the aldehyde **3** (578 mg, 1.0 mmol) in ethanol (20 mL) was added sodium borohydride (30 mg in 0.1 mL of H_2O), and the mixture was stirred at room temperature for 15 min. A solution of NaOH (6 N, 0.4 mL) was added, and the mixture was heated on a steam bath for 5 min and then poured onto ice. The product was extracted with CH_2Cl_2 (3 × 20 mL) to give a white solid (550 mg): mp 128–130 °C; MS, *m/e* 580 (M^+); NMR δ 1.1 (6 H, t, Et), 1.3 (6 H, t, OEt), 2.0 (6 H, s, Me), 2.8 (4 H, q, Et), 4.1 (4 H, q, OEt), 5.0 (2 H, s, CH_2O), 5.3 (1 H, s, OH), 6.5 (1 H, s, methane CH), 7–7.77 (7 H, m, anthryl), 8.2 (1 H, s, 9H-an), 8.4 (2 H, br, NH). This solid was used in the next step without further purification.

8-(Hydroxymethyl)-1-[[4,4′-diethyl-3,3′-dimethyl-2,2′-dipyrryl]methyl]anthracene (4c). The diester dipyrrylmethane **4a** (500 mg, 0.86 mmol) was saponified by refluxing for 8 h in ethanol (10 mL) containing NaOH (300 mg) and water (1 mL). After the hydrolysate was concentrated to remove ethanol, water (20 mL) was added, and the solution was extracted with CH_2Cl_2 (20 mL). The aqueous layer was kept in an ice bath and neutralized with glacial acetic acid; the precipitated white solid was extracted into ether (3 × 20 mL). The crude diacid, after removal of solvent, was mixed with ethanolamine (3 mL) and heated to a gentle reflux under nitrogen for 1 h. The dark solution was poured into ice water; the resultant light yellow solid was collected by filtration. This material was chromatographed on silica gel (CH_2Cl_2) to give pure α-free dipyrrylmethane **4c** (360 mg): mp 98–100 °C; MS, *m/e* 436 (M^+); NMR δ 1.1 (6 H, t, Et), 2.0 (6 H, s, Me), 2.3 (4 H, q, Et), 5.0 (2 H, s, CH_2O), 5.2 (1 H, s, OH), 6.2 (1 H, s, methane CH), 6.3 (2 H, s, 5,5′-pyrrole), 7–7.77 (7 H, m, anthryl), 8.2 (1 H, s, 9-an), 8.4 (2 H, br, NH).

5-[8-(Hydroxymethyl)-1-anthryl]-2,8,13,17-tetraethyl-3,7,12,18-tetramethylporphine (7). To a solution of the decarboxylated pyrrylmethane **4c** (530 mg, 1.2 mmol) and the (diformyldipyrryl)methane **5**[14] (347 mg, 1.2 mmol) in dry methanol (70 mL) was added 70% perchloric acid (0.5 mL). The dark red solution was stirred for 12 h at room temperature in the dark; after which a solution of NaOAc (0.5 g) in methanol (10 mL) was added, followed by another solution of *o*-chloroanil (200 mg) in methanol (10 mL). After 1 h, the mixture was evaporated; the residue was taken up in CH_2Cl_2 (20 mL) and a solution of zinc acetate (200 mg) in methanol (10 mL) was added. After being stirred for 1 h, the mixture was evaporated and the residue separated by chromatography (silica gel, CH_2Cl_2). The isolated Zn(II) porphyrn was demetalated by washing with 10% HCl in CH_2Cl_2: yield of **7**; 400 mg, 48%; NMR δ −3.0 (2 H, d, NH), 1.7 (6 H, t, Et), 1.9 (6 H, t, Et), 2.1 (6 H, s, Me), 3.7 (6 H, s, Me), 3.8 (2 H, s, CH_2O), 3.9 (4 H, q, Et), 4.1 (4 H, q, Et), 10.0 (1 H, s, meso), 10.3 (2 H, s, meso), anthryl: 7.1 (1 H, d), 7.4 (1 H, t), 7.8 (2 H, m), 8.0 (1 H, d), 8.1 (1 H, d), 8.4 (1 H, d), 8.7 (1 H, s); UV-vis λ_{max} (ϵ_M) 624 nm (2400), 569 (6000), 535 (6500), 502 (13000), 405 (129000). Anal. Calcd for $C_{47}H_{48}N_4O$: C, 82.42; H, 7.06; N, 8.18. Found: C, 82.33; H, 7.15; N, 8.09.

