Phytochemistry, 1978, Vol 17, pp 305–309. Pergamon Press Printed in England.

DESMETHOXYABRESOLINE AND 10-*EPI*-DESMETHOXYABRESOLINE, NEW ESTER ALKALOIDS IN *HEIMIA SALICIFOLIA*

University of Connecticut, School of Pharmacy, Storrs, CT 06268, U.S.A.

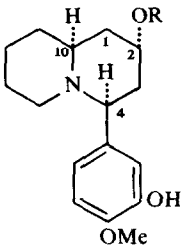
(*Received* 15 *July* 1977)

Key Word Index—*Heimia salicifolia*; Lythraceae; alkaloid; cinnamyl ester; desmethoxyabresoline; 10-*epi*-desmethoxyabresoline

Abstract—Two new ester alkaloids, desmethoxyabresoline and 10-*epi*-desmethoxyabresoline, have been isolated from young seedlings of *Heimia salicifolia* and have been synthesized. Chemical and physical properties of the natural and synthetic isomers are in agreement. The presence of these alkaloids adds support to the postulate that the biphenyl system of the lythraceous alkaloids is derived from *trans*-cinnamate esters of phenylquinolizidinols.

INTRODUCTION

Abresoline (**1**) the first non-biphenyl alkaloid isolated from *Heimia salicifolia* [1], represents an expected variant in the basic biogenetic theme of the lythraceous alkaloids. Its discovery in the species gave significant circumstantial support to a postulated biogenetic proposal [2], a scheme which was further sustained by the occurrence of the phenylquinolizidinols **2** and **3** in young *H. salicifolia* seedlings [3]. We report here on the occurrence of two new esters, desmethoxyabresoline (**4**) and 10-*epi*-desmethoxyabresoline (**5**), isolated from the same fraction of minor alkaloids as **1**.



1 R = feruloyl
2 R = H
4 R = *p*-coumaroyl

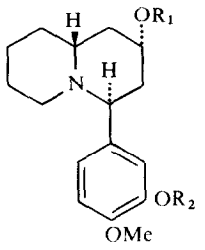
RESULTS

Desmethoxyabresoline (**4**) was obtained as a chromatographically pure, noncrystalline solid. It gave a positive phenol test and showed OH stretch absorptions in the IR spectrum (ν_{max} 3520, 3300 cm^{-1}). The presence of a conjugated carbonyl group could be inferred from absoption bands at 1700 and 1630 cm^{-1}. Of importance also was the presence of a band at 2800 cm^{-1}, a transition present in quinolizidines with a *trans* ring juncture [4].

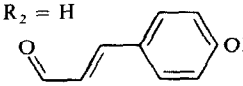
The mass spectrum gave the molecular composition ($C_{25}H_{29}NO_5$) and a fragmentation pattern which indicated that the compound was not a biphenyl lactone but was probably an ester alkaloid. The spectrum presents two intense peaks at *m/e* 259 (M-164) and 258. Transitions at these units are very characteristic for esters of the phenylquinolizidinols **2** and **3** [1b, 5b], and may originate by a fragmentation as shown in Scheme 1 (R_1 = R = H). The loss of 164 (147 + 17) from the molecular ion together with the presence of a peak at *m/e* 147 (acylium ion) pointed to the presence of a coumaryl group in the parent molecule. A fragment at 276 (M-147) is also observable in the spectrum.

Structure **4**, in agreement with the previous observations, is fully sustained by the PMR spectrum. It shows the characteristic quinolizidine ring proton resonances as well as the low field aromatic transitions; the latter have been detailed in the Experimental. Notable features include (a) two pairs of doublets (both of J = 16 Hz) at 6.36 and 7.65 ppm corresponding to the olefinic protons of a cinnamyl group with *trans* geometry, (b) the chemical shift of H-4 at 3.3 ppm found in 4-phenylquinolizidines with a *trans* ring juncture [6, 7] and (c) the H-2 resonance at 5.17 ppm of $W_{\frac{1}{2}}$ = 9 Hz suggesting an equatorial hydrogen. The latter assignment was confirmed by base hydrolysis followed by comparative TLC of the amino alcohol with both synthetic **2** (axial OH) and its C-2 epimer (equatorial OH). The product was identical to **2**. Finally, catalytic hydrogentation gave 2-(*p*-hydroxyhydrocinnamyloxy)-4-(3-hydroxy-4-methoxyphenyl)(*e*)-trans-quinolizidine, identical (TLC, IR, MS) to an authentic sample [5].

