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STEREOCHEMISTRY OF STRICTIC ACID AND RELATED FURANODITERPENES FROM *CONYZA JAPONICA* AND *GRANGEA MADERASPATANA*

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Key Word Index—*Conyza japonica*; *Grangea maderaspatana*; Compositae; Astereae; strictic acid; clerodanes; 5,7-dihydroxy-3,8,4′-trimethoxyflavone; 3-hydroxy-8-acetoxy-pentadeca-1,9,14-trien-4,6-diyne.

Abstract—Extraction of *Conyza japonica* gave strictic acid, *ent*-2β-hydroxy-15,16-epoxy-3,13(16),14-clerodatrien-18-oic acid and 5,7-dihydroxy-3,8,4′-trimethoxyflavone. Extraction of *Grangea maderaspatana* gave (−)-hardwickiic acid, *ent*-15,16-epoxy-1,3,13(16),14-clerodatetraen-18-oic acid and 3-hydroxy-8-acetoxypentadeca-1,9,14-trien-4,6-diyne. The structure of *ent*-2β-hydroxy-15,16-epoxy-3,13(16),14-cleroclatrien-18-oic acid was deduced by spectroscopic methods and by partial synthesis from (−)-hardwickiic acid and the stereochemistries of strictic acid and (*ent*-15,16-epoxy-1,3,13(16),14-clerodatraen-18-oic acid were established by correlation with *ent*-2β-hydroxy-15,16-epoxy-3,13(16),14-clerodatrien-18-oic acid.

INTRODUCTION

Published work on a furanoditerpene variously referred to as conyzic acid [1], seconidoresedic acid [2] and strictic acid [3] is surrounded by confusion. The substance, first isolated from *Conyza stricta* Willd., was originally assumed to be Δ^1-polyalthic acid. Bohlmann and Fritz [2] recognized that their material, isolated as the methyl ester from *Nidorella resedifolia*, was a 5,10-secoclerodane and assigned it, and its probable precursor also found in *N. resedifolia*, the stereochemistry shown in formulas **1b** and **2b**, respectively*. Tandon and Rastogi [6], without recognizing the identity of their strictic acid from *Conyza stricta* with conyzic acid, showed that strictic acid on heating was decarboxylated to a bicyclic diene and represented its structure as **5a** without further comment. Finally, Mahato and coworkers [7] showed that conyzic acid, seconidoresedic acid and strictic acid were identical but preferred formula **1a** on the apparently mistaken assumption that the diterpenes accompanying strictic acid in *N. resedifolia* were of type **3**.

Contributing to the confusion is a report on the constituents of a collection thought to be *Centipeda orbicularis* Lour. [8] but actually representing *Grangea maderaspatana* Poir† Structures of two furanoditerpene acids isolated as their methyl esters and stated to be known [8] but without literature references were listed as **2b** and **7b**; presumably the former was identical with the diene from *N. resedifolia*. As far as we are aware the literature contains no authentic compound with stereochemistry **7a** and we assume, in light of the results to be detailed below, that the authors meant to refer to methyl hardwickiate (**8b**).

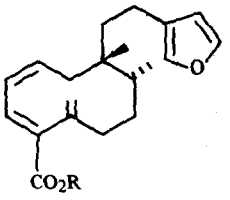
As a result of our work on the cosntituents of *Conyza japonica* (Thunb.) Less. and *Grangea maderaspatana* Poir. which is described in this report we have now clarified the situation. The stereochemistries of strictic acid (from *C. japonica*) and the diene clerodane (from *G. maderaspatana*) have been confirmed as **5a** and **6a** by photochemical conversion of **6a** to **5a** and by preparation of **6b** from a clerodane **9a** isolated in low yield from *C. japonica*. In turn, the structure of **9a** was established by partial synthesis from (−)-hardwickiic acid (**8a**) which was found in *G. maderaspatana*. *Conyza japonica* also gave 5,7-dihydroxy-3,8,4′-trimethoxyflavone (**16a**) previously isolated from *C. stricta* [9], whereas *G. maderaspatana* in addition to **6a** and **8a** gave an acetylenic alcohol **17a** previously isolated from the roots of *Helianthus angustifolius* [10].

RESULTS AND DISCUSSION

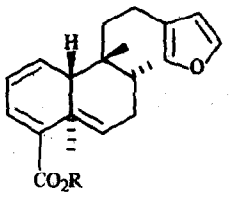
We discuss first the structure of **9a**, characterized as the methyl ester $C_{21}H_{30}O_4$ (high resolution mass spectrum), from *C. japonica* since this is central to the correlations with **5a** and **6a**. That the substance was a furanoclerodane was evident from the mass spectrum (strong peaks at *m/z* 95 and 81) and ^{1}H NMR spectrum (see Experimental) which exhibited the typical signals of a 3-substituted furan as well as two methyl singlets and a methyl doublet. The distribution of functional groups in ring A was also clear

*These formulae are either misprints or are based on a mistaken analogy. It was claimed [2] that another furanoditerpene from *N. resedifolia* was identical with, and had the same rotation as, a supposed compound **3** earlier obtained from *Solidago* species [3–5]. In fact the substance described in refs. [3] and [4] is the *cis*-clerodane **4**.

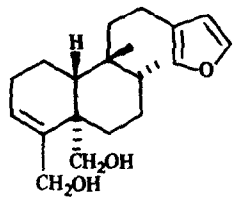
†The material used by the German workers was collected by staff members of the RRL, Jorhat. The misidentification, corrected by the Botanical Survey of India, Shillong, Meghalaya, was brought to our attention after we had independently begun work on *Grangea maderaspatana*.



