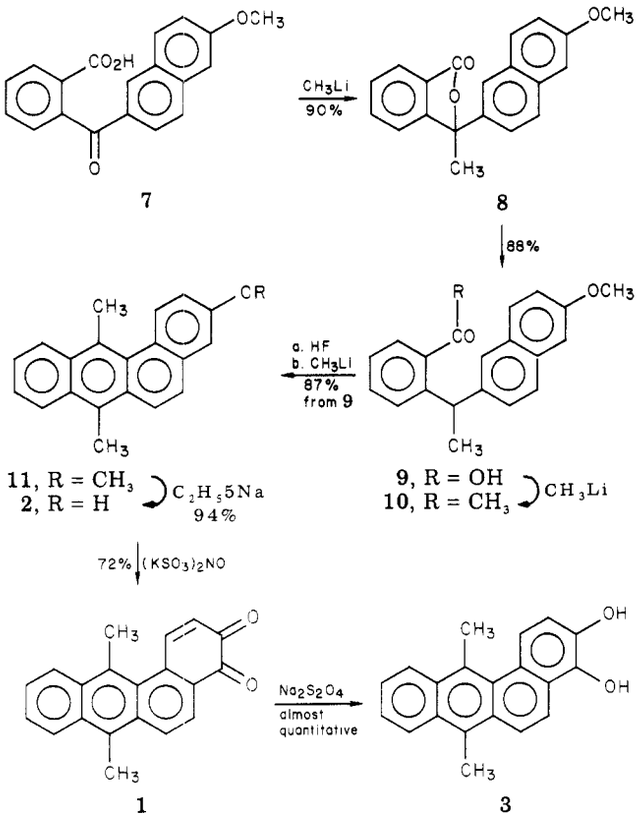
Scheme I



at room temperature. The dark green solid produced was collected and chromatographed over silica gel using benzene to produce 300 mg (22%) of **2** from the early fractions and 800 mg (72% based on the recovery of **2**) of **1**, mp 155.5–156.5 °C.[11]

3,4-Dihydroxy-7,12-dimethylbenz[*a*]anthracene (3).[12] To a well-stirred solution of 200 mg of **1** in 100 mL of benzene saturated with N_2 was added under N_2 a solution of $Na_2S_2O_4$ in 30 mL of water. After 15 min (the blue color changed to yellow in a few minutes) the usual workup afforded 180 mg (90%) of **3**, mp 174–175 °C, as pale yellow crystals.

7,12-Dimethylbenz[*a*]anthracene-1,4-dione (5).[12] By a procedure entirely analogous to the oxidation of **2** to **1**, 3.0 g of **4**[4] was oxidized by 9.0 g of Fremy's salt to give 1.47 g (94% based on recovery of 47% of **4**) of **5**, mp 199–201 °C, as deep violet crystals.

1,4-Dihydroxy-7,12-dimethylbenz[*a*]anthracene (6).[12] By a method entirely analogous to that used in the reduction of **1** above there was obtained 180 mg (90%) of **6**, mp 114–116 °C.

Registry No. 1, 70092-13-6; 2, 57266-83-8; 3, 71964-72-2; 4, 66240-13-9; 5, 71964-73-3; 6, 71964-74-4; 7, 71964-75-5; 8, 71964-76-6; 9, 71964-77-7; 10, 71974-97-5; 11, 66240-02-6; 2-bromo-6-methoxynaphthalene, 5111-65-9; phthalic anhydride, 85-44-9.