The mixture of minor alkaloids from which **1** and **4** had been separated contained another new compound, of similar chromogenic character but lower chromatographic mobility than **1** and **4**. These properties, together with reflections on the biogenetic relationship among the heimia alkaloids, suggested that the compound might be an ester of the phenylquinolizidinol with a *cis* ring juncture [3]; the mass spectrum together with an hydrolysis experiment indicated that we were dealing with the *p*-coumaryl ester (**5**). The amount available was low and therefore we decided to establish the proof of structure by a synthetic approach.



3 $R_1 = R_2 = H$

5 R_1 =  OH ; $R_2 = H$

6 $R_1 = H$; $R_2 = CH_2COC_6H_4Br$

7 $R_1 = COCH{=}CHC_6H_4OR_3$; $R_2 = R_3 = CH_2COC_6H_4Br$

8 $R_1 = COCH{=}CHC_6H_4OCH_2COC_6H_4Br$; $R_2 = H$

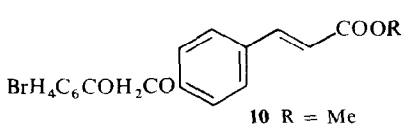
9 $R_1 = COC_6H_4Br$;
$R_2 = COCH{=}CHC_6H_4OCH_2COC_6H_4Br$

12 $R_1 = COC_6H_4Br$, $R_2 = H$

We previously had synthesized [3] the 4-phenylquinolizidinol (**3**) which was the starting material for this work. The phenolic hydroxyl was protected with the *p*-bromophenacyl group as described by Hendrickson and Kandall [8] to give **6**. Similarly, *p*-hydroxycinnamic acid was converted into *p*-bromophenacyloxycinnamic acid (**11**).

Esterification was achieved by the method of Hanaoka *et al.* for the synthesis of the lactonic lythraceous alkaloids (9), by reflux of **6** and *p*-bromophenacyloxycinnamic acid (**11**) in benzene in the presence of *p*-toluenesulfonic acid. Two major **7** and **8** and a minor **9** product were obtained. Various other esterification methods were tried without any, or only with limited, success, and even the above procedure which we found to be very good on a comparative basis, gave low yields (25% conversion of **6** into **7** + **8**). Correlation of the spectrometric data of **7** with the expected diether ester was straight forward and is detailed in the Experimental. The structural assignment of **8** and **9** was more complicated and merits comment here.

Compound **8** gives a positive phenol test; an OH absorption band is present in the IR spectrum. The presence of the cinnamyl group is evidenced by the IR spectrum (ν_{max} 1695 and 1625 cm^{-1}) and the PMR spectrum (doublet at 6.26, J = 16 Hz). The latter also shows that there is one bromophenacyl group (δ 5.25, *s*, 2H,—OCH_2CO— per methoxyl group in the molecule. The mass spectrum gave the molecular formula, $C_{33}H_{34}O_6NBr$, and a fragmentation pattern characteristic of esters of the 4-phenylquinolizidinols. Of significance is the presence of a pair of peaks at m/e 360 and 362.



10 R = Me

11 R = H

These units are also components of the spectrum of **7** and **9** but are not detectable in the spectra of compounds **1**–**6**. High resolution MS gave the elemental composition for that ion, $C_{17}H_{13}O_4Br$, which may be assigned to a bromophenacylcoumaric ion (iii) formed by a McLafferty-type rearrangement as shown in Scheme 1 (R_1 = H, R = $CH_2COC_6H_4Br$). The structure of **8** was thus established.