R
1a H
1b Me



R
2a H
2b Me



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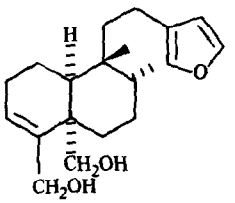

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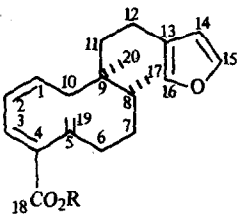
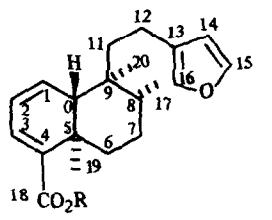
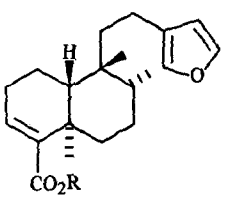


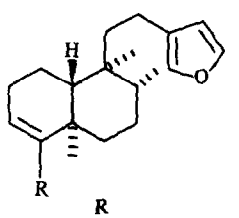
R
5a H
5b Me



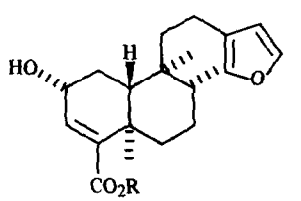
R
6a H
6b Me



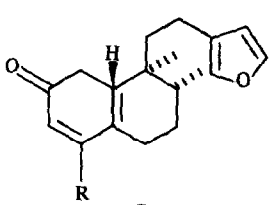
R
7a H
7b Me



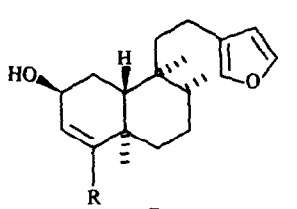
R
8a CO_2H
8b CO_2Me
8c CH_2OH
8d CH_2OAc



R
9a H
9b Me



R
10a CHO
10b CO_2Me
10c CH_2OH
10d CH_2OAc



R
11a CO_2Me
11b CH_2OH

from the chemical shift of H-3, a narrowly split *dd*, $J = 2.5$, 1.5 Hz, at $\delta 6.47$ coupled to the broadened *t*, $J = 7$ Hz, of H-2 at $\delta 4.35$, and it seemed plausible to assume that the A/B ring junction of **9a** was the same as that of (−)-hardwickiic acid (**8a**). If so, the appearance of the H-2 signal was different from that reported for H-2 of a substance **11** from *Dodonaea boronifolia* and seemed more in keeping with that of its C-2 epimer obtained as the major product by sodium borohydride of ketone **10b** [11].

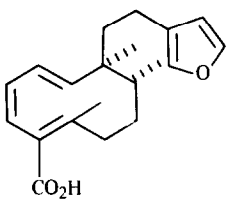
An authentic sample of **9b** was synthesized from (−)-methyl hardwickiate (**8b**) by the following route. Lithium aluminium hydride–aluminium chloride reduction of **8b** to **8c** [11], acetylation to **8d** and oxidation of the latter with CrO_3–pyridine afforded **10** which was hydrolysed to **10c**. Manganese dioxide oxidation of **10c** gave a ketoaldehyde whose spectral properties corresponded to those of ketoaldehyde **10a** prepared by oxidation of **11b** [11]. Oxidation of **10a** by the literature method (KCN, MnO_2, HOAc, MeOH) [11] furnished **10b** whose reduction with sodium borohydride gave as major product **9b**, identical in all respects with the clerodane from *C. japonica*, and as

minor product its C-2 epimer **11a**.

Dehydration of **9b** with *p*-toluenesulfonic acid gave **6b**, identical with the methyl ester of **6a** isolated from *G. maderaspatana*. Consequently the stereochemistry of this substance at C-8 and C-9 is as shown in the formula.

Photolysis of **6a** resulted in conversion to **5a**, thus providing proof for the stereochemistry of strictic acid. The reaction, monitored by TLC, proved to be rather complex and resulted in gradual conversion of **6a** to a stationary mixture containing mainly one stereoisomer of starting material. This was followed by gradual appearance of strictic acid which was isolated and identified by direct comparison with authentic material. We interpret these results as follows. Photolysis (conrotatory opening) of **6a** should furnish **12** which may be in photolytic equilibrium with **13** by alternative conrotatory ring closure or in thermal equilibrium (disrotatory ring closure) with **14** or **15** [12–16]. Strictic acid is subsequently formed by a thermally allowed photochemically disallowed 1,7-hydride shift in **12**, as in the conversion of previtamin D to vitamin D [17, 18]. The mixture containing **13**, **14** or **15** presumably contains some **12** as well. This can be inferred from the following observation. As **5a**, **6a** and the mixture exhibit considerably different R_f values, the presence of **5a** in the mixture as originally isolated in Jorhat by prep. TLC can be excluded. However, the presence of **5a** in the mixture received in Tallahassee approximately two weeks later was evident from NMR spectrometry and then by TLC. We ascribe this to the conversion of **12** to **5a** in the time which elapsed between isolation of the photolysis products and their examination by high resolution NMR spectrometry.

