

HYDROGENATION DERIVATIVES OF NEO-CLERODANES AND THEIR ANTIFEEDANT ACTIVITY

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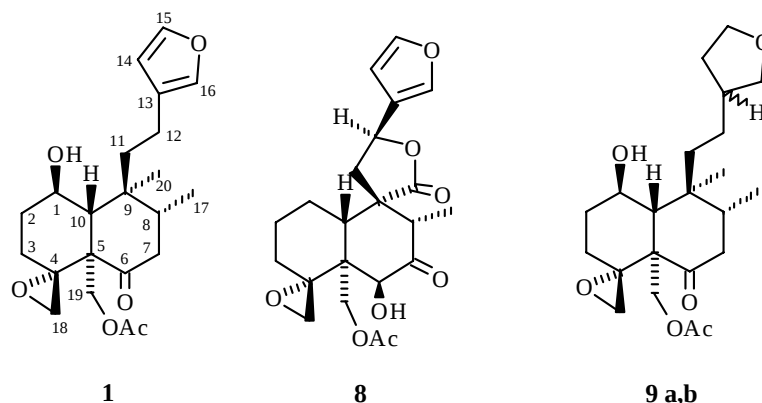
Abstract - Hydrogenation of some natural neo-clerodanes on 10% Pd/C resulted in the saturation of the furan ring and in some cases hydrogenolysis of the epoxide system and or γ -lactone ring. Overall, reduction of the furan ring found in the natural compounds resulted in a decrease in the antifeedant activity of the compounds against the lepidopteran pests, *Heliocoverpa armigera* and *Spodoptera frugiperda*. However, two of the most active derivatives had both the furan ring and the lactone ring hydrogenated but the epoxide intact.

The genus *Teucrium* (family Labiatae) is a rich source¹ of neo-clerodanes and many of them exhibit potent antifeedant activity against pest insects. The structure-activity relationship of the functional groups on these compounds, especially the furan ring, is unresolved.

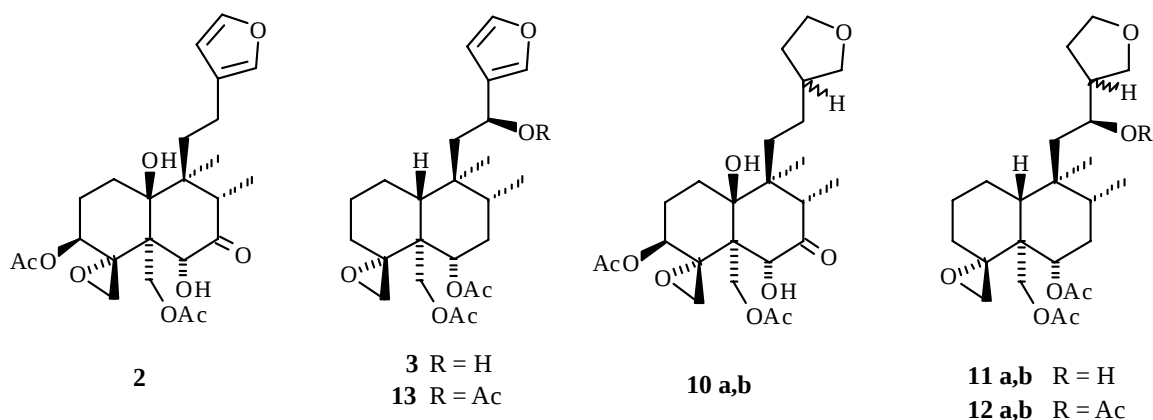
We report here on the catalytic hydrogenation of seven diterpenes isolated from *Teucrium* species, i.e. fruticolone (1),² teucrolivin B (2),³ 6,19-diacetylteumassilin (3),⁴ montanin C (4),⁵ isoeriocephalin (5),⁶ teucrin A (6)⁷ and deacetylajugarin II (7).⁴ All these compounds have a β -substituted furan ring, except deacetylajugarin II (7) whose heterocyclic ring occurs as a β -substituted α,β -unsaturated γ -lactone system.

The catalytic hydrogenations of natural neo-clerodanes from *Teucrium* had been reported previously. For example, reduction of the acetyl derivative of picropolin (8) on 10% Pd/C⁸ gave two products: the first was considered to be a tetrahydrofuran derivative, whereas in the second product the γ -lactone had also been transformed by hydrogenolysis into a carboxylic acid. Two products were also obtained in the 10% Pd/C treatment⁵ of montanin C (4). However, in both these examples the derivatives were not fully characterised. More recently, teucrin A (6) was hydrogenated⁹ on 5%, Rh/C yielding a tetrahydrofuran derivative.

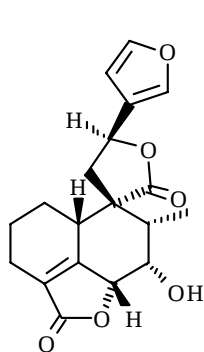
The first product we submitted to hydrogenation on 10% Pd/C was fruticolone (**1**): only the furan ring was saturated, yielding a mixture of tetrahydro derivatives (**9a**) and (**9b**), epimeric at C-13. The products were isolated after several radial chromatographies and characterized; however, it was not possible to attribute the 13*S* or 13*R* absolute configuration.