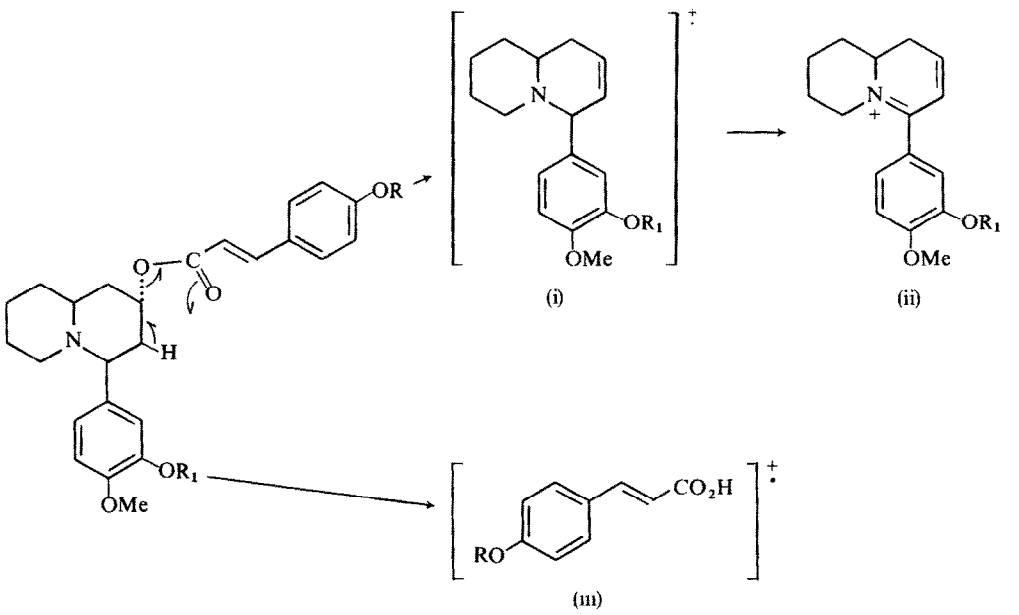
The minor compound (**9**) showed similar chromatographic mobility as **7** and gave a negative phenol test. These observations suggest that the compound lacks a free hydroxyl group, a supposition that is confirmed by the IR spectrum. The presence of a *trans*-cinnamyl group is evidenced by the NMR spectrum (δ 6.32, *d*, J = 16 Hz) as well as the IR spectrum (ν_{max} 1740, 1710 and 1640 cm^{-1}). The overall appearance of the PMR spectrum is very similar to that of **8** although there is a larger number of low field aromatic resonances. This spectrum gives evidence for the presence of only one bromophenacyl group (δ 5.25, *s*, 2H). The high mass region of the MS of **9** shows a pattern almost superimposable to that of **7** but with a shift of 14 units to lower mass. High resolution gave the molecular formula $C_{40}H_{37}NO_7Br_2$ and the elemental composition of the fragment ion, $C_{23}H_{23}NO_3Br$. (M-H + bromophenacylcoumaric acid). Hydrolysis and TLC analysis of the produets gave **3**, **11** and *p*-bromobenzoic acid.

Treatment of **9** with Zn/HOAc gave, after extraction, a compound (**12**) that gave a positive phenol test and evidence for the presence of both OH (ν_{max} 3400–3500 cm^{-1}) and CO (1718 cm^{-1}) in the IR spectrum but no conjugated olefinic bond (absence of absorption at *ca* 1635 cm^{-1}) was observed. The mass spectrum gave the elemental composition, $C_{23}H_{26}NO_4Br$, and a fragmentation pattern, detailed in the Experimental, characteristic of esters of the phenylquinolizidinols.

The hydrolytic cleavage of the cinnamyl ester of **9**, upon treatment with Zn/HOAc, was unexpected; phenolic esters of these phenylquinolizidinols though are relatively labile. We had observed previously that attempts to crystallize the diacetate of **3** gave the monoacetate [3]. We are unable to propose a mechanism for the formation of **9**, although one may rationalize its formation by the presence of *p*-bromophenacyl alcohol, formed upon hydrolysis of a *p*-bromophenacyl ether group, in reaction mixture. Reaction of **5** with *p*-bromophenacyl bromide in acetone [8] does not yield **9**. The desired *p*-hydroxycinnamyl ester (**5**) was obtained upon removal of the phenacyl group [8] from both **7** and **8**.

The mass spectrum of **5** shows the important M-147, M-164 and M-259 fragments; the spectrum is similar to that of desmethoxyabresoline (**4**). The presence of the *trans*-cinnamyl group is demonstrated by both the IR spectrum (ν_{max} 1710 and 1635 cm^{-1}) and the PMR spectrum (δ 6.35, *d*, J = 16 Hz). Evidence for the *cis*-quinolizidine ring juncture is found by the absence of Bohlmann IR frequencies [4] as well as the PMR chemical shift of H-4 at 4.0 ppm [6, 7]. The H-2 signal is found at 5.25 ppm, a very broad singlet suggesting, that (**5**) exists in solution (DMSO) in equilibrium of conformers as **3** [3].