Extensive NMR decoupling experiments established the structure of a divinylhydroxyacetoxydiyne from *C. japonica* as **17a**, a substance isolated earlier from *Helianthus angustifolius* roots [10] and a lower homologue of a C_{17}-analogue found in '*Centipeda orbicularis*' [18]. ^{13}C NMR spectra of **17a** and its previously unreported hydrolysis product whose properties confirmed the postulated structure are listed in Table 1. Catalytic



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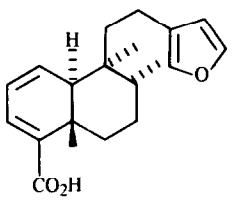

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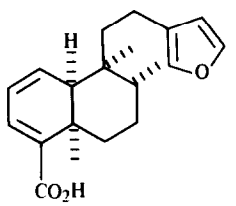

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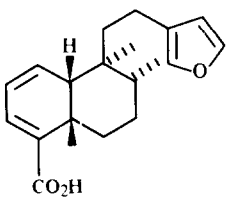

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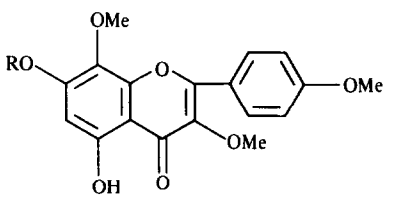
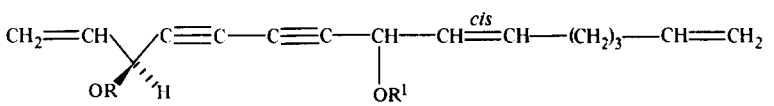
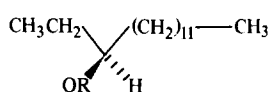


R
16a H
16b Me



17a R=H,R^1=Ac
17b R,R^1=Ac
17c R,R^1=H



R
18a H
18b Ac

Table 1. ^{13}C NMR spectra of compounds **17a** and **17c***†

Carbon	**17a**	**17c**	**17c**‡
1	117.18 *t*	117.12 *t*	116.52 *t*
2	135.57 *d*	135.66 *d*	136.46 *d*
3	63.37 *d*	63.31 *d*	63.45 *d*
4	78.49	78.28	79.36
5	70.03§	70.17§	70.62§
6	69.22§	68.70§	69.30§
7	||	79.73	80.73
8	60.04 *d*	58.44 *d*	58.77 *d*
9	123.96 *d*	127.92 *d*	128.96 *d*
10	135.71 *d*	133.83 *d*	133.36 *d*
11	27.22 *t*	26.99 *t*	27.17 *t*
12	28.26 *t*	28.35 *t*	28.64 *t*
13	33.07 *t*	33.07 *t*	33.35 *t*
14	138.00 *d*	138.12 *d*	138.56 *d*
15	114.78 *t*	114.12 *t*	115.00 *t*
Ac	169.22		
	20.88 *q*		

*Run at 67.89 MHz in $CDCl_3$ using TMS as internal standard.

†All multiplets were identified by selective decoupling.

‡Run in C_6D_6.

§Assignments may be interchanged.

||Obscured by solvent signal.

hydrogenation of **17a** was accompanied by hydrogenolysis and yielded **18a** which was further characterized as the acetate **18b**. Alcohol **17a** possesses two asymmetric centres. Application of the Horeau method of partial esterification to **17a** gave (+)-*S*-phenylbutyric acid in 24% optical yield; if the vinyl group were the 'larger' of the two groups attached to C-3 (an assumption which is subject to some doubt) the absolute configuration should be 3*R**. The configuration at C-8 remains unknown.

The chemistry of *Conyza japonica* is essentially identical with that reported for *Conyza stricta* [1, 6, 9]† and somewhat similar to that of *C. ivaefolia* which also yields furanoclerodanes [20], but different from that of a number of other *Conyza* species which have been studied recently [21]. Our collection of *Grangea maderaspatana* did not yield the two flavonoids reported by Bohlmann and Mahanta from '*Centipeda orbicularis*' [8] but appears to be similar in other respects. An article on steroids from *G. maderaspatana* has appeared [22].

*The situation is somewhat confusing as by the Cahn-Ingold-Prelog rules the diacetylene moiety has higher priority than the vinyl group.

†According to Hooker [19], *Conyza stricta* Willd. extends from Kashmir eastwards up to 5000 ft and is found in the Khasia mountains at 2000–6000 ft, whereas *C. japonica* Less. (which embraces *inter alia* what has been called *C. stricta* Wall. earlier) is found from Simla east and the Khasia mountains up to 5000 ft. While the ranges in India overlap, "the excessively fastigiately branched leaf habit of *C. stricta* Willd. and its minute head distinguish it from all others".

EXPERIMENTAL

Extraction of Conyza japonica. Above ground parts of *Conyza japonica* (Thunb.) Less. (0.5 kg), collected in the hills of Dehradoon, U.P., India, in September 1982, were extracted with $CHCl_3$ in a Soxhlet apparatus for 8 hr. Evaporation of the solvent at red. pres. gave 5 g of residue which was dissolved in 200 ml MeOH containing 10% H_2O and left overnight at room temp. After filtration, the filtrate was washed with petrol (bp 60–80°), until the washings were almost colourless. Most of the MeOH was removed at red. pres.; the residue was extracted with $CHCl_3$ (6 × 100 ml) and the washed and dried extract was evaporated at red. pres. The residue (1.5 g) was chromatographed over 150 g silica gel (60–120 mesh, BDH India), 200 ml fractions being collected as follows. Fractions 1–3 (C_6H_6), 4–7 (C_6H_6–EtOAc, 9:1), 8–18 (C_6H_6–EtOAc, 4:1), 19–33 (C_6H_6–EtOAc, 2:1), 34–40 (C_6H_6–EtOAc, 1:1), 41–45 (C_6H_6–EtOAc, 1:2), 46–50 (EtOAc), 51–53 (EtOAc–MeOH, 50:1), 54–59 (EtOAc–MeOH, 20:1), 60–64 (EtOAc–MeOH, 10:1), 65–66 (EtOAc–MeOH, 7:1), 67–68 (EtOAc–MeOH, 5:1), 69–70 (EtOAc–MeOH, 4:1) and 71–72 (EtOAc–MeOH, 2:1).

