Problems in Electron State Assignment Based on Circular Dichroism. Optical Activity of Diazines

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Abstract: Uv and CD spectra of 1,4- and 1,2-diazines with rigid molecular structure indicate that deviations between these types of spectra may be taken as a clue to hidden electronic states only with precaution. The necessity for a careful analysis of vibrational coupling is emphasized. Reversal of sign by vibrational coupling is not restricted to weak CD bands; it may be more common than hitherto accepted. We were not able to locate and identify the higher lying $^1(n,\pi^*)$ state in a diazine by CD measurements.

A large body of evidence concerning the electronic structure of diazines has been accumulated.[1] The π,π^* states are quite well understood.[2] The diazine molecules are planar; the n $\rightarrow$ π^* transition is polarized perpendicular to that plane. In the diazines there are two n $\rightarrow$ π^* transitions to be expected corresponding to the two n orbitals of the nitrogen atoms. The n-orbital split has been determined by photoelectron (PE) spectroscopy.[3] However, up to now only the n $\rightarrow$ π^* transitions at long wavelengths have been assigned with certainty, as n $\rightarrow$ π^* transitions are too weak to be found in the uv spectrum unless they are separated from the intense π $\rightarrow$ π^* bands. Attempts of band assignments to the high energy n $\rightarrow$ π^* transition of diazines are highly tentative.[1]

This paper is concerned with the application of circular dichroism (CD) to the determination of position and identity of hidden bands, especially the high energy n $\rightarrow$ π^* transitions in diazines. The selection rules for uv and CD spectra are different ones. Accordingly,

$$\text{Uv:} \quad f = \frac{8\pi^2 m}{3e^2 h} \nu_{0i} |\langle \psi_0 | \mu_e | \psi_i \rangle|^2$$

$$\text{CD:} \quad R = Im\{\langle \psi_0 | \mu_e | \psi_i \rangle \cdot \langle \psi_i | \mu_m | \psi_0 \rangle\}$$

transitions with small electric but large magnetic transition moments, as have the n $\rightarrow$ π^* transitions, may appear stronger in the CD than in the uv spectrum. Moreover, CD bands may have positive or negative sign which in many cases facilitates the recognition of bands in the CD spectrum. There is little information about optically active pyrazines and pyridazines in the literature.[4] In order to minimize effects of temperature and solvent, we selected the diazines I–IV with constant distance between the optically active center and the chromophore.
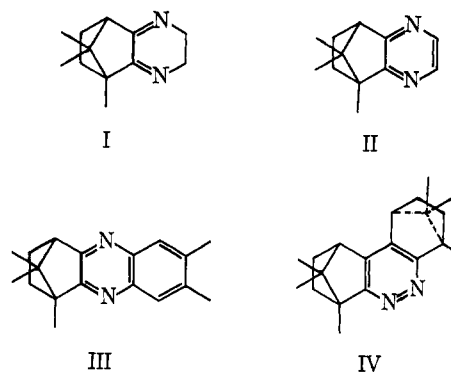
Experimental Section

(1R)-Bornano[2,3-b]-5,6-dihydropyrazine (I) was obtained by condensation of d-camphorquinone and ethylenediamine as a yellow solid with melting point at room temperature. Caution has

I   II

III   IV

to be taken to avoid dehydration of the product to the corresponding pyrazine. (1R)-Bornano[2,3-b]pyrazine (II) was made from the dihydro compound by oxidation with sulfur, mp 87–89°. (1R)-Bornano[2,3-b]-6,7-dimethylquinoxaline (III) was formed by condensation of d-camphorquinone and dimethyl-o-phenylenediamine as white needles, mp 80–81°. Di[(1R)-bornano][2,3-c:2′,3′-e]pyridazine (IV) was prepared according to the literature.[5] L-Phenyl glycol (V) was obtained from L-mandelic acid by reduction with LiAlH4, mp 72–74°.

