samples were estimated spectrophotometrically on the basis of ϵ 29 870 at 300 nm for (±)-1 in CCl_4.[2]

Registry No. (±)-1, 88130-94-3; (+)-1, 74443-33-7; (−)-1, 74453-39-7; poly(triphenylmethyl methacrylate), 27497-74-1.

The Identity of 4-Bromo-3-phenylisoçoumarin.[1] A Facile Preparation by Bromolactonization of Alkyl 2-(2-Phenylethynyl)benzoates

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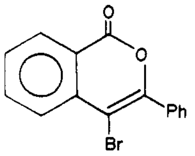
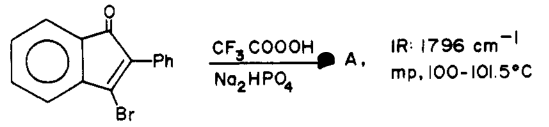
In a recent report[2] on syntheses of halo enol lactones, the title compound 1 was suggested as the product (A) of



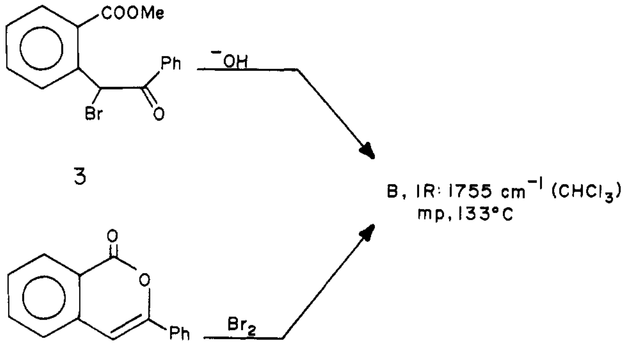
1

the reaction of 3-bromo-2-phenylinden-1-one (2) and trifluoroperacetic acid in the presence of sodium diphosphate.



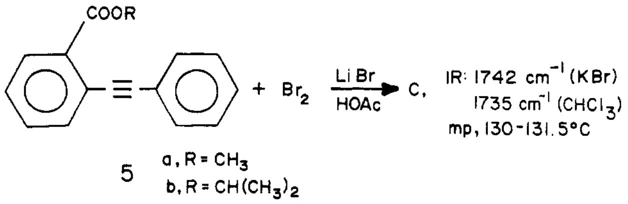
2

Compound 1 had been previously suggested[3] as the product (B) in the base-catalyzed cyclization of methyl 2-(1-bromo-2-oxo-2-phenylethyl)benzoate (3). The latter claim was bolstered by the fact that B was isolated[3] in the bromination of 3-phenylisocoumarin (3-phenyl-1*H*-benzo-2-pyran-1-one, 4).



4

This discrepancy was noticed in this laboratory as a result of an unsuccessful attempt to prepare some 1,2-dibromo-1,2-diphenylethene derivatives. Product C was isolated in 78% yield from the bromination of the substituted ethyne methyl 2-(2-phenylethynyl)benzoate (5a) in acetic acid containing lithium bromide. The reaction was also conducted in ether and CCl_4 at temperatures ranging from −40 to 25 °C; C was the only product isolated. Bromination of the isopropyl ester **5b** at −40 °C in ether afforded C in 92% crude yield. Numerous attempts to grow a single crystal for X-ray analysis failed.

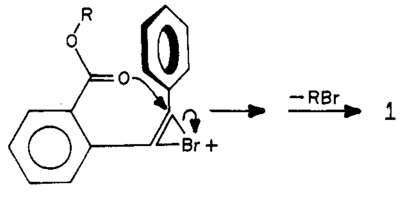


When C was treated with tributyltin hydride, 4 was the only product isolated other than starting material. The ^{1}H NMR spectrum and MS data of C matched those reported for B.

Based on these data, it is proposed that B and C are the same compound, viz., 1. The carbonyl stretch for 1 lies in the reported[4] range, 1670–1755 cm^{-1}, for a series of isocoumarins. Product A is outside this range and the range reported for coumarins.[4] In the absence of data other than the IR data, a speculation is that A is the epoxide of 2. The carbonyl stretch for A suggests a five-membered ring.

