

1.30-1.70 (m, 4, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.20 (m, 2, H<sub>2</sub>'2''), 2.66 (t, 2, ArCH<sub>2</sub>), 3.91 (m, 2, H<sub>5</sub>'5''), 4.24 (m, 1, H<sub>3</sub>'), 6.18 (t, 1, H<sub>1</sub>'), 6.44 (s, 1, H<sub>5</sub>), 8.68 (s, 1, H<sub>4</sub>). Anal. Calcd for C<sub>15</sub>H<sub>20</sub>N<sub>2</sub>O<sub>5</sub>: C, 58.43; H, 6.54; N, 9.09. Found: C, 58.37; H, 6.43; N, 8.91.

**Method B.** To a solution of 308 mg (1 mmol) of **9c** in 4 mL of dioxane/H<sub>2</sub>O (1:1) was added 10 mg of HgSO<sub>4</sub>, and the mixture was stirred at 25 °C for 48 h. The major, highly fluorescent product (110 mg, 36%) was isolated by preparative TLC and shown to be **16** (mp 150-152 °C), identical with the product of method A.

**Acknowledgment.** We thank the National Cancer Institute of Canada, the Natural Sciences and Engineering Research Council of Canada (Grant No. A5890), and The University of Alberta for generous support. M.J.R. thanks Professor A. D. Broom for facilities and hospitality provided during a visiting professorship at the University of Utah, 1981-1982.

**Registry No.** **1**, 45774-47-8; **2a**, 77875-79-7; **2b**, 77875-82-2; **2c**, 85267-59-0; **3a**, 77875-80-0; **3c**, 85267-72-7; **4**, 1956-30-5; **5a**, 85267-60-3; **5b**, 85267-61-4; **6a**, 85282-15-1; **6b**, 59864-07-2; **6c**, 85267-70-5; **7**, 31356-86-2; **8a**, 77875-86-6; **8b**, 77875-87-7; **8c**,

85267-63-6; **8d**, 77875-89-9; **8e**, 77875-90-2; **8f**, 77875-92-4; **8g**, 77875-91-3; **8h**, 69075-43-0; **8i**, 77875-93-5; **8j**, 85267-64-7; **8k**, 77875-94-6; **8l**, 77882-22-5; **8m**, 85267-65-8; **8n**, 85267-66-9; **8p**, 77875-95-7; **9a**, 77875-96-8; **9b**, 77887-18-4; **9c**, 77875-97-9; **9d**, 77875-98-0; **9e**, 77887-19-5; **9f**, 77887-20-8; **9g**, 61135-33-9; **9j**, 77875-99-1; **9m**, 77876-00-7; **9n**, 84559-05-7; **9o**, 84582-78-5; **9q**, 77876-01-8; **10**, 85267-69-2; **11**, 85267-68-1; **12**, 15176-29-1; **13**, 57741-93-2; **14**, 84621-32-9; **15**, 69304-47-8; **16**, 85267-76-1; **17**, 85267-71-6; **18**, 85267-73-8; **19**, 85267-74-9; **20**, 85267-75-0; (Ph<sub>3</sub>P)<sub>2</sub>PdCl<sub>2</sub>, 13965-03-2; CuI, 7681-65-4; 4-(*p*-toluoyloxy)butyne, 77875-81-1; 3-butynol, 2028-63-9; 5-(*p*-toluoyloxy)pentyne, 77875-85-5; 4-pentynol, 2117-11-5; hexyne, 693-02-7; 3',5'-di-*O*-acetyl-2'-deoxyuridine, 13030-62-1; (trimethylsilyl)acetylene, 1066-54-2; 4-[(triphenylmethyl)oxy]butyne, 75014-48-1; 3-(3,5-di-*O*-acetyl-2-deoxy-β-D-erythro-pentofuranosyl)-6-(2-hydroxyethyl)furano[2,3-*d*]pyrimidin-2-one, 85267-77-2; 3-(2-deoxy-β-D-erythro-pentofuranosyl)-6-(2-hydroxyethyl)furano[2,3-*d*]pyrimidin-2-one, 85267-62-5; 1-butyne, 107-00-6; 1-pentyne, 627-19-0; 1-heptyne, 628-71-7; 3,3-dimethyl-1-butyne, 917-92-0; benzene-ethyne, 536-74-3; trimethylsilylethyne, 1066-54-2; 3-(tetrahydropyranyloxy)-1-propyne, 6089-04-9; 4-(tetrahydropyranyloxy)-1-butyne, 40365-61-5; 2',3',5'-tri-*O*-*p*-toluyl-5-[4-(*p*-toluyl-oxyl)butynyl]uridine, 77875-84-4; 5-iodo-2',3',5'-tri-*O*-*p*-toluyl-uridine, 77875-83-3; 5-(4-hydroxybutynyl)uridine, 85267-67-0.

## Synthesis and Photophysical Properties of Some *endo*-6-Substituted Norcamphors and Pentacyclo[5.4.0.0<sup>2,6</sup>.0<sup>3,10</sup>.0<sup>5,9</sup>]undecan-8-ones

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The reactivity of the π\* region of photoexcited carbonyl groups was studied by monitoring the fluorescence of a series of substituted norcamphors and pentacycloundecanones. These substrates contained various probes so positioned as to be able to interact directly with the π\*-orbital system of the carbonyl group but not the n-orbital system. No significant perturbation of carbonyl fluorescence was caused by weak electron donors (Cl, OR, SR, and OTs), proton sources (OH, CO<sub>2</sub>H), electron sinks (C≡N), and abstractable hydrogen atoms (CH<sub>3</sub>, CH<sub>2</sub>X). By contrast, the dimethylamino group was able to completely quench fluorescence, presumably via an electron-transfer mechanism. These results support the concept of reduced electrophilicity of the π\* region of an excited carbonyl group.

