Pergamon

Tetrahedron 57 (2001) 10033–10038

TETRAHEDRON

Semi-synthesis and insecticidal activity of dyshomoerythrine derivatives

Joanne B. Hart,[a] Jennifer M. Mason[a,*] and Philippa J. Gerard[b]

[a]*Industrial Research Limited, P.O. Box 31310, Gracefield Road, Lower Hutt, New Zealand*
[b]*AgResearch Ltd, Ruakura Research Centre, Private Bag 3123, Hamilton, New Zealand*

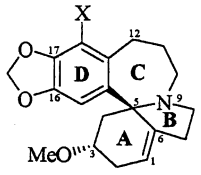
Received 16 July 2001; revised 19 September 2001; accepted 11 October 2001

Abstract—Several novel insecticidal homoerythrinans and dibenzazecines have been synthesised from the alkaloid dyshomoerythrine.
© 2001 Elsevier Science Ltd. All rights reserved.

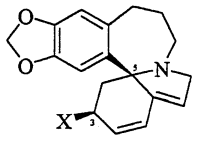
1. Introduction

The homoerythrinan alkaloid dyshomoerythrine **1** was first isolated from *Dysoxylum lenticellare* and shown to be molluscicidal.[1–3] It was subsequently isolated as the major alkaloid from *Lagarostrobos colensoi* (New Zealand silver pine) and shown to be active against some agriculturally important insect pests.[4,5] The C-homoerythrina alkaloids, of which dyshomoerythrine is a typical example, were for many years thought to be a small subgroup of the parent erythrina series. Recently it has become apparent that they are nearly as numerous as, and more widespread in the plant kingdom than, the erythrina alkaloids.[6,7]

Elucidation and, hopefully, enhancement of the insecticidal activity of dyshomoerythrine requires synthesis of a family of analogues. Even in the light of recent advances, de novo synthesis of the homoerythrinans presents a considerable challenge.[6–10] Therefore, we opined that the insecticidal properties of the dyshomoerythran system might be best explored through semi-synthetic modifications of the natural product. Semi-synthesis of this kind was once a common means of elucidating the structure of natural products but has gone out of fashion with the rise of non-destructive spectroscopic methods. However, an excellent paper on the chemistry of dyshomoerythrine's close relative schellhammeridine **3** showed that we could expect to prepare derivatives with both homoerythrinan and dibenzazecine structures (e.g. **7**).[11] Dibenzazecines are formed by cleavage of the C–5–N bond followed by elimination and aromatisation of the A-ring. For example, demethylation of schellhammeridine **3** by reflux in 10% HCl gives not only the expected C-3 (allyl) alcohol **4** and its epimer but also a 13% yield of dibenzazecine **7**.[11] Under the same conditions

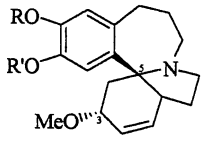


1 X = OMe
2 X = H

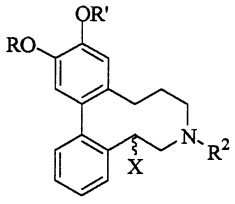


3 X = OMe
4 X = OH

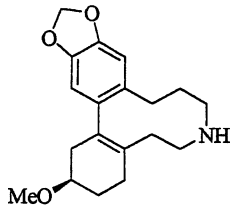
comosidine **5** gives dibenzazecine **8** as well as a mixture of C-3 alcohols.[12] Schellhammeridine **3** is converted quantitively to dibenzazecine **9** on reflux in acetic anhydride and von Braun degradation (BrCN) of both 3-epi-schellhammericine **2** and 6α,7-dihydrohomoerythraline **6** gives dibenzazecine **10**.[6,11,12] Under mild conditions C–N bond cleavage