Fractions 10–14 which showed a single spot on TLC (C_6H_6–EtOAc, 9:1) were combined to give 75 mg of strictic acid (**5a**), mp 160° (petrol–EtOAc) lit. 160° [6], $[\alpha]_D$ −190° (*c* 1.1, $CHCl_3$), lit. −182° (*c* 1.3, $CHCl_3$) [3]; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3200–2700 (*br*), 1775–1690 (*br*), 1655, 1640, 1615 (*w*), 1100 and 950; ^1H NMR (270 MHz, $CDCl_3$) and ^{13}C NMR (67.89 MHz, $CDCl_3$) as reported for conyzic acid. Methylation of 30 mg of **5a** with ethereal CH_2N_2 followed by the usual work up gave 30 mg of **5b**, mp 98°, $[\alpha]_D$ −195° (*c* 0.5, $CHCl_3$), lit. mp 98°, $[\alpha]_D$ −215° (*c* 0.8, $CHCl_3$) [3]; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700, 1635, 1025 and 910; ^1H NMR (270 MHz, $CDCl_3$): δ7.33 (*br*, H-15), 7.24 (part. obsc. by $CDCl_3$, H-3), 7.20 (*br*, H-16), 6.28 (*br*, H-14), 5.91 (*br d*, *J* = 12 Hz, H-2), 5.39 (*br t*, *J* = 12 Hz, H-1), 5.03 (*br*, H-19a), 4.82 (*br*, H-19b), 3.77 (OMe), 2.59 (*br d*, *J* = 18 Hz) and 1.81 (*br d*, *J* = 18 Hz, H-6 or H-10), 2.38 (2H, *t*, *J* = 8, H-12a, b), 2.32 (*dd*, 13, 12, H-?), 2.07 (*dd*, 12, 3, H-?), 0.76 (*d*, *J* = 17, H-17), 0.71 (H-20); MS *m/z*: 328 $[M]^+$, 313, 297, 296, 281, 269, 268, 233, 201, 173, 164, 163, 161, 159, 149, 145, 131, 121, 119, 117, 105, 95 (C_6H_7O), 91 and 81 (C_5H_5O, base peak); CD curve (*c* 8.35 × 10^{-4}, EtOH) $\Delta\varepsilon_{253}$ +2.16 (max).

Fractions 27–31 which showed a single spot on TLC (C_6H_6–EtOAc, 4:1) were combined to give 0.40 g of **16a**, mp 170° (petrol–EtOAc), lit. 172–173° [9]; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700 (*w*), 1650, 1600, 1015 and 910; UV λ_{max}^{MeOH} nm: 360, 270; λ_{max}^{NaOAc} nm: 282. ^1H NMR (270 MHz, $CDCl_3$): δ12.44 (5-OH), 8.11 (2H, *d*, *J* = 10.5 Hz, H-2′ and H-6′), 7.04 (2H, *d*, *J* = 10.5 Hz, H-3′ and H-5′), 6.41 (H-6), 3.98, 3.88, 3.84 (OMe); MS *m/z*: 344 $[M]^+$, 343, 329, 315, 314, 311, 301, 286, 283, 273, 271, 234, 203, 161, 161, 159, 145, 129, 115 and 105. Methylation of 50 mg **16a** with excess ethereal CH_2N_2 followed by the usual work-up gave 50 mg of flindulatin (**16b**), mp 169–170°, lit. 161° [9]; ^1H NMR (270 MHz, $CDCl_3$): δ12.50 (5-OH), 8.16 (2H, *d*, *J* = 10.5 Hz, H-2′ and H-6′), 7.04 (2H, *d*, *J* = 10.5 Hz, H-3′ and H-5′), 6.40 (H-6), 3.39, 3.91, 3.89 (OMe); MS *m/z*: 357 $[M-1]^+$, 343, 329, 328, 327, 325, 315, 309, 271, 165, 149 and 135.

Fractions 43–48 which showed a single spot on TLC (EtOAc–C_6H_6, 1:1) were combined and repurified to give 25 mg of gummy **9a**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 3100–2700 (*br*), 1700, 1630, 1039, 925 and 875, which was converted to the methyl ester. Purification by TLC gave gummy **9b**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1705, 1625, 1070, 1025, 915, 870 and 840; ^1H NMR (270 MHz, $CDCl_3$): δ7.35 (*t*, *J* = 1.5 Hz, H-15), 7.20 (*br*, $W_{1/2}$ = 3.5 Hz, H-16), 6.25 (*br*, $W_{1/2}$ = 3.5 Hz, H-14), 6.47 (*dd*, *J* = 2.5, 1.5 Hz, H-3), 4.35 (*br t*, *J* = 7 Hz, H-2), 3.70 (OMe), 1.32 (H-19), 0.83 (*d*, *J* = 7 Hz, H-17), 0.77 (H-20). [Calc. for $C_{21}H_{30}O_4$: MW, 346.2144.

Found: MW(MS) 346.2137 (17%).] Other significant ions were at *m/z* (rel. int.): 331 ($C_{20}H_{27}O_4$, 2.1), 316 ($C_{20}H_{28}O_3$, 2.6), 315 ($C_{20}H_{27}O_3$, 3.8), 314 ($C_{20}H_{26}O_3$, 6.7), 299 ($C_{19}H_{23}O_3$, 27.6), 287 ($C_{19}H_{27}O_2$, 9.4), 250 ($C_{15}H_{22}O_3$, 3.5), 219 ($C_{14}H_{17}O_2$, 9.2), 217 ($C_{14}H_{17}O_2$, 5.1), 203 ($C_{10}H_{19}O_4$, 8.2), 191 ($C_{13}H_{19}O$, 11.1), 180 ($C_{10}H_{12}O_3$, 11.0), 179 ($C_{10}H_{11}O_3$, 16.9), 175 ($C_9H_{19}O_3$, 9.3), 81 (C_5H_5O, 100).