With few exceptions the photochemistry of saturated carbonyl compounds has been rationalized in terms of the properties of the electron-deficient (in plane) molecular orbital system that results from promotion of a n electron to the π\* orbital. The diminished electron density in the (delocalized) n-orbital system gives rise to its well-known electrophilic properties, e.g., hydrogen abstractions, additions to electron-rich olefins, and type I and II cleavages. On the other hand, relatively little chemistry has been associated with the electron-rich region above and below the plane of the carbonyl group.<sup>2-4</sup> In fact, much of the experimental work does not differentiate between reactions

occurring in the two orthogonal planes since no fixed geometrical relationships were imposed on the reacting centers. We have initiated a program whose objectives are to design experiments that will delineate the stereoelectronic requirements of common photochemical reactions. Our approach to these objectives is to examine the properties of rigidly oriented systems that contain various internal probes positioned to interact *only* with the electronic system above (or below) the plane of the carbonyl group.

In this report we detail some studies that utilize the fluorescent properties of alkanones to monitor the reactivity of various probes with π\* systems of excited carbonyl groups. The two molecular systems evaluated were a series of 6-*endo*-norcamphors (**1a-f** and **2**) and some pentacycloundecanones (**3a-h**).

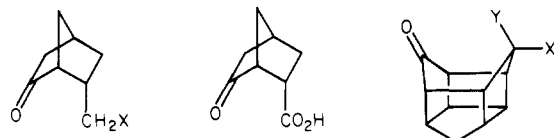
**Syntheses: Norcamphors.** The key starting material for the syntheses of **1a-f** was the keto acid **2** first reported by Beckmann and Geiger.<sup>5</sup> This compound was converted in one step to the methyl ester dimethyl ketal **4** by heating

(1) On leave from Helwan University, Giza, Egypt.  
(2) For references and a summary, see: Turro, N. J.; Dalton, J. C.; Farrington, G.; Niemczyk, M.; Pond, D. M. *J. Am. Chem. Soc.* 1970, 92, 6978.

(3) Zimmerman, H. E. *Adv. Photochem.* 1963, 1, 183.

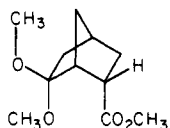
(4) A recent theoretical treatment of the problem of hydrogen-atom abstraction by π\* orbitals has been presented: Chandra, A. K. *J. Photochem.* 1979, 11, 347. It was concluded that the activation energy for this kind of abstraction was higher than that for in-plane abstraction by a half-filled n orbital.

(5) Beckmann, S.; Geiger, H. *Chem. Ber.* 1961, 94, 48.

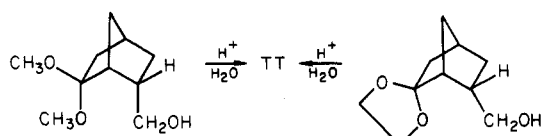


1 a, X = OH  
 1 b, X = Cl  
 1 c, X = OSO<sub>2</sub>C<sub>6</sub>H<sub>5</sub>  
 1 d, X = CN  
 1 e, X = SCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>  
 1 f, X = N(CO)<sub>2</sub>C<sub>6</sub>H<sub>4</sub>

2  
 3 a, X, Y = H  
 3 b, X, Y = OCH<sub>2</sub>CH<sub>2</sub>O  
 3 c, X, Y = SCH<sub>2</sub>CH<sub>2</sub>S  
 3 d, X, Y = O  
 3 e, X = C<sub>6</sub>H<sub>5</sub>; Y = H  
 3 f, X, Y = OCH<sub>3</sub>  
 3 g, X = H; Y = N(CH<sub>3</sub>)<sub>2</sub>  
 3 h, X = H; Y = CH<sub>3</sub>



4



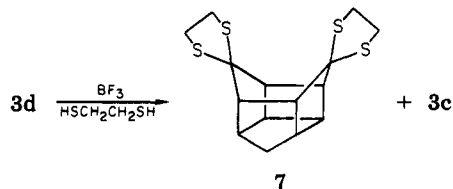
5

6

with trimethyl orthoformate in the presence of acid. Reduction of the latter compound by lithium aluminum hydride gave the ketal 5, which was hydrolyzed to give 1a. The stereochemistry of 1a was confirmed by an alternate synthesis from 6 a molecule whose structure had been proven earlier.<sup>6</sup>

The chloride 1b was prepared from 1a by using thionyl chloride in pyridine, and the tosylate 1c by Tipson's procedure.<sup>7</sup> The other three compounds were prepared by displacement reactions using cyanide ion,<sup>8</sup> benzylmercaptide ion, and phthalimido ion.<sup>9</sup>

**Pentacycloundecanones.** Compounds 3a,<sup>10</sup> 3b,<sup>11</sup> and 3d<sup>12</sup> were prepared by literature procedures. Compound 3c was not readily obtained on treatment of diketone 3d with HSCH<sub>2</sub>CH<sub>2</sub>SH·BF<sub>3</sub>.<sup>13</sup> Instead, we obtained a mixture of products, one of which had physical properties consistent with those expected for a bis(thioacetal), i.e., 7.