5-(8-Formyl-1-anthryl)-2,8,13,17-tetraethyl-3,7,12,18-tetramethylporphine (8). Oxidation of the anthracene alcohol was effected by addition of **7** (280 mg) in pyridine (30 mL) to a solution of CrO_3 (325 mg) in pyridine (20 mL). The mixture was stirred at room temperature for 4 h and then poured into water (100 mL). The product was extracted into CH_2Cl_2 (3 × 50 mL) and purified by chromatography (siica gel, CH_2Cl_2) to give **8** in quantitative yield: NMR δ −3.1 (2 H, d, NH), 1.67 (6 H, t, Et), 1.85 (6 H, t, Et), 2.03 (6 H, s, Me), 3.68 (6 H, s, Me), 3.85 (4 H, q, Et), 4.03 (4 H, q, Et), 9.38 (1 H, s, CHO), 9.91 (1 H, s, meso), 10.15 (1 H, s, meso), anthryl: 7.40 (1 H, t), 7.67 (1 H, d), 7.85 (1 H, t), 8.10 (1 H, d), 8.28 (1 H, d), 8.46 (1 H, d), 8.75 (1 H, s), 9.00 (1 H, s); UV-vis λ_{max} (ϵ_M) 624 nm (2400), 569 (6100), 535 (6600), 502 (13500), 404 (140000).

***trans*-5,15-Bis[8-[5-(2,8,13,17-tetraethyl-3,7,12,18-tetramethylporphyrinyl)]-1-anthryl]-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphine (1).** To the porphyrin–aldehyde **8** (50 mg, 0.073 mmol) suspended in methanol (10 mL) was added first the α-free dipyrrylmethane **6**[8b] (17.3 mg, 0.073 mmol) and then toluenesulfonic acid (3.4 mg, 0.018 mmol).[8a] The mixture was stirred at room temperature for 10 h before the solvent was pumped dry. The residue was dissolved in THF (10 mL), treated with a solution of *o*-chloranil (10 mg) in THF (5 mL), and stirred for 1 h, and the solvent was removed again by evaporation. This mixture contained a large amount of unreacted **8** which can be recovered during the isolation of trimer **1**. The chromatography was carried out with a silica gel column, using pure CH_2Cl_2 to elute **8** and 5% MeOH–CH_2Cl_2 for **1**. The trimer thus obtained was purified further by converting into and chromatography of the Zn complex, which moves much faster than the free base, to remove impurities of low R_f values. Pure triporphyrin **1** was then derived by demetalation of the zinc complex using 10% HCl: yield, 7 mg; NMR δ −4.5 (6 H, three singlets clustered together, NH, see Figure 1), 0.95 (12 H, t, Et), 1.10 (12 H, t, Et), 1.45 (12 H, t), 1.60 (12 H, s, Me), 1.80 (12 H, s, Me), 3.02 (12 H, s, Me), 3.20 (8 H, q, Et), 3.41 (8 H, q, Et), 3.55 (8 H, q, Et), anthryl: 6.81 (2 H, d), 7.35 (2 H, d), 7.50 (2 H, t), 7.59 (2 H, d), 7.60 (2 H, s), 8.05 (2 H, s), 8.45 (2 H, t), 8.72 (2 H, s), meso: 8.95 (2 H, s), 9.25 (4 H, s), 9.30 (2 H, s); UV-vis λ_{max} (ϵ_M) 625 (3900), 573 (9300), 538 (9300), 506 (18000), 395 (169000). Anal. Calcd for $C_{124}H_{126}N_{12}$: C, 83.46; H, 7.12; N, 9.42. Found: C, 83.75; H, 7.30; N, 9.32. High-resolution positive ion mass spectra of **1** have been obtained on a Kratos MS-50RF equipped with Ionteck FAB gun, operated at 8 kV. The sample was prepared in 1-thioglycerol matrix containing trifluoroacetic acid.[15] Calcd for monoprotonated **1**: 1784.0306. Found: 1784.0140.