5 R, R' = Me
6 R, R' = -CH_2-



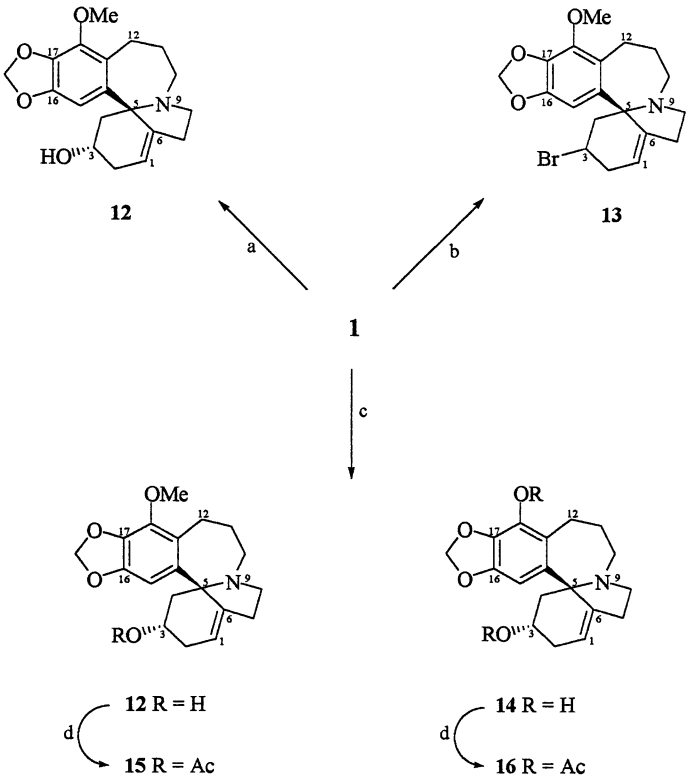
7 X = OH R, R'= -CH_2- R^2= H
8 X = H R, R'= CH_3 R^2= H
9 X = Ac R, R'= -CH_2- R^2= Ac
10 X = H R, R'= -CH_2- R^2= CN



11

Keywords: alkaloids; biaryls; insecticides.
* Corresponding author. Fax: +64-4-569-0055; e-mail: j.mason@irl.cri.nz

0040–4020/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0040-4020(01)01037-7



Scheme 1. (a) Pyridinium hydrochloride, 140°C, 20%; (b) BBr_3, 0°C, 16%; (c) pyridinium hydrochloride, 155°C; (d) pyridine–acetic anhydride, 27% (**15**) and 1.7% (**16**) from **1**.

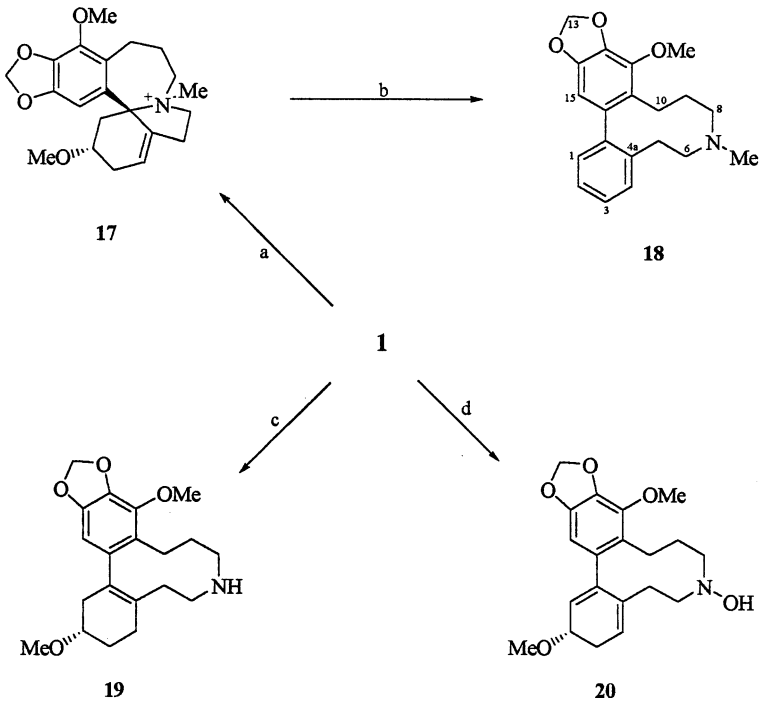
may occur without aromatisation. Catalytic hydrogenation of schellhammeridine **3** gives traces of **11** along with full and partly hydrogenated homoerythrinans.[6,11]

2. Results and discussion

Our first task was to extract a quantity of dyshomoerythrine **1** from *L. colensoi*. Green leaves and twigs (0.6 kg) were extracted with methanol. An alkaloidal fraction was isolated from the extract by standard techniques. The crude alkaloids were chromatographed on a column of silica gel eluted with hexanes–ethyl acetate. Fractions were assayed by GLC and those containing dyshomoerythrine were pooled to give 0.35 g of material. The dyshomoerythrine **1** thus isolated was of greater than 85% purity (by GLC peak area) and was used in all the work described here.

