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IMPROVED METHODS OF SYNTHESIS OF LIGNAN ARYLNAPHTHALENE LACTONES VIA ARYLPROPARGYL ARYLPROPIOLATE ESTERS

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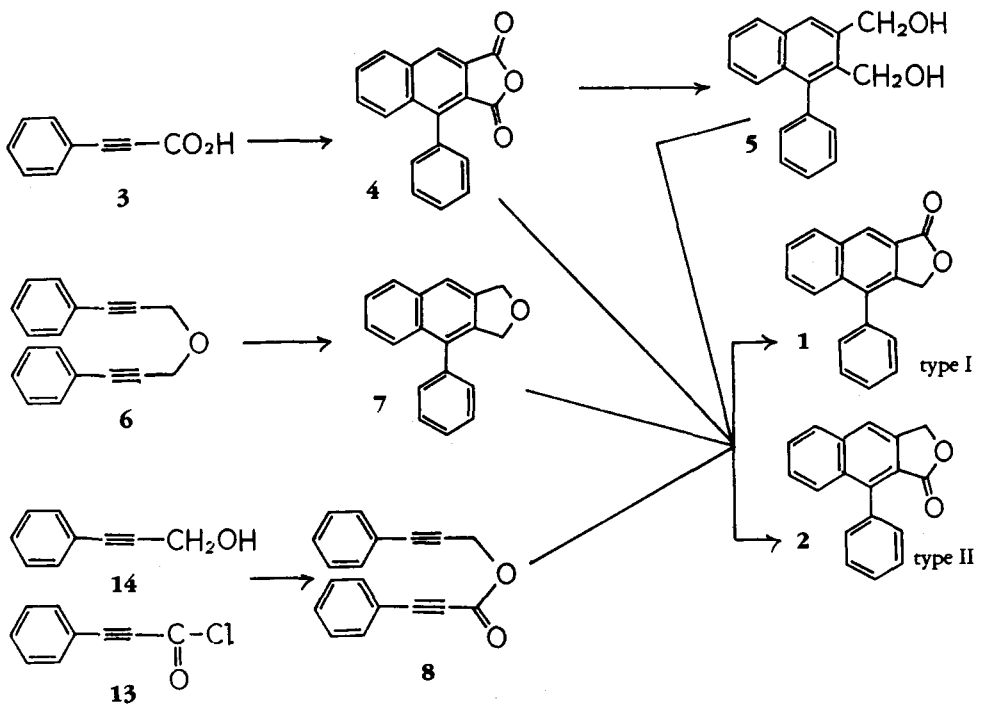
ABSTRACT.—The solid-phase copolymer of 4-vinylpyridine (P4-VP) is an excellent reagent for conversion of arylpropiolic acids to 1-arylnaphthalene-2,3-dicarboxylic acid anhydrides. Treatment of an acid chloride with P4-VP followed by alcohol addition provides a convenient esterification procedure, applicable to the formation of diynic esters, e.g., **8** from phenylpropiolic acid [**3**] and phenylpropargyl alcohol [**14**]. By heating under reflux in xylene, phenylpropargyl phenylpropiolates (e.g., **8**) are converted in excellent yield to the arylnaphthalene type I and type II lactones **1** and **2**, respectively, in a 1:1 ratio. Using these procedures, the lignan arylnaphthalene lactones, justicidin E [**9**], taiwanin C [**10**], helioxanthin [**18**], retrohelioxanthin [**19**], dehydrodimethylconidendrin [**23**], and dehydrodimethylretrodendrin [**24**], have been synthesized.

The increasingly diverse structures of natural lignans have created an interest which is reflected in the frequent review of their chemistry (1–6). A wide range of associated biological activity (antitumor, antimitotic, antiviral, antimicrobial, fungistatic, and enzyme inhibitory) is now recognized and was reviewed in 1984 (7). More recently, it has been discovered that several lignans are platelet-activating factor antagonists (8–10) with potential for therapeutic application to the variety of physiopathological conditions (e.g., inflammation, acute allergy, asthma, toxic shock, gastric ulceration) implicated with this mediator (11).

Arylnaphthalene lignans, of which more than 30 natural members are known, are a well-recognized subclass, over 90% of which are lactones, structurally based upon 1-phenyl-2-hydroxymethylnaphthalene-3-carboxylic acid lactone [**1**] (Type I) or 1-phenyl-3-hydroxymethylnaphthalene-2-carboxylic acid lactone [**2**] (Type II). Procedures that have been developed for the synthesis of **1** and **2** should be applicable to the preparation of arylnaphthalene lignans that bear aryl ether and/or phenolic functionality in rings A and C. In this connection, intramolecular cyclization procedures are of particular interest in view of starting material structural simplicity and economy of involved steps. These are summarized in Scheme 1.