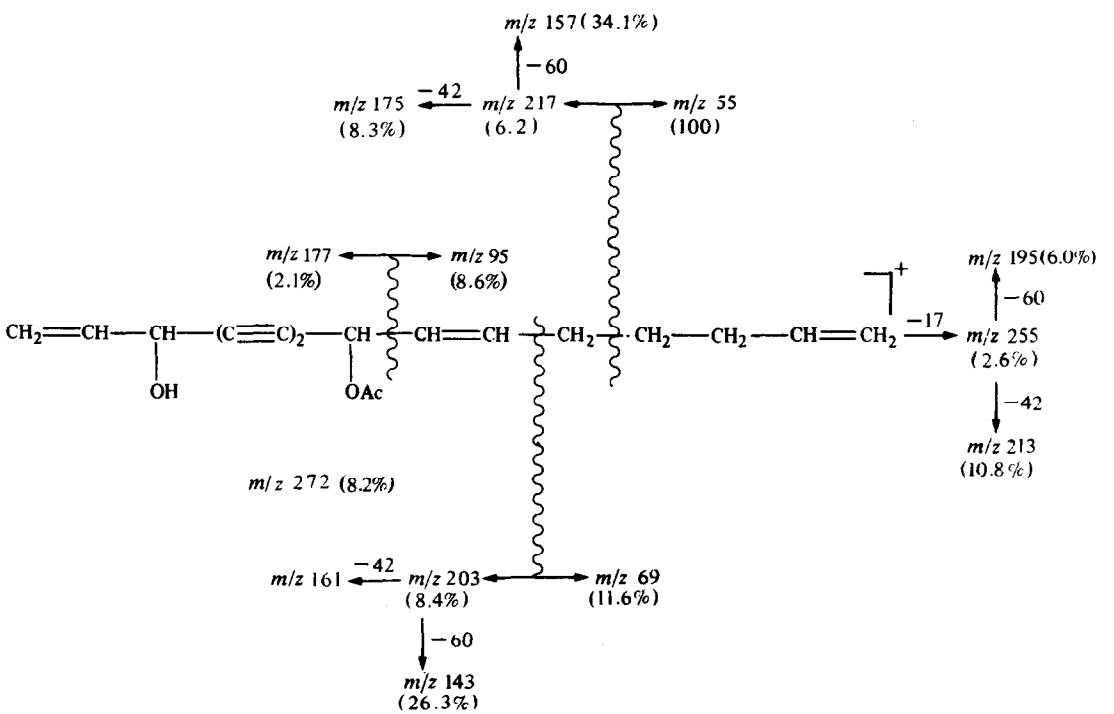
Extraction of Grangea maderaspatana. Above ground parts of *Grangea maderaspatana* Poir (2 kg), collected in the Janjimukh area of the Sibsagar district, Assam, India, in March 1982 were extracted with MeOH (10 l.) at room temp. for 7 days. The extract was concd to 300 ml at red. pres., diluted with 30 ml H_2O and allowed to stand overnight at room temp. The ppt was filtered, the filtrate was extracted with petrol (bp 60–80°, 6 × 200 ml), concd at red. pres. and the residue extracted with $CHCl_3$ (5 × 100 ml). The washed and dried $CHCl_3$ extract was concd at red. pres. and the residue (42 g) chromatographed over 500 g of silica gel (60–120 mesh, BDH India) packed in C_6H_6, 200 ml fractions being collected as follows. Fractions 1–20 (C_6H_6), 21–30 (C_6H_6–$CHCl_3$, 50:1), 31–36 (C_6H_6–$CHCl_3$, 24:1), 37–42 (C_6H_6–$CHCl_3$, 9:1), 43–53 (C_6H_6–$CHCl_3$, 4:1), 54–60 (C_6H_6–$CHCl_3$, 2:1), 61–65 (C_6H_6–$CHCl_3$, 1:1), 66–71 (C_6H_6–$CHCl_3$, 1:2), 72–80 ($CHCl_3$), 81–90 ($CHCl_3$–MeOH, 90:1), 91–95 ($CHCl_3$–MeOH, 24:1), 96–100 ($CHCl_3$–MeOH, 19:1), 101–105 ($CHCl_3$–MeOH, 9:1).

Fractions 10–15 (10 g) were a mixture of two major components by TLC (EtOAc–C_6H_6, 1:4) and were combined. Further purification of 2 g of this material by prep. TLC (C_6H_6–EtOAc, 4:1, six developments) gave 0.40 g of gummy (−)-hardwickiic acid (**8a**), $[\alpha]_D$ −135.6° ($CHCl_3$), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–2400 (*br*), 1675, 1625, 1250, 1140, 925, 875 and 850; ^1H NMR (270 MHz, $CDCl_3$): δ7.36 (*br*, H-15), 7.21 (*br*, H-16), 6.89 (*m*, H-3), 6.27 (*br*, H-14), 1.25 (H-19), 0.86 (*d*, *J* = 6 Hz, H-17), 0.79 (H-20); MS *m/z* 316 $[M]^+$, 299, 283, 221, 203, 95 and 81. Methylation of **8a** (50 mg) with excess CH_2N_2 in Et_2O gave 50 mg of gummy **8b**, $[\alpha]_D$ −120° ($CHCl_3$), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705, 1650, 1100, 1050, 950 and 875; ^1H NMR: δ7.34 (*t*, *J* = 1.5 Hz, H-15), 7.20 (*br*, H-16), 6.59 (*br t*, *J* = 3 Hz, H-3), 6.25 (*br*, H-14), 3.68 (OMe), 1.26 (H-19), 0.83 (*d*, *J* = 6 Hz, H-17), 0.76 (H-20). Comparison with an authentic sample of methyl hardwickiate supplied by Dr. Sukh Dev established identity.