Our initial synthetic efforts focused on cleavage, preferably selective, of the ether and methylenedioxy moieties (Scheme 1). Conventional reagents met with little success, treatment of **1** with boron trichloride or iodotrimethylsilane gave only low and unreliable yields of alcohol **12** and recovery of most of the starting material, whilst reaction with sodium methanethiolate yielded no isolable products. Reaction of **1** with boron tribromide gave a 16% yield of bromide **13** and traces of demethylated products. Secondary alkyl bromides are often the product of cleavage of methyl ethers of secondary alcohols with this reagent.[13,14] A literature search unearthed an old, but little used, method for cleavage of phenol ethers by fusion with pyridinium hydrochloride.[15] We found that heating dyshomoerythrine with excess pyridinium hydrochloride at 140°C for 2 h selectively cleaved the A-ring methyl ether to give a 20% yield of alcohol **12**. More vigorous heating (160°C, 3 h) resulted in some cleavage of the phenolic ether group and gave both alcohol **12** (27%) and diol **14** (1.7%). These compounds were more readily isolated as their chromatographically amenable acetates (**15** and **16**).

Dyshomoerythrine **1** was readily N-methylated under conventional conditions (methyl iodide–diethyl ether) in good yield (Scheme 2). Exposing the resulting quaternary salt **17** to classical Hofmann elimination conditions gave only traces of isolable products. However, the chloride salt of **17** reacted cleanly upon heating with sodium iodide in acetone to give **18**, the structure of which was deduced from its mass and NMR spectra. The high-resolution mass spectrum gave a molecular formula of $C_{20}H_{23}NO_3$, indicating a loss of MeOH and H^+ from the starting material **17**. Comparison of the ^{13}C NMR spectrum of **18** with that of dyshomoerythrine **1** showed that the D ring of dyshomoerythrine remained intact in the new compound, but the A ring had undergone extensive modification since the distinctive resonances corresponding to dyshomoerythrine C-1, C-3, C-5 and 3-methoxyl were missing. Instead, the ^{13}C NMR spectrum of **18** contained four new aromatic methine resonances (125.3–130.1 ppm) and an N-methyl group (44.5 ppm). There were also five aliphatic methylene groups, two of which were deshielded by attachment to nitrogen (59.5 and 50.6 ppm). ^1H–^1H and ^{13}C–^1H COSY experiments showed that these five methylene groups comprised two independent spin systems of two and three methylenes. Taking into account the origin of this



Scheme 2. (a) MeI; (b) NaI, acetone, 80°C, 55% from **1**; (c) H_2, 20 psi, 5 days, 29%; (d) *m*-CPBA, 80%.

compound as a reaction product of dyshomoerythrine we assigned to **18** the dibenzazecine structure shown.

Biphenyl **18** was optically active ($[\alpha]^{20}_D=+32$) and HPLC on a chiral column showed the enantiomeric ratio to be 3:1. Therefore the transformation of dyshomoerythrine **1** into compound **18** has proceeded stereoselectively with transfer of chirality from the *spiro*-centre to the biphenyl axis. The same process occurs in the ring opening reactions of schellhammeridine **3**.[11]

1,6-Ene homoerythrinans and erythrinans are resistant to hydrogenation under all but the most vigorous conditions.[6,7] Indeed, they are often the product of hydrogenation of dienoid alkaloids such as schellhammeridine **3**.[11] Therefore we were not surprised to find that dyshomoerythrine **1** could not be hydrogenated at ambient temperature and pressure. However, under 20 psi of hydrogen, dyshomoerythrine **1** was slowly converted to a single compound **19** that had a molecular weight consistent with a hydrogenation product. It was evident though that the homoerythrinan ring system was not intact since the ^{13}C NMR spectrum of **19** did not contain a resonance at ~69 ppm, characteristic of C-5. Also the ^1H NMR spectrum contained no olefinic resonances and a D_2O shake indicated that an exchangeable proton was present. Full analysis of the ^1H–^1H and ^{13}C–^1H COSY NMR spectra lead us to the structure (**19**) shown.

Table 1. LD_{50} of homoerythrinans and dibenzazecines against *L. cuprina* larvae

Compound	LD_{50} (ppm±SD)
Batch 1	
1	22±5
12	251±38
13	148±20
15	21±3
16	>300
20	217±13
Batch 2	
1	73±6
18	171±17
19	730±37

Treatment of dyshomoerythrine **1** with *m*-chloroperbenzoic acid did not give the expected *N*-oxide, but instead another product of C–5–N cleavage. Comparison of the ^{13}C NMR spectrum of the product **20** with that of dyshomoerythrine **1** showed that again the D ring of dyshomoerythrine remained intact in the new compound. The ^1H NMR spectrum of the product contained two olefinic resonances that were shown to be part of the A ring by ^1H–^1H and ^{13}C–^1H COSY which demonstrated their correlation to H-3. HRMS gave a formula of $C_{20}H_{25}NO_5$, consistent with the proposed structure **20**.