In the earliest procedure, dating from 1895 (12), the product obtained by heating phenylpropiolic acid [**3**] with Ac_2O under reflux proved to be 1-phenylnaphthalene-2,3-dicarboxylic anhydride [**4**] (13–16). The general applicability of this procedure for many phenylpropiolic acids is now established, notably in the work of Baddar and coworkers (17). In cases where the severity of the conditions resulted in undesirable side reactions, it was shown that the desired self-condensation could be obtained at 0° by treatment of the arylpropiolic acid with *N,N*-dicyclohexylcarbodiimide (18,19), and the scope of this procedure modification has been explored (20). Reduction of the anhydride **4** with zinc and HOAc gave both lactones **1** and **2** in approximately equal amounts, and with $LiAlH_4$ at 0°, there was a regio preference for formation of the type I lactone **1** in a ratio of ca. 2:1 (21). Alternatively, as shown in lignan lactone synthesis, reduction of the anhydride with excess $LiAlH_4$ to the diol **5** followed by Fétizon oxidation gives a strong preference (ca. 9:1) for the type I lactone (22).

A second approach involves the base-promoted cyclization of bis-(3-phenyl-2-propenyl) ether [**6**] to yield the phenyldihydronaphthofuran **7** (21,23), which on benzylic oxidation with Jones' reagent gave both lactones **1** and **2** with oxidation predominating as expected (ratio ca. 2.7:1) at the less hindered C-3 site. This procedure as extended to lignan synthesis, however, may have limited generality. In a reported synthesis of



SCHEME 1

taiwanin C [**10**], the oxidation of the relevant phenyldihydronaphthofuran with Jones' reagent failed, and of the two possible lactone isomers **9** and **10**, only **10** was isolated in low yield after oxidation with chromium trioxide in a basic solvent system (24).

In a series of papers under the wide rubric of Intramolecular Diels-Alder Reactions (25), Klemm and co-workers in the period 1963–1976 examined the cyclization inter alia of phenylpropargyl phenylpropiolate esters, i.e., functionality designed to produce arylnaphthalene lactones essentially in one step. Thus, when the diynic ester **8** was heated under reflux with Ac_2O, the only reported product isolated (in 39% yield) was the lactone **2** (26). When these conditions were applied to diynic esters with appropriate aryl ether lignan group functionality, there were clear indications that both type I and II lactones were formed, although the very low yields (generally <25% combined) precluded reliable assessment of the modal selectivity of cyclization (27).

RESULTS AND DISCUSSION

We report here improved procedures for the synthesis of arylnaphthalene-2,3-dicarboxylic anhydrides, the preparation of arylpropargyl propiolate esters, and the cyclization of the latter to arylnaphthalene lactones of natural occurrence.

It has recently been shown that a solid-phase co-polymer of 4-vinylpyridine (P4-VP) is a highly effective reagent/catalyst for formation of mixed anhydrides from equimolar quantities of carboxylic acids and acid chlorides and of simple (symmetric) anhydrides by treatment of a carboxylic acid with a half equivalent of thionyl chloride (28,29). On subjecting phenylpropiolic acid [**3**] to these latter conditions at room temperature, we find that the cyclized anhydride **4** was formed and readily isolated in 88% yield. The mildness of the reaction conditions and the additional advantage that the released HCl will be bound to the solid phase suggested that this procedure would be particularly useful for the synthesis of those lignan arylnaphthalene lactones which bear identical substituents on rings A and C, such as justicidin E [**9**] and taiwanin C [**10**].

Accordingly, 3,4-methylenedioxyphenylpropiolic acid [**11**] was reacted with thionyl chloride and P4-VP in CH_2Cl_2 under reflux (for solubility reasons) and gave in 87% yield the cyclized anhydride **12**, the reduction of which to the natural lactones **9** and **10** has been previously reported (22,30).

