5
4 (4')	152.4	152.5	159.2	152.2
4a (4a')	123.2	123.0	117.5	121.9
4b (4b')	129.3	129.4	128.2	129.4
5 (5')	129.2	128.9	130.2	109.5
6 (6')	119.6	119.6	120.8	150.4
7 (7')	149.0	148.7	148.5	139.8
8 (8')	121.0	120.9	119.5	121.1
8a (8a')	133.8	133.7	133.5	128.6
9 (9')	127.0	126.9	128.5	126.6
10 (10')	125.4	127.4	125.7	123.1
10a (10a')	127.6	127.42	134.4	127.5
OMe	61.0 (OMe at C-4)	61.2	56.1	61.1
	60.0 (OMe at C-3)	60.05	–	60.1
				55.8
OCOMe	169.7, 20.9	169.2, 20.8	169.3, 20.8	168.4, 19.5
	168.5, 19.9	169.5, 21.3	169.7, 21.3	169.3, 20.4

*Carbon atoms with and without parenthesis correspond to those of the dimeric phenanthrene derivatives and those without parenthesis correspond to those of the monomers.

^aSpectra were run in CDCl_3 and the chemical shifts were measured with $\delta_{\text{TMS}} = \delta_{\text{CDCl}_3} + 76.9$ ppm.

dd, J_1 9.36 Hz and J_2 2.50 Hz) of **4b** assigned to its H-6 (H-6') exhibited two 3-bond correlations with the carbon signals at δ_{C} 129.3 and 121.0 assigned to its C-4b (C-4b') and C-8 (C-8'), respectively. Similarly, the protons at δ 7.52 (2H, d, J 2.50 Hz) which corresponded to H-8 (H-8') of **4b** displayed three strong 3-bond and one 2-bond fairly strong correlations with the carbon resonances at δ_{C} 119.6, 129.3, 127.0 and 149.0 which were assigned to its C-6 (C-6'), C-4b (C-4b'), C-9 (C-9') and C-7 (C-7'), respectively. Again, the protons at δ 7.39 (2H, d, J 9.09 Hz) assigned to H-9 (H-9') of **4b** exhibited three strong 3-bond correlations with the carbon signals at δ_{C} 121.0, 129.3 and 127.6 which corresponded to its C-8 (C-8'), C-4b (C-4b') and C-10a (C-10a'), respectively. Similarly, the protons at δ 7.02 (2H, d, J 9.09 Hz) attributed to H-10 (H-10') of **4b** showed three strong 3-bond correlations and one 2-bond weak correlation with the carbon resonances at δ_{C} 133.8, 123.2, 121.9 and 127.6 which were assigned to its C-8a (C-8a'), C-4a (C-4a'), C-1 (C-1') and C-10a (C-10a'), respectively. The methoxyl protons at δ 4.09 and 4.11 exhibited strong 3-bond corre-

lations with the carbon signals at δ_{C} 142.5 and 152.4 which corresponded to its C-3 (C-3') and C-4 (C-4'), respectively. All the above correlations observed in the HMBC spectrum of **4b** are shown on its structural diagram (Fig. 1), which further confirmed its assigned structure and hence that of the parent rigidanthrin (**4a**).

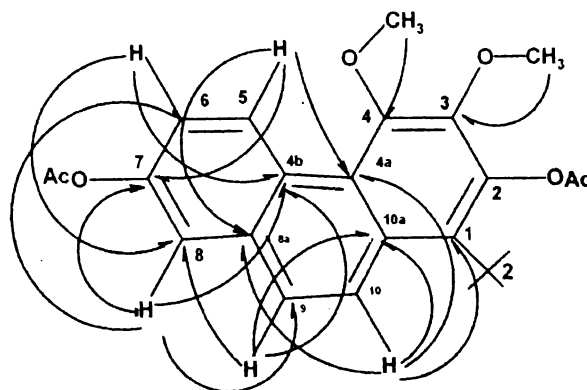
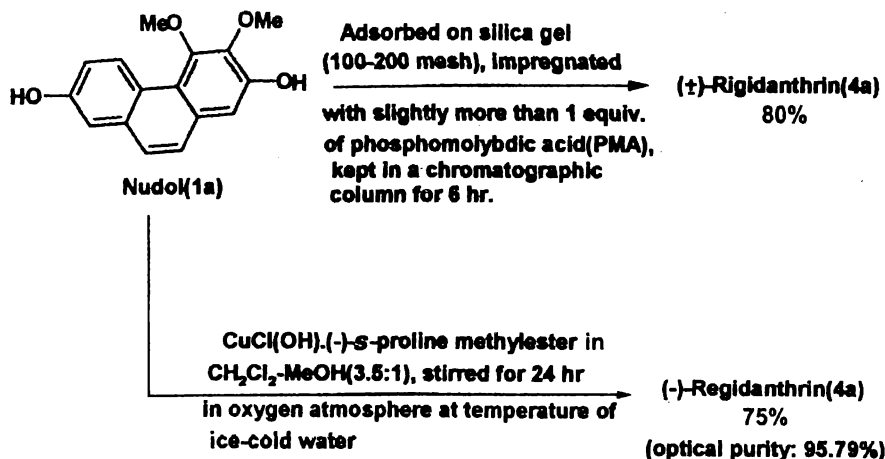