Compounds **1**, **12**, **13**, **15**, **16**, **18**, **19** and **20** were assayed against larvae of *Lucilia cuprina* (Australian blowfly) in two batches. (Table 1).[5,17] Of the compounds retaining the dyshomoerythrine skeleton mono-acetate **15** retained all the activity of the parent compound, bromide **13** and alcohol **12** were moderately active whilst diacetate **16** showed surprisingly little activity. Of the ring-opened compounds, the tertiary amine **18** was the most active. Work is in progress in our laboratories on the synthesis of **18** and its analogues.

3. Experimental

3.1. General

NMR spectra were recorded on either a Bruker AC-300

spectrometer at 300 MHz (^{1}H) or 75 MHz (^{13}C) or on a Varian Unity spectrometer equipped with a 5 mm inverse probe at 500 MHz (^{1}H) or 125 MHz (^{13}C). Both high and low-resolution mass spectra were recorded on a VG70-250S spectrometer at HortResearch, Palmerston North, New Zealand. Optical rotation was determined on a Perkin–Elmer 241 polarimeter. HPLC was performed on a Hewlett Packard 1050 chromatograph with a UV detector. Gas chromatography was performed on a Hewlett Packard 5890 GC. Anhydrous solvents were purchased from Aldrich Chemicals. Except for pentane, chromatography solvents were distilled prior to use. 'Hexanes' refers to a petroleum fraction boiling around 68°C. Column chromatography was performed on silica gel (230–400 mesh). Preparative TLC was performed on Merck silica gel F_{254} glass backed plates (0.25 mm). All other chemicals were commercially available and used without further purification.

3.1.1. Dyshomoerythrine 1 by extraction of *L. colensoi*. *L. colensoi* needles and branchlets were collected from Tongariro Forest, New Zealand under the supervision of Department of Conservation staff. Shredded material (0.6 kg) was extracted with methanol (3×2.5 L). The combined extracts were concentrated under reduced pressure to approximately 500 mL and then acidified with HCl (2 M, 2 L). Solids were removed by filtration and the filtrate washed with dichloromethane (3×500 mL). The aqueous phase was brought to pH 12 by addition of concentrated ammonia solution and extracted with dichloromethane (5×1 L). The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give a yellow oil, which darkened on standing (4.8 g). The oil was chromatographed on a column using ethyl acetate–hexanes (1:1) as eluant. Fractions were assayed by GLC (BP1, 250°C isothermal) and those containing more than 85% dyshomoerythrine (R_T 6.5 min) were pooled. Removal of the solvent under reduced pressure gave dyshomoerythrine **1** (0.35 g) which had ^{1}H NMR and mass spectra consistent with literature data.[16] ^{13}C NMR ($CDCl_3$) δ 145.7 (quat), 142.9 (C-6), 141.2, 136.3, 136.1, 127.7 (all quat.), 115.8 (C-1), 106.0 (C-15), 100.8 (–O*C*H$_2$O–), 74.1 (C-3), 69.0 (C-5), 60.0 (aromatic –O*C*H$_3$), 55.6 (aliphatic –O*C*H$_3$), 50.2 (C-10), 46.4 (C-8), 38.1 (C-4), 31.9 (C-2), 27.5 (C-7), 25.0 (C-12), 22.8 (C-11).

3.1.2. 3-Bromo-18-methoxy-16,17-methylenedioxy-$\Delta^{1,6}$-homoerythrinan 13. A solution of dyshomoerythrine **1** (22.8 mg, 0.066 mmol) in dry dichloromethane (2 mL) was stirred with $NaSO_4$ (20 mg) under argon at 0°C. After the addition of BBr_3 (1 M in dichloromethane, 170 μL, 2.5 equiv.) the reaction was stirred for 1 h and then quenched with saturated aqueous sodium carbonate. Extractive workup (CH_2Cl_2–aqueous Na_2CO_3) followed by preparative TLC (silica gel, *n*-pentane–ethyl acetate 1:1) gave the title bromide as a yellow oil (4.2 mg, 16%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.63 (1H, s, H-15), 5.89 (2H, m, –OC*H*$_2$O–), 5.62 (1H, m, H-1), 4.25 (1H, m, H-3), 3.89 (3H, s, –OC*H*$_3$), 3.60 (1H, m, H-10), 3.50 (1H, m, H-12), 3.15 (1H, m, H-10′), 3.12 (1H, m, H-4), 2.78 (2H, m, H-8, H-8′), 2.60 (1H, m, H-2), 2.50 (2H, m, H-2′, H-12′), 2.40 (2H, m, H-4′, H-7), 2.35 (1H, m, H-7′), 1.76 (1H, m, H-11), 1.60 (1H, m, H-11′). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.3, 142.5, 140.5, 136.1, 136.0, 127.8, all quat., 117.1 (C-1), 104.1 (C-15), 101.1 (–O*C*H$_2$O–), 68.8 (C-5), 60.2 (–O*C*H$_3$), 49.5 (C-10), 46.5 (C-3, C-8), 41.1 (C-4), 35.4 (C-2), 27.6 (C-7), 24.8 (C-12), 23.1 (C-11). Mass spectrum (EI) *m*/*z* (rel. int.) 393 (5%, [M$^+$(^{81}Br)]), 391 (5%, [M$^+$(^{79}Br)]), 313 (20), 312 (100). HRMS Calcd for $C_{19}H_{22}{}^{81}BrO_3$ (M$^+$) 393.0763; found 393.0767.