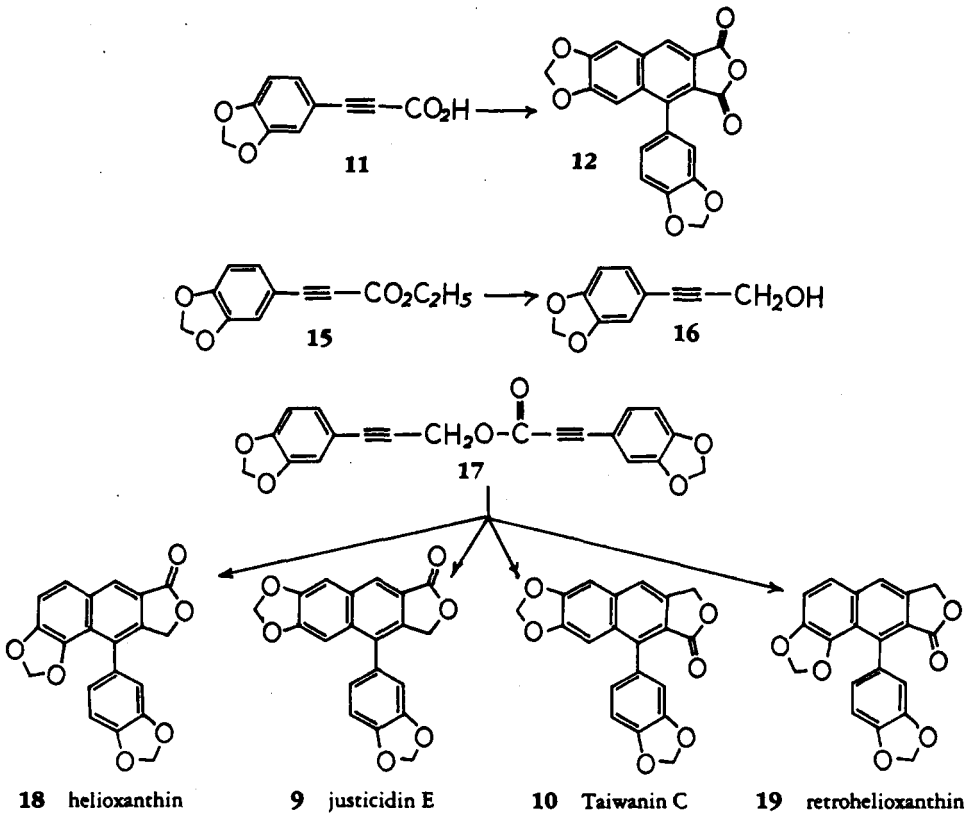
We considered that this polymer-mediated methodology might be extended advantageously to the preparation and subsequent cyclization of diynic esters of the phenylpropargyl phenylpropiolate type (e.g., **8**). To develop conditions for general simple ester formation, we examined the reaction of benzoyl chloride with a variety of alcohols. The polymer P4-VP was stirred with the acid chloride in CH_2Cl_2 for 15 min, and the alcohol was added with overnight stirring at room temperature. In this manner the benzoate esters of MeOH, EtOH, iPrOH, *t*-BuOH, and *trans*-cinnamyl alcohol were obtained in isolated yields surpassing 93%. When phenylpropiolic acid chloride [**13**] was similarly reacted with alcohols in equimolar ratio, the ester yields were in the 35–45% range. When the acid chloride to alcohol ratio of 2:1 was used, however, yields were restored to 91–93%. Under these latter conditions **13**, obtained from **3** by the action of thionyl chloride, was reacted with phenylpropargyl alcohol [**14**] and gave the desired diynic ester **8** in 71% yield.

It was reported by Klemm *et al.* (26) that the ester **8** on heating with Ac_2O for 5 h gave the type II lactone **2** in 39% yield. In our hands under the same conditions, in addition to lactone **2** obtained in comparable yield, the type I lactone **1** in 6% yield and unchanged ester (36%) were also isolated. In an examination of alternative solvent systems (C_6H_6, toluene, xylenes, and DMF) in which to effect the cyclization step, we found the most efficient to be xylenes in which the ester **8** was quantitatively cyclized, but significantly to a 1:1 mixture of both type I **1** and type II **2** lactones.

We next examined the application of these improved experimental conditions to the synthesis of the natural piperonyl analogues, justicidin E [**9**], first isolated from *Justicia procumbens* (31), and taiwanin C [**10**], first isolated from *Taiwania cryptomeriodes* (32). The intermediate diynic ester [**17**] required for this purpose was obtained in the following way. Piperonal was treated with triethyl phosphonoacetate under the conditions devised by Wadsworth and Emmons (33) for formation of propiolate esters; this yielded ethyl 3,4-methylenedioxyphenylpropiolate [**15**] which was then reduced with diisobutylaluminium hydride to yield 3,4-methylenedioxyphenylpropargyl alcohol [**16**]. Conversion of the acid **11** to the acid chloride and reaction with **16** under the P4-VP polymer-mediated conditions gave **17** in 92% yield.

The crude product mixture obtained by thermal treatment (refluxing xylenes for 5 h) of the diynic ester **17** was examined by analytical tlc, and total conversion to four products was revealed (Scheme 2). These proved to be the expected major products **9** and **10** accompanied in lesser amounts by the ring-A analogues with C-7,-8 methylenedioxy substitution. These minor products are helioxanthin [**18**], a natural product isolated from the roots of *Heliopsis helianthoides* (34) and the known (19) type II lactone analogue retrohelioxanthin [**19**]. Flash chromatography of the mixture on Si gel afforded a ready separation of type I from type II lactones, and from these fractions the major and minor constituents were then separated by preparative tlc. The ratio of type I to type II lactones was again 1:1, and the 6,7-disubstituted to 7,8-disubstituted product ratio was ca. 2.5:1. Each product was identified by the characteristic nmr spectrum (see Table 1) and comparison with authentic specimens.