It is of interest to contrast the bromination of 5 with an ethene analogue,[5] 2-(2-phenylethenyl)benzoic acid. In the case of the latter, lactonization occurs in acetic acid or chloroform but dibromide is formed in carbon tetrachloride. No such solvent effect is observed with 5. Whether this difference is due to the triple bond or the ester group remains to be explored.

The regioselectivity seen in the bromolactonization of 5 is predictable. Baldwin's rules[6] for cyclization permit both 6-Endo-Dig and 5-Exo-Dig, although many lactonizations of acetylenic compounds[2,7] give the exo product. In this reaction, cyclization likely occurs after formation of a bridged bromonium ion. Cyclization can then occur as a 6-Endo-Trig or 5-Exo-Trig process; both are permitted by Baldwin's rules. The factor that dominates the regioselectivity in these cyclizations is the relative charge density on the two carbons of the putative bridged cationic intermediate. For 5, the electron-donating phenyl group stabilizes its side of the bromonium ion intermediate more so than does the (alkoxycarbonyl)phenyl group. The (alkoxycarbonyl)phenyl group is also less effective in stabilizing positive charge on its end of the bridged ion because the cyclic transition structure constrains the π system of this aryl group to be orthogonal to the π orbitals involved in the complexing of the bromonium ion. The phenyl group, being free to rotate, can provide stabilization.[8] This stabilization likely produces the observed regiospecificity.



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(8) We thank referee I for this suggestion.

0022-3263/84/1949-0558$01.50/0

The high yield of the lactonization step coupled with the ease of preparation of the ethynes[9] makes this procedure a potentially useful approach to isocoumarins (1*H*-benzo-2-pyran-1-ones). The presence of bromine at the 4 position permits ready elaboration to more complex derivatives.

Experimental Section

4-Bromo-3-phenyl-1*H*-benzo-2-pyran-1-one (1). A solution of bromine (0.2 mL) in 10 mL of acetic acid was added dropwise to a mixture of 0.48 g of methyl 2-(2-phenylethynyl)benzoate,[9] (**5a**, 2.0 mmol) and 0.25 g of lithium bromide (2.9 mmol) in 10 mL of acetic acid, and the reaction was stirred overnight. The reaction mixture was added to 50 mL of water and the product filtered. The filter cake was washed with water, a sodium thiosulfate solution, and again with water and dried to give 0.47 g of **1**: mp (uncorr) 130–131.5 °C (recrystallized from cyclohexane) (lit.[3] 133 °C); mass spectrum, *m/e* (relative intensity) 302 (84), 300 (98), 274 (52), 272 (53), 221 (9), 193 (88), 165 (83), 164 (27), 105 (100), 88 (39), 77 (97); IR (KBr) 1742, 1623, 1603, 1478, 1403, 1236, 1090, 1080, 1058, 1035, 1025, 964, 761, 754, 692, 647 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.33–8.26 (m, 1 H), 7.94–7.87 (m, 1 H) 7.85–7.72 (m, 3 H) 7.60–7.50 (m, 1 H) 7.50–7.41 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHZ) δ 160.88 (s), 151.64 (s), 136.44 (s), 135.29 (d), 132.64 (s), 130.08 (d), 129.59 (d), 129.53 (d), 129.01 (d), 127.98 (d), 126.48 (d), 120.45 (s), 101.19 (s).

3-Phenyl-1*H*-benzo-2-pyran-1-one (4). Tributyltin hydride (45 mg) and **1** (32 mg) were stirred together (no solvent) at 145 °C for 14 h. The crude product was purified by TLC (silica gel, $CHCl_3$) to give 12 mg of **4** (51%) and 13 mg of **1** (41%): mp (uncorr) 91.5–92.5 °C (recrystallized from cyclohexane) (lit.[10] 91–92 °C; IR (KBr) 1719 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 8.36–8.27 (m, 1 H), 7.94–7.86 (m, 2 H), 7.78–7.67 (m, 1 H), 7.56–7.43 (m, 5 H), 6.96 (s 1 H).

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Registry No. 1, 22115-36-2; 4, 4809-08-9; **5a**, 33578-05-1; **5b**, 88180-65-8.