3.1.3. 3α-Hydroxy-18-methoxy-16,17-methylenedioxy-$\Delta^{1,6}$-homoerythrinan 12. Dyshomoerythrine **1** (15.5 mg, 0.045 mmol) and pyridinium hydrochloride (50 mg, excess) were heated in a sealed tube at 140–145°C (bath temperature) for 2 h. Extractive work up (CH_2Cl_2–aqueous K_2CO_3) followed by column chromatography (pentane–acetone, 2:1) gave alcohol **12** (3 mg, 20%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.47 (1H, s, H-15), 5.83 (2H, m, –OC*H*$_2$O–), 5.43 (1H, bs, H-1), 3.82 (3H, s, –OC*H*$_3$), 3.72 (1H, m, H-3), 3.44 (2H, m, H-10, H-12), 3.16 (1H, bd, H-10′), 2.72 (2H, m, H-8, H-8′), 2.63 (1H, dd, H-4), 2.47 (3H, m, H-2, H-7, H-12′), 2.23 (1H, m, H-7′), 1.98 (1H, m, H-2′), 1.64 (2H, m, H-4′, H-11), 1.50 (1H, m, H-11′). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 142.8, 141.4, 136.4, 135.6, 128.0, all quat., 116.4 (C-1), 106.3 (C-15), 101.0 (–O*C*H$_2$O–), 69.6 (C-5), 65.9 (C-3), 60.2 (–O*C*H$_3$), 50.4 (C-10), 46.4 (C-8), 41.7 (C-4), 35.4 (C-2), 27.5 (C-7), 25.2 (C-12), 22.9 (C-11). Mass spectrum (EI) *m*/*z* (rel. int.) 329 (22%, M$^+$), 312 (9), 285 (51), 284 (58), 164 (100). HRMS Calcd for $C_{19}H_{23}NO_4$ (M$^+$) 329.1627; found 329.1632.

3.1.4. 3α-Acetoxy-18-methoxy-16,17-methylenedioxy-$\Delta^{1,63}$-homoerythrinan 15 and 3α,18-Diacetoxy-16,17-methylenedioxy-$\Delta^{1,6}$-homoerythrinan 16. Dyshomoerythrine **1** (20.1 mg, 0.059 mmol) and pyridinium hydrochloride (52 mg, excess) were heated in a sealed tube at 155–160°C (bath temperature) for 3 h. This melt was cooled and taken up in pyridine (10 drops) and acetic anhydride (10 drops) and stirred overnight. Extractive work up (CH_2Cl_2–aqueous K_2CO_3) followed by column chromatography (pentane–acetone 4:1, 2:1) gave acetate **15** and diacetate **16**.