Acknowledgment. This work was supported by the NSF. We thank Brian Musselman for obtaining the high-resolution mass spectra. C.K.C. is an Alfred P. Sloan Fellow, 1980–84, and a recipient of a Camille and Henry Dreyfus Teacher–Scholar Grant, 1981–85.

Registry No. **1**, 94347-88-3; **2**, 4949-58-0; **3**, 94324-82-0; **4a**, 94324-83-1; **4b**, 94324-84-2; **4c**, 94324-85-3; **5**, 967-68-0; **6**, 92415-30-0; **7**, 94347-89-4; **7** Zn(II) complex, 94324-87-5; **8**, 94324-86-4; 1,8-anthracenedicarboxaldehyde, 34824-75-4.

(14) Chong, R.; Clezy, P. S.; Liepa, A. J.; Nichol, A. W. *Aust. J. Chem.* **1969**, *22*, 229.

(15) Musselman, B.; Chang, C. K., manuscript in preparation.

A Spontaneous Sulfoxide Dehydration

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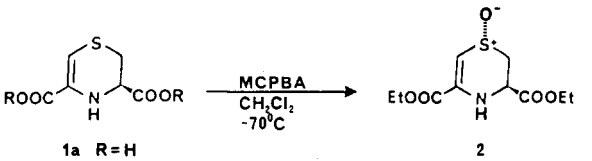
In the course of studies on 3,4-dihydro-2*H*-1,4-thiazine-3,5-dicarboxylic acid (**1a**), diester **1b** was oxidized with 1 equiv of *m*-chloroperbenzoic acid. A proton NMR spectrum of the product before chromatography suggested that predominantly one compound had formed which, when compared with spectra obtained by Kitchin and Stoodley[1] on 3,4-dihydro-1-oxo-2*H*-1,4-thiazine-3,6-dicarboxylates, appeared to be the trans sulfoxide **2**. This stereochemical assignment was supported by an aromatic solvent-induced shift study (see Table I). It has been



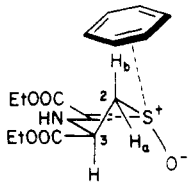
1a R=H
1b R=Et

2

(1) Kitchin, J.; Stoodley, R. J. *Tetrahedron* **1973**, *29*, 3023.
(2) Strom, E. T.; Snowden, B. S.; Toldan, P. A. *J. Chem. Soc., Chem. Commun.* **1969**, 50.
(3) Fraser, R. R.; Durst, T.; McClory, M. R.; Viau, R.; Wigfield, Y. Y. *Int. J. Sulfur Chem.*, Part *A* **1971**, *1*, 133.

0022-3263/85/1950-0413$01.50/0

Table I. Aromatic Solvent-Induced Shifts

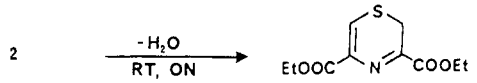


proton	ppm downfield from Me_4Si[a]		
	CCl_4	C_6D_6	$\Delta(CCl_4 - C_6D_6)$
2a	3.23	2.99	0.24
2b	2.19	1.58	0.61
3	4.23	4.35	0.12

[a] J(2a,3) = small; J(2b,3) = 13.5 Hz; J(2a,2b) = 13.5 Hz ($CDCl_3$).

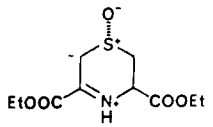
reported[2,3] that benzene solvates the positive end of the sulfoxide dipole and therefore is closer to the vicinal proton trans (H_{2b}) to the sulfoxide and shields it more than the proton cis (H_{2a}) to it. The large coupling of H_3 to H_{2b} and its small coupling to H_{2a} indicate that H_3 is trans to H_{2b} and therefore is cis to the sulfoxide as in structure **2**.