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A second compound, mp 117 °C, was also isolated from this reaction. Its properties were those anticipated for the monothioacetal 3c except that our melting point differed

Table I. Absorption and Relative Fluorescence Data of Norcamphors

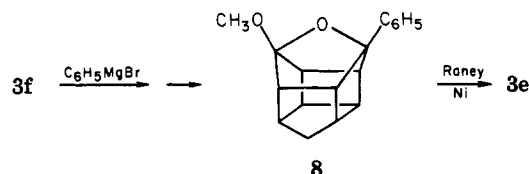
compd	concn, M	$\lambda_{\max}$ ( $\pm 2$ nm)	$\epsilon_{\max}$ ( $\pm 5\%$ )	$V_f^{a,b}$ ( $\pm 5$ nm)	$\phi_f^{rel,c}$ ( $\pm 15\%$ )
norcamphor	0.040	291	25	404	1.0
1a	0.040	293	36	410	0.80
1b	0.040	292	38	413	0.84
1c	0.040	294	36	410	1.2
1d	0.042	290	40	395	1.1
1e	0.0059	289	87	405	1.3
1f	0.00046	292	1879	383	
2	0.040	292	45	404	0.92

<sup>a</sup> Acetonitrile solutions. <sup>b</sup> Excitation at 310 or 313 nm.

<sup>c</sup> Ratios corrected for unequal light absorption or determined at equal absorbance; cf: Parker, C. A. "Photoluminescence of Solutions"; American Elsevier: New York, 1968; pp 15-21.

from that reported (lit.<sup>13</sup> mp 85–86 °C). We also obtained the product with mp 117 °C from the reaction of 3d with ethanedithiol catalyzed with *p*-toluenesulfonic acid. It is possible that the two compounds are polymorphs since the only discrepancy appears to be in the melting points.

The phenyl ketone 3e was to be prepared by reacting the mono ketal 3f<sup>14</sup> with phenylmagnesium bromide followed by hydrogenolysis. The expected ketal carbinol was not produced in the Grignard synthesis. Instead, the product (NH<sub>4</sub>Cl workup) displayed only one methoxyl group (NMR) and no hydroxyl group (IR). We conclude that the reaction product was 8. In any event, when



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compound 8 was subjected to hydrogenolysis using Raney nickel, a phenyl ketone was produced.<sup>15</sup> The stereochemistry of the phenyl ring was deduced from an analysis of the NMR spectrum in the presence and absence of the shift reagent Eu(fod)<sub>3</sub>.<sup>16</sup> Before addition of the shift reagent we had assigned a sharp singlet (width at half-height  $\cong$  2.5 Hz) at  $\delta$  3.1 to the benzylic proton. It was concluded that this proton must have the syn configuration since significant coupling with the protons on C<sub>1</sub> and C<sub>10</sub> would be expected for the anti configuration (dihedral angles  $\sim$  40°) but not the syn configuration (dihedral angles  $\sim$  80°). This assignment was confirmed when it was found that the peak at  $\delta$  3.1 and two other protons were the most strongly shifted protons on addition of Eu(fod)<sub>3</sub>.<sup>17</sup>

The method of Borch and Hassid<sup>18</sup> was used to prepare the dimethylamino ketone 3g. The configuration was assigned by analysis of spectroscopic data, which indicated transannular interaction between the carbonyl group and the amine. For example, whereas most of the compounds in this series display carbonyl absorptions between 5.8 and

(6) Sauers, R. R.; Oppelt, J. C. *Tetrahedron* 1969, 25, 613. See also: Kropp, P. J.; Worsham, P. R.; Davidson, R. I.; Jones, T. H. *J. Am. Chem. Soc.* 1982, 104, 3972. Werstiuk, N. H.; Taillefer, R. *Can. J. Chem.* 1978, 56, 1134.

(7) Tipson, R. S. *J. Org. Chem.* 1944, 9, 235.

(8) Pawson, B. A.; Cheung, H.-C.; Gurbaxani, S.; Saucy, G. *J. Am. Chem. Soc.* 1970, 92, 336.

(9) Sheehan, J. C.; Bolhofer, W. A. *J. Am. Chem. Soc.* 1950, 72, 2786.

(10) Dekker, T. G.; and Oliver, D. W. *S. Afr. J. Chem.* 1979, 32, 45.

(11) Eaton, P. E.; Cassar, L.; Hudson, R. A.; Huang, D. R. *J. Org. Chem.* 1976, 41, 1445.

(12) Cookson, R. C.; Crundwell, E.; Hill, R. R.; Hudec, J. *J. Chem. Soc.* 1964, 3062.

(13) Lerman, B. M.; Galin, F. Z.; Umanskaya, L. A.; Tolsitkov, G. A. *J. Org. Chem. USSR (Engl. Transl.)* 1978, 14, 2336.

(14) Barborak, J. C.; Khoury, D.; Maier, W. F.; Schleyer, P. v. R.; Smith, E. C.; Smith, W. F., Jr.; Wyrick, C. *J. Org. Chem.* 1979, 44, 4761.

(15) The use of Raney nickel to cleave  $\alpha$ -phenyltetrahydrofurans has been reported to proceed with retention of configuration. See: Mitsui, S.; Senda, Y.; Konno, K. *Chem. Ind. (London)* 1963, 1354. We obtained the same product using Pd/C.

(16) Tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octadecanedionato)europium.

(17) Raber, D. J.; Janks, C. M.; Johnston, M. D., Jr.; Raber, N. K. *J. Am. Chem. Soc.* 1980, 102, 6591. The two bridgehead protons at C<sub>7</sub> and C<sub>9</sub> and the syn-H<sub>11</sub> proton are similarly disposed in the complex.

(18) Borch, R. F.; Hassid, A. I. *J. Org. Chem.* 1972, 37, 1673.

