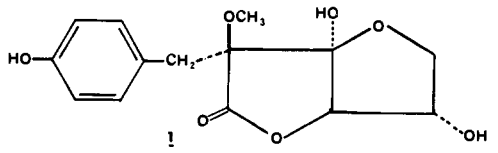


1

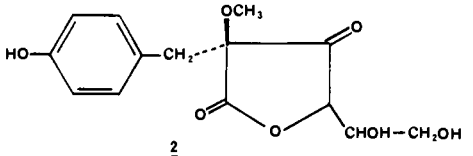
and with very few analogues among naturally occurring compounds. To our knowledge only piptoside,[2,3] ascorbigen,[4] and to a lesser extent conocarpine[5] and leucodrin[6] display some common features with delesserine (**1**). The compound was isolated from the marine alga *Delesseria sanguinea*,[7] belonging to the family Delesseriaceae. This family has, as yet attracted relatively little attention from marine natural products chemists,[8] despite the powerful anticoagulant properties displayed by the aqueous extracts of *D. sanguinea*.[9]

The ether-soluble material of the water–ethanol extract of *D. sanguinea*[10] gave some polar compounds. From this mixture the purification of delesserine (**1**) was achieved by a multiple-step procedure including chromatography on sephadex LH20 and silica gel and by HPLC on C_{18}-bondapak (H_2O–CH_3CN–MeOH, 75:20:5).

Delesserine (**1**) ($[\alpha]^{20}_D$ + 36° (*c* 0.72, MeOH)) was obtained as an amorphous powder which gave crystals from MeOH (mp 117 °C). The elemental composition $C_{14}H_{16}O_7$ was determined from high-resolution mass spectrometry (calcd for $C_{14}H_{16}O_7$ 296.0896, found 296.0895). The presence of a *para*-hydroxybenzyl moiety was deduced from the mass spectrum (*m/e* 107, C_7H_7O), from UV ((λ_{max} (EtOH) 225 (15 000), 277 (4500); λ_{max} (EtOH/KOH) 220 (35 000), 293 (3000)), from ^1H NMR (δ 6.75 (d), 7.17 (d)), and from ^{13}C NMR (δ 157.9, 134.8 (2C), 128.1, 118.3 (2C)).[11] In addition, the presence of OH (IR 3400 cm^{-1}), lactone (IR 1770–1800 cm^{-1}, ^{13}C NMR δ 177.6), and OMe (^1H NMR δ 3.64 (s); ^{13}C NMR δ 55.8) were also established.

In fact, the ^{13}C NMR spectrum displayed signals for 28 carbons, suggesting that delesserine in solution exists in two forms. In view of this possibility, plus its lack of stability, an X-ray crystallographic study was performed on a single crystal obtained from MeOH. The structure of the crystalline form of delesserine was then determined to be **1** with the relative configuration shown.

In solution, as suggested above, delesserine exists in two forms by opening of the hemiketal function. The main form has structure **1**, while the minor form is the open form **2** as shown by the ^{13}C



2

NMR spectrum. Indeed, in this spectrum there were two different series of signals differing in relative intensity (which is, in fact, temperature dependent). Signals of the most intense series (δ 177.6, 157.9, 134.8, 128.1, 118.3, 111.4, 90.4, 87.2, 78.5, 75.9, 55.8, 38.3)[12] were assigned to the closed form **1**; signals of the minor series (δ 212.6, 177.0, 158.7, 134.8, 125.6, 118.8, 87.4, 85.3, 73.1, 64.2, 59.0, 44.5)[12] were due to the open form **2**. The structure of this form was secured by the presence of an ketone (δ 212.6) and a $CHOHCH_2OH$ group (δ 73.1, 64.2) similar to that of glycerol[13] and ascorbic acid.[14] The biosynthetic origin of delesserine is probably a condensation of a C^6–C^1 unit with a 3-dehydrohexonic acid moiety. A similar biosynthesis has been proposed for piptoside.[2] The biological properties of delesserine are currently under investigation.