10-*epi*-Desmethoxyabresoline (**5**) is homogenous in various TLC systems but in one system (XIb, see Experimental) it gives evidence for the presence of traces of another phenolic alkaloid of slightly lower R_f. The pro-



Scheme 1.

portion of the latter is greater in samples that have been in prolonged contact with Si gel, reaching approximately 30%. Efforts to obtain the minor component in a pure state by PLC were unsuccessful, after separation and extraction of the lower band. Such samples on rechromatography gave evidence of the presence of **5**. This phenomenon suggested an isomerization at the olefinic bond as it has been observed for *trans*-4′-hydroxycinnamyl lupinine [10]. Indeed, exposure of **5** on Si gel to UV light accelerated the conversion. Hydrolysis of a sample representing a mixture of **5** and the minor alkaloid gave, in addition to **3** a mixture of *trans*- and *cis*-*p*-coumaric acids. The chromatographic behavior of synthetic **5** is identical to that of the natural product. We now find an explanation for the difficulties that we had in our early attempts to purify the natural product by PLC on Si gel.

The identity of the natural alkaloid with synthetic (**5**) was further verified by comparative IR, UV and MS spectrometric analysis. In addition, the natural product was treated with *p*-bromophenacyl bromide to give a mixture of **7** and **8**. The monophenacyl ether (**8**) was isolated and its identity with synthetic **8** was proven by TLC and IR spectrometry.

EXPERIMENTAL

General. PMR spectra were determined in $CDCl_3$ unless otherwise indicated. Chemical shifts are quoted in δ units relative to TMS. MeOH was the solvent for UV spectra. Mps were determined with a Kofler microstage and are uncorr. The following systems were used throughout for both TLC and PLC: Al_2O_3–GF_{254}: (Ia) C_6H_6 satd with NH_4OH–MeOH (19:1); (Ib) C_6H_6 satd with NH_4OH–MeOH (19:3); (IIa) $CHCl_3$ satd with NH_4OH–EtOH (19:0.5); (IIb) $CHCl_3$ satd with NH_4OH–EtOH (19:1.2 and/or 19:1.5); (IIc) $CHCl_3$ satd with NH_4OH–MeOH (19:1.5); (III) EtOAc satd with NH_4OH; (IV) EtOAc satd with NH_4OH–MeOH (19:0.3); (V) EtOAc satd with NH_4OH–C_6H_6 satd with NH_4OH (2:1). Si gel–GF_{254}. (VIa) C_6H_6 satd with NH_4OH–MeOH (19:1 and/or 19:1.5); (VIb) C_6H_6 satd with NH_4OH–MeOH (19:2 and/or 19:2.5); (VIc) C_6H_6 satd with NH_4OH–MeOH (19:3 and/or 19:4); (VII) C_6H_6 satd with NH_4OH–*iso*-PrOH (19:3); (VIII) C_6H_6 satd with NH_4OH–Me_2CO (1:1); (IX) C_6H_6–MeOH (20:3 and/or 20:4); (X) $CHCl_3$ satd with NH_4OH; (XIa) $CHCl_3$ satd with NH_4OH–EtOH (19:0.5); (XIb) $CHCl_3$ satd with NH_4OH (19:1 and/or 19:1.5); (XIc) $CHCl_3$ satd with NH_4OH (19:1.8); (XII) $CHCl_3$ satd with NH_4OH–Me_2CO (15:5); (XIII) $CHCl_3$ satd with NH_4OH–MeCN (1:1); (XIVa) $CHCl_3$ satd with NH_4OH–C_6H_6 satd with NH_4OH (1:1); (XIVb) $CHCl_3$ satd with NH_4OH–C_6H_6 satd with NH_4OH (3:1); (XV) EtOAc satd with NH_4OH; (XVIa) EtOAc satd with NH_4OH–EtOH (18:1 and/or 18:2); (XVIb) EtOAc satd with NH_4OH–EtOH (18:3 and/or 18:5); (XVIIa) EtOAc satd with NH_4OH–$CHCl_3$ satd with NH_4OH (1:1); (XVIIb) EtOAc satd with NH_4OH–$CHCl_3$ satd with NH_4OH (1:3); (XVIIIa) EtOAc satd with NH_4OH–C_6H_6 satd with NH_4OH (1:1); (XVIIIb) EtOAc satd with NH_4OH–C_6H_6 satd with NH_4OH (1:2); (XVIIIc) EtOAc satd with NH_4OH–C_6H_6 satd with NH_4OH (2:1); (IXX) EtOAc–MeOH (18:2); (XX) EtOAc–C_6H_6 (12:10); (XXI) C_6H_6–MeOH–HOAc (23:2:2 and/or 23:1:1); (XXII) hexane–Me_2CO–HCO_2H (10:7.5:0.5); (XXIII) C_6H_6–dioxane–HOAc (18:5:0.8). Cellulose: (XXIV) C_6H_6–HOAc–MeOH (23:1:1); (XXV) 0.4% AcOH [10]; (XXVI) M $(NH_4)_2SO_4$ in H_2O [10]. Visualization was with Dragendorff's and diazotized *p*-nitroaniline reagents. Elution of alkaloidal bands after PLC was with (a) $CHCl_3$–EtOAc–MeOH for hydroxylic, and (b) $CHCl_3$–EtOAc for nonpolar compounds. Residual Si was separated from the alkaloids either by repeated filtration or by partition between aq. $NaHCO_3$ soln (pH 8.5) and $CHCl_3$–MeOH (4:1).