Sulfoxide **2** is remarkably labile; simply standing overnight in methylene chloride solution at room temperature, it was transformed into a new substance (warming at 60 °C for <1 h also effected this change). Exact mass spectral and elemental analyses[4] on the product indicated that 1 mol of water has been lost from **2**. Structure **3** was assigned to the product on the basis of ^1H and ^{13}C NMR spectra (see Table II). The proton spectrum of **3** differed

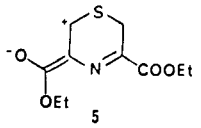


3

from that of **2** in the following ways: it had one less proton on carbon, the two protons of the methylene had become equivalent, and the resonance of the olefinic proton had shifted downfield by 1.36 ppm. The ^{13}C spectrum of **3** showed an additional trigonal carbon not bearing a proton and one less tetrahedral carbon as well as a significant (30 ppm) downfield shift for the olefinic carbon bearing a proton. These results indicated that a new double bond had formed involving only one carbon atom and that the asymmetry of the sulfoxide had been lost. The significant downfield shifts can be understood by considering the most important polar resonance-contributing forms involving the 6-position of these molecules (see **4** and **5**). The carbon



4



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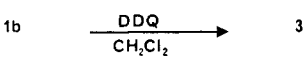
atom at position 6 in structure **3** is expected to be much more electropositive than the one in structure **2** and, therefore, both it and the attached proton should be strongly deshielded relative to the corresponding nuclei in **2**.

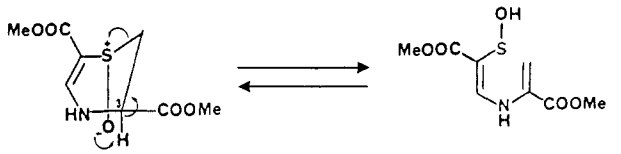


(4) Compounds **1b–3** were obtained as oils which retained small amounts of the methylene chloride used in their preparation or chromatographic purification. Acceptable elemental analyses (<±0.3) were obtained for all three compounds when the amount of methylene chloride (5, 10, and 20 mol %, respectively) detected in the ^1H NMR spectrum was included in the calculations.

(5) Sica, D.; Paolillo, L.; Ferretti, J. A. *Ric. Sci.* **1967**, *37*, 629.

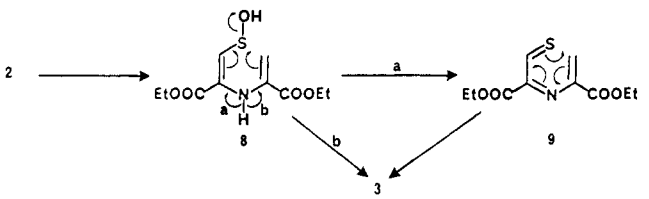
The structural assignment of the dehydration product was confirmed by its synthesis from **1** by dehydrogenation using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

No precedent for such a mild sulfoxide dehydration was found in the literature.[6] The mechanism of the surprisingly facile reaction reported here is of particular interest. Stoodley and Wilkins[7] have reported the thermal (~40 °C) racemization of *trans*-3,4-dihydro-1-oxo-2*H*-1,4-thiazine-3,6-dicarboxylates (**6** and related structures) and have provided evidence that this reaction involves a cycloelimination to produce an achiral sulfenic acid intermediate (**7**) which recloses to give back the trans sulfoxide as a racemate. Since only the trans isomers undergo



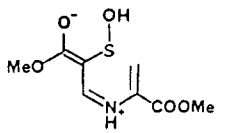
6 **7**

racemization, it was proposed that the cycloelimination reaction required a cis-axial arrangement of the sulfinyl group and the hydrogen atom at the 3-position. Our starting dihydrothiazine **1** was optically active, but the oxidation product **2** was racemic. Since this sulfoxide was prepared at −70 °C, the workup at room temperature must have been responsible for the racemization. Clearly, this compound must readily ring-open like Stoodley's sulfoxides, supporting its assignment as the trans isomer. In addition to being able to reclose to give racemized sulfoxide, ring-opened intermediate **8** could also undergo other reactions. For example, 1,4 elimination of water[8] (path a) would give **9** which could undergo an electrocylic reaction to give thiazine **3**. Alternatively, **8** could undergo direct



8 **9** **3**

cyclization by enamine attack on the sulfenic acid (path b). Stoodley did not report any dehydration reactions for his sulfoxides; undoubtedly, these kinds of reactions are less likely to occur with intermediates in which the electron pair on the nitrogen atom is delocalized into the vinylogous urethane portion of the molecule as illustrated in resonance-contributing form **10**.