The materials were purified by passing them through alumina and silica columns until the uv spectrum was not altered by further purification. The purity was checked by thin-layer chromatography. The crystalline products were purified further by chromatography on a column of Sephadex LH-20 (2.5 × 90 cm). The column was developed with 96% ethanol of "uvasol" quality; the effluent was monitored with a LKB-uvicord. Hexane and ethanol were of "uvasol" quality, sulfuric acid *pro analysi*, and bromohexane was distilled and transparent at 300 nm to 80%, at 275 nm to 2%.

CD spectra were recorded with a Cary 60 spectropolarimeter, equipped with CD attachment 6002, at room temperature with fused silica cells of different pathlengths (1–20 mm). The bandwidth was 3 nm. The law of Lambert–Beer was valid. The uv spectra of the solutions used for CD measurements were recorded with a Zeiss DMR 21 spectrophotometer.

Results

We want to emphasize our efforts in elimination of impurities and generalize that the reliability of ORD and CD spectra depends critically on the care dedicated to the purification of the samples. All samples used in this study were purified by chromatography until no change of the CD spectrum could be obtained by further chromatographic treatment.

The uv and CD spectra of I (Figure 1) are almost identical in the long-wavelength region. The n $\rightarrow$ π^* band centered at 28 kK is shifted in the polar solvent

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(3) (a) R. Gleiter, E. Heilbronner, and V. Hornung, *Helv. Chim. Acta*, **55**, 255 (1972); (b) K. A. Muszkat and J. Schäublin, *Chem. Phys. Lett.*, **13**, 301 (1972).

(4) H. E. Smith and A. A. Hicks, *Chem. Commun.*, 1112 (1970).

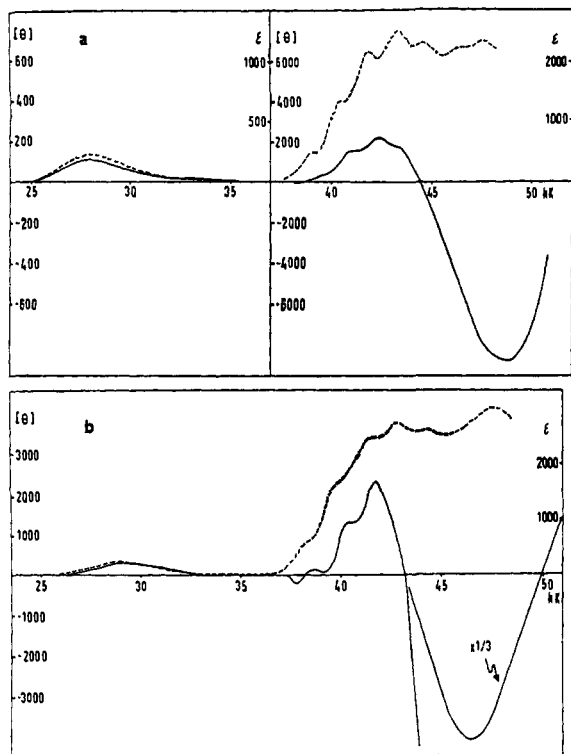(5) G. Oddo, *Gazz. Chim. Ital.*, **27**, I, 149 (1897).

Figure 1. (1R)-Bornano[2,3-b]-5,6-dihydropyrazine (I) in (a) hexane and (b) ethanol; (-----) uv, (———) CD spectrum.

to shorter wavelengths in both spectra. The band centered near 40 kK is shifted in the opposite direction. The vibrational structure of some 1.5 kK spacing observed in the $\pi \rightarrow \pi^*$ band is more pronounced in the uv spectrum for hexane as a solvent; however, for ethanol as a solvent the CD spectrum is structured more sharply. The vibrational sequence of the band in both hexane and ethanol solutions starts with a negative peak which is smaller in the hexane solution. Thus the sign of the CD band is changed in the region of the $\pi \rightarrow \pi^*$ absorption band. There is no hint to the second $n \rightarrow \pi^*$ transition if we take the negative band near 38.5 kK in hexane and near 37.8 kK in ethanol as a member of the vibrational progression, which seems to be justified by the solvent dependence of this band (for details see Discussion).

It was not possible to take a spectrum of I in acid solution as the compound decomposes and the spectrum is that of camphorquinone.