Table II. Absorption and Relative Fluorescence of Pentacycloundecanones 3

compd	concn, M	$\lambda_{\max}$ ( $\pm 2$ nm)	$\epsilon_{\max}$ ( $\pm 5\%$ )	$V_f^{a,b}$ ( $\pm 5$ nm)	$\phi_f^{\text{rel c}}$ ( $\pm 15\%$ )
3a	0.020	299	18	411	1.0
3b	0.020	295	19	410	0.44
3c	0.020	303	30	410	0.40
3d	0.020	301	31	450	0.36
3e	0.040	297	22	405	1.24
3g	0.020-0.010	280 <sup>d</sup>	44		~0
3h	0.020	295 <sup>e</sup>	19	410	0.85

<sup>a-c</sup> See Table I. <sup>d</sup> Inflection. <sup>e</sup> Unpublished results, H. Shams.

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5.7  $\mu\text{m}$ , compound **3g** absorbs at 5.87  $\mu\text{m}$ . In addition, the ultraviolet spectrum displays a charge-transfer band at 219 nm. ( $\epsilon$  4810) in accord with the studies of Leonard and co-workers on monocyclic amino ketones.<sup>19</sup>

### Results and Discussion

The absorption and fluorescence characteristics of compounds **1a-f**, **2**, and norcamphor are listed in Table I. It can be seen that there is relatively little perturbation of the carbonyl emission by the probes in compounds **1a-e** and **2**. In other words, during the lifetime of the carbonyl singlet states, ca. 5 ns,<sup>20</sup> there are no new decay mechanisms introduced by the probes.

Since it is known that alkyl chlorides<sup>21</sup> and sulfur-containing compounds<sup>22</sup> rapidly quench carbonyl excited states intermolecularly we tentatively conclude that there is a stereoelectronic requirement that is not being met in the norcamphor derivatives.<sup>23</sup> The situation with the phthalimide derivative is somewhat different in that light is absorbed exclusively by the probe. We observed only unperturbed fluorescence from this moiety as evidenced by the coincidence of the spectrum with that of *n*-propylphthalimide.<sup>24</sup>

In the pentacycloundecanones (**3**) in which the relative geometry of the probes and carbonyl groups is fixed, one sees (Table II) normal  $n, \pi^*$  absorptions in the 280–300-nm region. On the other hand, the fluorescence results with derivatives of **3** revealed a spectrum of behavior. For example, compounds **3e** and **3h** displayed fluorescence intensity comparable to that of the model, pentacycloundecanone **3a**, despite the presence of a  $\gamma$ -benzylic hy-

drogen in **3e** and a methyl group in **3h** that is directly positioned over the  $\pi^*$ -orbital system.<sup>25</sup> It is also noteworthy that neither of these ketones led to low-molecular-weight products after prolonged irradiation ( $\lambda > 290$  nm) in benzene.<sup>26,27</sup>

At the other extreme, we observed no fluorescence from the amino ketone **3g** upon excitation from 310 to 220 nm at two different concentrations. We conclude that intramolecular quenching of the excited carbonyl group has occurred, probably via an electron-transfer mechanism.<sup>19c,22,28,29</sup> In a qualitative sense, the lowered fluorescence yields from the thioketal **3c** and ketal **3b** may also be due to (less efficient<sup>22</sup>) electron-transfer interactions, but other factors, e.g., geometrical differences<sup>30</sup> and *n*-orbital size, may also contribute to the ease of intramolecular electron transfer.

### Summary

Most of the compounds studied displayed a relatively high relative fluorescence yield despite the presence of built-in quenchers. These results are consistent with quenching mechanisms that require interaction of the probes with the (inaccessible) *n* orbitals of the photoexcited carbonyl groups combined with a low reactivity of the  $\pi^*$  region toward (accessible) electrons and C–H bonds.

### Experimental Section

Infrared spectra were determined as liquid films or as noted on a Perkin-Elmer Model 727B spectrometer. Nuclear magnetic resonance spectra were determined in carbon tetrachloride on a Varian Model T-60 spectrometer using internal tetramethylsilane as a standard. Integration data were consistent with the assigned structures to an accuracy of  $\pm 10\%$ . Fluorescence spectra were determined on a Perkin-Elmer spectrometer, Model MPF-3L. Absorption spectra were measured on a Cary spectrometer, Model 17D.

**6-endo-Carbomethoxybicyclo[2.2.1]heptan-2-one dimethyl ketal (4)** was prepared by heating a solution of 41.32 g (0.268 mol) of keto acid **2**<sup>5</sup> with 123.86 g (1.17 mol) of trimethyl orthoformate and 2.58 g of *p*-toluenesulfonic acid in 339 mL of reagent-grade methanol. After 17 h at reflux temperature, the solution was cooled and treated with sodium methoxide to neutralize the acid. Rotoevaporation was followed by distillation to give 30.14 g (52.5%) of **4**: bp 65–70 °C (0.05 torr); NMR  $\delta$  3.65 (s, CO<sub>3</sub>CH<sub>2</sub>), 3.20 and 3.10 (two s, C(OCH<sub>3</sub>)<sub>2</sub>), 2.90–1.0 (m); IR (neat) 5.68 (s, C=O)  $\mu\text{m}$ . Anal. Calcd for C<sub>11</sub>H<sub>18</sub>O<sub>4</sub>: C, 61.66; H, 8.47. Found: C, 61.89; H, 8.28.

(25) The quantum yield of fluorescence of 5-methyl-2-hexanone is ca. one-sixth that of acetone: Dalton, J. C.; Turro, N. J. *J. Am. Chem. Soc.* 1971, 93, 3569. See also: Dalton, J. C.; Dawes, K.; Turro, N. J.; Weiss, D. S.; Barlthrop, J. A.; Coyle, J. D. *Ibid.* 1971, 93, 7213.