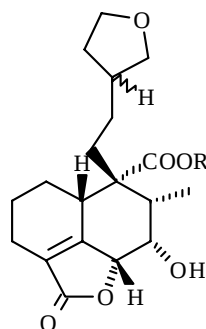
The reduction of teucrolivin B (**2**) yielded a mixture of two C-13 epimeric tetrahydrofurans (**10a**) and (**10b**); it was not possible to separate the compounds. The same result was obtained with 6,19-diacetylteumassilin (**3**). It gave a mixture of the two C-13 epimeric tetrahydrofurans (**11a**) and (**11b**). The mixture was then acetylated to give a mixture of two epimers of 6,12,19-triacetyl-tetrahydroteumassilin, (**12a**) and (**12b**). The same mixture was obtained by acetylation of **3** to triacetylteumassilin⁴ (**13**) and subsequent hydrogenation.



Hydrogenation on 10% Pd/C of teucrin A (**6**) resulted in a mixture of products (**14a**) and (**14b**), arising from saturation of the furan ring and contextual hydrogenolysis of the 20,12- γ -lactone ring. Diazomethane treatment transformed the two carboxylic acids into the inseparable mixture of their methyl esters (**15a**) and (**15b**). We did not isolate the tetrahydro derivative reported⁹ previously from teucrin A.



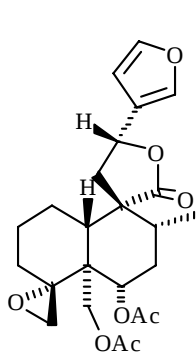
6



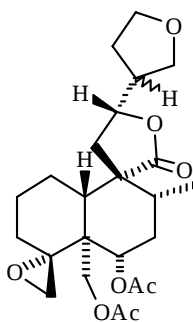
14 a,b R = H

15 a,b R = CH₃

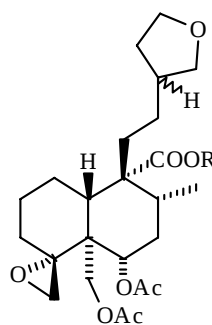
In the case of montanin C (**4**) the hydrogenation yielded two products, as suggested previously⁷: the first was the inseparable mixture of the tetrahydrofuran epimers (**16a**) and (**16b**), the second the also inseparable mixture of the carboxylic acid epimers (**17a**) and (**17b**), transformed by diazomethane treatment to a mixture of **18a** and **18b**. In the case of isoeriocephalin (**5**), not only was the saturation of the furan ring observed but the 4,18-epoxy ring was opened, giving an inseparable mixture of epimers, (**19a**) and (**19b**), both with 4 α -OH and 4 β -CH₃.



4

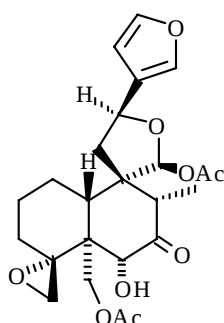


16 a,b

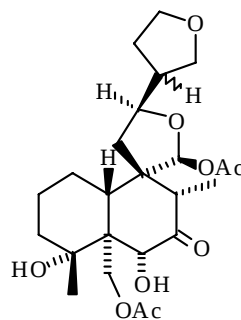


17 a,b R = H

18 a,b R = CH₃



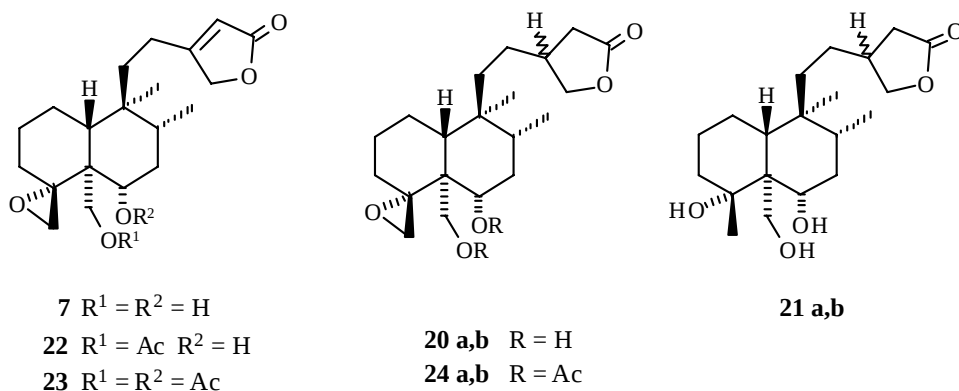
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19 a,b

An analogous result occurred in the reduction of deacetylajugarin II (**7**): we obtained a mixture of the two inseparable epimers (**20a**) and (**20b**), arising from the saturation of the double bond of the α,β -

unsaturated γ -lactone, besides an inseparable mixture of **21a** and **21b** epimers in which the epoxy ring had undergone hydrogenolysis. We also prepared ajugarin II (**22**)¹⁰ and ajugarin I (**23**)¹⁰ by selective acetylation of **7**: the reduction of **23** gave only the inseparable dihydro epimers (**24a**) and (**24b**), but no hydrogenolysis of the epoxy ring occurred.