The well-known solvent dependence of the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ bands can be seen in the uv spectrum of II (Figures 2a and b). In the CD spectrum a negative band appears near 35 kK. In the EtOH–H$_2$SO$_4$ solution (Figure 2c) the type of the spectrum is changed: the long-wavelength $\pi \rightarrow \pi^*$ uv band seems to possess two components which contribute to the CD spectrum with opposite sign. An assignment to $n \rightarrow \pi^*$ or $\pi \rightarrow \pi^*$ transitions is impossible.

In the uv spectrum of III the long-wavelength $n \rightarrow \pi^*$ band which is visible in the spectrum of the plain quinoxaline,[6] has disappeared in the envelope of the sharply structured $\pi \rightarrow \pi^*$ band at 31 kK (Figures 3a and b). For experimental reasons it is impossible to record a reliable CD spectrum in the spectral region around 32

(6) F. Dörr, H. Gropper, and N. Mika, *Ber. Bunsenges. Phys. Chem.*, **67**, 202 (1963).
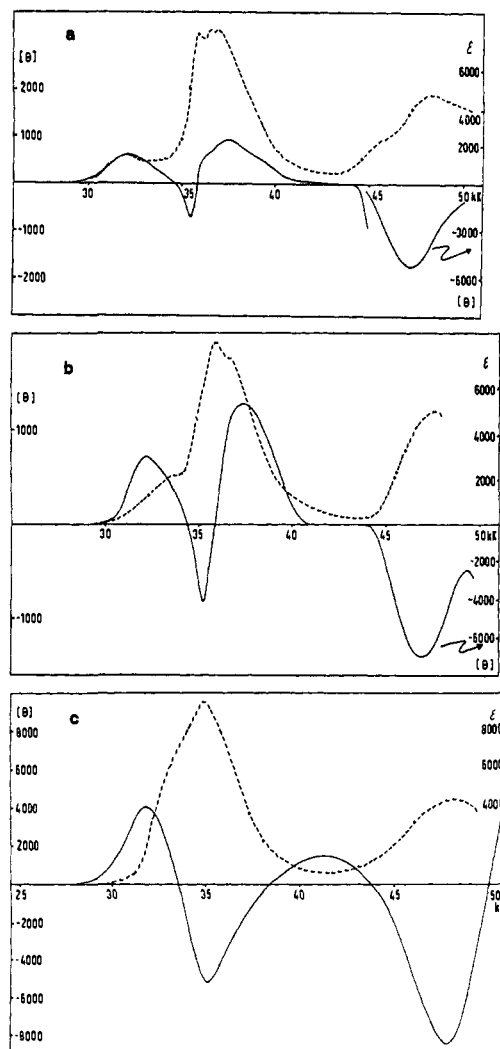

Figure 2. (1R)-Bornano[2,3-b]-pyrazine (II) in (a) hexane, (b) ethanol, and (c) ethanol–sulfuric acid: (-----) uv, (———) CD spectrum.

kK. In the CD spectrum of III we observe a negative band near 40 kK which is missing in the uv spectrum, quite similar to the spectra of I. Again this negative band is shifted to the red when the polarity of the solvent is increased. The CD spectrum in acid solution (Figure 3c) resolves the long-wavelength absorption band into two components of opposite sign similarly to the spectrum of II. The absorption band at 38.4 kK seems to meet the same fate.

In contrast to the bornano-1,4-diazines the sign of the $n \rightarrow \pi^*$ and longest wavelength $\pi \rightarrow \pi^*$ bands of IV are negative (Figure 4). Here the ellipticities of the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions are about equal. The solvent effect is normal. In hexane solution we observe an additional very weak band at 29 kK with positive sign which is not detectable in ethanol solution. Even solutions with high concentrations do not reveal the positive band.