(26) H. Shams, unpublished results.

(27) Related results were obtained by Sugiyama et al. (Sugiyama, N.; Nishio, T.; Yamada, K.; Aoyama, H. *Bull. Soc. Chem. Jpn.* 1970, 43, 1879. These workers rationalized the low photoreactivity of several polycyclic ketones on the inability of the hydrogens to approach the half-vacant nonbonding orbital on the carbonyl group. For examples in the solid state, see: Chang, H. C.; Popovitz-Biro, R.; Lahav, M.; Leiserowitz, L. *J. Am. Chem. Soc.* 1982, 104, 614.

(28) The fluorescence of 2-pentanone is quenched by triethylamine with a rate constant equal to  $2.2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ : Encina, M. V.; Soto, H.; Liisi, E. A. *J. Photochem.* 1974/5, 3, 467. See also: Yip, R. W.; Loutfy, R. O.; Chow, Y. L.; Magdzinski, L. K. *Can. J. Chem.* 1972, 50, 3426.

(29) In a different context, the fluorescence of an aliphatic amine has been reported to be quenched by intramolecular energy transfer to a proximate carbonyl group: Halpern, A. M.; Walter, R. B. *Chem. Phys. Lett.* 1974, 25, 393.

(30) The importance of geometric factors has been pointed out (Paquette, L. A.; Wise, L. D. *J. Am. Chem. Soc.* 1967, 89, 6659). The low value of  $\epsilon$  (292) for the short wavelength absorption of **3c** is suggestive of only a modest degree of S–CO interaction as compared to 1-thiacycloctan-5-one ( $\epsilon$  1690).

(31) Vogel, A. I. "A Textbook of Practical Organic Chemistry", 3rd ed.; Wiley: New York, 1962, pp 423–424.

(19) (a) Leonard, N. J.; Oki, M.; Brader, J.; Boaz, H. *J. Am. Chem. Soc.* 1955, 77, 6237. (b) Leonard, N. J.; Oki, M. *Ibid.* 77, 1955, 6239. (c) Since the molecule in question also has a maximum of normal intensity and wavelength (Table II), it is possible that more than one conformer of the dimethylamino group exists.

(20) Norcamphor fluoresces with a quantum yield of 0.0033 and has a singlet state lifetime of  $\sim 4.9$ –5.7 ns; Halpern, A. M.; Walter, R. B. *Chem. Phys. Lett.* 1974, 25, 393. Turro, N. J.; Farrington, G. L. *J. Am. Chem. Soc.* 1980, 102, 6051.

(21) Alkyl chlorides quench the fluorescence of 2-butanone with a rate constant equal to  $1.8 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ ; see: Harriman, A.; Rockett, B. W. *J. Chem. Soc., Perkin Trans. 2* 1974, 1235.

(22) Rapid quenching ( $k \sim 8.3 \cdot 10^8 \text{ M}^{-1} \text{ s}^{-1}$ ) of benzophenone triplets by sulfides has been reported: Guttenplan, J. B.; and Cohen, S. G. *J. Am. Chem. Soc.* 1972, 94, 4040. See also: Fox, M. A.; Miller, P. K.; Reiner, M. D. *J. Org. Chem.* 1979, 44, 1103. Zepp, R. G.; Wagner, P. J. *J. Chem. Soc., Chem. Commun.* 1972, 167.

(23) It is unlikely that adverse conformational factors are at fault here, especially in view of the appearance of a short wavelength CT absorption band in **1e**. In addition, intramolecularity probably enhances reactivity by a factor of at least  $10^3$ ; see: Kirby, A. J. *Adv. Phys. Org. Chem.* 1980, 17, 183.

(24) For a discussion of fluorescence of phthalimides, see: Coyle, J. D.; Newport, G. L.; Harriman, A. *J. Chem. Soc., Perkin Trans. 2* 1978, 133.

**6-endo-(Hydroxymethyl)bicyclo[2.2.1]heptan-2-one (1a).**  
**A. From 4.** The ketal ester 4 (29.79 g, 0.139 mol) was reduced with a slurry of 6.38 g (0.168 mol) of lithium aluminum hydride in 638 mL of anhydrous ether. After the mixture was stirred for 3 h at 25 °C, 3 mL of water was added. The precipitate was removed by filtration, and the ether was evaporated under reduced pressure to give 23.44 g (90.5%) of the dimethyl ketal of 6-endo-hydroxymethylbicyclo[2.2.1]heptan-2-one (5): NMR  $\delta$  3.36 (d, CH<sub>2</sub>O), 3.18 and 3.12 (two s, OCH<sub>3</sub>); IR 2.90 (br, OH)  $\mu$ m.

A solution of 5.52 g (30 mmol) of the ketal in 61 mL of ether was stirred for 17 h with 61 mL of 1 N HCl. The ether layer was separated, and the aqueous phase was extracted with four portions of CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried (MgSO<sub>4</sub>) and rotoevaporated to give an oil. Distillation at 100 °C (0.05 torr) gave 2.36 g (56%) of 1a: NMR 3.8 (br, OH), 3.4 (m, CH<sub>2</sub>O), 2.8–1.0 (m). Anal. Calcd for C<sub>8</sub>H<sub>12</sub>O<sub>2</sub>: C, 68.54; H, 8.63. Found: C, 68.71; H, 8.92.

**B. From 6.** A small sample of ketal 6<sup>6</sup> was hydrolyzed by the above procedure to give 1a: bp 109–120 °C (0.07 torr). The NMR spectrum was essentially the same as that obtained from 4.