In summary, the reaction performed on fruticolone (**1**), teucrolivin B (**2**), diacetylteumassilin (**3**) and triacetylteumassilin (**13**) led to products in which only the furan ring had undergone hydrogenation. From montanin C (**4**), both the product of hydrogenation and the product of hydrogenation-hydrogenolysis of the γ -lactone were obtained. From teucrin A (**6**) only the product of hydrogenation and hydrogenation-hydrogenolysis of the γ -lactone was obtained. From isoeriocephalin (**5**) the saturation of the furan system was accompanied by the hydrogenolysis of the epoxy ring. The same hydrogenolysis occurred on deacetyl-ajugarin II (**7**) but not on ajugarin I (**23**).

Nine of the 23 compounds, tested at 100 ppm, elicited significant antifeedant responses from larvæ of one or both species of Lepidoptera (Table 5). Hydrogenation of just the furan ring in five (**1**, **2**, **3**, **13**, and **23**) of these active compounds resulted in a decrease of activity. However hydrogenation of furan ring does not always lead to inactive compounds as shown by the activity of the hydrogenated products (**19a/19b**, **17a/17b** and **18a/18b**). Previous studies have indicated that an epoxide at C-4, C-18 and acetyl groups at C-6 and C-19 are often present in active compounds.^{11-13, 16} For example, these three functional groups are present in the active compounds (**3**, **13**, **17a/17b**, **18a/18b** and **23**) but not in the active **19a/19b**. The importance of the C-20, C-12 γ -lactone ring to the activity is also unclear. Hydrogenation of the furan and lactone rings in **6** did not increase its activity. However neither **6** nor its product (**15a/15b**) had the C-4, C-18 epoxide or the C-6, C-19 acetyl groups. In contrast hydrogenation of the furan and lactone rings in **4**, which does have the epoxide and acetyl group, results in products (**17a/17b** and **18a/18b**) which have significant levels of antifeedant activity.

Overall, the trend in the behavioural responses of both species of Lepidoptera to the hydrogenated compounds was similar. Thus there does appear to be a structure-activity relationship in the behavioural responses of these larvæ. However it is unclear as to how this relationship is modulated by the structure and configuration of any one specific functional group but it could be associated with the conformation of the whole molecule and properties such as lipophilicity.

Because of the potential use of these compounds in pest control further studies in to their structure-activity relationships are justified.

EXPERIMENTAL

IR spectra (KBr) were obtained on a Perkin-Elmer 1310. ^1H -NMR spectra were recorded in CDCl_3 or pyridine- d_5 solution using a Bruker AC 250 E apparatus at 250 MHz and chemical shifts are reported with respect to residual CHCl_3 (δ 7.27) or pyridine (δ 7.21, 7.57, 8.72). ^{13}C -NMR spectra were recorded in CDCl_3 , pyridine- d_5 on the same apparatus at 62.7 MHz, and chemical shifts are reported with respect to solvent signals (δ_{CDCl_3} 77.0, δ_{pyridine} 123.5, 135.5, 149.5). ^{13}C -NMR assignments were determined by DEPT spectra. MS were recorded on a Finnigan TSQ70 instrument (70 eV, direct inlet). Elemental analyses were made with Perkin Elmer 240 apparatus. Merck Si gel no. 7734 (70-230 mesh) deactivated with 15% H_2O , w/v, was used for column chromatography. Radial chromatography has been performed on a Chromatotron 7924 T apparatus using Merck Si gel no. 7749 60 PF_{254} as plate adsorbent. Starting materials were isolated from the following species: fruticolone (**1**) from *Teucrium fruticans*,² teucrolivin B (**2**) from *Teucrium oliverianum*,³ 6,19 diacetylteumassilin (**3**), deacetylajugarin I (**7**) and montanin C (**4**) from *Teucrium massiliense*,⁴ isoeriocephalin (**5**) from *Teucrium lanigerum*,⁶ teucrin A (**12**) from *Teucrium microphyllum*.¹⁴ The hydrogenation catalyst was Pd/C 10% (Avocado 7440-05-3).

Antifeedant Bioassay

The compounds were tested against final stadium larvae of the lepidopteran pests, *Spodoptera littoralis* and *Helioverpa armigera*, in a binary choice test on glass-fibre discs that had been pre-treated with the phagostimulant sucrose.¹⁵

Hydrogenation procedure

The substrates (28-80 mg) to be reduced were dissolved in MeOH (50-100 mL) and treated for 24 h at rt under H_2 (2 atm) in the presence of 10% Pd/C (25-110 mg) as catalyst. After filtration, the solvent was evaporated at 30 °C under reduced pressure.