It would have been straightforward to use (1R)-bornano[2,3-a]benzene for comparison with the pure aromatic system. As we have not been successful in synthesizing this compound we used L-phenyl glycol which lacks the rigidity of the molecular framework. The uv and CD spectra of this compound have the same number of bands with similar structure (Figure 5).
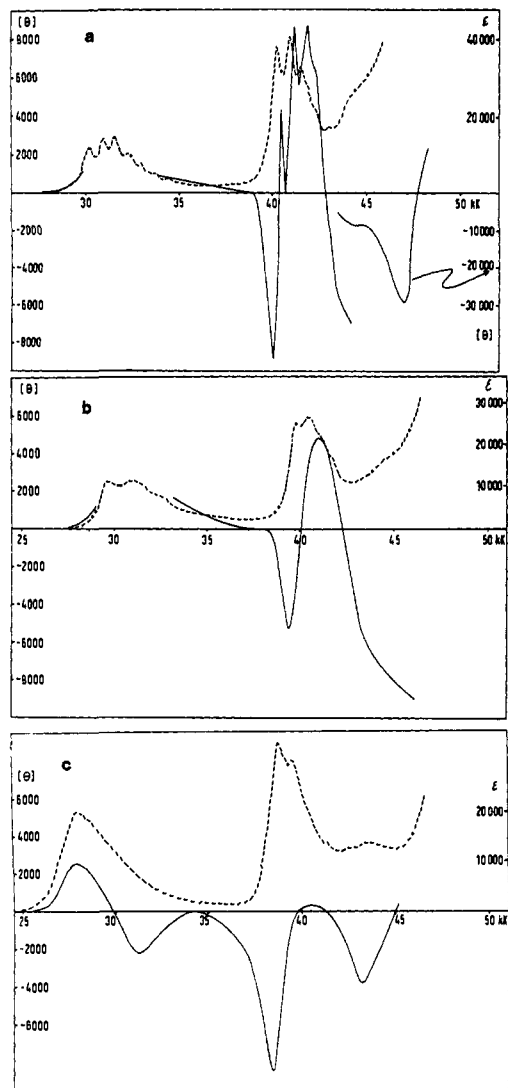
Figure 3. (1R)-Bornano[2,3-b]-6,7-dimethylquinoxaline (III) in (a) hexane, (b) ethanol, and (c) ethanol–sulfuric acid: (-----) uv, (——) CD spectrum.
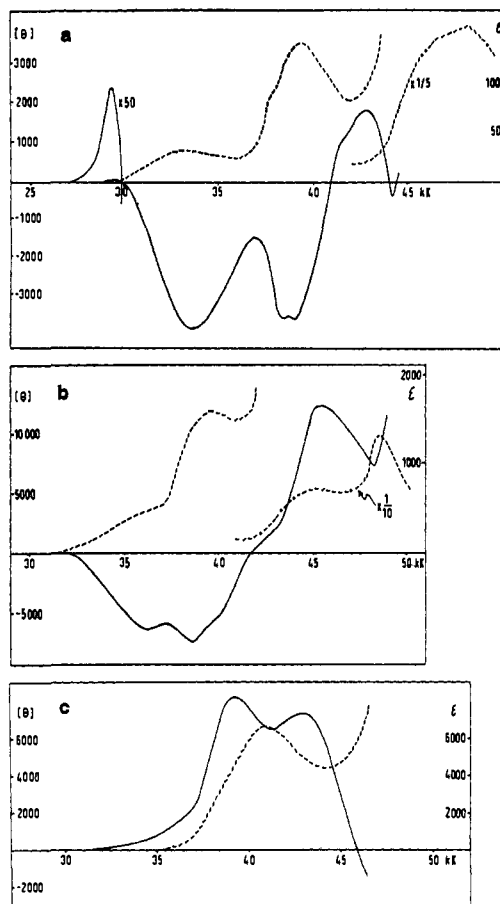
Figure 4. Di[(1R)-bornano][2,3-c:2'3'-e]pyridazine (IV) in (a) hexane, (b) ethanol, and (c) ethanol–sulfuric acid: (-----) uv, (——) CD spectrum.

Protonization of the diazines causes a reversal of the sign of the CD bands belonging to the $\pi \to \pi^*$ transition of lowest energy (Figures 2c, 3c, and 4c). This is an astonishing result as there is no conformational change possible in the rigid structures of the molecules investigated.