The veratryl analogues of justicidin E and taiwanin C are known respectively as dehydrodimethylconidendrin [**23**] and dehydrodimethylretrodendrin (**24**). Although not yet apparently reported to be naturally occurring, they have been significant in the structure elucidation of natural aryltetralin lactone lignans from which they are obtained by dehydrogenation processes. They are now conveniently synthesized by this



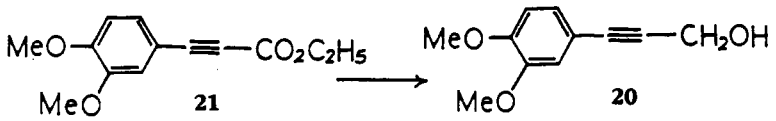
SCHEME 2

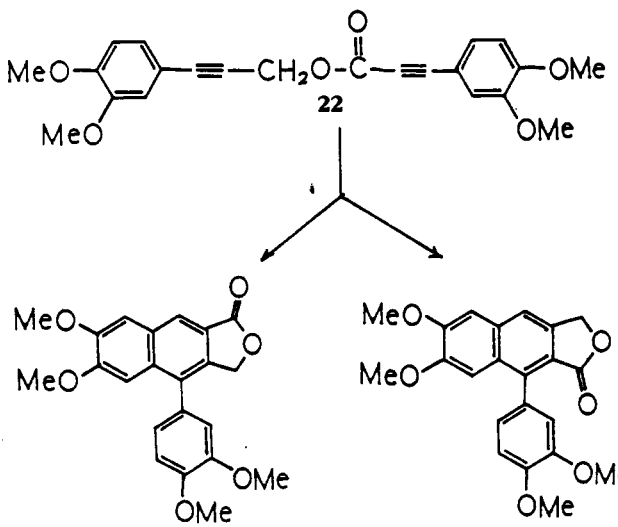
present method. 3,4-Dimethoxyphenylpropargyl alcohol [**20**] was obtained by DIBAL reduction of ethyl 3,4-dimethoxyphenylpropiolate [**21**], prepared from veratraldehyde via the Wadsworth-Emmons procedure. Esterification of **20** with 3,4-di-

TABLE 1. Synthetic/Natural Lactone ^{1}H-Nmr Comparison Data.

Proton	Compound			
	18	**9**	**10**	**19**
Lactone -CH_2-	5.19 s	5.17 s	5.38 s	5.38 s
Ring A -OCH_2O-	5.96 s	6.07 s	6.07 s	5.91 d (J=2)
Ring C -OCH_2O-	6.07 s	6.07 s	6.07 s	6.04 d (J=1)
H-4	8.42 s	8.27 s	7.69 s	7.83 s
H-5	7.72 d (J=9.5)	7.32 s	7.20 s	7.58 d (J=8)
H-6	7.31 d (J=9.5)	—	—	7.32 d (J=8)
H-8	—	7.10 s	7.13 s	—
H-2′	6.81–6.86 m	6.82 d (J=1)	6.82 d (J=1)	6.74–7.08 m
H-5′		6.98 d (J=8)	6.98 d (J=8)	
H-6′		6.77 dd (J=8,1)	6.78 dd (J=8,1)	

methoxyphenylpropiolic acid chloride in the presence of P4-VP gave the diynic ester **22**, which without purification was heated in xylenes. Flash chromatography of the product readily separated **23** and **24** and, interestingly, without significant formation of the expected 7,8-dimethoxy isomers (Scheme 3).





23 dehydrodimethylconidendrin **24** dehydrodimethylretrodendrin

SCHEME 3

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—^{1}H-nmr spectra were determined in $CDCl_3$ solution with TMS as internal standard, using Varian EM390 and XL300 spectrometers. Tlc analyses were performed on Kodak Chromagram Sheets Si gel with fluorescent indicator (20 × 20 cm) and were developed by I_2 vapor exposure or uv irradiation. Cc was conducted on Si gel (Kieselgel 40, 70–239 mesh, EM Science) or neutral alumina (alumina Woelm, activity grade 1). Flash chromatography was conducted with Universal Adsorbents Si gel 32–63, 40 μm mesh under a positive pressure of N_2. Preparative tlc was conducted on Analtech Si gel GF (1000 μm, 20 × 20 cm). Petroleum ether (bp 20–40°) was from J.T. Baker, and C_6H_6 was distilled from a solution containing the blue ketyl formed by reaction of Na metal with a small quantity of benzophenone. P4-VP-Reillex 425 (Reilly Tar and Chemical Corporation) was oven-dried at 125° to constant weight (ca. 24 h).