The more polar component **6a** of fractions 10–15 (1.2 g), had mp 82–84° (EtOAc), $[\alpha]_D$ −139° ($CHCl_3$, *c* 0.49 g/100 ml); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–2400 (*br*), 1675, 1650, 1620, 1250, 1125, 975, 875 and 850; ^1H NMR (270 MHz, $CDCl_3$): δ7.33 (*t*, *J* = 1.5 Hz, H-15), 7.19 (*t*, *J* = 1 Hz, H-16), 6.95 (*dd*, *J* = 4, 1.5 Hz, H-3), 6.23 (*br*, H-14), 6.19 (*m*, centre of AB system, H-1, H-2), 1.08 (H-19), 0.91 (H-20), 0.87 (*d*, *J* = 6 Hz, H-17); MS *m/z*: 314 $[M]^+$, 298, 297, 219, 95, 81. Methylation with CH_2N_2 gave gummy **6b**; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700, 1650, 1075, 1000, 900 and 875; ^1H NMR: δ7.33 (*t*, *J* = 1.5 Hz, H-15), 7.18 (*t*, *J* = 1 Hz, H-16), 6.73 (*dd*, *J* = 4, 1.5 Hz, H-3), 6.23 (*br*, H-14), 6.15 (*m*, centre of AB system, H-1 and H-2), 1.09 (H-19), 0.90 (H-20), 0.87 (*d*, *J* = 6 Hz, H-17); MS *m/z*: 328 $[M]^+$, 269, 95, 81.

Fractions 18–22 (1.5 g) which contained one major and several minor components were purified by prep. TLC (C_6H_6–EtOAc, 20:1) to give 0.8 g of gummy **17**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3360, 2840, 1640, 1250, 1100, 1000, 980, 925 and 950; ^1H NMR (270 MHz, $CDCl_3$): δ5.26 (*dt*, *J* = 10.5, 1.5 Hz, H-1_{cis}), 5.47 (*dt*, *J* = 16.5, 1.5 Hz, H-1_{trans}), 5.94 (*ddd*, *J* = 16, 10.5, 5.5 Hz, H-2), 4.94 (*br d*, *J* = 5.5 Hz, H-3), 6.14 (*br d*, *J* = 9 Hz, H-8), 5.50 (*tt*, *J* = 10, 1.5 Hz, H-9), 5.67 (*dtd*, *J* = 1.5, 7, 10 Hz, H-10), 2.17 (2H, *dq*, *J* = 1.5, 7 Hz, H-11), 1.49 (2H, *quint*, *J* = 7 Hz, H-12), 2.06 (2H, *dq*, *J* = 1.5, 7 Hz, H-13), 5.80 (*tdd*, *J* = 16, 10, 7 Hz, H-14), 4.95 (*dt*, *J* = 10, 1.5 Hz, H-15), 5.02 (*dt*, *J* = 16, 1.5 Hz, H-15_t), 2.05 (Ac). [Calc. for $C_{15}H_{20}O_3$: MW, 272.1411. Found: MW(MS) 272.1412.] Significant peaks in the MS are shown in Scheme 1. The ^{13}C NMR spectrum is listed in Table 1.

Photolysis of **6a**. A soln of 20 mg of **6a** in 10 ml of dry C_6H_6 was photolysed in a quartz cell using a 125 W bare arc mercury



Scheme 1. The mass spectral fragmentation of compound **17a**.

lamp. The reaction was monitored by TLC. The appearance of material less polar than **6a** was noted initially; as the reaction progressed a spot corresponding to **5a** which is more polar than **6a** developed gradually. After 2 hr the solvent was evaporated *in vacuo* and the residue was purified by prep. TLC (C_6H_6–EtOAc, 4:1, three developments). The more polar material was obtained as a solid, mp 160°, and was identical with strictic acid (**5a**) in all respects. Methylation with CH_2N_2 gave methyl strictate which was identical (TLC, IR and ^1H NMR) with authentic **5b**. The less polar product (4 mg) was mainly a stereoisomer of **6a** which exhibited ^1H NMR signals at 7:30 (*t*, J = 1.5 Hz, H-15), 7.14 (*br*, H-16), 6.90 (*br d*, J = 5.5 Hz, H-3), 6.22 (*dd*, J = 10, 5 Hz, H-1), 6.19 (*br*, H-14), 6.09 (*br dd*, J = 10, 5.5 Hz, H-2), 1.14 (H-19), 1.00 (*d*, J = 6 Hz, H-17), 0.90 (H-20) contaminated by impurities. One of these appeared to be a second stereoisomer of **6a** as evidenced by the appearance of a new C-17 methyl doublet near 0.98; a second was **5a** (TLC and NMR spectrum), probably arising from **12** in the time elapsing between preparation and analysis as the material originally was free of **5a** (TLC).

Conversion of **8b** *to* **9b** *and* **6b**. To a soln of 0.200 g of $LiAlH_4$ and 0.200 g of dry $AlCl_3$ in 3 ml of dry Et_2O was added at 0° with stirring a soln of 0.100 g of **8b** in 2 ml of dry Et_2O. After 1 hr at 0°, excess $LiAlH_4$ and $AlCl_3$ were decomposed by addition of cold satd NH_4Cl in H_2O and an additional 50 ml of H_2O. The mixture was extracted with EtOAc (5 × 50 ml); the washed and dried extract was evaporated at red. pres. and purified by prep. TLC (EtOAc–petrol, 3:2). This resulted in 80 mg of gummy **8c**, [11] IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1250, 1115, 975 and 825; ^1H NMR (270 MHz, $CDCl_3$): δ7.36 (*t*, J = 1.5 Hz, H-15), 7.21 (*br*, H-16), 6.27 (*br*, H-14), 5.58 (*m*, H-3), 4.10 (2H, *br*, H-19), 1.09 (*br*, H-19), 0.82 (*d*, J = 6 Hz, H-17), 0.76 (*br*, H-20); MS *m/z*: 302, 287, 284, 271, 269, 207, 189, 95 and 81. Acetylation of 40 mg of **8c** (Ac_2O–pyridine), work-up in the usual fashion and purification by prep. TLC (C_6H_6–EtOAc, 20:1) gave 36 mg of **8d**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725, 1250, 1110, 950 and 875; ^1H NMR (270 MHz, $CDCl_3$): δ7.36 (*t*, J = 1.5 Hz, H-15), 7.21 (*br*, H-16), 6.27 (*br*, H-14), 5.61 (*br t*, J = 3 Hz, H-3), 4.55 (2H, *br*, H-18), 2.07 (Ac), 1.10 (*br*, H-19), 0.84 (*d*, J = 6 Hz, H-17), 0.76 (*br*, H-20); MS *m/z*: 344 $[M]^+$, 284, 269, 189, 95 and 81.