Discussion

The spectrum of the hexane solution of IV (Figure 4a) shows a very weak additional CD band of positive sign. This suggests an electronically excited state 3–5 kK below the lowest lying $^1(n,\pi^*)$ state. The transition to that state from the ground state must be highly forbidden in the electric dipole approximation. According to the exciton theory such a state should be expected[7] giving rise to a CD band of opposite sign as that of the 34-kK n $\to$ π^* band.[8] However, exciton theory is not applicable to molecules like the diazines on the basis of the PE spectra[3] and theoretical considerations.[9,10]
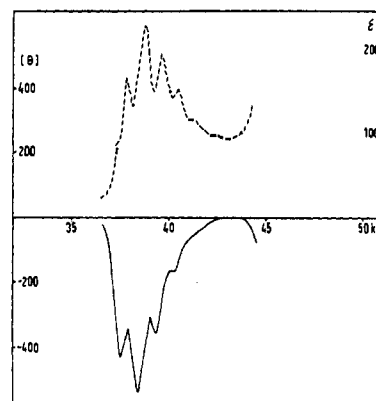
Figure 5. L-Phenyl glycol (V) in ethanol: (-----) uv, (——) CD spectrum.

In ethanol solution this weak CD band has disappeared. It seems blue shifted and concealed under the n $\to$ π^* band of the CD spectrum (Figure 4b). This behavior would suggest the assignment of this band to a n $\to$ π^* transition. Considering the uv and PE spectra we are only left with an assignment to the $^3(n,\pi^*)$ state. With unsubstituted pyridazine this triplet state was localized at 24 251 cm^{-1} in the crystal spectrum[11] and at 22 487.1

(7) M. Kasha, H. R. Rawles, and M. Ashraf El-Bayoumi, Pure Appl. Chem., 11, 371 (1965).

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(9) D. R. Kearns and M. Ashraf El-Bayoumi, J. Chem. Phys., 38, 1508 (1963).

(10) (a) E. Clementi, J. Chem. Phys., 46, 4737 (1967); (b) M. Hack-meier and J. L. Whitten, J. Chem. Phys., 54, 3739 (1971).

(11) R. M. Hochstrasser and C. Marzzacco, J. Chem. Phys., 46, 4155 (1967).

cm^{-1} in the vapor phase spectrum.[12] This is in correspondence with calculations for this triplet state of pyridazine.[13] We tried to confirm this assignment of the CD band in question to a singlet–triplet transition by making use of the heavy atom effect, but the ellipticity of this band is the same in hexane and bromohexane. So we have to postpone an unequivocal assignment until current investigations of the CD behavior of singlet–triplet transitions have provided further evidence.

According to the pyridazine PE spectra the short wavelength n $\rightarrow$ π^* transition should be expected some 15 kK at higher energies than the long wavelength n $\rightarrow$ π^* transition. In this spectral region, however, not a single one of the CD spectra displayed a clue to a transition which might be hidden in the uv spectrum.

Much more expressed are the differences between the uv and CD spectra of the diazines I, II, and III in the region of the low-energy $\pi \rightarrow \pi^*$ bands. It is remarkable that the new negative bands of the CD spectrum in the hexane solution spectrum [of I at 37.8 kK, of II at 35.5 kK, and of III at 40 kK (Figures 1a, 2a, and 3a)] always mark the long-wavelength ascent of a $\pi \rightarrow \pi^*$ band. A closer look at the solvent influence reveals a red shift of the negative CD bands in more polar solvents. This rules out an identification of the transition as being of the n $\rightarrow$ π^* type.

Conventionally from spectra like that of, e.g., Figure 3b, the conclusion is drawn that the envelope of the uv band contained two electronic transitions, one of which has a positive, the other a negative Cotton effect. However, calculations[2] do not require an additional $^1(\pi,\pi^*)$ state in this region of the spectrum and it seems unjustified on grounds of the high optical activity to postulate a triplet state. For benzene, where there is evidence for a state not yet identified quite near the $^1B_{2u}$ state[14] there is no CD band without correspondence in the uv spectrum (Figure 5 in correspondence with ref 15). It seems to be justified to accept the band assignments founded on the results of absorption and fluorescence measurements and of calculations. So we are left with the question whether it is necessary at all to introduce new electronic states into the discussion of the CD spectra. This cannot be answered without the consideration of vibrational effects.