Acknowledgment. This work was supported by CNEXO (Centre National pour l'exploitation des Océans), CNRS (Centre National de la Recherche Scientifique), and INRA (Institut National de la Recherche Agronomique). We are indebted to Professor P. Courtot and the "Université de Bretagne Occidentale" for help and providing facilities. We thank Ph. Amade and D. Buestel for collecting material and J. Y. Le Gall for recording NMR spectra.

Registry No. **1**, 82198-78-5; **2**, 82198-79-6.

Supplementary Material Available: X-ray crystal structure, positional and thermal parameters, final bond distances and angles, observed and calculated structure factors for **1**, and mass and ^1H NMR spectral data for delesserine (8 pages). Ordering information is given on any current masthead page.

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(11) For the main signals of the predominating form in solution.
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Synthesis of a Cofacial Porphyrin–Quinone via Entropically Favored Macropolycyclization

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The precise, 3-dimensional orientation of molecular components achieved in macropolycyclic molecules makes them well-suited for use in model systems of biological processes.[1] The key role of porphyrin pigments and of quinones in the primary reactions of bacterial photosynthesis[2] provides impetus for the synthesis of porphyrin–quinone compounds. These syntheses have provided monosubstituted benzoquinone flexibly tethered or directly bonded to tetraphenylporphyrin.[3] However, the crucial requirements of distance and orientation in fast electron-transfer reactions[4] requires the synthesis of molecules with defined geometry, as occur in the photosynthetic systems.

We present the synthesis of a molecule containing a porphyrin and a quinone rigidly held 10 Å apart in cofacial parallel planes. Though capped,[5] bridged,[6] and cofacial[7] porphyrins have been

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prepared via macrocyclization, the syntheses are laborious and of low yield. The entropically favored macropolycyclization described here proceeds in high yield under the gentle conditions of mild acid catalysis in dilute solution at ambient temperature. It achieves the desired rigidity and represents a general approach for the efficient synthesis of compounds of this type.

A tetrabenzaldehyde-substituted quinone was prepared by alkoxylation of fluoranil (0.6 M) in dry CH_3CN with 5 equiv of 4-(2-hydroxyethoxy)benzaldehyde (I)[8] and excess CsF[9] (Figure 1). Mild heating for over 10 h gave 2,3,5,6-tetrakis[2-(4-formylphenoxy)ethoxy]benzoquinone (II)[10] in 47% yield after crystallization. The $\alpha,\alpha,\alpha,\alpha$-atropisomer of *meso*-tetrakis(*o*-aminophenyl)porphyrin (III) was prepared in high yield by isomerization in the presence of silica gel.[11]

Equimolar amounts of II and III were condensed in CH_3CN containing 10% dimethylacetamide (5×10^{-4} M) at room temperature in the presence of 4 equiv of trifluoroacetic acid. Schiff base formation was monitored spectrally at 330 nm, and kinetic analysis of the reaction composition was performed with HPLC. Intermediate condensation products PQ(n) (the porphyrin–quinone molecules with n = 1, 2, or 3 Schiff bases formed) rapidly appear and then slowly disappear as the product PQ(4) steadily accumulates. After 24 h, over 85% of the original porphyrin and quinone have been converted to PQ(4). Isolation of PQ(n) by column chromatography (alumina, 1:1 CH_2Cl_2/ethyl acetate) followed by acid hydrolysis regenerates the original porphyrin and quinone in a 1:1 ratio. PQ(n) isolated after 10 h of reaction was analyzed with the ^{252}Cf fission fragment mass spectral technique.[12] Observed parent ion masses $(M + H)^+$ of 1367.3, 1385.3, and 1403.3 mass units correspond to PQ(4), PQ(3), and PQ(2), the loss of one molecule of H_2O occurring with the formation of each Schiff base (calculated masses (M) are 1366.4, 1384.4, and 1402.4, respectively).