A soln of 0.200 g of **8d** in 3.5 ml of dry pyridine containing 0.180 g of CrO_3 (dried over P_2O_5) was allowed to stand for 4 days after which time excess reagent was decomposed by addition of 1 ml EtOH. The mixture was diluted with H_2O and extracted repeatedly with EtOAc. Concn of the extract at red. pres. and purification of the residue by TLC (C_6H_6–EtOAc, 20:1) gave 40 mg of **10d**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725, 1655, 1250, 1200, 1100 and 875; ^1H NMR (270 MHz, $CDCl_3$): δ7.34 (*br*, H-15), 7.19 (*br*, H-16), 6.24 (*br*, H-14), 5.91 (*t*, J = 1.5 Hz, H-3), 4.79 (2H, *d*, J = 1.5 Hz, H-18), 2.44 (*d*, J = 8 Hz, probably H-12), 2.14 (Ac), 1.25 (H-19), 0.88 (*d*, J = 6 Hz, H-17), 0.86 (H-20); CD curve $[\theta]_{329}$ −1800 (neg. max), $[\theta]_{286}$ −632 (min), $[\theta]_{275}$ −722 (neg. max), $[\theta]_{238}$ +9030 (last reading). The molecular ion could not be detected in the high resolution MS; the peak of highest *m/z* was 298 (M^+ − HOAc, $C_{20}H_{26}O_2$, 26.2%).

A soln of 48 mg of **10a** in 4 ml of MeOH and five drops of 5% KOH was stirred at room temp. (N_2 atmosphere) for 10 min, neutralized with dil HOAc, diluted with H_2O and extracted with $CHCl_3$ (5 × 50 ml). Evaporation of the washed and dried extract followed by prep. TLC (EtOAc–C_6H_6, 9:1) of the residue gave 38 mg of **10c** as a gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1700, 1150, 1110, 1000 and 870; ^1H NMR (270 MHz, $CDCl_3$): δ7.35 (*t*, J = 1.5 Hz, H-15), 7.20 (*br*, H-16), 6.24 (*br*, H-14), 6.11 (*t*, J = 1.5 Hz, H-3), 4.38 (2H, *br*, H-18), 1.21 (*br*, H-19), 0.87 (*d*, J = 6 Hz, H-17), 0.84 (*br*, H-20); MS *m/z*: 316 $[M]^+$ 285, 220, 189, 173, 95 and 81. A mixture of 35 mg of **10c** and 400 mg of active MnO_2 in 4 ml of THF was stirred at room temp. for 30 min and filtered. Evaporation of the combined filtrate and $CHCl_3$ washings gave 28 mg of crystalline **10a**, mp 128–129°, lit. 129–130° [11], IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2700, 1715–1660 (*br*), 1100, 950 and 870; ^1H NMR (270 MHz, $CDCl_3$): δ9.72 (H-18), 7.36 (*t*, J = 1.5 Hz, H-15), 7.21 (*br*, H-16), 6.37 (*br*, H-3), 6.25 (*br*, H-14), 1.32 (*br*, H-19), 0.88 (*d*, J = 6 Hz, H-17), 0.85 (*br*, H-20); MS *m/z*: 314 $[M]^+$, 299, 285, 220, 95 and 81.

A mixture of 28 mg of **10a** in 3 ml of MeOH, 0.300 g of MnO_2, 30 mg of KCN and 0.1 ml of glacial HOAc was stirred for 10 hr at room temp. and filtered. The solid material was washed thoroughly with MeOH and the combined filtrate and washing were evaporated at red. pres. The residue was diluted with H_2O and extracted with $CHCl_3$. The residue obtained from the washed and dried extract (25 mg) was purified by prep. TLC (C_6H_6–petrol, 2:1, three developments) to give 15 mg of **10b**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715, 1665, 1200, 975 and 875; ^1H NMR: δ7.35 (*t*, J = 1.5 Hz, H-15), 7.19 (*br*, H-16), 6.24 (2H, *br*, H-3 and H-14), 3.81 (OMe), 1.41 (*br*, H-19), 0.87 (*d*, J = 6 Hz, H-17), 0.84 (*br*, H-20); MS *m/z*: 344 $[M]^+$, 329, 313, 297, 285, 250, 218, 217, 191, 189, 95 and 81.

A soln of 11 mg of **10b** in 1.5 ml MeOH cooled to 10–15° was reduced with 8 mg $NaBH_4$ by stirring for 30 min at 10–15°, diluted with H_2O and extracted with $CHCl_3$ (5 × 50 ml). The washed and dried extract was evaporated and the residue (8 mg) purified by TLC (C_6H_6–EtOAc, 9:1, two developments). The more polar major product was **9b** (4 mg) identical in all respects (TLC, IR, ^1H NMR, MS) with **9b** prepared from naturally-occurring **9a**. The less polar material (1.5 mg) was **11**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1705, 1625, 1050 and 875; ^1H NMR (270 MHz, $CDCl_3$): δ7.33 (*t*, J = 1.5 Hz, H-15) 7.20 (*br*, H-16), 6.46 (*br*, H-14), 6.23 (*br*, H-3), 4.32 (*br*, $W_{1/2}$ ~ 8 Hz, H-2), 3.72 (OMe), 1.23 (H-19), 0.85 (*d*, J = 6 Hz, H-17), 0.77 (H-20).