Symmetrical chromophores become optically active only by a perturbation by an asymmetric center and this perturbation is a static one and independent from the dynamic perturbation of the electronic states of the chromophore by vibrational coupling. So it is not of necessity that the contribution to circular dichroism caused by the static asymmetric perturbation must be greater than the contribution reflecting the sensitivity of the electric and/or magnetic transition dipole moment to vibrations.[16] The effect of vibrational coupling thus may result in contributions to a CD band equal to or even larger than those of the vibrationally unperturbed states. Consider the vibrational structure of

the 40-kK band in the CD spectrum of III in hexane solution (Figure 3a). The vibrations of 650–700 cm^{-1} of the uv spectrum can be assigned to a totally symmetric vibration, obviously the same that determines the long progression of the uv band near 30 kK. The vibrational structure of the 40-kK band of the CD spectrum (Figure 3a) may be analyzed in terms of two progressions: (1) 40,000 + n680 cm^{-1}, where n = 0,1,2... and (2) 40,000 + 450 + m680 cm,$^{-1}$ where m = 0,1,2..., the first progression carrying negative, the second positive rotator strength. Under the assumption that the totally symmetric vibrations do not contribute to vibrational coupling in this case the 0–0 transition and the bands of the first progression reflect the influence of the asymmetric perturbation of the chromophore. The positive progression "steals" its intensity by coupling of the second excited $^1(\pi,\pi^*)$ state with other electronic states under the perturbation of the 450-cm^{-1} vibration which is not totally symmetric. We are not able to determine the symmetry representation of this vibration to obtain a clue as to whether the influence on the electric or the magnetic dipole transition moment might be responsible for this vibrational progression. The effect of vibrational coupling is quite large, however, and causes a reversal of sign in the region of the corresponding uv band. Our molecule III is an example for an exception to the rule of Weigang[17] that such a reversal of sign by vibrational coupling should be restricted to ellipticities smaller than 3000 [deg cm/dmol]. The effect of vibrational coupling thus may be larger than hitherto accepted. The same line of argument holds for the case of I (Figure 1a), where the totally symmetric vibration is characterized by 1500 cm^{-1} quanta, the nontotally symmetric by quanta of 600 cm^{-1}. Here the vibrationally induced positive rotator strength is much greater than the negative one caused by electrostatic perturbation. Molecule I is still within the limits of Weigang's rule.

In ethanol solution the influence of vibronic coupling is not as easily recognized as in hydrocarbon solution. Looking at the 40-kK band of III in ethanol solution (Figure 3b) one would, without careful investigation in nonpolar solvents, be tempted to localize two bands of opposite sign within the envelope of the uv band. The same holds for the hexane and ethanol solutions of II (Figures 2a and b). Thus extreme care has to be taken if one tries to identify two electronic transitions on the basis of resolution of uv bands in the CD spectrum. A special feature should be pointed out by inspection of Figure 1b. The sharpness of the vibrational structure of the CD spectrum of I in ethanol is increased in comparison to that of the uv spectrum. The two progressions of opposite sign are shifted relative to one another in such a way that the minima of the positive and the maxima of the negative progressions nearly coincide. This may be generalized, so in cases where the vibrational structure in the CD spectrum is sharper than in the uv spectrum attention must be paid to vibrational coupling effects.

The molecules which we used in this study have rigid structures and thus correspond to the "low temperature limit." Only small influences of temperature and solvent are to be expected. Investigations of riboflavine where these geometric restrictions are relaxed show a

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(13) L. Goodman and R. W. Harrell, J. Chem. Phys., 30, 1131 (1959).

(14) J. H. Callomon, J. E. Parkin, and R. Lopez-Delgado, Chem. Phys. Lett., 13, 125 (1972).

(15) P. Salvadori, L. Lardicci, R. Menicagli, and C. Bertucci, J. Amer. Chem. Soc., 94, 8598 (1972).