10

The involvement of a direct, acid-catalyzed, 1,4 dehydration of **2** as illustrated by structures **11** and **12** is unlikely since no strong acid was present in the reaction solution. Sulfoxides are weakly basic (pK_a −1.6 to −3.0),[9]

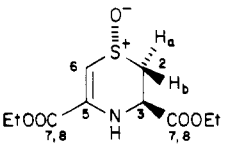
(6) Olefinic products have been reported for Pummerer reactions employing carboxylic anhydrides and elevated temperatures. Horner, L.; Kaiser, P. *Liebigs Ann. Chem.* **1959**, *626*, 19.

(7) Stoodley, R. J.; Wilkins, R. B. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1572.

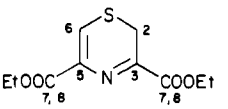
(8) 1,2 Elimination of water from a sulfenic acid intermediate has been proposed. Yoshida, A.; Oida, S.; Ohki, E. *Chem. Pharm. Bull.* **1975**, *23*, 2518.

(9) Landini, D.; Modena, G.; Scorrano, G.; Taddei, F. *J. Am. Chem. Soc.* **1969**, *91*, 6703.

Table II



I



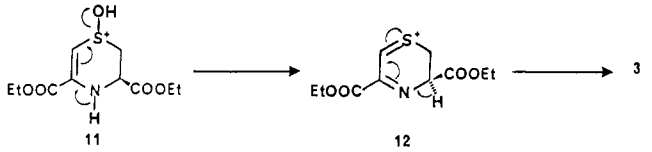
II

^{1}H NMR Spectra in $CDCl_3$						
	I				II	
	2a	2b	3	6	2	6
δ	3.37	2.28	~4.3	6.24	3.40	7.54
mult	(br)(d)	(dd)	(obsc)	(br)	(d)	(t)
J, Hz	13.4	13.5			1.2[a]	1.2[a]
J, Hz		13.5				

^{13}C NMR Spectra (ppm) in $CDCl_3$							
I				II			
2,3	5	6	7,8	2	3,5	6	7,8
43.74	136.38	97.26	161.30	20.17 (t)	136.92 (s)	127.22 (d)	161.89 (s)
43.90			169.10		137.57 (s)		162.87 (s)

[a] Long-range coupling of this magnitude has been reported for 3,5-diphenyl-2*H*-1,4-thiazines.[5]

and acid-catalyzed Pummerer reactions have been carried out with strong acids such as hydrogen chloride or *p*-toluenesulfonic acid.[10,11]



11 12

Experimental Section

Proton magnetic resonance spectra were recorded on a Varian T-60 spectrometer with Me_4Si as internal reference. Carbon magnetic resonance spectra were obtained on a JEOL FX-90-Q spectrometer using $CDCl_3$ as internal reference. The molecular formulas of all compounds were confirmed by exact mass spectral measurements. Mass spectra were recorded on a Varian MAT CH5-DF spectrometer. Infrared spectra were taken on a Perkin-Elmer 137 spectrophotometer. Ultraviolet spectra were obtained on a Hewlett-Packard 8450-A spectrophotometer. Circular dichroism spectra were recorded on a Jasco J500C spectrophotometer. Chromatography was done at medium pressure using Baker silica gel for flash chromatography (40-μm average particle size). Et_3N was dried over NaOH.