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Ilikonapyrone Esters, Likely Defense Allomones of the Mollusc *Onchidium verruculatum*

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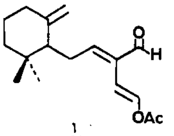
Naked gastropod molluscs belonging to the subclass *Opisthobranchia* have evolved various chemical defenses that include ingestion of functional coelenterate cnidoblasts from their prey and secretion of various repellents, including strong acids.(1) An observation(2) that the nudibranch *Phyllidia varicosa* secretes a defensive fluid led one of us (P.J.S.) to the first chemical elucidation of such an allomone, an isocyanosesquiterpene.(3) Members of the family Onchidacea are known to possess peripherally situated epidermal glands, described as "repugnatorial". The milky exudate from these glands reportedly deters predation and "when received upon one's tongue is found to sting like wild mustard".(4) Likewise this observation led one of use (C.M.I.) to the isolation of onchidal (1), the defensive allomone of *Onchidella binneyi*.(5) We now report the isolation of a mixture of esters, all based on the bispyrone alcohol ilikonapyrone (**2**),(6) as probable defense allomones of the Hawaiian onchid *Onchidium verruculatum* (Cuvier, 1830).



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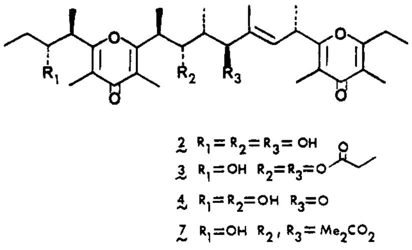


2 $R_1 = R_2 = R_3 =$ OH

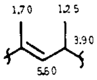
3 $R_1 =$ OH $R_2 = R_3 =$ O

4 $R_1 = R_2 =$ OH $R_3 =$ O

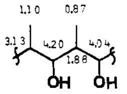
7 $R_1 =$ OH R_2, $R_3 = Me_2CO_2$

O. verruculatum from Portlock, Oahu, HI were stored whole in acetone for 24 h. The acetone filtrate was evaporated and the residue partitioned between ether and H_2O to give 0.53 g of organic oil. Chromatography of the oil on Sephadex LH-20 (CH_2Cl_2/hexane, 4:1) and Bio-Sil A (EtOAc) gave a mixture of UV absorbing esters (IR 1735 cm^{-1}) that could only be partially resolved chromatographically to give small amounts of pure **3**. However, saponification greatly simplified the mixture, yielding a single alcohol **2**.

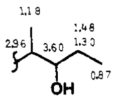
The triol **2** ($C_{32}H_{48}O_7$; HRMS obsd *m/z* 544.335, calcd 544.340) exhibited data for two fully substituted γ-pyrone rings bearing methyl groups at the β carbons [IR 1660, 1610 cm^{-1}; UV 260 nm (ϵ 12700); ^{13}C NMR ($CDCl_3$) δ 180.1 (s), 180.0 (s), 165.5 (s), 165.3 (s), 164.7 (s), 164.6 (s), 119.3 (s), 119.2 (s), 118.0 (s), 117.3 (s), 9.7 (q), 9.6 (q, 3 C); ^1H NMR ($CDCl_3$) δ 1.93 (s, 3 H), 1.92 (s, 3 H), 1.91 (s, 3 H), 1.89 (s, 3 H)] and the isolated spin systems a–d as defined by proton decoupling. The electron-impact mass spectrum of **2** (Scheme I) exhibited prominent ions at *m/z* 486 and 180, resulting from consecutive McLafferty rearrangements, indicating that b and c are attached to the same pyrone ring. Treatment of **2** with MnO_2 in CH_2Cl_2 furnished α,β-unsaturated ketone **4** [IR 1675, 1660, 1600 cm^{-1}; UV 242 nm (ϵ 13800), 257 (13300); ^1H NMR ($CDCl_3$) δ 1.76 (d, 3 H, *J* = 1 Hz), 6.43 (dd, 1 H, *J* = 9, 1 Hz)], indicating that a and b are also joined. Finally, treatment



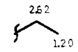
a



b



c



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(6) Ilikona is the Hawaiian translation of the Latin *verrucula*, the specific name of the animal meaning "wart".

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