Two Novel Lactams from the Marine Sponge *Halichondria melanodocia*

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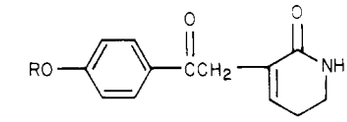
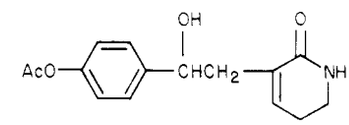
Although one of the earliest marine natural products to be extracted and used commercially, Tyrian purple, proved to be an indole derivative,[1] few other indole-related compounds have been reported among the numerous marine metabolites described in the past two decades.[2] Quite recently, however, several indoles and indole-based compounds have been isolated from sponges[3] and algae.[4] In this note we report the isolation of two novel lactams, one of them an indole derivative, from an algae-infested Caribbean sponge, *Halichondria melanodocia*.[5]

Specimens of *H. melanodocia* were collected at 2–4 ft depths near Summerland Key, Fla. The new lactams were obtained from isopropyl alcohol extracts of the wet sponge through a sequence of solvent partitioning followed by chromatography over Sephadex LH-20 and finally silica gel. Crystallization of one of the fractions from the silica gel chromatography yielded a white solid, **1a**, mp



1a, R = H
b, R = Ac



2

235.0–235.5 °C, $C_{13}H_{13}NO_3$ (high resolution mass spectrum 231.087; calcd 231.089). The infrared spectrum (KBr) of **1a** showed absorption at 3377 (sharp, OH), 3200 (brd, NH), 1680 (sh at 1689), and 1635 cm^{-1}, consistent with hydroxyl, α,β-unsaturated ketone, and primary amide groups. The ultraviolet absorption spectrum showed maxima at 273 (ϵ 20 600) and 218 nm (ϵ 17 800), indicative of a *p*-hydroxybenzoyl moeity.[6] Further evidence for this structural feature was obtained from the ^1H NMR spectrum ($CDCl_3$–CD_3OD) which contained a pair of two-proton doublets at δ 6.86 and 7.92 (J = 9 Hz) and also the mass spectrum which exhibited a base peak at 121 (high resolution mass spectrum 121.028; calcd for $C_7H_5O_2$ 121.029).

In addition to the aromatic proton signals, the downfield region of the ^1H NMR spectrum of **1a** contained a one-proton triplet signal at 6.56 ppm (J = 4 Hz) attributable to the β proton of an α,β-unsaturated carbonyl system. This proton was coupled to a broad two-proton multiplet at δ 2.44 (overlapping dt J = ~4, ~7.5 Hz), which in turn was coupled to a two-proton triplet appearing at δ 3.46 ppm ($J \simeq$ 7.5 Hz). Irradiation of the signal at 2.44 not only collapsed the triplets at δ 6.56 and 3.46 to singlets, but also sharpened a broad two-proton singlet at δ 3.92. Hence, the methylene groups resonating δ 2.44 and 3.92 were confirmed to have a homoallylic relationship. These chemical shifts and proton interrelationships were best accounted for by the partial structure $-CH_2C(CO)=$

(1) J. T. Baker and M. D. Sutherland, *Tetrahedron Lett.*, 43 (1968); J. T. Baker, *Pure Appl. Chem.*, **48**, 35 (1976), and references cited therein.

(2) For leading references see: P. J. Scheuer, Ed., "Marine Natural Products", Vol. II, Academic Press, New York, 1978; P. J. Scheuer, "Chemistry of Marine Natural Products", Academic Press, New York, 1973; J. T. Baker and V. Murphy, "Handbook of Marine Science", Vol. I, The Chemical Rubber Publishing Co., Cleveland, Ohio, 1976; D. J. Faulkner, *Tetrahedron*, **33**, 1421 (1977).

(3) G. E. Van Lear, G. O. Morton, and W. Fulmor, *Tetrahedron Lett.*, 299 (1973); W. D. Raverty, R. H. Thomson, and T. J. King, *J. Chem. Soc., Perkin Trans. 1*, 1204 (1977); R. Kazlauskas, P. T. Murphy, R. J. Quinn, and R. J. Wells, *Tetrahedron Lett.*, 61 (1977); K. H. Hollenbeak and F. J. Schmitz, *Lloydia*, **40**, 479 (1977); R. J. Anderson, *ibid.*, 2541 (1978).

(4) (a) M. R. Brennan and K. L. Erickson, *Tetrahedron Lett.*, 1637 (1978); (b) G. T. Carter, K. L. Rinehart, Jr., L. H. Li, S. L. Kuentzel, and J. L. Connor, *ibid.*, 4479 (1978).