Isolation of the alkaloids. Leaf and stem material of *H. salicifolia* Link & Otto was extracted and the alkaloids were separated as previously described [1]. The mixture remaining after separation of abresoline (**1**) was further resolved by PLC (system XVIb) to yield, in order of decreasing chromatographic mobility, crude desmethoxyabresoline (**4**) and crude, 10-*epi*-desmethoxyabresoline (**5**).

Desmethoxyabresoline (**4**). The fractions containing desmethoxyabresoline were purified by PLC (system VIb) elution and rechromatography in XIc-triple development). The alkaloid

was noncrystalline but chromatographically pure (TLC systems VIa, XIb, c, XV, XVIIb). XIb, c the alkaloid resolved into a major (**4**) and a very minor phenolic component of slightly lower mobility; attempts to obtain the latter compound in a homogeneous state from the PLC run in system XIc were unsuccessful. We believe that we are dealing with an *trans*→*cis* isomerization of the olefinic bond [10] as discussed for **5**. MS *m/e* (rel. int.) [fragment, see Scheme 1, R = R_1 = H]: 423.2032 [M^+ (4), $C_{25}H_{29}NO_5$ requires 423.2038], 276 [M − COCH=CHC_6H_4OH], 259 (100) [i], 258 (100) [ii], 244 (20), 218 (11), 211.5 (1) [M^{++}], 177 (33), 147 (24) [COCH=CH−C_6H_4OH], 136 (32) and 84 (67); $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520, 3300, 2800, 1700 and 1630. PMR (220 MHz): 0.7–2.9 (*m*), 3.25 (*s*, $W_{\frac{1}{2}}$ = 19 Hz), 3.85 (*s*, 3H), 5.17 (*s*, $W_{\frac{1}{2}}$ = 9 Hz), 6.36 (*d*, *J* = 16 Hz, 1H), 6.77 (*s*, 2H), 6.84 (*d*, *J* = 7.5 Hz, 2H), 6.95 (*s*, 1H), 7.45 (*d*, *J* = 7.5 Hz, 2H), 7.65 (*d*, *J* = 16 Hz, 1H).

*4-(2-*p*-Bromophenyl-2-oxo-ethyloxy) cinnamic acid* (**11**). Methyl 4-(2-*p*-bromophenyl-2-oxo-ethyloxy) cinnamate (**10**) was obtained in 81% yield upon reflux (8 hr) of methyl *p*-hydroxycinnamate [11] (9.97 g) with *p*-bromophenacyl bromide (19.12 g) and K_2CO_3 (12.9 g) in Me_2CO (200 ml) [8]. Recrystallization from $CHCl_3$–MeOH gave mp 148–149; PMR (60 MHz). 3.72 (*s*, 3H), 5.19 (*s*, 2H), 6.20 (*d*, *J* = 16 Hz), 6.84 (*d*, *J* = 9 Hz), 7.40 (*d*, *J* = 9 Hz), 7.54 (*d*, *J* = 9 Hz), 7.57 (*d*, *J* = 16 Hz), 7.82 (*d*, *J* = 9 Hz). Hydrolysis of **10** (4N NaOH, reflux, 16 hr) gave the acid (**11**), in 70% yield. Recrystallization from Me_2CO or MeCN–*iso*–PrOH gave mp 215–216. MS *m/e* (rel. int.): 362 (18), 360.00000 M^+ (20), $C_{17}H_{13}O_4Br$ requires 359.99939, 185 (92), 183 (100), 160 (26), 157 (16.5), 155 (17).