Preparation of compounds (9a) and (9b).

Fruticolone (**1**) (32 mg) was reduced yielding a mixture (31 mg) of epimers (**9a**) and (**9b**). After several radial chromatographies (CH₂Cl₂-MeOH 99:1) it was possible to isolate 4 mg of compound (**9a**) and 7 mg of compound (**9b**).

Compound (9a).

Colourless needles; mp 148-150 °C (petrol-EtOAc); IR $\nu_{\max}$ cm⁻¹: 3400, 1725, 1250; ¹H NMR: see Table 1; ¹³C NMR: see Table 3; EIMS m/z [M]⁺ absent, 321 [M-CH₂OAc]⁺ (32), 303 (18), 205 (16), 107 (18), 83 (40), 69 (73), 43 (100); Anal. Calcd for C₂₂H₃₄O₆: C 66.98, H 8.69. Found: C 67.11, H 8.62.

Compound (9b).

Colourless needles; mp 148-150 °C (petrol-EtOAc); IR $\nu_{\max}$ cm⁻¹: 3400, 1725, 1250; ¹H NMR: see Table 1; ¹³C NMR: see Table 3; EIMS m/z [M]⁺ absent, 321 [M-CH₂OAc]⁺ (30), 303 (17), 205 (16), 107 (19), 83 (43), 69 (73), 43 (100); Anal. Calcd for C₂₂H₃₄O₆: C 66.98, H 8.69. Found: C 67.14, H 8.74.

Preparation of compounds (10a) and (10b).

Teucrolivin B (**2**) (28 mg) an unresolvable mixture (24 mg) of the epimers (**10a**) and (**10b**). Amorphous solid; IR $\nu_{\max}$ cm⁻¹: 3390, 3080, 1730, 1715, 1660, 1250; ¹H NMR: see Table 1; ¹³C NMR: see Table 3; EIMS m/z 468 [M]⁺ (2), 450 [M-H₂O]⁺ (2), 409 [M-OAc]⁺ (5), 369 (38), 289 (76), 197 (67), 166 (100), 137 (74), 83 (62); Anal. Calcd for C₂₄H₃₆O₉: C 61.52, H 7.75. Found: C 61.39, H 7.81.

Preparation of compounds (11a) and (11b).

6,19 diacetylteumassilin (**3**) (38 mg) was reduced yielding, after CC, an unresolvable mixture (31 mg) of the epimers (**11a**) and (**11b**). Amorphous solid; IR $\nu_{\max}$ cm⁻¹: 3480, 3080, 1725, 1250; ¹H NMR: see Table 1; ¹³C NMR: see Table 3; EIMS m/z 438 [M]⁺ (1), 420 [M-H₂O]⁺ (1), 395 (8), 323 (65), 305 (100), 203 (80), 191 (96), 105 (82), 95 (90); Anal. Calcd for C₂₄H₃₈O₇: C 65.73, H 8.73. Found: C 65.61, H 8.80.

Preparation of compounds (12a) and (12b).

The mixture of compounds (**11a**) and (**11b**) (20 mg) was treated with 1:1 mixture (2 mL) of Ac₂O-pyridine for 24 h at rt giving; after usual work-up, an unresolvable mixture (18 mg) of **12a** and **12b**. Amorphous solid; IR $\nu_{\max}$ cm⁻¹: 3040, 1740, 1240, 1230, 1210; ¹H NMR: see Table 1; EIMS m/z 480 [M]⁺ (1), 437 [M-COCH₃]⁺ (22), 407 [M-CH₂OAc]⁺ (12), 365 (24), 203 (14), 107 (16), 93 (27), 69 (45), 43 (100); Anal. Calcd for C₂₆H₄₀O₈: C 64.98, H 8.39. Found: C 64.86, H 8.30.

The same products were obtained by hydrogenation of triacetylteumassilin (**13**), prepared as described previously⁴ and identified by its physical and spectroscopic data and by comparison with authentic sample.

Preparation of compounds (15a) and (15b).

Teucrin A (**6**) (50 mg) was reduced yielding, after CC, the inseparable mixture (33 mg) of the **14a** and **14b** epimers. It was treated with an Et₂O solution of CH₂N₂ to give the mixture of methyl esters (**15a**) and (**15b**), also not separable.

Amorphous solid; IR $\nu_{\max}$ cm⁻¹: 3370, 1730, 1250; ¹H NMR: see Table 1; ¹³C NMR: see Table 4; EIMS m/z 364 [M]⁺ (3), 333 [M-OCH₃]⁺ (6), 187 (7), 154 (13), 136 (47), 107 (30), 91 (46), 79 (78), 55 (100); Anal. Calcd for C₂₀H₂₈O₆: C 65.91, H 7.74. Found: C 65.83, H 7.61.

Preparation of compounds (20a), (20b), (21a), and (21b).