(5) F. Wiedenmayer, "Shallow-Water Sponges of the Bahamas", Birkhauser Verlag, Basel, 1977, p 149.

(6) A. I. Scott, "Ultraviolet Spectra of Natural Products", Macmillan, New York, 1964, p 104.

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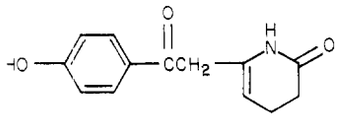
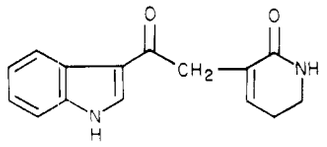
$CHCH_2CH_2NH$–. Joining of the carbonyl carbon in this formula to the nitrogen to form a δ lactam accounted for the amide carbonyl absorption and also the final degree of unsaturation required by the molecular formula. Attachment of the *p*-hydroxybenzoyl group to the remaining free valence on the terminal methylene group of this partial formula leads to **1a** as the preferred structure for the new lactam. The alternative structure **3** is consistent with the



3



4

decoupling data but is incompatible with the chemical shift data. Specifically, the olefinic proton in **3** would be expected to resonate at ~4.2–4.6,[7] and the protons α to the amide carbonyl group would be expected to resonate at ~1.8–2.5.[7]

Definitive evidence for attaching the *p*-hydroxybenzoyl group to the allylic methylene group as in **1a** was obtained by selective reduction of the ketone in the derived acetate **1b**. This acetate, M^+ 273, showed nearly the same ^1H NMR spectrum as **1a**, except for the addition of an acetate methyl signal at δ 2.30. The mass spectrum of **1b** exhibited a significant peak at *m/e* 173 (35%), corresponding to the acetylated *p*-hydroxybenzoyl fragment. Reduction of 0.5 mg of **1b** with sodium borohydride in ethanol at room temperature for 15 min afforded 0.2 mg of **2**: M^+ 275; IR 3430, 1750, 1665, 1605 cm^{-1}. The ^1H NMR spectrum of **2** differed from that of **1b** primarily in the occurrence of an additional one-proton triplet at 4.89 (J = 6 Hz [–C**H**(OH)CH_2–] and the replacement of the two-proton broad singlet at δ 3.94 with a two-proton doublet at δ 2.66 (J = 6 Hz). Thus, structures **2** and, by inference, **1a** are supported.

The second lactam, a white solid, mp 194.0–194.5 °C, $C_{15}H_{14}N_2O_2$ (high resolution MS 254.107, calcd 254.106), had important IR absorptions (KBr) at 3300 (NH), 1686, (ketone), 1646, 1636 (amide), 1619, and 1522 cm^{-1}. These were indicative of –NH–, α,β-unsaturated ketone and amide groups, and an aromatic ring.

The ^1H NMR spectrum ($CDCl_3$–CD_3OH) of this second lactam, **4**, was superimposable in the region from δ 0–6.64 with that of **1a**, and this confirmed that the same substituted lactam ring was present in both compounds. The low-field region of the spectrum of **4** contained signals at δ 7.20–7.35 (2 H, m), 7.40–7.54 (1 H, m), 8.16 (1 H, s), and 8.20–8.35 (1 H, m), which were virtually superimposable with those of 3-acetylindole, except that the one-proton singlet in the latter occurred at slightly higher field, δ 8.02. Thus, structure **4** was inferred for the second lactam. This assignment was corroborated by the mass spectrum which showed a base peak at *m/e* 144.045, C_9H_6ON (calcd 144.045), corresponding to the indolylcarbonyl moiety, and the UV spectrum (CH_3OH) 294, 254, 238 nm (ε 12 700, 9 800, and 13 800), which was in excellent agreement with that of 3-acetylindole.[8]

As is the case with other sponge metabolites, it is not known whether lactams **1a** and **4** are produced by the sponge or associated alage and bacteria or whether they are of dietary origin.