rel-(2S, 4S, 10R)-*2-Hydroxy-4-[3(2-*p*-bromophenyl-2-oxo-ethyloxy)-4-methoxyphenyl] quinolizidine* (**6**). A mixture of **3** [3] (2.17 g), *p*-bromophenacyl bromide (5.13 g) and K_2CO_3 (5.7 g) in Me_2CO (250 ml) was heated at reflux [8] (3 hr). TLC indicated *ca* 70% conversion of **3**. Additional K_2CO_3 (0.3 g) and *p*-bromophenacyl bromide (2.3 g) in Me_2CO (25 ml) was added and reflux was continued (16 hr). The product was by column chromatography on Si gel (Woelm, for partition chromatography) eluting with $CHCl_3$→0.5% EtOH in $CHCl_3$ to give noncrystalline, but TLC homogeneous **6** (2.225 g; 60% yield), MS *m/e* (rel. int.): 475 (5.8), 473.1187 M^+ (6), $C_{24}H_{28}O_4NBr$ requires 473.11949, 276 (32) [M-R_2], 218 (9), 185 (44) and 183 (50) [COC_6H_4Br], 154 (100), 110 (37); PMR (60 MHz): 1.0–3.0 (*m*), 3.79 (*s*, 3H), 4.08 (*s*, *br*), 5.21 (*s*, 2H), 6.81 (*s*, 2H), 6.98 (*s*, 1H), 7.51 (*d*, *J* = 9 Hz, 2H), 7.85 (*d*, *J* = 9 Hz, 2H).

Esterification. The acid (**11**) (3 × 236 mg) was dissolved in boiling C_6H_6 (3 × 1.300 ml) (reflux, 1 hr). After cooling, **6** (3 × 236 mg) and *p*-TsOH.H_2O (3 × 1.5 g) was added and the mixture was heated under reflux and worked up as in ref. [9]. TLC indicated that the reaction product was composed of 2 major and 3 minor Dragendorff-positive compounds. PLC (double development, systems XIVa and XVIIa, elution and rechromatography in XVIIa) gave **7** (175 mg, 15% yield based on **6**), **8** (97 mg, 11% yield based on **6**), and **9** (25 mg, 2% yield based on **6**). The other minor products were not studied further.

rel-(2S, 4S, 10R)-*2-[4-(2-*p*-Bromophenyl-2-oxo-ethyloxy) cinnamyloxy]-4-[3, 4-(2-*p*-bromphenyl-2-oxo-ethyloxy) cinnamyloxy-4-methoxyphenyl] quinolizidine* (**7**). Noncrystalline but TLC (systems XVIIb, XVIIIb, XIa) homogenous. MS *m/e* (rel. int.) [fragment, see Scheme 1, R = R_1 = $CH_2COC_6H_4Br$] 817 (0.4), 815.0993 (0.3) [M^+, $C_{41}H_{39}O_7NBr_2$ requires 815.1092], 620 and 618 (3) [M -R_1], 457 and 433 (9) [i], 456 and 454 (10) [ii], 416 and 414 (17.5) [ii—C_3H_5] 362 and 360 (6) [iii], 259 (44) [i-R_1 + H], 258 (87.5) [i-R_1], 218 (14), 185 and 183 (100) [COC_6H_4Br], 84 (31); $\nu_{max}^{CHCl_3}$ cm^{-1}: 1695, 1680 *sh*, 1630; PMR (60 MHz): 1.1–3.5 (*m*), 3.87 (*s*, 3H), 4.18 (*t*, *J* = 6 Hz), 5.29 (*s*, 2H), 5.38 (*s*, 2H), 5.36 (*br*, *s*), 6.32 (*d*, *J* = 17 Hz, 1H), 6.78–8.08 (*m*).