15: yellowish oil, 6.0 mg, 27%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.48 (1H, s, H-15), 5.84 (2H, m, –OC*H*$_2$O–), 5.42 (1H, bs, H-1,) 4.68 (1H, m, H-3), 3.83 (3H, s, –OC*H*$_3$), 3.44 (2H, m, H-10, H-12), 3.17 (1H, m, H-10′), 2.69 (3H, m, H-4, H-8, H-8′), 2.60 (1H, bd, H-2), 2.47 (2H, m, H-12′, H-7), 2.23 (1H, m, H-7′), 1.98 (1H, m, H-2′), 1.92 (3H, s, acetate), 1.64 (2H, m, H-4′, H-11), 1.48 (1H, m, H-11′). ^{13}C NMR. (125 MHz, $CDCl_3$) δ 170.5, 145.9, 143.0, 141.4, 136.4, 135.6, 127.8 (all quat.), 115.5 (C-1), 106.2 (C-15), 100.9 (–O*C*H$_2$O–), 69.1 (C-3), 68.7 (C-5), 60.1 (–O*C*H$_3$), 50.4 (C-10), 46.6 (C-8), 38.0 (C-4), 31.7 (C-2), 27.6 (C-7), 25.1 (C-12), 22.9 (C-11), 22.3 (acetate). Mass spectrum (EI) *m*/*z* (rel. int.) 371 (7%, M$^+$), 325 (17), 312 (7), 285 (20), 284 (18), 282 (12), 255 (10), 254 (13), 253 (10), 238 (13), 196 (21), 178 (16), 163 (57), 150 (55), 135 (100). HRMS calcd for $C_{21}H_{25}NO_5$ (M$^+$) 371.1733; found 371.1733.

16: yellowish oil, 0.4 mg, 1.7%, ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.65 (1H, s, H-15), 5.87 (2H, dd, –OC*H*$_2$O–), 5.43 (1H, bs, H-1), 4.68 (1H, m, H-3), 3.41 (1H, t, H-10), 3.19 (1H, bd, H-10′), 2.95 (1H, dd, H-12), 2.71 (2H, m, H-8, H-8′), 2.66 (1H, dd, H-4), 2.60 (2H, m, H-2, H-12′), 2.38

(1H, m, H-7), 2.26 (3H, s, 18-acetate), 2.20 (1H, m, H-7′), 1.98 (1H, m, H-2′), 1.92 (3H, s, 3-acetate), 1.69 (2H, m, H-4′, H-11), 1.42 (1H, m, H-11′). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 168.0, 146.0, 144.0, 142.1 135.9, 135.6, 128.5 (all quat) 116.0 (C-1), 109.2 (C-15), 102.0 (–O*C*H_2O–), 69.2 (C-5), 69.0 (C-3), 50.4 (C-10), 46.6 (C-8), 38.1 (C-4), 31.8 (C-2), 27.6 (C-6), 26.4 (C-12), 22.6 (C-11), 21.4, 20.5 acetates. Mass spectrum (EI) *m/z* (rel. int.) 399 (20%, M^+), 341 (15), 340 (62), 314 (14), 313 (73), 312 (42), 298 (22), 271 (12), 270 (31), 206 (16), 178 (33), 146 (100). HRMS Calcd for $C_{22}H_{25}NO_6$ (M^+) 399.1682; found 399.1694.

3.1.5. 11-Methoxy-7-methyl-5,6,7,8,9,10-hexahydro-7-aza-benzo[1,3]benzodioxolocyclodecene 18. A solution of dyshomoerythrine **1** (27.4 mg, 0.080 mmol) and methyl iodide (0.2 mL) in diethyl ether (1 mL) was stirred overnight at room temperature. The solvent was decanted and the precipitate taken up in methanol and eluted through a column of Amberlite IRA 900 (Cl^- form) with more methanol. Evaporation of the solvent gave crude methyl dyshomoerythrinium chloride that was heated at 80°C in a sealed tube for 8 h with sodium iodide (75 mg) and acetone (1.25 mL). The slurry was blown down and the residue was partitioned between dichloromethane and potassium carbonate solution (10%, aqueous). The organic phase was concentrated under reduced pressure and dried by addition and evaporation of toluene. Column chromatography with pentane–acetone (2:1, 1:1) as eluent gave compound **18** as a pale yellow oil (12 mg, 0.035 mmol, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (2H, m, H-1 or H-4, H-2 or H-3), 7.06 (1H, t, J=7.2 Hz, H-2 or H-3), 6.87 (1H, d, J=7.6 Hz, H-1 or H-4), 6.18 (1H, s, H-15), 5.86 (2H, s, –OCH_2O–), 3.95 (3H, s, –OCH_3), 2.67 (1H, m, H-5), 2.58 (1H, m, H-6), 2.44 (1H, m, H-10), 2.37 (3H, m, H-5′, H-6′, H-10′), 2.24 (1H, m, H-8), 1.98 (3H, s, –NCH_3), 1.65 (2H, m, H-8′, H-9), 1.48 (1H, m, H-9′). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.7, 142.9, 142.0, 140.2, 137.0, 135.7 (all quat.), 130.1 (C-1 or C-4), 128.4, 127.6 (C-1 or C-4, C-2 or C-3) 125.3 (C-2 or C-3), 104.3 (C-15), 100.8 (–O*C*H_2O–), 59.5 (C-6), 59.3 (–O*C*H_3), 50.6 (C-8), 44.5 (-N*C*H_3), 30.6 (C-5), 26.0 (C-9), 25.1 (C-10). Mass spectrum (EI) *m/z* (rel. int.) 325 (93%, M^+), 324 (17), 310 (28), 295 (17), 294 (23), 282 (17), 253 (35), 70 (100). HRMS Calcd for $C_{19}H_{23}NO_3$ (M^+) 325.1678; found 325.1677. $[\alpha]^{20}_D$=+32 (c=0.87, CH_2Cl_2). HPLC (Chirobiotic-V (Vancomycin) 250×4.6 mm^2, MeOH–AcOH–Et_3N 100:0.1:0.1, 1 mL min^{-1}) R_T 8.5 min, 27%, 9.3 min, 73%.