**6-endo-(Chloromethyl)bicyclo[2.2.1]heptan-2-one (1b)** was prepared by addition over 1 h of 2.02 g (17 mmol) of thionyl chloride to an ice-cold solution containing 2.38 g (17 mmol) of 1a and 2.29 g (29 mmol) of pyridine in 9.6 mL of benzene. The mixture was allowed to warm to 25 °C and heated at reflux for 6 h. After ice quenching, the product was extracted into ether. The combined extracts were washed with dilute HCl followed by washing with aqueous NaHCO<sub>3</sub> and H<sub>2</sub>O. After drying (MgSO<sub>4</sub>), the ether was removed by evaporation to give an oil, which was distilled at 51 °C (0.025 torr): NMR  $\delta$  3.2–3.7 (m, CH<sub>2</sub>Cl), 2.87–1.10 (m); IR 5.75 (C=O)  $\mu$ m. Anal. Calcd for C<sub>8</sub>H<sub>11</sub>OCl: C, 60.58; H, 6.99. Found: C, 60.79; H, 6.99.

**6-endo-[(Benzylthio)methyl]bicyclo[2.2.1]heptan-2-one (1e).** A mixture consisting of 2.0 g (13 mmol) of 1b, 1.58 g (12.6 mmol) of benzyl mercaptan, 0.52 g (13 mmol) of NaOH, and 21.7 mL of 50% aqueous ethanol was heated at reflux for 20 h. Twenty milliliters of water was added, and the resulting solution was extracted with ether. The dried (MgSO<sub>4</sub>) extracts were evaporated to give an oil: bp 140 °C (0.035 torr); yield 1.92 g (65%); NMR  $\delta$  7.27 (ArH), 3.67 (s, CH<sub>2</sub>S), 2.77–1.13 (m); IR 5.75 (C=O)  $\mu$ m; UV  $\lambda_{\max}$  243 ( $\epsilon$  1525). Anal. Calcd for C<sub>15</sub>H<sub>18</sub>OS: C, 73.13; H, 7.36. Found: C, 73.23; H, 7.43.

**6-endo-(N-Phthalimidomethyl)bicyclo[2.2.1]heptan-2-one (1f)** was prepared by heating a solution of 1.31 g (8.3 mmol) of 1b with 1.63 g (8.8 mmol) of potassium phthalimide in 20 mL of dimethyl formamide for 5 h at 90–95 °C.<sup>9</sup> The solution was cooled, diluted with 12 mL of CHCl<sub>3</sub>, and poured into 48 mL of H<sub>2</sub>O. The layers were separated, and the aqueous phase was extracted twice with CHCl<sub>3</sub>. The combined extracts were washed with 1 N NaOH and H<sub>2</sub>O. The dried (Na<sub>2</sub>SO<sub>4</sub>) extracts were evaporated to give 200 mg of a brown powder. This material was purified by flash chromatography using ethyl acetate–hexane (60:40) as eluant to give 0.12 g (5.5%) of white crystals: mp 144–145 °C; NMR  $\delta$  7.84 (m, ArH), 3.65 (d,  $J$  = 8 Hz, CH<sub>2</sub>N), 2.90–1.50 (m). Anal. Calcd for C<sub>16</sub>H<sub>15</sub>NO<sub>3</sub>: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.18; H, 5.73; N, 5.02.

**6-endo-(Cyanomethyl)bicyclo[2.2.1]heptan-2-one (1d).** The *p*-bromobenzenesulfonate ester of 1a was prepared from 2.2 g (15.7 mmol) of 1a by reaction with 4.41 g (17.3 mmol) of *p*-bromobenzenesulfonyl chloride in 2.2 mL of dry pyridine.<sup>7</sup> There was obtained 1.87 g of crude ester. A solution of 1.27 g (3.4 mmol) of the brosylate in 110 mL of dimethyl sulfoxide was allowed to react with 0.24 g (5 mmol) of sodium cyanide for 4.5 h at 85–95 °C.<sup>8</sup> The reaction mixture was poured into 20 mL of 10% aqueous NH<sub>4</sub>Cl, which was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The extracts were washed with H<sub>2</sub>O and dried (Na<sub>2</sub>SO<sub>4</sub>) prior to rotoevaporation. The resulting oil was distilled at 85–93 °C (0.025 torr) to give 0.30 g (59%) of 1d: NMR  $\delta$  2.8 (br, s), 2.6–1.5 (m); IR 4.48 (C≡N), 5.73 (C=O)  $\mu$ m. Anal. Calcd for C<sub>9</sub>H<sub>11</sub>NO: C, 72.45; H, 7.43. Found: C, 72.68; H, 7.62.

**Pentacyclo[5.4.0.0<sup>2,6</sup>.0<sup>3,10</sup>.0<sup>5,9</sup>]undecan-8-one (3a)** was prepared according to 11 and was purified by gas chromatography (SE-30, 148 °C): mp 210–212 °C (lit.<sup>11</sup> mp 194–195 °C). Anal. Calcd for C<sub>11</sub>H<sub>12</sub>O: C, 82.46; H, 7.55. Found: C, 82.25; H, 7.80. The 2,4-dinitrophenylhydrazone derivative was prepared in the usual way and had mp 155 °C (lit.<sup>13</sup> mp 159–161 °C) after

crystallization from 95% ethanol. Anal. Calcd for C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O<sub>4</sub>·H<sub>2</sub>O: C, 56.98; H, 5.06; N, 15.63. Found: 56.42; H, 4.72; N, 15.60.