Fig. 1. Long range ^1H - ^{13}C correlations (HMBC) observed in the spectrum of **4b**.



Scheme 1. Synthesis of (±) and (-)-rigidanthrin (4a).

The structure of rigidanthrin was finally confirmed by its regioselective biomimetic synthesis from its naturally occurring monomer nudol (1a) with slightly more than one equivalent of phosphomolybdic acid (PMA) on silica gel surface³² in 80% yield (Scheme 1). The product, is, however, a *dl*-mixture.

More importantly, an efficient regio- and enantio-selective biomimetic synthesis of natural (-)-rigidanthrin was achieved with an optical purity of 95.79% [calculated on the basis of the pure natural (-)-rigidanthrin to have the $[\alpha]_D - 9.50^\circ$ (MeOH) as has been actually observed] involving oxidative phenol-coupling reaction of nudol (1a) with CuCl(OH).(-)-(*S*)-proline methyl ester, a new chiral reagent developed by us, in about 75% yield (Scheme 1). A detailed account of the above reagent and its application would be described in a forthcoming communication. Similar oxidative phenol-coupling reaction with achiral reagent CuCl(OH).TMEDA has been initially employed by Noji *et al.*³³ and later by Majumder and his co-workers^{8,34} to get the *dl*-product.

Biogenetically, rigidanthrin (4a) may be assumed to be formed by oxidative coupling of its monomeric congener nudol (1a). The co-occurrence of nudol (1a) and rigidanthrin (4a) in the same orchid *Bulbophyllum rigidum* has provided a strong circumstantial evidence in support of the above contention. Rigidanthrin (4a) is, thus, a new addition to the growing list of naturally occurring biphenanthryl derivatives.

Experimental

M.p.s : uncorr. CC : silica gel (100–200 mesh). TLC : silica gel G. IR : KBr discs. ¹H and ¹³C NMR : 300 MHz and 75 MHz, respectively. NMR spectra were recorded in *d*₆-acetone (4a) and CDCl₃ (4b and others) using TMS as internal standard. Chemical shifts were expressed in δ_{ppm} . The HMQC and HMBC spectra of 4b were recorded in CDCl₃ in a 500 MHz instrument with *J*_{C-H} parameters set to 160 Hz and 7 Hz, respectively. MS : direct inlet system, 70 eV. All analyt. samples were routinely dried over P₂O₅ for 24 h *in vacuo* and were tested for purity by TLC and MS. The petrol used had b.p. 60–80 °C. Anhydrous Na₂SO₄ was used for drying organic solvents.

Plant materials :

Bulbophyllum rigidum King and Pantling was collected from Kalimpong (Darjeeling, India) in August 2002. A voucher specimen (Majumder s.n.) was deposited in the Herbarium of the Department of Botany, University of Calcutta (CUH).

Isolation of rigidanthrin (4a), nudol (1a), gymnopusin (2) and 3 :

Air-dried finely powdered whole plant of *B. rigidum* (4 kg) was kept soaked in MeOH (10 L) for four weeks at room temperature. The MeOH extract was concentrated to ca. 100 ml, diluted with H₂O (750 ml) and exhaustively extracted with Et₂O. The Et₂O extract was frac-

tionated into acidic and non-acidic fractions with 2 M NaOH solution. The aqueous alkaline solution was acidified in the cold with conc. HCl and the liberated solids were extracted with Et₂O, washed with H₂O, dried and the solvent was removed. The Et₂O extract containing the non-acidic constituents (left after treatment with 2 M NaOH) was also washed with H₂O, dried and the solvent removed. The residues containing the acidic and non-acidic (neutral) compounds were separately chromatographed.