3.1.6. 2,11-Dimethoxy-1,2,3,4,5,6,7,8,9,10-decahydro-7-aza-benzo[1,3]benzodioxolocyclodecene 19. A solution of dyshomoerythrine (20.5 mg, 0.060 mmol) in ethanol (1 mL) was shaken with palladium-on-carbon under hydrogen (20 psi) for 5 days. The solution was filtered through Celite, concentrated and applied to a column. Elution with pentane–acetone (2:1) and then methanol gave compound **19** as a pale yellow oil (6.9 mg, 29%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.17 (1H, s, H-15), 5.90 (2H, s, –OCH_2O–), 3.98 (3H, s, –OCH_3), 3.61 (1H, m, H-2), 3.37 (3H, s, –OCH_3), 3.00 (2H, m, H-6, N*H*), 2.78 (1H, m, H-10), 2.66 (1H, m, H-8), 2.63 (1H, dd, J=13.1, 4.9 Hz, H-5), 2.54 (1H, dt, J=13.5, 4.4 Hz, H-10′), 2.46 (1H, dm, J=14.1 Hz, H-6′), 2.33 (1H, m, H-4), 2.30 (1H, m, H-1), 2.16 (1H, m, H-1′), 2.10 (1H, m, H-8′), 1.94 (2H, m, H-9, H-3), 1.87 (1H, m, H-4′), 1.77 (2H, m, H-3′, H-9′), 1.67 (1H, bd, J=14.2 Hz, H-5′). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 142.2, 137.3, 135.5, 135.3, 129.5, 122.6 (all quat.), 102.8 (C-15), 100.8 (–O*C*H_2O–), 74.5 (C-2), 59.4, 56.0 (–O*C*H_3), 43.3 (C-6), 42.4 (C-8), 38.6 (C-1), 30.3 (C-5), 25.9 (C-3, C-9), 23.9 (C-4), 23.1 (C-10). Mass spectrum (EI) *m/z* (rel. int.) 345 (59%, M^+), 149 (100). HRMS Calcd for $C_{20}H_{27}NO_4$ (M^+) 345.1940; found 345.1942.

3.1.7. 2,11-Dimethoxy-7-hydroxy-2,3,5,6,7,8,9,10-octa-hydro-7-aza-benzo[1,3]benzodioxolocyclodecene 20. Dyshomoerythrine **1** (21 mg, 0.061 mmol) was dissolved in dry CH_2Cl_2 (1 mL) and *m*-CPBA (50%, 25.3 mg, 1.2 equiv.) was added to the resulting solution. After stirring at room temperature for 2 h, $Ca(OH)_2$ (ca. 100 mg) was added to the reaction mixture. The mixture was filtered through a bed of Celite and column chromatographed, eluting with $CHCl_3$. The solvent was removed from the filtrate to give the title compound **20** (17.5 mg, 0.049 mmol, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.00 (1H, s, H-15), 5.82 (3H, bs, –O*H*, –OCH_2O–), 5.61 (1H, m, H-4), 5.51 (1H, d, J=5.8 Hz, H-1), 3.93 (4H, s, –OCH_3, H-2), 3.28 (3H, s, –OCH_3), 3.15 (1H, m, H-10), 2.83 (1H, m, H-6), 2.80 (1H, m, H-6′), 2.56 (1H, m, H-10′), 2.50 (1H, m, H-3), 2.40 (1H, m, H-3′), 2.30 (1H, m, H-8), 2.10 (1H, m, H-8′), 1.98 (2H, m, H-7, H-7′), 1.78 (1H, m, H-9), 1.58 (1H, m, H-9′). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.8, 144.5, 142.0, 137.3, 136.0, 135.4, 124.9 (all quat.), 122.4 (C-4), 120.6 (C-1), 102.9 (C-15), 100.7 (–O*C*H_2O–), 70.5 (C-2), 64.7 (C-6), 59.5, 55.0 (–O*C*H_3), 53.3 (C-8), 30.9 (C-5), 29.2 (C-3), 25.6 (C-9), 23.4 (C-10). Mass spectrum (EI) *m/z* (rel. int.) 359 (12%, M^+), 327 (100), 325 (80), 308 (57). HRMS Calcd for $C_{20}H_{25}NO_5$ (M^+) 359.1733; found 359.1730.