Experimental Section

Isolation of 1a.[9] Specimens of *H. melanodocia* collected near Summerland Key, Fla., were immersed immediately after collection in isopropyl alcohol and stored in sealed cans until workup. The alcohol extract was recovered by decantation and filtration and concentrated on a rotary evaporator at reduced pressure. The concentrate was diluted with water and extracted continuously with dichloromethane, and then the organic solubles were dissolved in 10% aqueous methanol and partitioned against hexane. The methanol phase was diluted to 20:80 water–methanol and partitioned against carbon tetrachloride. Finally, the methanol phase was diluted to 30:70 water–methanol and extracted with chloroform. The chloroform solubles (6 g) were chromatographed over Sephadex LH-20, using chloroform–methanol (1:1), to give six fractions after combinations based on TLC analysis. Fraction 4 (500 mg) was chromatographed over 40 g of TLC grade silica gel, using dichloromethane–methanol mixtures in which the methanol content was gradually increased, to give 15 fractions. The fourth fraction crystallized, and upon recrystallization from chloroform–methanol 2 mg of pure **1a** was obtained. The total yield of pure **1a**, 10 mg (see isolation of **4** below), was 2.8×10^{-4}% of the wet sponge weight: mp 235.0–235.5 °C; IR 3377, 1689, 1680, 1635, 1608, 1593, 1277, 1225, 1020, 845 cm^{-1}; for UV and ^1H NMR see text; mass spectrum *m/e* (%) M^+ 231 (30), 121 (100), 93 (44), 65 (50), 53 (38); high resolution mass spectrum, see text.

Acetylation of 1a. The phenol **1a**, 0.7 mg, was mixed with 0.1 mL of pyridine and 0.05 mL of acetic anhydride at room temperature, and the resulting solution was allowed to stand at 0 °C overnight. After the addition of a few drops of water, the reaction mixture was extracted with ethyl acetate, and the organic layer was washed successively with 1 N HCl, water, 5% $NaHCO_3$, and water. After evaporation of the solvent, 0.7 mg of the acetate **1b** was obtained: IR ($CHCl_3$) 3420, 1755, 1690, 1675, 1630, 1190, 1110 cm^{-1}; ^1H NMR ($CDCl_3$/acetone-d_6) δ 2.30 (3 H, s), 2.41 (2 H, brd q),[10] 3.46 (2 H, t, J = 7 Hz), 3.94 (2 H, s), 6.54 (1 H, t, J = 4 Hz), 7.23 (2 H, d, J = 9 Hz), 8.06 (2 H, d, J = 9 Hz); mass spectrum, *m/e* (%) 273 (M^+ 8.1), 163 (35), 121 (100), 93 (9.5).

Reduction of 1b. A solution of 0.5 mg of **1b** in 0.3 mL of ethanol was treated with four drops of a saturated solution of sodium borohydride in ethanol at room temperature and then stirred for 15 min. A few drops of water were added, the solution was extracted with ethyl acetate, and the organic layer was dried (Na_2SO_4) and evaporated at reduced pressure to give **2** as a white solid: IR ($CHCl_3$) 3430, 1750, 1665, 1605 cm^{-1}; ^1H NMR ($CDCl_3$/acetone-d_6) δ 2.30 (3 H, s), 2.40 (2 H, brd q),[10] 2.66 (2 H, d, J = 6 Hz), 3.47 (2 H, t, J = 7 Hz), 4.89 (1 H, t, J = 6 Hz), 6.41 (1 H, t, J = 4 Hz), 7.08 (2 H, d, J = 9 Hz), 7.42 (2 H, d, J = 9 Hz); mass spectrum, *m/e* (%) 275 (M^+, 5.8), 163 (2.6), 123 (29), 121 (19), 112 (52), 111 (100), 95 (13), 82 (38), 77 (12).