**Pentacyclo[5.4.0<sup>2,6</sup>.0<sup>3,10</sup>.0<sup>5,9</sup>]undecan-8,11-dione Monoethylene Thioketal (3c).** When the directions given in ref 14 were followed, a mixture of 3c (60%) and 7 (25%) was obtained, which was separated by fractional crystallization from ethanol–petroleum ether. Compound 7 had mp 159–160 °C and showed no carbonyl absorption in the 5–6- $\mu$ m region. Anal. Calcd for C<sub>15</sub>H<sub>18</sub>S<sub>4</sub>: C, 55.21; H, 5.52; S, 39.26. Found: C, 55.39; H, 5.60; S, 39.35.

Compound 3c had mp 117 °C on crystallization from ethanol–ether; NMR  $\delta$  3.3 (s, CH<sub>2</sub>S, 4 H), 3.2–2.3 (m, 8 H), 1.77 (q,  $J_{AB}$  = 12 Hz, CH<sub>2</sub>); IR (mull) 5.71, 8.85, 12.5  $\mu$ m; UV  $\lambda_{\max}$  252 nm ( $\epsilon$  292). Anal. Calcd for C<sub>13</sub>H<sub>14</sub>OS<sub>2</sub>: C, 62.36; H, 5.64; S, 25.61. Found: C, 62.61; H, 5.56; S, 25.37.

**anti-11-Phenylpentacyclo[5.4.0<sup>2,6</sup>.0<sup>3,10</sup>.0<sup>5,9</sup>]undecan-8-one (3e).** A solution of phenylmagnesium bromide was prepared by reaction of 20.7 g (0.132 mol) of bromobenzene with 3.21 g (0.132 mol) of magnesium in 45 mL of anhydrous ether. A solution of ketal 3f<sup>15</sup> (19.4 g, 0.088 mol) in 80 mL of ether was added at a rate sufficient to maintain reflux. The resulting mixture was stirred at 25 °C for 17 h. The reaction mixture was quenched by pouring it onto a mixture of ice and 200 mL of saturated NH<sub>4</sub>Cl solution. The pH of the aqueous phase was adjusted to 5 by addition of dilute HCl. The layers were separated, and the aqueous layer was extracted three times with ether. The organic layers were washed with aqueous NaHCO<sub>3</sub> (3 $\times$ ) and water (3 $\times$ ). The dried (MgSO<sub>4</sub>) extracts were evaporated to give 22.9 g (98%) of crude 8: crystallization from CH<sub>3</sub>OH gave white plates, mp 74–76 °C; NMR  $\delta$  7.34 (s, ArH), 3.55 (s, 1 CH<sub>3</sub>), 2.8 (m, 8 H), 1.8 (q,  $J_{AB}$  = 10 Hz, CH<sub>2</sub>). Anal. Calcd for C<sub>18</sub>H<sub>18</sub>O<sub>2</sub>: C, 81.17; H, 6.82. Found: C, 81.11; H, 6.87.

A slurry of ca. 50 g of Raney nickel in 350 mL of absolute ethanol was prepared by repeated washing and decanting a commercial sample<sup>32</sup> of a 50% aqueous slurry. To this was added 9.97 g of 8, and the mixture was heated at reflux for 20 h. The nickel was removed by filtration, and the ethanol was removed by evaporative distillation to yield 10.1 g of a semisolid mass. This material showed a weak carbonyl absorption at 5.77  $\mu$ m and hydroxyl absorption at 2.76 and 2.9  $\mu$ m. The alcoholic contaminant was removed by stirring a solution of 7.15 g of crude product in 234 mL of ether for 1 h at 0 °C with an aqueous solution comprised of 45 g of Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>·2H<sub>2</sub>O and 33.75 mL of 96% H<sub>2</sub>SO<sub>4</sub> diluted to 225 mL.<sup>33</sup> The layers were separated, and the aqueous phase was extracted with ether (3 $\times$ ). The combined extracts were washed with aqueous NaHCO<sub>3</sub> and water, dried (MgSO<sub>4</sub>), and evaporated to give 5.88 g of crude ketone. The infrared spectrum of this material showed no hydroxyl absorption and an intense carbonyl peak at 5.77  $\mu$ m. TLC on silica showed at least two spots at *R*<sub>f</sub> 0.4 and 0.25 with a mixture of petroleum ether–ethyl acetate (81:19) as eluent. The major component at 0.4 was isolated by flash chromatography and had mp 96–100 °C: IR (CHCl<sub>3</sub>) 5.77 (C=O)  $\mu$ m;  $\lambda_{\max}$  258 nm ( $\epsilon$  230); NMR  $\delta$  7.2 (m, ArH), 3.6–2.2 (m, CH), 3.05 (s, CH), 1.73 (q,  $J_{AB}$  = 12 Hz, CH<sub>2</sub>). Anal. Calcd for C<sub>17</sub>H<sub>16</sub>O: C, 86.40; H, 6.83. Found: C, 86.07; H, 6.95.