Chromatography of the acidic fraction :

The petrol-EtOAc (80 : 1) eluate afforded a compound (0.12 g) as a semisolid mass which was characterized as ethyl 4-hydroxy-3-methoxy-cinnamate (**3**). Washing the main column with petrol-EtOAc (10 : 1) gave gymnopusin (**2**), [0.12 g], crystallized from petrol-EtOAc, m.p. 192 °C. The petrol-EtOAc (5 : 1) eluate afforded nudol (**1a**) [0.3 g], as amorphous powder. ¹H NMR : δ 9.33 (1H, d, *J* 10.0 Hz, H-5), 8.65 and 8.00 (each 1H, br.s, ArOH), 7.63 (2H, ABq, *J* 8 Hz, H-9 and H-10), 7.35 (1H, d, *J* 3.0 Hz, H-8), 7.33 (1H, s, H-1), 7.30 (1H, dd, *J*₁ 10.0 Hz and *J*₂ 3.0 Hz, H-6), 4.05 and 4.00 (each 3H, s, ArOMe). Acetylation of **1a** with Ac₂O and pyridine gave the corresponding diacetate **1b**, crystallized from petrol-EtOAc, m.p. 156 °C. ¹H NMR : δ 9.38 (1H, d, *J* 10.0 Hz, H-5), 7.90 (2H, s, H-9 and H-10), 7.80 (1H, d, *J* 3.0 Hz, H-8), 7.55 (1H, dd, *J*₁ 10.0 Hz and *J*₂ 3.0 Hz, H-6), 7.55 (1H, s, H-1), 4.05 and 4.00 (each 3H, s, ArOMe), 2.45 and 2.38 (each 3H, s, OAc at C-7 and C-2).

Further elution of the column with petrol-EtOAc (1 : 1) gave crude rigidanthrin (**4a**) which on repeated chromatography afforded pure **4a** (0.28 g) as an amorphous solid (Found : C, 71.34; H, 4.81. C₃₂H₂₆O₈ requires : C, 71.37; H, 4.83%); IR (KBr) ν_{max} cm⁻¹ : 3400 (phenolic -OH), 1610, 1570, 850, 830 and 780 (aromatic nucleus); ¹H NMR : δ 9.48 (2H, d, *J* 9.0 Hz, H-5 and H-5'), 8.57 and 7.87 (each 2H, s, Ar-OH), 7.33 (2H, d, *J* 9.0 Hz, H-9 and H-9'), 7.26 (2H, d, *J* 3.0 Hz, H-8 and H-8'), 7.21 (2H, dd, *J*₁ 9.0 Hz and *J*₂ 3.0 Hz, H-6 and H-6'), 7.03 (2H, d, *J* 9.0 Hz, H-10 and H-10'), 4.09 (12H, s, 4 × ArOMe); MS (EI) *m/z* (rel. int.) : 538 [M⁺] (100), 269 (37), 253 (15), 241 (10), 224 (22), 210 (12), 189 (11), 169 (19), 146 (18) and 132 (19). Rigidanthrin (**4a**) was acetylated with Ac₂O and pyridine in the usual manner to

give the corresponding tetraacetyl derivative **4b**, crystallized from petrol-EtOAc, m.p. 150 °C (Found : C, 67.95; H, 4.80. C₄₀H₃₄O₁₂ requires : C, 67.99; H, 4.82%); UV λ_{max} nm : 218, 262, 296 and 309 (log ε 4.62, 4.93, 4.35 and 4.39); IR (KBr) ν_{max} cm⁻¹ : 1255 and 1760 (OAc), 1610, 885, 830 and 790 (aromatic nucleus); ¹H NMR : δ 9.72 (2H, d, *J* 9.36 Hz, H-5 and H-5'), 7.52 (2H, d, *J* 2.50 Hz, H-8 and H-8'), 7.42 (2H, dd, *J*₁ 9.36 Hz and *J*₂ 2.50 Hz, H-6 and H-6'), 7.39 (2H, d, *J* 9.09 Hz, H-9 and H-9'), 7.02 (2H, d, *J* 9.09 Hz, H-10 and H-10'), 4.11 and 4.09 (each 6H, s, 4 × ArOMe), 2.37 (6H, s, OAc at C-7 and C-7') and 1.94 (6H, s, OAc at C-2 and C-2'); MS (EI) *m/z* (rel. int.) : 706 [M⁺] (15), 664 (82), 622 (100), 580 (65), 538 (30) and 269 (68).