Isolation of 4. The mother liquors of the fraction from which **1a** crystallized plus two other chromatography fractions in which **1a** was detected by TLC were combined and rechromatographed by high-pressure liquid chromatography, using a 10 × 250 mm 5 μm microparticle silica gel column (Altex Lichrosorb 60) and methanol–dichloromethane (5:95) as the eluting solvent to give 8 mg of **1a** and 3 mg of **4** (8.3×10^{-5}% yield from wet sponge weight): mp 194–194.5 °C after recrystallization from methanol–chloroform; IR (KBr) 3300, 1686, 1646, 1636, 1619, 1522, 1435, 1125, 765 vm^{-1}; UV (MeOH), see text; ^1H NMR (CD_3OD/$CDCl_3$) δ 2.44 (2 H, brd q),[10] 3.46 (2 H, t, J = 7 Hz), 3.90 (2 H, bs), 6.64

(7) Cf. H. Weitkamp and F. Korte, *Chem. Ber.*, **95**, 2896 (1962).
(8) (a) J. E. Saxton, *J. Chem. Soc.*, 3592 (1952); (b) F. Chastrette, *Bull. Soc. Chim. Fr.*, 1151 (1970).

(9) Melting points are uncorrected. Infrared spectra were taken on Beckman 4250 or Acculab 3 spectrophotometers. NMR spectra were acquired on Varian T-60 or XL-100 instruments in the solvents specified; signals are reported in parts per million (δ) downfield from internal tetramethylsilane. Mass spectra were obtained on Hewlett-Packard 5985 and CEC (Dupont, Monrovia, Calif.) 100 mass spectrometers. The column chromatographic adsorbent used was Silica Gel 60H (E. Merck).
(10) This broad quartet is identical with the corresponding signal in **1a** which was shown by decoupling to be an overlapping dt, $J \simeq 4$, 7.5 Hz, see text.

(1 H, t, J = 4 Hz), 7.29–7.35 (2 H, m), 7.40–7.54 (1 H, m), 8.16 (1 H, s), 8.20–9.35 (1 H, m); mass spectrum, m/e (%) 254 (M^+ 25), 196 (6), 144 (100), 137 (12), 117 (25), 116 (33); high resolution mass spectrum, 254.107, calcd for $C_{15}H_{14}N_2O_2$, 254.106.

3-Acetylindole was prepared according to the procedure of Saxton:[4a] mp 191–192 °C (lit. mp 191 °C); UV (CH_3OH) 291, 252, 238 nm (ϵ 15080, 11590, 14600) [lit.[4b] 296, 257, 240 (ϵ 12300, 8511, 11480)]; ^1H NMR (100 MHz, $CDCl_3/CD_3OD$) 2.51 (3 H, s), 7.23 (2 H, m), 7.46 (1 H, m), 8.02 (1 H, s), 8.26 (1 H, m).

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Registry No. **1a**, 71886-38-9; **1b**, 71886-39-0; **2**, 71901-59-2; **4**, 71886-40-3; 3-acetylindole, 703-80-0.

Elaboration of Aldehydes and Ketones to Alkynes: Improved Methodology

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Received June 12, 1979

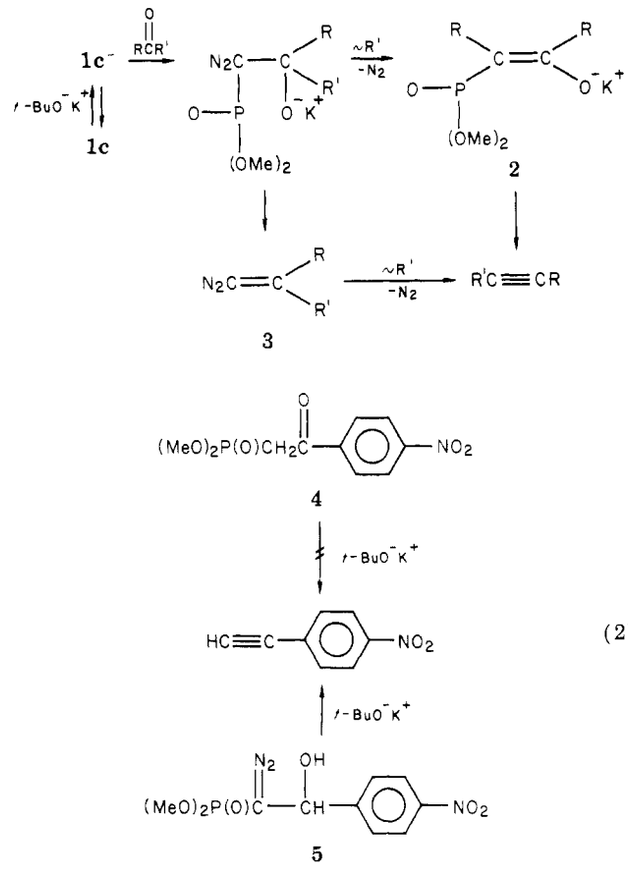
Recently, Colvin and Hamill reported the use of silicon- and phosphorus-substituted diazomethanes, **1**, to convert certain *aryl* ketones and aldehydes to alkynes in a single step (eq 1).[1] The scope of this potentially quite useful