**syn-11-(Dimethylamino)pentacyclo[5.4.0<sup>2,6</sup>.0<sup>3,10</sup>.0<sup>5,9</sup>]undecan-8-one (3g).** To a solution containing 1.72 g (0.010 mol) of diketone 3d and 1.72 g (0.015 mol) of 40% aqueous dimethylamine in 40 mL of acetonitrile was added 1.0 g (0.015 mol) of sodium cyanoborohydride in small portions. The resulting slurry was neutralized periodically by addition of acetic acid. After being stirred for 3 h, the solvent was evaporated under reduced pressure. The residue was basified with aqueous KOH followed by extraction with methylene chloride. The extracts were evaporated and the residue was dissolved in dilute HCl. After extraction with ether (3 $\times$ ) the aqueous layer was made basic with KOH, and the amine was extracted into methylene chloride. The extracts were dried (MgSO<sub>4</sub>) and evaporated. Distillation of the residue in a molecular still (block temperature 100–105 °C, 0.05 mm) gave 0.50 g (22%) of a colorless oil: IR 5.87 (s, C=O)  $\mu$ m; NMR  $\delta$  2.13 (s, 2CH<sub>3</sub>) 1.6 (q,  $J_{AB}$  = 10 Hz, CH<sub>2</sub>); UV  $\lambda_{\max}$  219 nm ( $\epsilon$  4810). Anal. Calcd for C<sub>13</sub>H<sub>17</sub>ON: C, 76.81; H, 8.43; N,

(32) Aldrich Chemical Co.

(33) Brown, H. C.; Garg, C. P. *J. Am. Chem. Soc.* 1961, 83, 2952.

6.89. Found: C, 76.75; H, 8.18; N, 7.31.

A picrate was prepared in chloroform and crystallized from 90% ethanol; mp 248-250 °C. Anal. Calcd for  $C_{19}H_{20}O_9N_4$ : C, 52.78; H, 4.66; N, 12.96. Found: C, 52.80; H, 4.58; N, 12.95.

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## Sesquiterpenoid Constituents of Eight Porostome Nudibranchs

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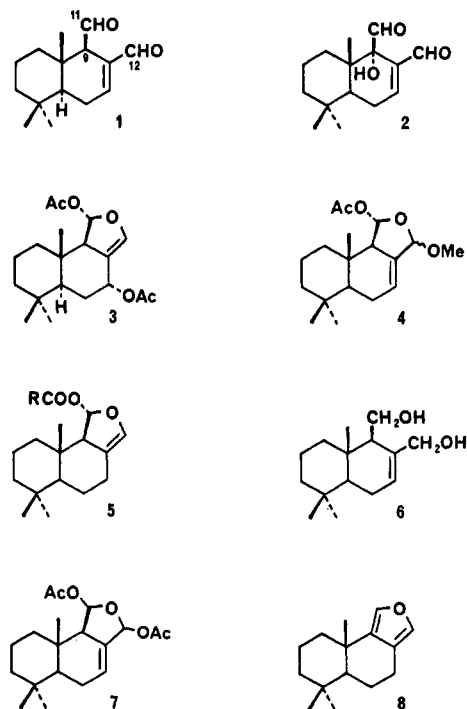
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Sesquiterpenes of the drimane series were isolated from eight porostome nudibranchs. A mixture of polygodial (1) and olepupuane (3), a new sesquiterpene diacetate, was obtained from *Dendrodoris nigra*, *Dendrodoris tuberculosa*, and *Dendrodoris krebsii*. Olepupuane (3) and the sesquiterpene esters 5 were found in *Doriopsilla albopunctata*, *Doriopsilla janaina*, and an undescribed yellow porostome, although one collection of *Doriopsilla albopunctata* contained only olepupuane (3) while a second collection contained a related methoxy acetal 4. Two undescribed porostomes contained only the sesquiterpene esters 5 found previously in *Dendrodoris limbata*. The structures of olepupuane (3) and the methoxy acetal 4 are based on interpretation of spectral data.

The porostome nudibranchs, of which the genera *Dendrodoris* and *Doriopsilla* are examples, are a group of dorid nudibranchs distinguished by the absence of a radula. Like other dorid nudibranchs,<sup>1</sup> the porostomes appear to employ a chemical defense mechanism. The chemicals implicated in their defense are all sesquiterpenes of the drimane series and are closely related to the known insect antifeedants polygodial (1) and warburganal (2) (Chart I), first isolated from a number of terrestrial plants.<sup>2</sup> We now report the structural elucidations of the novel sesquiterpenes olepupuane (3) and the methoxy acetal 4 and several new sources of polygodial (1) and the mixed sesquiterpene esters 5, previously found in *Dendrodoris limbata*.<sup>3,4</sup>

Specimens of *Dendrodoris nigra* were collected at Ala Moana reef, at Fort Kamehameha, and at Pupukea, all on Oahu; *Dendrodoris tuberculosa* were found at Ala Moana and at Pupukea; *Dendrodoris krebsii* were obtained from Bahia de los Angeles, Baja California, Mexico. Collections of *Doriopsilla albopunctata* were made at La Jolla, CA, Sunset Cliffs, San Diego, CA and Bahia de los Angeles. *Doriopsilla janaina*, the "gulf yellow porostome",<sup>5</sup> the "giant brown porostome", and "Fay's porostome" were all collected at Bahia de los Angeles. *D. nigra* and *D. tuberculosa* were extracted by immersion in distilled hexane for 5-10 min and then transferred to fresh solvent for 1-2

Chart I



(1) Schulte, G. R.; Scheuer, P. J. *Tetrahedron* 1982, 38, 1857. Thompson, J. E.; Walker, R. P.; Wratten, S. J.; Faulkner, D. J. *Ibid* 1982, 38, 1865.

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(5) The trivial names employed in this paper allow biologists who are familiar with Gulf of California fauna to identify these animals prior to their formal description.

days. In all cases the initial extract contained the sesquiterpenes of interest while the second extract contained largely fats, sterols, and pigments in addition to smaller quantities of sesquiterpenes. The specimens of *Doriopsilla albopunctata* from San Diego and La Jolla were extracted with cold methanol (-20 °C) while all other specimens were extracted with cold acetone for the length of time required to return the samples to the laboratory (1-3 weeks). In every case the sesquiterpenes were easily purified by