The desired porphyrin–quinone (labeled IV in Figure 1) is obtained by selective reduction of the Schiff bases in PQ(n) to benzylanilines. A total of 5 equiv of $NaBH_3CN$ is added after 20 h of reaction of II plus III, and the level of acidity is maintained with additional trifluoroacetic acid. Porphyrin–quinone is obtained in yields of 80–95% from II and III and gives a unique parent ion mass $(M + H)^+$ of 1375.5 mass units upon analysis (Figure 2).[13]

The quantitative evaluation of the entropic driving force for the formation of PQ(4) was obtained by comparison of the equilibrium positions of the PQ(n) condensation and that of the condensation of porphyrin with *p*-anisaldehyde (A). In contrast to the favorable formation of PQ(4) where aldehyde and amine are in a 1:1 ratio, a large excess (100-fold) of *p*-anisaldehyde was necessary to achieve significant condensation to PA(n). Reduction of PA(n) with $NaBH_3CN$ yielded PA_4 in quantitative fashion,[14] to be used for comparative photochemical purposes.

To prove the reversibility of the Schiff base formation and to measure the equilibrium point, we performed a mixed, competitive condensation with 1 equiv of quinone, 100 equiv of *p*-anisaldehyde, and 1 equiv of porphyrin (5×10^{-4} M) in benzonitrile/10% dimethylacetamide. The equilibrium composition consisted of 28% PQ(4), 34% PA(n) components, and 38% mixed condensation products of porphyrin, quinone, and *p*-anisaldehyde. This composition remains time invariant. The identical composition was obtained by the addition of 100 equiv of *p*-anisaldehyde to the PQ(n) equilibrium mixture (formed from 1 equiv of porphyrin and 1 equiv of quinone), or by the addition of 1 equiv of quinone to the PA(n) equilibrium mixture (formed from 1 equiv of porphyrin and 100 equiv of *p*-anisaldehyde). The PA(n) fraction consists of several components, and the distribution profile of these is dependent on the anisaldehyde concentration. The ratio of equilibrium constants, $K_{PQ(4)}/K_{PA(4)} = [PQ(4)][A]^4/[PA(4)][Q]$, can be obtained from the respective equilibrium constants, $K_{PQ(4)} = [PQ(4)][H_2O]^4/[P][Q]$ and $K_{PA(4)} = [PA(4)][H_2O]^4/[P][A]^4$, and the total PA($n$) fraction is used as an upper bound on the PA(4) content. Because the enthalpy of Schiff base formation is approximately the same in both compounds, the ratio of equilibrium constants provides a measure of the entropy of cyclization.[15]

In PA(4) each Schiff base is the result of an independent, second-order intermolecular reaction. In PQ(4) only one Schiff base is the result of intermolecular reaction, and the other three are due to first-order intramolecular cyclizations. Schiff base hydrolysis is a stoichiometric second-order reaction in all cases; thus, the number of molecules remains the same in the PA(4) condensation. Three additional molecules are gained, however, upon formation of PQ(4). These differences in orders of reaction and effective reaction concentrations are the source of the entropic advantage that favors cyclization.

Many macropolycyclizations use rather irreversible reactions, and the product yield is often low. Following the thermodynamic treatment of reversible cyclizations,[16] there exists a critical concentration below which quantitative cyclization occurs. This concentration can be quite high when the most probable molecular geometry is one predisposed to cyclization. Though cyclization to form a conformationally restricted state entails a loss of rotational entropy, this loss is minimized by using conformationally restricted precursors.[17] Macropolycycles of any reasonable shape and unlimited size can be prepared in high yields by joining rigid molecules that fit together through reversible condensations.

This thermodynamic favoring of macrocycle formation was previously observed in the porphyrinogens.[15] These compounds occur on the biosynthetic pathway to porphyrins. The prevalence of porphyrins in nature can be attributed to entropic causes more than to aromatic stabilization, which requires oxidation of the leuco compounds.

Preliminary measurements show the fluorescence emissions and yields of porphyrin–quinone and PA_4 are the same, but the fluorescence yield of Zn–PQ is quenched by 60% in comparison to that of Zn–PA_4. The photochemical properties of porphyrin–

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(10) Yellow-orange needles from CH_3CN; mp 149–151 °C; UV max (CH_3CN) 270 nm (ϵ 73 600), 400 nm (ϵ 184); IR ν_{max} (KBr) 825, 1060, 1160, 1250, 1605, 1690, 2730 cm^{-1}; ^1H NMR (60 MHz, 4.4 mM in $CDCl_3$) δ 9.88 (4 H, s, CHO), 7.38 (16 H, d, J = 8 Hz, PhH), 4.58 (8 H, m, CH_2O), 4.31 (8 H, m, CH_2O); Anal. Calcd ($C_{42}H_{36}O_{14}$) C, H, O; chemical ionization MS, $(M + 1)^+$ 765.5, relative abundance 22%, calcd mass (M) 764.2.