Deacetylajugarin II (**7**) (80 mg) was reduced yielding, after CC (CH₂Cl₂-MeOH 49:1), the inseparable mixture (38 mg) of the epimers (**20a**) and (**20b**) and the inseparable mixture (25 mg) of the epimers (**21a**) and (**21b**).

Mixture of **20a** and **20b**: amorphous solid; IR $\nu_{\max}$ cm⁻¹: 3480, 3380, 3075, 1780; ¹H NMR: see Table 2; ¹³C NMR: see Table 4; EIMS m/z [M]⁺ absent, 334 [M-H₂O]⁺ (10), 321 (40), 304 (39), 191 (32), 163 (27), 125 (76), 118 (100); Anal. Calcd for C₂₀H₃₂O₅: C 68.15, H 9.15. Found: C 68.22, H 9.09.

Mixture of (**21a**) and (**21b**): amorphous solid; IR $\nu_{\max}$ cm⁻¹: 3340, 3370, 1780; ¹H NMR: see Table 2; ¹³C NMR: see Table 4; EIMS m/z 354 [M]⁺ (9), 336 [M-H₂O]⁺ (50), 318 [M-2H₂O]⁺ (58), 301 (45), 279 (10), 205 (30), 168 (100), 150 (38), 107 (25), 85 (20); Anal. Calcd for C₂₀H₃₄O₅: C 67.76, H 9.67. Found: C 67.88, H 9.74.

Preparation of ajugarin II (22).

Deacetylajugarin II (**7**) (30 mg) was treated with 1:1 mixture (2 mL) Ac₂O-pyridine at rt for 2 h, yielding ajugarin II (**22**) (26 mg) after usual work-up. mp 188-189 °C; IR $\nu_{\max}$ cm⁻¹: 3075, 1770, 1730, 1250; ¹H NMR: see Table 2; ¹³C NMR: see Table 4; EIMS m/z 392 [M]⁺ (8), 374 [M-H₂O]⁺ (9), 333 [M-OAc]⁺ (9), 319 [M-CH₂OAc]⁺ (100), 301 (10), 209 (14), 167 (21), 133 (16), 123 (36), 98 (17).

Preparation of ajugarin I (23).

Deacetylajugarin II (**7**) (30 mg) was treated with 1:1 mixture (2 mL) Ac₂O-pyridine at rt for 48 h, giving ajugarin I (**23**) (25 mg) after usual work-up. mp 158-160 °C. Physical and spectroscopic data in agreement with those reported.¹⁰

Preparation of compounds (24a) and (24b).

Ajugarin I (23) (30 mg) was reduced yielding, after CC, the inseparable mixture (27 mg) of the epimers (24a) and (24b).

Amorphous solid; IR $\nu_{\max}$ cm^{-1} : 3080, 1780, 1720, 1260; ^1H NMR see Table 2; ^{13}C NMR: see Table 4; EIMS m/z $[\text{M}]^+$ absent, 393 $[\text{M}-\text{COCH}_3]^+$ (37), 363 $[\text{M}-\text{CH}_2\text{OAc}]^+$ (28), 321 (94), 303 (27), 291 (18), 105 (67), 69 (100); Anal. Calcd for $\text{C}_{24}\text{H}_{36}\text{O}_7$: C 66.03, H 8.31. Found: C 65.89, H 8.24.

Preparation of compounds (19a) and (19b).

Isoeriocephalin (5) (30 mg) was reduced yielding, after CC, the inseparable mixture (20 mg) of the epimers (19a) and (19b).

Amorphous solid; IR $\nu_{\max}$ cm^{-1} : 3390, 1745, 1730, 1715, 1660, 1250; ^1H NMR: see Table 2; ^{13}C NMR: see Table 4; EIMS m/z $[\text{M}]^+$ absent, 393 $[\text{M}-\text{COCH}_3]^+$ (37), 363 $[\text{M}-\text{CH}_2\text{OAc}]^+$ (28), 321 (94), 303 (27), 291 (18), 105 (67), 69 (100); Anal. Calcd for $\text{C}_{24}\text{H}_{36}\text{O}_9$: C 61.52, H 7.75. Found: C 61.66, H 7.69.

Preparation of compounds (16a), (16b), (17a), (17b), (18a) and (18b).

Montanin C (4) (30 mg) was reduced yielding, after CC (petrol-EtOAc 7:3, 1:1, 3:7), the inseparable mixture (16 mg) of the epimers (16a) and (16b) and the inseparable mixture (6 mg) of the epimers (17a) and (17b). The latter was treated with an Et_2O solution of CH_2N_2 to give the inseparable mixture of the methyl esters (18a) and (18b).

Mixture of 16a and 16b: amorphous solid; IR $\nu_{\max}$ cm^{-1} : 3080, 1760, 1725, 1720, 1250; ^1H NMR: see Table 2; EIMS m/z $[\text{M}]^+$ absent, 391 $[\text{M}-\text{OAc}]^+$ (5), 334 $[\text{M}-\text{COCH}_3-\text{CH}_2\text{OAc}]^+$ (91), 317 (90), 183 (76), 165 (52), 55 (60), 43 (100); Anal. Calcd for $\text{C}_{24}\text{H}_{34}\text{O}_8$: C 63.98, H 7.61. Found: C 63.87, H 7.69.