$$\mathrm{RCHN_2} \xrightarrow[2.\ \mathrm{ArCOR'/-78\ ^\circ C}]{1.\ n\text{-BuLi or } t\text{-BuOK/}-78\ ^\circ\mathrm{C}} \mathrm{ArC{\equiv}CR'} \quad (1)$$

1a, R = Me_3Si
b, R = $(Ph)_2P(O)$
c, R = $(MeO)_2P(O)$

synthetic method, as delineated by the previous workers, was disappointingly narrow. Thus, the transformation occurred in high yields with a number of diaryl ketones (e.g., various benzophenones, dinaphthyl ketone) and with *p*-nitrobenzaldehyde. Attempts to extend the reaction to ketones or aldehydes containing enolizable protons (e.g., acetophenone, phenylacetaldehyde) or α,β-unsaturation (cinnamaldehyde) were unsatisfactory at best in that yields of alkynes ranged from 0–30%. Moreover, benzaldehyde failed to give any phenylacetylene, leading the authors to conclude that only "highly electrophilic" aromatic aldehydes could be used as substrates.[1] We wish now to report preliminary results of a simple modification of the Colvin/Hamill approach that dramatically enhances the breadth and efficiency of this type of transformation.

Scheme I. Possible Reactions Mechanisms



The experimental method most often used by the previous workers was to form the anion of **1** irreversibly with the aid of *n*-butyllithium, add the carbonyl-containing substrate, and *immediately* allow the resulting mixture to warm to ambient temperature. This same general sequence of steps was also apparently followed in the one reported instance in which potassium *tert*-butoxide was employed as the base. We have found that stirring a slurry of approximately equimolar amounts of **1c**, potassium *tert*-butoxide, and a ketone or aldehyde for 12–16 h at −78 °C and then allowing the reaction mixture to warm to ambient temperature affords high yields of alkynes even with substrates bearing enolizable protons. Our preliminary results are summarized in Table I.

Runs 1–4 exemplify the efficacy of the method with enolizable substrates. In the case of acetophenone (run 4), some unchanged ketone was observed which may be indicative of the use of less than optimal reaction conditions. It is noteworthy that no aldol-type products could be detected by ^1H NMR analysis of the reaction mixtures obtained in any of the runs.

The result of run 5 clearly compromises the previous conclusion regarding the necessary electrophilicity of the carbonyl carbon atom.[1] Given our observation, we suspect that the reaction will be successful over essentially the full range of substituents normally encountered on aromatic aldehydes, obvious exceptions likely being *o*- and/or *p*-hydroxy.

The method was applied to furfural (run 6) in an effort to prepare an alkyne which previous authors had reported to be highly susceptible to polymerization.[3] As the table indicates, our technique succeeds in producing the mo-

(1) (a) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Chem. Commun.* **1973**, 151. (b) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Perkin Trans. 1* **1977**, 869.

(2) Schlosser, M.; Ladenberger, V. *Chem. Ber.* **1967**, *100*, 3901.

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