1-PHENYLNAPHTHALENE-2,3-DICARBOXYLIC ACID ANHYDRIDE [**4**].—A solution of thionyl chloride (0.32 g) in CH_2Cl_2 (20 ml) was added dropwise over 20 min with stirring to a solution of phenylpropiolic acid (0.73 g, 5 mmol) in the same solvent (10 ml) with suspended P4-VP polymer (2.2 g). Stirring was continued for 1 h, and the mixture was filtered. The polymer was washed with CH_2Cl_2 (3 × 25 ml) and the combined filtrate and washings evaporated to yield a foam residue which on one crystallization from $CHCl_3/Et_2O$ gave the anhydride **4** as a pale yellow solid (1.2 g), mp and mmp 254–255° [lit. (12) mp 255–256°]; ^{1}H nmr δ ($CDCl_3$) 7.4–8.2 (complex m, 9 ArH), 8.57 (s, H-4); ir ν (KBr) 1828, 1776 cm^{-1} (anhydride C=O).

6,7-METHYLENEDIOXY-1-(3′,4′-METHYLENEDIOXYPHENYL)NAPHTHALENE-2,3-DICARBOXYLIC ACID ANHYDRIDE [**12**].—A solution of thionyl chloride (0.32 g) in CH_2Cl_2 (10 ml) was added dropwise over 20 min to a refluxing solution of 3,4-methylenedioxyphenylpropiolic acid (0.95 g, 5 mmol) and sus-

pension of P4-VP polymer (2.2 g) in the same solvent (125 ml). After refluxing for 6 h, the mixture was filtered and washed with hot solvent (3 × 25 ml), and the combined filtrate and washings were evaporated under reduced pressure. The residual oil was dissolved in C_6H_6 filtered through a 1-in. plug of Si gel. Crystallization of the eluted yellow foam from $CHCl_3$/petroleum ether (bp 37–55°) gave the anhydride as a yellow solid (0.79 g): mp 244–245° [lit. (35) mp 244–246°]; ^{1}H nmr δ [$(CD_3)_2SO$] 6.15 (dd, J = 3.5, 0.9 Hz, -OCH_2O-), 6.57 (s, -OCH_2O-), 6.81 (dd, J = 6.2, 1.8 Hz, H-6′), 6.98 (d, J = 1.8 Hz, H-2′), 7.05 (d, J = 0.8 Hz, H-8), 7.09 (d, J = 6.2 Hz, H-5′), 7.75 (s, H-5), 8.52 (s, H-4); ir ν (KBr) 1829, 1779 cm^{-1} (anhydride C=O).

POLYMER-MEDIATED ESTER FORMATION FROM BENZOYL CHLORIDE.—Benzoyl chloride (0.7 ml, 6 mmol) was added to a stirred suspension of P4-VP polymer (2 g) in CH_2Cl_2 (20 ml). After stirring for 15 min, MeOH (0.2 g, 6 mmol) in CH_2Cl_2 (5 ml) was added dropwise over 5 min, and the mixture was stirred overnight and filtered. The filtrate and CH_2Cl_2 polymer washings (3 × 25 ml) were combined and evaporated. Distillation of the residual oil gave methyl benzoate (99% yield). By the same procedure there were obtained ethyl benzoate, isopropyl benzoate, *t*-butyl benzoate, and *trans*-cinnamyl benzoate in yields surpassing 93%.

POLYMER-MEDIATED ESTER FORMATION FROM PHENYLPROPIOLIC ACID CHLORIDE.—Esterifications conducted as for benzoyl chloride above gave with phenylpropiolic acid chloride (prepared from phenylpropiolic acid without isolation) and respective alcohol (in 1:1 molar ratio) isopropyl phenylpropiolate (37% yield), *t*-butyl phenylpropiolate (45% yield), and *trans*-cinnamyl phenylpropiolate (36% yield). By using an acid to alcohol mol ratio of 2:1, the yields in each case were raised to 91–93%.

PHENYLPROPARGYL PHENYLPROPIOLATE [**8**].—Phenylpropiolic acid (0.72 g, 5 mmol) was added with stirring to freshly distilled thionyl chloride (5 ml) at room temperature until solution was complete (ca. 3 h). Excess thionyl chloride was removed by repeated addition of C_6H_6 and evaporation under reduced pressure. The product acid chloride [ir ν ($CHCl_3$) 2222 (C≡C), 1770 and 1733 cm^{-1} (COCl)] was dissolved in CH_2Cl_2 (10 ml) and added to a stirred suspension of P4-VP polymer (2 g) in CH_2Cl_2. After stirring for 15 min, phenylpropargyl alcohol (0.33 g, 2.5 mmol) was added, and the mixture was stirred overnight and worked up in the usual way. The residual gum product was chromatographed on Si gel, and elution with $CHCl_3$-petroleum ether (1:1) yielded the ester **8** as a pale yellow oil (470 mg): ir ν ($CHCl_3$) 1786 cm^{-1} (C=O); ^{1}H nmr δ 5.00 (s, CH_2), 7.19–7.79 (complex m, ten ArH).