Mixture of (17a) and (17b): amorphous solid; IR $\nu_{\max}$ cm^{-1} : 3100, 1725, 1720, 1245; EIMS m/z $[\text{M}]^+$ absent, 393 $[\text{M}-\text{OAc}]^+$ (23), 349 $[\text{M}-\text{AcOH}-\text{COCH}_3]^+$ (53), 291 (52), 263 (70), 55 (75), 43 (100); Anal. Calcd for $\text{C}_{24}\text{H}_{36}\text{O}_8$: C 63.70, H 8.02. Found: C 63.58, H 7.92.

Mixture of (18a) and (18b): amorphous solid; ^1H NMR: see Table 2.

ACKNOWLEDGEMENTS

The insects were reared under licence from the Ministry of Agriculture, UK. We thank Martin Cullum (Birkbeck College) and Paul Green (Kew) for technical assistance.

Table 1. ¹H-NMR Spectral Data of Compounds (**9a**, **9b**, **10a**, **10b**, **11a**, **11b**, **12a**, **12b**, **15a**, **15b**, **19a** and **19b**).

H	9a	9b	10a,b	11a	11b	12a	12b	15a,b	19a	19b
1β	4.38m	4.38m								
3α	2.63m	2.63m	5.28dd							
6β			4.74br s	4.75br dd	4.75br dd	4.72br dd	4.72br dd	4.71br s	4.31br s	4.31br s
7α	2.72dd	2.75dd								
7β								4.15m		
8β			3.35br q						2.62q	2.62q
10β								2.64m		
12α				3.71m*	3.71m*	5.17m	5.17m		3.80m*	3.80m*
15A	3.72ddd	3.75ddd	3.74ddd	3.71m*	3.71m*	3.70m	3.70m	3.77m	3.73m*	3.73m*
15B	3.82ddd	3.86ddd	3.90m*	3.89m	3.89m	3.82m*	3.82m*	3.90m*	3.80m*	3.80m*
16A	3.30dd	3.32dd	3.20m	3.53dd	3.53dd	3.52dd	3.44dd	3.38m	3.53dd	3.53dd
16B	3.90dd	3.90dd	3.90m*	3.82dd	3.82dd	3.82m*	3.82m*	3.90m*	3.80m*	3.80m*
Me17	0.86d	0.88d	1.03d	0.81d	0.79d	0.81d	0.80d	1.13d	1.46d	1.46d
18A†	2.28d	2.29d	3.07d	2.20d	2.20d	2.18d	2.17d			
18B‡	3.46dd	3.48dd	3.18d	2.99dd	2.99dd	2.97dd	2.97dd			
Me18									1.51s	1.51s
19A	4.92d	4.93d	4.08d	4.37br d	4.37br d	4.33br d	4.33br d		4.14d	4.19d
19B	5.37d	5.40d	4.38d	4.87d	4.88d	4.82d	4.82d		4.59d	4.57d
Me20	1.30s	1.32s	0.78s	0.69s	0.68s	0.68s	0.67s			
20									6.05s	6.04s
OAc	2.03s	2.05s	2.11s	2.11s	2.11s	2.10s	2.09s		2.03s	2.04s
OAc			2.04s	1.96s	1.96s	2.05s	2.04s		1.94s	1.95s
OAc						1.95s	1.94s			
OH			3.57br s							
OMe								3.69s		
J _{H,H} (Hz)	9a	9b	10a,b	11a	11b	12a	12b	15a,b	19a	19b
2α,3			5.5							
2β,3			12.1							
3β,18B	2.1	2.1		2.1	2.1	2.1	2.1			
6β,7α				11.0	11.0	11.0	11.0			
6β,7β				5.5	5.5	5.5	5.5			
7α,7β	13.8	13.8								
7α,8β	13.8	13.8								
8β,17	6.6	6.6	6.6	6.6	6.6	6.6	6.6	7.0	6.7	6.7
13,16A	6.7	6.7	6.7	6.7	6.7	6.7	6.7		5.6	5.6
13,16B	7.4	7.4		7.5	7.5	7.5	7.5			
14A,15A	6.9	6.9	6.9							
14A,15B	7.9	7.9								
14B,15A	6.9	6.9	6.9							
14B,15B	4.0	4.0								
15A,15B	7.9	7.9	7.9							
16A,16B	8.2	8.2		8.8	8.8	8.8	8.8		8.9	8.9
18A,18B	5.6	5.6	3.8	3.8	3.8	3.8	3.8			
19A,19B	12.7	12.7	12.3	12.0	12.0	12.3	12.3		12.9	12.9

CDCl₃ solution

* Overlapped signal

Table 2. ¹H-NMR Spectral Data of Compounds (20a, 20b, 22, 24a, 24b, 21a, 21b, 16a, 16b, 18a and 18b)