3.2. Bioassay

Activity of compounds against *L cuprina* was determined at the Ruakura Research Centre, New Zealand. The bioassay was based on published methods.[5,17] Compounds were dissolved in ethanol and seven serial dilutions prepared. Two replicate strips of chromatography paper were each treated with 200 μL of each rate of test sample. The strips were rolled and placed in glass vials. Newly hatched *L. cuprina* larvae (mean 24) were placed into each vial along with 400 μL of sheep serum fortified with 2% yeast extract and 0.5% KH_2PO_4. The vials were plugged and held at 25 (±0.2)°C in constant light for 24 h. The contents of the vials were washed with warm water into a glass dish and the number of active larvae were counted. The results were analysed by regression analysis.

Acknowledgements

The authors would like to thank A. Falshaw for collection of *L. colensoi*, extraction of dyshomoerythrine and for help with preparation of the manuscript, S. Lynds for extraction of dyshomoerythrine, G. Russell for his gift of *L. colensoi* extract, staff of the Turangi office of the Department of Conservation for help with collection of *L. colensoi*,

H. Wong for his superb NMR service, L. Brocklebank for HPLC and staff of the Mass Spectrometry Unit, HortResearch, Palmerston North for mass spectra. The New Zealand Foundation for Research, Science and Technology provided funding.

References

1. Aladesanmi, A. J.; Adewunmi, C. O.; Kelley, C. J.; Leary, J. D.; Bischoff, T. A.; Zhang, X.; Snyder, J. K. *Phytochemistry* **1988**, *27*, 3789–3792.
2. Adewunmi, C. O.; Aladesanmi, A. J. *Phytother. Res.* **1988**, *2*, 104–106.
3. Aladesanmi, A. J.; Kelley, C. J.; Leary, J. D.; Onan, K. D. *J.Chem. Res., Synop.* **1984**, 108–109.
4. Bloor, S. J.; Benner, J. P.; Irwin, D.; Boother, P. *Phytochemistry* **1996**, *41*, 801–802.
5. Gerard, P. J.; Ruf, L. D.; Lorimer, S. D.; Heath, A. C. *NZ J. Agric. Res.* **1997**, *40*, 261–267.
6. Tsuda, Y.; Sano, T. Erythina and Related Alkaloids. *The Alkaloids*; Cordell, G., Ed.; Academic: New York, 1996; Vol. 48, pp. 249–337.
7. Dyke, S. F.; Quessy, S. N. Erythrina and Related Alkaloids. *The Alkaloids*; Rodrigo, R. G. A., Ed.; Academic: New York, 1981; Vol. 18, pp. 1–98.
8. Tsuda, Y.; Ohshima, T.; Hosoi, S.; Kaneuchi, S.; Kuichi, F.; Toda, J.; Sano, T. *Chem. Pharm. Bull.* **1996**, *44*, 500–508.
9. Tsuda, Y.; Murata, M.; Hosoi, S.; Ikeda, M.; Sano, T. *Chem. Pharm. Bull.* **1996**, *44*, 515–524.
10. Tsuda, Y. *Heterocycles* **1998**, *48*, 1599–1608.
11. Johns, S. R.; Lamberton, J. A.; Sioumis, A. A.; Suares, H. *Aust. J. Chem.* **1969**, *22*, 2203–2218.
12. Langlios, N.; Razafimbelo, J. *J. Nat. Prod.* **1988**, *51*, 499–503.
13. Kuehne, M.; Pitner, J. *J. Org. Chem.* **1989**, *54*, 4553–4569.
14. Youssefyeh, R.; Mazur, Y. *Chem. Ind. (London)* **1963**, 609–610.
15. Prey, V. *Ber. Bunsen-Ges.* **1941**, *74B*, 1219–1225 *Chem. Abstr.* **1942**, *6*, 4809.
16. Aladesanmi, A. J. *Tetrahedron* **1988**, *44*, 3749–3756.
17. Levot, G. W. *J. Aust. Entomol. Soc.* **1990**, *29*, 295–300.