INTRAMOLECULAR CYCLIZATION OF PHENYLPROPARGYL PHENYLPROPIOLATE [**8**].—*In* C_6H_6.—A solution of the ester **8** (100 mg) was heated under reflux in C_6H_6 (5 ml) for 5 h, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography on Si gel with hexane-EtOAc (9:1) with collection of 20-ml fractions (analyzed by tlc). Fractions 1–4 gave no residue. Fractions 5–7 yielded unchanged ester **8** (60 mg, 60%). Fractions 8–10 gave no residue, followed by fractions 11–16 which contained 1-phenyl-2-hydroxymethylnaphthalene-3-carboxylic acid lactone [**1**] (16 mg, 16%) which crystallized from $CHCl_3$/petroleum ether as prisms: mp 165–166° [lit. (21) mp 164.5–165.5°]; ^{1}H nmr δ ($CDCl_3$) 5.24 (s, lactone CH_2), 7.31–8.19 (complex m, nine ArH), 8.49 (s, H-4). After fractions 17–18 gave no residue, fractions 19–22 gave 1-phenyl-3-hydroxymethylnaphthalene-2-carboxylic acid lactone [**2**] (16 mg, 16% yield) as needles: mp 186–190° [lit. (26) mp 185–187°]; ^{1}H nmr δ ($CDCl_3$), 5.46 (s, lactone CH_2), 7.23–8.08 (complex m, ten ArH).

In toluene.—As conducted in C_6H_6 above, there was obtained unchanged ester (36%) and lactone mixture (1:1 ratio, 59%).

In xylenes.—Xylenes were from Fisher Scientific (Certified ACS). As conducted in C_6H_6 above, the lactone mixture (1:1 ratio) was isolated in 96% yield.

In DMF.—There was obtained unchanged ester (22%), lactone **1** in 29% yield, and lactone **2** in 44% yield.

In Ac_2O.—There was obtained unchanged ester (36%), lactone **1** in 6% yield, and lactone **2** in 38% yield.

ETHYL 3,4-METHYLENEDIOXYPHENYLPROPIOLATE [**15**].—Triethyl phosphonoacetate (8.4 g) was added dropwise over 30 min to a stirred suspension of 60% NaH (1.5 g) in dry THF (40 ml) with the temperature maintained below 10°. After H_2 evolution had ceased (ca. 20 min), a solution of I_2 (9.5 g) in dry THF (30 ml) was added dropwise with stirring and cooling below 10°. After 30 min, 60% NaH (3 g) was added, and the temperature allowed to rise to 25° with stirring until gas evolution again ceased. A solution of piperonal (5.6 g) in THF (60 ml) was then added over 15 min, and the mixture stirred at 35–40° for 3 h, cooled below 10°, and diluted with H_2O (300 ml). The precipitate (6.46 g) which resulted on overnight standing was collected and recrystallized from petroleum ether (bp 37–50°) to give the ethyl propio-

late ester **15** as a solid (5.21 g, 66% yield): mp 82–83° [lit. (36) mp 83.5–84°]; ir ν ($CHCl_3$) 2224 (C≡C), 1703 (C=O) cm^{-1}; ^1H nmr δ ($CDCl_3$) 1.39 (t, J = 9 Hz, Me), 4.31 (q, J = 9 Hz, OCH_2Me), 6.04 (s, OCH_2O), 6.81 (d, J = 9 Hz, H-5), 7.08 (d, J = 2 Hz, H-2), 7.21 (dd, J = 9 Hz, H-6).

3,4-METHYLENEDIOXYPHENYLPROPARGYL ALCOHOL [**16**].—Di-isobutylaluminium hydride (12.3 ml of a 1.0 M solution in hexane) was added by syringe to a solution of ethyl 3,4-methylenedioxyphenylpropiolate (1.16 g) in THF (15 ml) at −78° under N_2. After the mixture had warmed to room temperature, addition of saturated NH_4Cl solution (1.5 ml) produced a gel that was dispersed by addition of 10% HCl (3 ml). Et_2O (25 ml) was added and the organic layer washed with 10% HCl (2 × 20 ml), brine, and H_2O. Evaporation of the dried extract gave a solid, which on crystallization from C_6H_6/petroleum ether gave 3,4-methylenedioxyphenylpropargyl alcohol [**16**] as a solid (1.1 g): mp 74–76° [lit. (27) mp 75–76°]; ir ν ($CHCl_3$) 3600 (OH), 2221 (C≡C) cm^{-1}; ^1H nmr δ ($CDCl_3$) 2.98 (br s, OH), 4.39 (s, CH_2), 5.91 (s, OCH_2O), 6.51 (d, J = 9 Hz, H-5), 6.69 (d, J = 2 Hz, H-2), 6.93 (dd, J = 9,2 Hz, H-6).