H	22	24a,b	20a,b	21a,b	18a,b	16a,b
6β	3.54m	4.68ddd	3.58m	4.02br dd	4.73ddd	4.78ddd
12α						4.19ddd
13		2.43m	2.40m	2.42m		
14	5.85					
14A		2.13br dd	2.14br dd	2.15br dd		
14B		2.64ddd	2.65ddd	2.66ddd		
15A					3.78m	3.73m
15B					3.87m	3.80m
16A	4.74d	3.88br dd	3.90br dd	3.90br dd	3.34dd	3.53dd
16B	4.74d	4.42ddd	4.43ddd	4.45ddd	3.95m	3.90m
Me17	0.86d	0.79d	0.82d	0.86d	1.00d	1.03d
18A†	2.45d	2.20d	2.44d		2.23d	2.22d
18B‡	3.23dd	2.97d	3.16dd		3.03dd	2.95dd
Me18				1.44s		
19A	4.53d	4.33d	4.00br d	4.38br d	4.28d	4.50dd
19B	4.57d	4.80d	4.31d	4.48d	4.79d	5.32d
Me20	0.76s	0.70s	0.65s	0.71s		
OAc	2.11s	2.08s			2.10s	2.09s
OAc		1.93s			1.97s	1.98s
OMe					3.72s	
J _{H,H} (Hz)	22	24 a,b	20a,b	21a,b	18a,b	16a,b
3β,18B	2.3	2.3	2.6		2.4	2.4
6β,7α	*	10.0	*	9.0	11.7	11.7
6β,7β	*	6.0	*	6.0	4.0	4.0
6β,19A		0.8			1.2	1.2
8β,17	5.8	5.2	6.4	6.5	6.7	6.7
12,11A						7.9
12,11B						7.9
12,13						7.9
13,14A		7.6	7.6	7.6		
13,14B		8.2	8.2	8.2		
13,16A		7.0	7.0	7.0	5.4	5.4
13,16B		7.4	7.0	7.0		
14A,14B		17.1	17.1	17.1		
14B,16B		1.1	1.1	1.1		
14,16	1.4					
16A,16B		8.9	8.9	8.8	9.0	9.0
18A,18B	3.4	4.0	3.4			4.1
19A,19B	12.1	12.2	12.2	12.7	12.4	12.6

CDCl₃ solution

* Overlapped signal

† Exo hydrogen with respect to ring B

‡ Endo hydrogen with respect to ring B

Table 3. ¹³C-NMR Spectral Data of Compounds (**9a,9b,10a,10b,11a,11b,19a** and **19b**).

C	9a ^a	9b ^a	10a ^a	10b ^a	11a ^a	11b ^a	19a ^a	19b ^a	19a ^b	19b ^b
1	66.9	66.8	27.3	27.2	21.7	21.6	23.3	23.3	23.6	23.6
2	37.6	37.6	25.7	25.7	24.7	24.7	22.7	22.7	23.2	23.2
3	34.9	34.9	65.9	65.9	32.8	32.8	36.1	36.1	37.1	37.1
4	61.5	61.5	63.5	63.5	65.1	65.1	75.0	75.0	75.5	75.5
5	55.1	55.1	55.0	55.0	45.4	45.4	52.4	52.4	52.7	52.7
6	206.7	206.7	73.2	73.0	72.4	72.4	78.9	78.9	80.2	80.2
7	45.0	45.0	209.0	209.0	33.0	33.0	208.1	208.1	208.4	208.4
8	38.4	38.3	45.2	45.0	35.1	35.0	50.6	50.6	50.6	50.6
9	39.7	39.7	49.9	49.9	38.9	38.9	56.9	56.9	57.2	57.1
10	52.6	52.7	81.7	81.7	47.3	47.3	49.0	49.0	49.2	49.2
11	28.5	28.4	37.7	37.5	43.1	43.2	44.9	45.0	44.7	45.0
12	26.4	26.2	30.3	29.9	70.0	70.5	77.5	78.5	78.5	79.3
13	32.5	32.5	32.4	32.3	48.5	48.5	45.2	45.2	45.8	46.0
14	29.7	29.7	29.7	29.7	29.4	27.6	29.4	29.7	29.8	30.0
15	67.9	67.8	67.9	67.8	68.4	68.2	68.0	67.8	68.1	67.9
16	73.4	73.3	75.3	75.3	70.0	70.8	69.5	71.2	69.7	71.3
17	15.3	15.4	8.0	7.9	15.5	15.5	10.3	10.3	11.1	11.2
18	49.4	49.4	45.5	45.5	48.5	48.5	25.6	25.6	25.9	25.9
19	64.2	64.1	63.3	63.3	61.8	61.8	61.2	61.3	62.1	62.1
20	19.4	19.3	18.7	18.5	17.4	17.4	97.0	97.1	98.0	98.2
OAc	171.0	171.0	170.6	170.6	171.0	171.0	170.0	170.0	170.1	170.1
			169.4	169.4	170.2	170.2	169.3	169.2	169.6	169.6
			21.0	21.0	21.2	21.2	21.2	21.2	21.1	21.1
			20.8	20.8	21.2	21.2	21.1	21.1	20.8	20.8

^a CDCl₃ solution^b Pyridine -d₅ solution

Table 4. ¹³C-NMR Spectral Data of Compounds (**22**, **20a**, **20b**, **24a**, **24b**, **21a**, **21b**, **15a** and **15b**).