rel-(2S, 4S, 10R)-*2-[4-(2-*p*-Bromophenyl-2-oxo-ethyloxy) cinnamyloxy]-4-(3-hydroxy-4-methoxyphenyl) quinolizidine* (**8**) Noncrystalline but TLC homogeneous (systems IIa, VIb, XIa,b, XVIIb, XVIIIc). MS *m/e* (rel. int) [fragment, see Scheme 1, R_1 = H, R = $CH_2COC_6H_4Br$] 621 (0.4), 619.1559 (0.5) [M^+, $C_{33}H_{34}O_6NBr$ requires 619.15609], 422 (3) [M-R] 362 and 359.9995 [iii, $C_{17}H_{13}O_4Br$ requires 359.99939], 276 (2) [M−COCH=CHC_6H_4OR] 259 (58.5) [i], 258 (46) [ii], 218 (61), 185 and 183 (100) [COC_6H_4Br] 84 (37); $\nu_{max}^{CHCl_3}$ cm^{-1}: 3510, 1695, 1670 *sh*, 1625; PMR (60 MHz): 0.7–3.1 (*m*), 3.80 (*s*, 3H), 4.22 (*s*, $W_{\frac{1}{2}}$ = 19 Hz, 1H), 5.25 (*s*, 2H), 5.38 (*s*, *br*, 1H), 6.26 (*d*, *J* = 16 Hz, 1H), 6.65–7.90 (*m*).

rel-(2S, 4S, 10R)-*2-(*p*-Bromobenzoyloxy)-4-[3, 4-(2-*p*-bromophenyl-2-oxo-ethyloxycinnamyloxy-4-methoxyphenyl] quinolizidine* (**9**). Noncrystalline but TLC homogeneous (systems XIa, XVIIb, XVIIIb). MS *m/e* (rel. int.) [fragment] 803 (0.1), 801.0950 (0.1) [M^+, $C_{40}H_{37}NO_7Br_2$ requires 801.0933], 443 (10) and 441 (12) [M − HOR_2], 442 (12) and 440.0857 (10) [M-(HOR_2 + H), $C_{23}H_{23}NO_3Br$ requires 440.0857], 402 and 400.0564 (18) [M-(HOR_2 + C_3H_5), $C_{20}H_{19}NO_3Br$ requires 400.0544], 362 (7) and 360 (10) [HOR_2], 345 (4) and 343 (2.5) [R_2], 218 (36), 202 (58), 200 (94), 198 (60), 185 (96) and 183 (96) [COC_6H_4Br], 177 (94), 157 (96) and 155 (100) [C_6H_4Br], 84 (70); $\nu_{max}^{CHCl_3}$ cm^{-1} 1740, 1710, 1690 *sh*, 1640; PMR (60 MHz): 0.7–3.2 (*m*), 3.80 (*s*, 3H), 4.18 (*s*, $W_{\frac{1}{2}}$ = 18 Hz), 5.25 (*s*, 2H), 5.30 (*br* s, 1H), 6.32 (*d*, *J* = 16 Hz, 1H), 6.8–8.2 (*m*). Hydrolysis (4N NaOH, reflux 30 min) followed by extraction and TLC gave **3**, **11** and *p*-bromobenzoic acid.

rel-(2S, 4S, 10R)-*2-(*p*-Bromobenzoyloxy)-4-(3-hydroxy-4-methoxyphenyl) quinolizidine* (**12**). Obtained when **9** was stirred (22°, 2 hr) with Zn (200 mg) in HOAc (0.5 ml), followed by filtration, washing of the inorganic salt with HOAc and MeOH and extraction of the alkaloid compound into MeOH–$CHCl_3$ at pH 8.5. Recrystallization from MeOH gave mp 164–166°. MS (rel. int.) [fragment] 461 (8) 459.1030 [M^+, $C_{23}H_{26}NO_4Br$ requires 459.1042], 276 (3) [M-R_1], 260 (50), 259 (70) [M-HOR_1], 258 (80) [M-(HOR_1 + H)], 218 (25), 185 (19) and 183 (20) [COC_6H_4Br], 177 (80), 150 (28), 136 (70), 84 (100); ν_{max}^{KBr} cm^{-1}: 3500–3400, 1718, 1700*sh*. Compound **12** co-chromatographs with **8** in TLC systems IIa, XIa, b, XVIIa, b, but it is of slightly lower mobility in system VIb.