3,4-METHYLENEDIOXYPHENYLPROPARGYL 3,4-METHYLENEDIOXYPHENYLPROPIOLATE [**17**].—3,4-Methylenedioxyphenylpropiolic acid [**11**] (600 mg) was added to freshly distilled thionyl chloride (4 ml) at room temperature until solution was complete (3 h). Excess thionyl chloride was removed by repeated addition of C_6H_6 and evaporation under reduced pressure. The residual orange oil was dissolved in CH_2Cl_2 (10 ml) and added to a suspension of P4-VP polymer (1.5 g) in CH_2Cl_2 (20 ml) with stirring for 15 min. A solution of 3,4-methylenedioxyphenylpropargyl alcohol [**16**] (540 mg) in CH_2Cl_2 (5 ml) was then added, and the mixture was stirred at room temperature for 24 h and worked up in the usual way. The residual oil product (1.06 g) was chromatographed on neutral alumina, and elution with Et_2O-petroleum ether (1:1) gave the ester **17** as an oil that crystallized from Et_2O as a colorless solid (1.0 g): mp 135–138°; ir ν ($CHCl_3$) 2225 (C≡C), 1722 (C=O) cm^{-1}; ^1H nmr δ ($CDCl_3$) 4.99 (s, CH_2), 5.95 and 5.98 (s, two OCH_2O groups), 6.61–7.31 (m, six ArH).

INTRAMOLECULAR CYCLIZATION OF 3,4-METHYLENEDIOXYPHENYLPROPARGYL 3,4-METHYLENEDIOXYPHENYLPROPIOLATE [**17**].—*Isolation of helioxanthin* [**18**], *justicidin E* [**9**], *taiwanin C* [**10**] *and retrohelioxanthin* [**19**].—A solution of the ester **17** (500 mg) in xylenes (5 ml) was heated under reflux for 5 h and the solvent removed under reduced pressure. The residual oil [two broad spots, R_f 0.68 and 0.57 on tlc analysis on silica with hexane-EtOAc (4:1)] was subjected to flash chromatography on Si gel with hexane-EtOAc (4:1) under a positive pressure of N_2 with 20-ml aliquots being collected and assayed by tlc in the same manner as above.

After fractions 1–9 gave no product, fractions 10–23 yielded a colorless oil (135 mg, R_f 0.72 and 0.68) which was subjected to preparative tlc [hexane-EtOAc (95:5), multiple elution]. The faster running zone (corresponding to R_f 0.72) on elution with EtOAc gave a solid which after one crystallization from EtOH gave helioxanthin [**18**] as pale yellow prisms (49 mg): mp 244–245° [lit. (19) mp 243–244°]; ir ν ($CHCl_3$) 1764 (C=O) cm^{-1}; ^1H nmr (see Table 1). The slower running zone (corresponding to R_f 0.68) on similar extraction and crystallization from $CHCl_3$ gave justicidin E [**9**] as needles (50 mg): mp 270–271° [lit. (35) mp 264°, lit. (31) 265–271°, lit. (22) 271–272°]; ir ν ($CHCl_3$) 1759 (C=O) cm^{-1}; ^1H nmr see Table 1. Fractions 24–33 gave a colorless oil which crystallized from $CHCl_3$ to yield a further quantity (60 mg) of justicidin E.

Fractions 34–49 gave a yellow oil (32 mg, R_f 0.68 and 0.54) which was similarly subjected to preparative tlc; the front-running zone (R_f 0.58) gave additional justicidin E (20 mg) and the slower-running zone (R_f 0.54) on crystallization from $CHCl_3$ gave taiwanin C [**10**] as a white solid (10 mg): mp 273–277° [lit. (35) mp 275°, lit. (32) 276°, lit. (22) 272–276.5°]; ir ν ($CHCl_3$) 1764 (C=O) cm^{-1}; ^1H nmr see Table 1. Fractions 50–77 gave a dark yellow oil (200 mg, R_f 0.54 and 0.50) which was re-subjected to flash chromatography as before. Fractions 16–28 gave further taiwanin C (90 mg), and fractions 29–53 gave an oil (87 mg, R_f 0.54 and 0.52). By preparative tlc of this product, the front-running zone gave more taiwanin C (24 mg) and the slow running zone gave an orange-brown solid, which on crystallization from MeOH gave retrohelioxanthin [**19**]: mp 263–270° [lit. (19) mp 264–268°]; ir ν ($CHCl_3$) 1762 (C=O) cm^{-1}; ^1H nmr see Table 1.