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(13) ^1H NMR (CD_2Cl_2) δ 8.87 (8 H, d, J = 30.1 Hz, β-pyrrole H), 7.84 (4 H, m, porphyrin PhH), 7.67 (4 H, m, porphyrin PhH), 7.14 (8 H, m, porphyrin PhH), 6.63 (8 H, d, J = 8.5 Hz, quinone PhH), 6.29 (8 H, d, J = 8.5 Hz, quinone PhH), 4.13 (8 H, m, OCH_2), 4.08 (8 H, s, $PhCH_2$), 3.76 (8 H, m, OCH_2), 3.41 (4 H, s, PhNH), −2.81 (2 H, s, porphyrin NH); porphyrin–quinone ($C_{86}H_{70}N_8O_{10}$), $(M + H)^+$ 1375.5, calcd mass (M) 1374.4. Microcrystals of Zn–PQ were obtained from toluene. Microcrystals of PQ(4) were also obtained from CH_3CN/methanol.

(14) PA_4, *meso*-tetrakis[*N*-(*p*-methoxybenzyl)-α-*o*-aminophenyl]-porphyrin: ^1H NMR (CD_2Cl_2) δ 8.89 (8 H, s, β-pyrrole H), 7.81 (4 H, m, porphyrin PhH), 7.59 (4 H, m, porphyrin PhH), 7.11 (4 H, m, porphyrin PhH), 7.01 (4 H, m, porphyrin PhH), 6.93 (8 H, d, J = 8.5 Hz, *p*-anisaldehyde PhH), 6.54 (8 H, d, J = 8.5 Hz, *p*-anisaldehyde PhH), 4.14 (8 H, s, CH_2), 3.75 (4 H, br s, PhNH), 3.51 (12 H, s, OCH_3), −2.67 (2 H, s, porphyrin NH); PA_4 ($C_{76}H_{66}N_8O_4$), $(M + H)^+$ 1155.5, calcd mol wt 1154.5.

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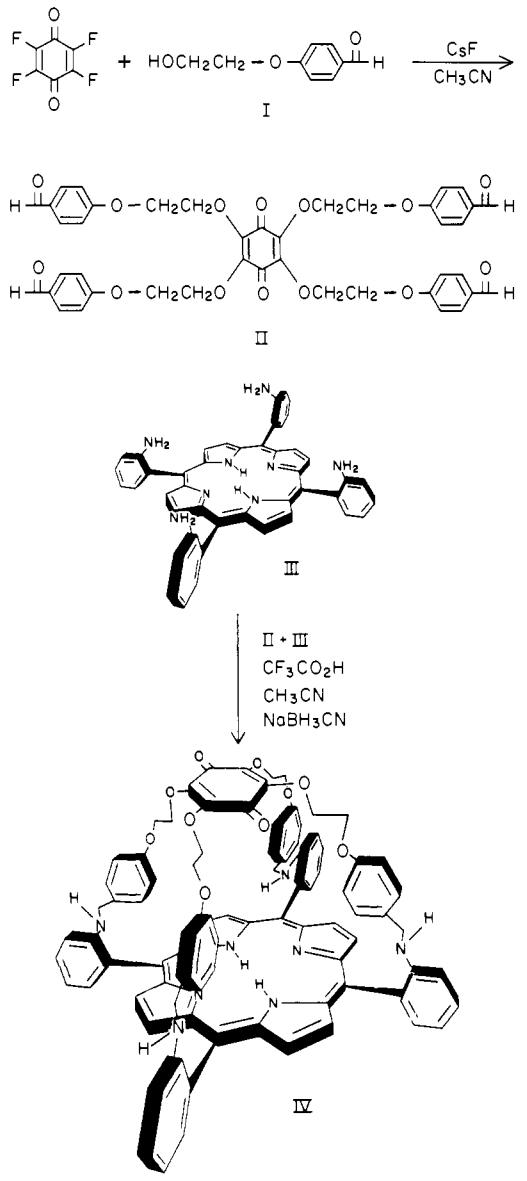

Figure 1. Synthetic scheme for preparation of porphyrin–quinone.