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huge influence of the solvent on the form of the CD bands.[18]

Cyclotetramerization of 2-Dimethylamino-4-tert-butylpyrrole. The Tetra-tert-butylporphyrins

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Abstract: The acid-catalyzed cyclotetramerization of 2-dimethylaminomethyl-4-tert-butylpyrrole was examined. A mixture of all four isomeric tetra-tert-butylporphyrins was produced. Each isomer was isolated in a pure form and characterized spectroscopically. The mechanism of the cyclization was investigated.

Among the questions dealing with the whys and wherefores of porphyrin biosynthesis, certainly foremost is the so-called Type III problem: What is the mechanism by which porphobilinogen (PBG) is enzymatically cyclotetramerized to uroporphyrinogen III (eq 1)?

$$(1)$$
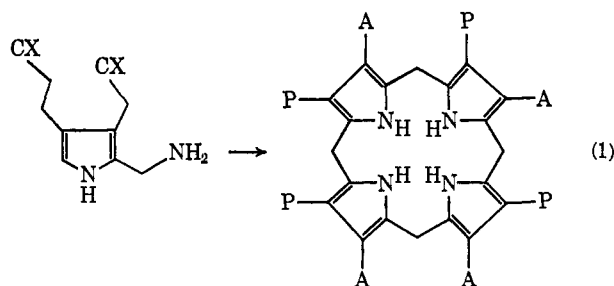
The nature of this process, and in particular the stage of the cyclotetramerization at which isomerization occurs, has been the subject of much work.[1-3] As a model of this reaction we have investigated the acid-catalyzed cyclotetramerization of the title compound (**5**). This pyrrole, being unsymmetrically substituted,


5
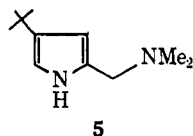
allows in principle a distinction between the isomeric

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(3) R. B. Frydman, A. Valasinas, and H. Rapoport, FEBS (Fed. Eur. Biochem. Soc.) Lett., 25, 309 (1972), report the role of i as a precursor of uroporphyrinogen III.

i
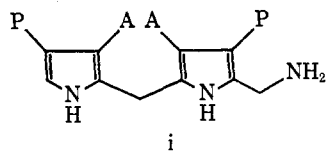
tetra-tert-butylporphyrins (Figure 1) formed from it. Moreover, as **5** bears only one substituent (tert-butyl) other than the dimethylaminomethyl group, it allows a test of the hypothesis that the facile cyclotetramerization of 2-aminomethylpyrroles such as PBG to porphyrinogens (as opposed to simple linear polymerization that is the predominant product when substitution is absent[4]) is at least partially a consequence of the steric bulk of the substituents present on the pyrrole ring.

Results

The preparation of **5** was carried out by conventional procedures and is detailed in the Experimental Section. When a solution of **5** in acetic acid was heated to reflux with air or oxygen being bubbled through the solution, there was isolated in 10-25% yield a purple crystalline material which from its uv-visible spectrum was porphyrin in nature. Elemental analysis and mass spectrometry were consistent with this conclusion. In particular, while the mass spectrum exhibited an intense parent ion at m/e 534 there was no peak at m/e 478 (tri-tert-butylporphyrins) or m/e 590 (penta-tert-butylporphyrins).[5] This makes it unlikely that any processes involving acid-catalyzed isomerization of tert-butylporphyrins are involved in the synthesis as this should lead to substantial amounts of de-tert-butylation.

The nmr spectrum of the product (Figures 2a and 3a) was clearly inconsistent with any one of the expected products. Although the areas of the high field (tert-butyl) and low field (CH=C-t-Bu and bridging methine) were in the proper ratio of 9:1:1 the latter consisted of a larger number of singlets than would be possible for any one of the isomers. By integration the multiplet at ca. δ 9.1 could be assigned to the CH=C-t-Bu protons of the pyrrole ring and the region from δ 10 to 11 to the bridging methine ("meso") protons.[6] The con-

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(5) A small peak at m/e 477 $(P - C_4H_9)^+$ was present.
(6) (a) R. J. Abraham, A. H. Jackson, and G. W. Kenner, J. Chem. Soc., 3468 (1961); (b) R. J. Abraham, P. A. Burbridge, A. H. Jackson, and D. B. MacDonald, J. Chem. Soc. B, 620 (1966).