ETHYL 3,4-DIMETHOXYPHENYLPROPIOLATE.—Compound **21** was prepared from triethyl phosphonoacetate and 3,4-dimethoxybenzaldehyde exactly as for the piperonal analogue [**15**]. Crystallization from Et_2O gave the ester as a solid: mp 43–46° in 59% yield; ir ν ($CHCl_3$) 2220 (C≡C), 1705 (C=O) cm^{-1}; ^1H nmr δ ($CDCl_3$) 1.31 (t, J = 7 Hz, Me), 3.81 (s, OMe), 3.84 (s, OMe), 4.24 (q, J = 7 Hz, OCH_2Me), 6.78 (d, J = 9 Hz, H-5), 7.03 (d, J = 2 Hz, H-2), 7.19 (dd, J = 9,2 Hz, H-6).

3,4-DIMETHOXYPHENYLPROPARGYL ALCOHOL [**20**].—Compound **20** was prepared from the above ester by reduction with di-isobutylaluminium hydride as in the preparation of **16**. Crystallization of the product from C_6H_6/petroleum ether (bp 60–110°) gave the alcohol **20** as needles: mp 54–55° [lit. (27)

mp 55–55.5°]; ir ν ($CHCl_3$) 3600 (OH), 2220 (C ≡ C) cm^{-1}; ^1H nmr δ ($CDCl_3$) 2.92 (br s, OH), 3.80 (s, OMe), 3.82 (s, OMe), 4.42 (s, CH_2), 6.72 (d, J = 8 Hz, H-5), 6.88 (br s, H-2), 6.97 (dd, J = 8,2 Hz, H-6).

3,4-DIMETHOXYPHENYLPROPARGYL 3,4-DIMETHOXYPHENYLPROPIOLATE [**22**].—Compound **22** was prepared as for the methylenedioxy analogue **17** and was isolated in 73% yield as a colorless oil: ir ν ($CHCl_3$) 2222 (C C), 1723 (C=O) cm^{-1}; ^1H nmr ($CDCl_3$) 3.81 (s, two OMe), 3.92 (s, two OMe), 4.99 (s, CH_2), 6.51–7.31 (m, six ArH).

INTRAMOLECULAR CYCLIZATION OF 3,4-DIMETHOXYPHENYLPROPARGYL 3,4-DIMETHOXYPHENYLPROPIOLATE [**22**].—*Isolation of dehydrodimethylconidendrin* [**23**] *and dehydrodimethylretrodendrin* [**24**].—A solution of the ester **22** (600 mg) in xylenes (5 ml) was heated under reflux for 5 h, then worked up and subjected to flash chromatography on Si gel with petroleum ether-EtOAc (9:1) as for the methylenedioxy analogues. After fractions 1–12 gave no product, fractions 13–29 gave an orange solid (143 mg) which on recrystallization from MeOH gave dehydrodimethylconidendrin [**23**] as needles: mp 216–217° [lit. (22) mp 215–216°]; ir ν ($CHCl_3$) 1771 (C=O) cm^{-1}; ^1H nmr δ ($CDCl_3$) 3.81 (s, 7-OMe), 3.89 (s, 3′-OMe), 3.99 (s, 4′-OMe), 4.04 (s, 6-OMe), 5.24 (s, CH_2), 6.86–7.09 (m, 3 ArH), 7.15 (s, H-8), 7.34 (s, H-5), 8.32 (s, H-4).

Fractions 30–44 gave an orange oil (200 mg, with R_f 0.57 and 0.44 indicating mixture of **23** and **24**), followed by fractions 45–58 which gave a light yellow oil (130 mg), which on crystallization from MeOH gave dehydrodimethylretrodendrin [**24**] as yellow rhombs: mp 254–255° [lit. (22) mp 253–255°]; ir ν ($CHCl_3$) 1758 (C=O) cm^{-1}; ^1H nmr δ ($CDCl_3$) 3.75 (s, 7-OMe), 3.88 (s, 3′-OMe), 4.04 (s, 4′- 6-OMe), 5.34 (s, CH_2), 6.91–7.05 (m, 3ArH), 7.18 (s, H-8), 7.22 (s, H-5), 7.73 (s, H-4).

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ERRATUM

The authors have requested the following corrections for the paper entitled "Two New Bioactive Carbazole Alkaloids from the Root Bark of *Clausena harmandiana*," *J. Nat. Prod.*, **51**, 1285 (1988).

The corrected ^{1}H-nmr assignments for compound **2** should be 6.81 (1H, dd, $J=8.2, J=2$, H-6), 6.99 (1H, d, $J=2$, H-8), 7.89 (1H, d, $J=8.2$, H-5).

ERRATUM

The authors have requested the following correction for the paper entitled "Phytochemical Studies of the Chinese Herb Tai-Zi-Shen, *Pseudostellaria heterophylla*," *J. Nat. Prod.*, **51**, 1236 (1988).

In Table 1, the COSY correlations should indicate that proton 2′ correlates with proton 4′ but not with proton 3′ as shown.