A soln of 5 mg of **9b** and 4 mg of *p*-toluene sulfonic acid in 1 ml of dry C_6H_6 was refluxed for 1 hr, and evaporated *in vacuo*. Purification of the residue by TLC (C_6H_6–EtOAc, 9:1) gave 4 mg of a substance identical in all respects (TLC, ^1H NMR) with **6b**.

Reactions of **17a**. (a) A soln of 60 mg of **17a** and 0.200 g of 2-phenylbutyric anhydride in 2 ml of pyridine was allowed to stand for 72 hr at room temp. diluted with 100 ml H_2O and left again overnight at room temp. The mixture was extracted with Et_2O (5 × 200 ml); the Et_2O extract was washed with 5% $NaHCO_3$ soln (5 × 50 ml) and the aq. phase washed with $CHCl_3$, acidified and extracted with CH_2Cl_2 (5 × 50 ml). The washed and dried extract yielded 115 mg of α-phenylbutyric acid, $[\alpha]_D$ +5.71° which corresponds to an optical yield of 24%.

(b) Acetylation of 50 mg of **17a** with Ac_2O–pyridine followed by the usual work-up and purification by prep. TLC (C_6H_6–EtOAc, 20:1) gave 50 mg of gummy **17b**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2950, 2900, 2860, 1740, 1200, 1000, 920, 870 and 840; ^1H NMR (270 MHz, $CDCl_3$) coupling constants as for **17a**: δ5.54 (*td*, H-1$_c$) 5.33 (*td*, H-1$_t$), 5.87 (*ddd*, H-2), 5.91 (*br d*, H-3), 6.13 (*br d*, H-8), 5.49 (*tt*, H-9), 5.67 (*dtd*, H-10), 2.16 (*dq*, H-11), 1.49 (*quint*, H-12), 2.06 (*br q*, H-13), 5.79 (*tdd*, H-14), 5.01 (*dt*, H-15$_c$), 4.97 (*dt*, H-15$_t$), 2.07, 2.09 (Ac); MS *m/z* (rel. int.): 314 $[M]^+$ (0.4), 259 (0.4), 245 (0.9), 217 (1.4), 203 (5.3), 199 (3.9), 185 (4), 161 (22.9), 157 (15.5), 143 (10.2), 139 (6.4), 125 (5.5), 95 (14.9) and 55 (83.4).

(c) A soln of 50 mg of **17a** in 10 ml of MeOH was absorbed on a column of 100 g of neutral alumina and allowed to stand for 20 hr. Elution with MeOH, evaporation of the eluate at red. pres. and prep. TLC of the residue (C_6H_6–EtOAc, 9:1) gave 10 mg of recovered **17a** and 22 mg of **17c**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560, 3350, 2900, 2840, 1660, 1100, 1000 and 925; ^1H NMR (270 MHz, $CDCl_3$, coupling constants as reported for **17a**): δ5.47 (*td*, H-1$_c$), 5.25 (*td*, H-1$_t$), 5.94 (*ddd*, H-2), 4.94 (*br d*, H-3), 5.19 (*br d*, H-8), 5.56 (*tt*, H-9), 5.61 (*dtd*, H-10), 2.13 (*dq*, H-11), 1.50 (*quint*, H-12), 2.07 (*br q*, H-13), 5.80 (*tdd*, H-14), 5.02 (*dt*, H-15), 4.97 (*dt*, H-15$_t$); ^{13}C NMR

spectrum listed in Table 1; MS m/z (rel. int.): 230 $[M]^+$ (0.2), 175 (1.4), 161 (2.7), 157 (6.9), 143 (6.6), 139 (1.5), 135 (2.6), 117 (14.9), 95 (8.9), 69 (20.2) and 55 (100).

(d) Hydrogenation of 0.015 g of **17a** in 25 ml of EtOAc over 0.250 g of 10% Pd-C in 1 atm of H_2 followed by filtration, evaporation and purification by prep. TLC (petrol–C_6H_6, 1:1) gave 30 mg of semi-solid **18a**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1200, 1050, 955, 925, 875 and 850; ^1H NMR (270 MHz, $CDCl_3$): δ3.52 (*m*, H-3), 1.47 (4H, *m*) 1.27 (*ca* 20H, *br*), 0.94 (3H, *t*, J = 7 Hz) and 0.89 (3H, *t*, J = 7 Hz, H-1 and H-15); MS m/z (rel. int.) 228 $[M]^+$ (0.1), 210 (5.3), 199 (27.3) and 59 (100). Acetylation of 15 mg of **18a** with Ac_2O–pyridine followed by the usual work-up and prep. TLC of the product gave 12 mg of **18b** as a gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725, 1250, 1100 and 1050; ^1H NMR ($CDCl_3$): δ4.81 (*quint*, J = 6 Hz, H-3), 2.04 (Ac), 1.54 (4H, *m*), 1.26 (*ca* 20H, *br*), 0.88 (6H, *t*, J = 7 Hz, H-1 and H-15); MS m/z (rel. int.): 271 $[M+1]^+$ (4.2) 241 (5.7), 211 (54.4), 210 (40.5), 181 (10.2) and 101 (100).

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NOTE ADDED IN PROOF

Strictic acid and its congener **6a** were formulated correctly without further discussion in an article dealing with the constituents of *Koanophyllum admantium* (Bohlmann, F., Abraham, W.-R., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1903).