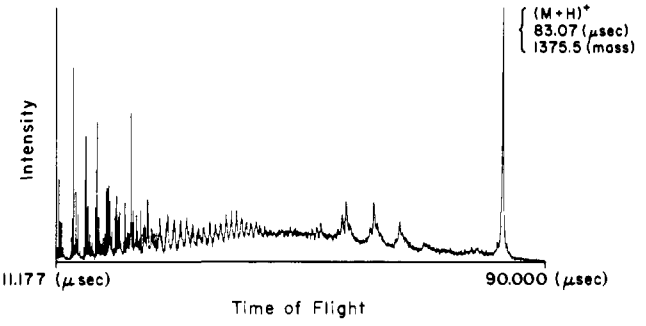

Figure 2. ^{252}Cf fission fragment time of flight mass spectrum of porphyrin–quinone. The times shown correspond to m/z values between 25 and 1622.

quinone and its metal derivatives will be reported shortly.

Acknowledgment. We thank James P. Tam for many helpful discussions pertaining to the synthesis. The mass spectrometric measurements were made by Brian Chait of the Rockefeller Mass Spectrometric Research Resource supported by the Division of Research Resources, NIH. This research was supported by The Rockefeller University Graduate Program and an NIH grant, No. GM25693. NMR spectra were obtained by using the 7 T spectrometer at the Rockefeller University purchased in part with funds from the National Science Foundation (PCM-7912083) and from the Camille and Henry Dreyfus Foundation.

Registry No. I, 22042-73-5; II, 82352-96-3; III, 52199-35-6; IV, 82352-97-4; fluoranil, 527-21-9.

Pivaloxy Decarboxylates Less Rapidly than Propionoxy: Steric Retardation of the Decarboxylation of Aliphatic Carboxylate Radicals

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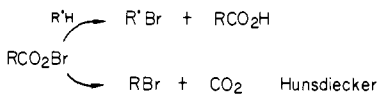
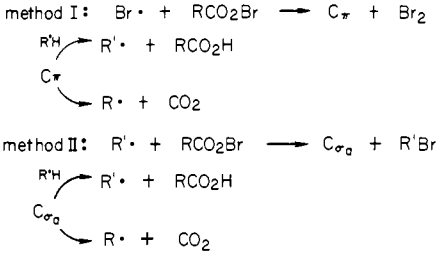
The conventional wisdom holds that pivaloxy radical (t-$BuCO_2\cdot$) decarboxylates more rapidly[1] than acetoxy radical. The rate of decarboxylation of acetoxy is reported[2] as 1.6×10^9 s^{-1} at 60 °C, giving it a half-life too short for reactions outside the solvent cage in which it is generated.[3] We report here reactions of propionoxy, isobutyroxy, and pivaloxy that occur outside the cage in which they are born. Also, we find pivaloxy decarboxylates less rapidly than acetoxy.

The chemistry of carboxylate radicals ($RCO_2\cdot$) are readily studied at temperatures between −60 and −100 °C in photoinitiated chain substitution reactions between acyl hypobromites (RCO_2Br) and alkanes in CCl_3F solvent.[4] These substitution reactions are in compeititon with the well-known Hunsdiecker process.[5] Earlier



studies employed high-temperature pyrolyses of peroxides to generate carboxylate radicals. Our reactions are carried out at low temperatures, by utilizing thermoneutral or exothermic chain steps (quantum yields >40).

We employ two different reaction systems to attain limiting conditions for the generation of carboxylate radicals. In method I, Br_2 is present at concentrations of 0.04–0.1 M. In method II,



vinylidene chloride (VC) is present as a bromine scavenger at concentrations of 0.026–3.6 M.[6] Selectivities (S) for formation

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