Chromatography of the neutral fraction gave only some uncharacterized oily mass.

Biomimetic synthesis of rigidanthrin (4a) involving oxidative phenol-coupling reaction :

(i) *Regioselective biomimetic synthesis of (±)-rigidanthrin with phosphomolybdic acid (PMA) on silica gel surface :*

A solution of nudol (**1a**) [0.10 g] in acetone (25 ml) was uniformly adsorbed on 15 g of silica gel (100–200 mesh) previously impregnated with an aqueous methanolic solution of phosphomolybdic acid (PMA) [0.70 g] (the silica gel after uniformly impregnated with PMA was dried in a vacuum desiccator for 1 h) and the solvent was removed by keeping the materials also in a vacuum desiccator for 30 min. The material was then placed on a bed of fresh silica gel (*ca.* 30 g) in a small chromatographic column and kept soaked with petrol for 6 h. The silica gel layer containing PMA and **1a** gradually turned intense blue in colour. The column was then washed with petrol-EtOAc (5 : 1). The eluate on removal of solvent gave small amounts of unreacted **1a** (0.02 g). Further washing the column with petrol-EtOAc (1 : 1) gave an eluate leaving behind the inorganic materials mostly in the column. The above eluate was washed with H₂O, dried and the solvent removed. The residue was chromatographed. The petrol-EtOAc (1 : 1) eluate afforded pure (±)-rigidanthrin (**4a**) [0.08 g; *ca.* 80%] as a white amorphous powder.

(ii) *Regio- and enantio-selective biomimetic synthesis of (-)-rigidanthrin (4a) with CuCl(OH).(-)-(S)-proline methyl ester* :

(-)-(S)-Proline (0.50 g) dissolved in MeOH (60 ml) was treated with a solution of 8 molar equivalent of CH_2N_2 in Et_2O (100 ml) and the mixture was kept overnight in an ice-bath. Removal of the solvent gave an oily residue which was taken in Et_2O , washed twice with NaHCO_3 solution and then with H_2O , dried and the solvent removed. The residue was chromatographed. The petrol-EtOAc (3 : 1) eluate gave pure (-)-(S)-proline methyl ester as an oily mass.

To a hot solution of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (7 g) and pure NaCl (1.84 g) in H_2O (25 ml) was added a solution of sodium metabisulphite (1.68 g) in 18 ml water during about 5 min with constant stirring. The mixture was then cooled in an ice bath, when CuCl was precipitated out. It was filtered, washed twice with cold water and then dried in vacuum desiccator.

A mixture of CuCl (1.5 g) and (-)-(S)-proline methyl ester (3.9 g), as prepared above, in 95% methanol was stirred under oxygen atmosphere at room temperature for 1 h. The resulting precipitate was collected by filtration, washed with acetone and dried in a vacuum desiccator to give CuCl(OH).(-)-(S)-proline methyl ester as a yellowish powder.

A mixture of nudol (**1a**) [0.27 g] and CuCl(OH).(-)-(S)-proline methyl ester (0.025 g) in 25 ml CH_2Cl_2 -MeOH (3.5 : 1) was stirred at a temperature of ice-cold H_2O for 25 h in an atmosphere of oxygen. The solvent was then removed under reduced pressure and the residue was extracted with Et_2O , washed with dil. HCl and then with H_2O , dried and the solvent removed. The residue was then chromatographed. The petrol-EtOAc (5 : 1) eluate gave unreacted **1a** (0.07 g). Further washing the column with petrol-EtOAc (1 : 1) afforded (-)-**4a** (0.20 g, ca. 75%) as an amorphous powder, $[\alpha]_D^{30} - 9.1^\circ$ (c, 0.10, MeOH) [optical purity was 95.79% calculated on the basis of pure (-)-rigidanthrin (**4a**) having $[\alpha]_D^{30} - 9.5^\circ$ (MeOH)].

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