rel-(2S, 4S, 10R)-*2-(*p*-Hydroxycinnamyloxy)-4-(3-hydroxy-4-methoxyphenyl) quinolizidine*; ± *10-epi--desmethoxyabresoline* (**5**). Removal of the phenacyl group [8] from both **7** and **8** gave **5**. Recrystallization from $CHCl_3$ gave mp 221–223. MS (rel. int.) [fragment, see Scheme 1, R = R_1 = H]: 423.2041 [M^+ $C_{25}H_{29}NO_5$ requires 423.2038], 277 (3), 276 (3) [M−COCH=CHC_6H_4OH], 259 (100) [i], 258 (94) [ii], 244 (17), 218 (61), 211.5 (1), [M^{++}], 177 (33), 150 (18), 147 (22) [COCH=CHC_6H_4OH], 120 (50), 84 (67); ν_{max}^{KBr} cm^{-1}, 3380, 1710, 1635; λ_{max} nm (log ε): 228 (4.3), 290*sh* (4.3), 298*sh* (4.3), 313 (4.4); PMR (60 M Hz, DMSO): 1–3.2 (*m*), 3.80 (*s*, 3H), 4.00 (*t*, *J* = 6 Hz), 5.25 (*s*, $W_{\frac{1}{2}}$ = 28 Hz), 6.35 (*d*, *J* = 16 Hz, 1H), 6.6–7.6 (*m*).

Natural 10–epi-*desmethoxyabresline* (**5**). The fractions obtained after separation of **1** [1] and which contained 10-*epi*-desmethoxyabresoline were purified by repeated PLC in the following order: systems XVIb, VIc, VIc, and VIc The natural product was shown to be identical, (MS; IR, UV; TLC; systems Ia triple development, IIb, VIa double development, VIb, VII, XIb, XIII, XVIa, XVIIa triple development). In system XIb the new alkaloid resolved into a major and a minor alkaloidal band. PLC (XIb) gave, from the major band **5**, and from the minor band a mixture of **5** and the isomer of **5** with a *cis*-olefinic bond Hydrolysis of the mixture (4N NaOH, reflux 30 min) gave **3** [3] (TLC systems IIc, VIa, XIb) and a mixture of *trans* and *cis* *p*-hydroxycinnamic acids (TLC, systems XXI, XXII, XXIV, and the cellulose systems [10] XXV and XXVI).

Compound **8** *from* **5**. To natural 10-*epi*-desmethoxyabresoline (**5**) (5.1 mg) in Me_2CO (0.8 ml) was added *p*-bromophenacyl bromide (24 mg) and K_2CO_3 (13 mg) and the mixture was heated under reflux for 4 hr. Additional *p*-bromophenacyl bromide (12 mg) and K_2CO_3 (5.3 mg) was added and reflux was continued for 3 hr. TLC inspection of the reaction product showed that both **7** and **8**, the major compound, had been formed PLC (system XVIIa) gave the monoether (8); **7** was

not isolated. This derivative (**8**) of the natural product was shown to be identical with **8** obtained in the sythetic sequence towards **5** by its IR spectrum and TLC (systems IIa, III, V, VIb, VIII, XIa, b, XII, XVIIIa, b).

Acknowledgement—The authors thank J. M. Edwards for his valuable assistance and advice during the course of this investigation and in the preparation of this manuscript.

REFERENCES

1. (a) Hörhammer, R. B., Schwarting, A. E. and Edwards, J. M. (1975) *J. Org. Chem.* **40**, 656; (b) Hörhammer, R B (1973) Ph.D. Thesis, University of Connecticut.
2. Ferris, J. P., Boyce, C. B. and Briner, R. C. (1966) *Tetrahedron Letters* 5129.
3. Rother, A. and Schwarting, A. E. (1975) *Lloydia* **38**, 477.
4. Bohlmann, F. (1958) *Chem. Ber.* **91**, 2157.
5. (a) Rosazza, J. P., Bobbitt, J. M. and Schwarting, A. E. (1970) *J. Org. Chem.* **35**, 2564; (b) Rosazza, J. P. (1968) Ph.D. Thesis, University of Connecticut.
6. Bohlmann, F., Schumann, D. and Arndt, Ch. (1965) *Tetrahedron Letters* 2705.
7. Crabb, T. A., Newton, R. F. and Jackson, D. (1971) *Chem. Rev.* **71**, 109.
8. Hendrickson, J. B. and Kandall, C. (1970) *Tetrahedron Letters* 343.
9. Hanaoka, M., Ogawa, N. and Arata, Y. (1976) *Chem. Pharm. Bull.* **24**, 1045.
10. Murakoshi, I., Sugimoto, K., Haginiwa, J., Ohmiya, S. and Otomasu, H. (1975) *Phytochemistry* **14**, 2714.
11. Schmid, H. and Karrer, P. (1945) *Helv. Chim. Acta* **28**, 722.