Diethyl (*R*)-3,4-Dihydro-2*H*-1,4-thiazine-3,5-dicarboxylate (1b). To a solution of 3.7 g (20 mmol) of L-cysteine ethyl ester hydrochloride and 5.6 mL (40 mmol) of dry Et_3N in 75 mL of CH_2Cl_2 under nitrogen was added over 10 min a solution of 3.9 g (20 mmol) of ethyl bromopyruvate in 25 mL of CH_2Cl_2.[12] After being stirred overnight, the yellow solution was washed twice with 25 mL of water and then dried over Na_2SO_4. Evaporation of the solvent left 5.1 g (~100%) of **1b** as a yellow syrup which required no further purification: IR (CH_2Cl_2) 3400 (w), 1725, 1700, 1605 (w), 1015 cm^{-1}; UV (CH_3CN) λ_{max} 214 nm (ϵ 5070), 313 (7760); CD (CH_3CN), extrema [θ] 206 nm (-2.4×10^3), 220 ($+3.2 \times 10^3$), 260 (-9.6×10^3), 310 ($+8.1 \times 10^3$); ^{1}H NMR ($CDCl_3$) δ 6.14 (s, 1 H, CH=), 4.22 (q + obscured m, 5 H, J = 7.2 Hz, CH_2CH_3 + CHN), 2.77–3.36 (m, 2 H, CH_2S), 1.28 (t, 6 H, J = 7.2 Hz, CH_3); exact mass, electron-impact ionization mode (70 eV), m/z 245.071 (calcd for $C_{10}H_{15}NO_4S$ 245.072).

Diethyl *trans*-3,4-Dihydro-1-oxo-2*H*-1,4-thiazine-3,5-dicarboxylate (2). To a solution of 490 mg (2 mmol) of **1b** in 10 mL of CH_2Cl_2 at −70 °C under nitrogen was added over 5 min a solution of 414 mg (2.4 mmol) of *m*-chloroperbenzoic acid in 13 mL of CH_2Cl_2. The reaction was allowed to stir at −70 °C for 20 min. After being warmed to room temperature, the reaction solution was washed with 8 mL of 5% $NaHCO_3$ and then 10 mL of water and dried over Na_2SO_4. Evaporation of the solvent left 443 mg (85%) of **2** as an amber syrup. An analytical sample was prepared by rapidly chromatographing on silica gel, eluting with 1% MeOH in CH_2Cl_2, and cooling the fractions with ice. Removal of the solvent in vacuo left a yellow oil: IR (CH_2Cl_2) 3400 (w), 1730, 1590, 1015 cm^{-1}; UV (CH_3CN) λ_{max} 290 nm (ϵ 5160); CD, no optical activity; NMR, see Tables I and II; exact mass, field desorption mode (7 kV), m/z 261.065 (calcd for $C_{10}H_{15}NO_5S$ 261.067).

Diethyl 2*H*-1,4-Thiazine-3,5-dicarboxylate (3). Method A. Sulfoxide Dehydration. A solution of 429 mg (1.64 mmol) of **2** in 2.5 mL of $CDCl_3$ in a test tube was heated in a bath of refluxing EtOH. After 20 min, very little sulfoxide remained as determined by proton NMR. The reaction product was purified by silica gel chromatography eluting with 0.5% MeOH in CH_2Cl_2 to give 111 mg of **3** as a yellow oil: IR (CH_2Cl_2) 1705, 1590 (w), 1015 cm^{-1}; UV (CH_3CN) λ_{max} 220 nm (ϵ 9600), 258 (5850), 365 (3600); NMR, see Table II; exact mass, electron-impact ionization mode, m/z 243.056 (calcd for $C_{10}H_{13}NO_4S$ 243.056).

Method B. Dehydrogenation of 1b. To a solution of 120 mg (0.53 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in 7 mL of CH_2Cl_2 was added a solution of 115 mg (0.47 mmol) of **1b** in 2 mL of CH_2Cl_2. The reaction was capped and stirred at room temperature for 0.5 h; it turned dark instantly, and a reddish brown precipitate formed. The solid was removed by filtration, and the solution was washed with 5% $NaHCO_3$. The organic layer was dried over Na_2SO_4 and evaporated to a yellow oil which gave ^{1}H NMR, IR, and UV spectra identical with those obtained for the sulfoxide dehydration product.

Acknowledgment. We are grateful to Dr. W. Holl for circular dichroism and ultraviolet spectral data and Mr. W. Johnson for mass spectral data. We thank Dr. G. Dunn for his encouragement.

Registry No. **1b**, 94110-58-4; **2**, 94110-59-5; **3**, 94110-60-8; L-cysteine ethyl ester hydrochloride, 868-59-7; ethyl bromopyruvate, 70-23-5.

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