C	22 ^a	20a ^a	20b ^a	24a ^a	24b ^a	21a ^a	21b ^a	15a ^a	15b ^a
1	20.8	20.6	20.6	21.0	21.0	20.7	20.7	21.9	21.9
2	25.0	25.1	25.1	25.0	25.0	23.2	23.2	23.4	23.4
3	31.9	31.7	31.7	32.6	32.6	36.9	36.9	19.4	19.4
4	66.8	67.5	67.5	65.0	65.0	80.1	80.1	128.0	128.0
5	45.1	46.2	46.2	45.1	45.1	47.5	47.5	159.8	159.8
6	73.4	74.5	74.5	72.3	72.3	77.2	77.2	80.4	80.4
7	33.8	33.8	33.8	32.9	32.9	36.2	36.2	73.3	73.3
8	34.7	34.7	34.8	34.5	34.5	35.1	35.2	36.8	36.8
9	38.6	38.2	38.2	38.2	38.2	38.4	38.4	55.2	55.2
10	47.3	46.8	46.9	47.9	48.0	43.4	43.5	37.3	37.4
11	34.6	34.6	34.6	34.6	34.6	34.6	34.6	39.6	39.6
12	22.1	26.5	26.5	26.2	26.2	26.6	26.6	27.7	27.7
13	171.0	36.0	36.0	36.1	36.1	36.1	36.1	32.5	32.5
14	115.4	35.4	35.4	35.3	35.3	35.4	35.4	31.3	31.3
15	169.8	176.8	176.8	176.6	176.6	176.8	176.8	67.9	67.9
16	72.9	73.3	73.2	73.2	73.1	73.3	73.2	72.3	72.3
17	15.4	15.4	15.4	15.3	15.3	15.6	15.6	13.2	13.2
18	48.7	48.0	48.0	48.5	48.5	23.8	23.8	172.7	172.7
19	61.9	61.5	61.5	61.9	61.8	63.7	63.7		
20	17.6	17.8	17.8	17.4	17.4	19.1	19.1	176.1	176.1
OAc	169.7			170.8	170.8				
				170.0	170.0				
	21.1			21.2	21.2				
				21.1	21.1				
OMe								52.4	52.4

^a CDCl₃ solution

Table 5. Effect of natural (1, 2, 3, 6, 7, 23, 5, 4) and semisynthetic neo-clerodanes tested at 100 ppm on the feeding behaviour of larvæ of *Helicoverpa armigera* and *Spodoptera frugiperda* (n=15-20).

Compound	<i>H. armigera</i>		<i>S. frugiperda</i>	
	Feeding Index %			
	Mean ± sem			
Fruticolone (1)	20 ±	11.2	32 ±	12.3*
(9a)	15 ±	6.1	10 ±	12.4
(9b)	15 ±	12.4	15 ±	4.6
Teucrolivin B (2)	25 ±	12.3	36 ±	11.7*
(10a,10b)	8 ±	11.6	14 ±	11.6
6,19-diacetylteumassilin (3)	63 ±	12.4*	24 ±	16.6 ^b
(11a,11b)	10 ±	18.4	10 ±	12.4
(13)	41 ±	11.2*	25 ±	6.4
(12A,12b)	2 ±	14.6	12 ±	6.8
Teucrin A (6)	11 ±	5.9	4 ±	13.8 ^b
(15a,15b)	16 ±	11.4	12 ±	7.2
Deacetylajugarin II (7)	23 ±	9.6	26 ±	8.4
(20a,20b)	15 ±	11.4	12 ±	6.4
(21a,21b)	8 ±	14.4	25 ±	6.4
Ajugarin II (22)	48 ±	7.4*	25 ±	7.8
Ajugarin I (23)	39 ±	9.6*	47 ±	7.3* ^c
(24a,24b)	20 ±	11.2	25 ±	6.8
Isoeriocephalin (5)	24 ±	11.6	29 ±	6.4 ^b
(19a,19b)	43 ±	8.6*	34 ±	6.5
Montanin C (4)	4 ±	12.9	6 ±	12.8 ^b
(16a,16b)	16 ±	6.8	24 ±	8.4
(17a,17b)	43 ±	6.7*	48 ±	3.4*
(18a,18b)	45 ±	9.9*	48 ±	12.4*

^a Feeding Index = ((C-T)/(C+T)) %, where C and T represent the amount of control and treatment discs eaten over a 18-14 h period. * P < 0.05, significant difference in the amount of treatment and control discs eaten, Wilcoxon ranked pairs test.

^b as cited in reference 16.

^c as cited in reference 11.

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