

Scheme 2. Reagents: (i), Br<sub>2</sub>-AcOH; (ii), *p*-BrC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>-DMSO

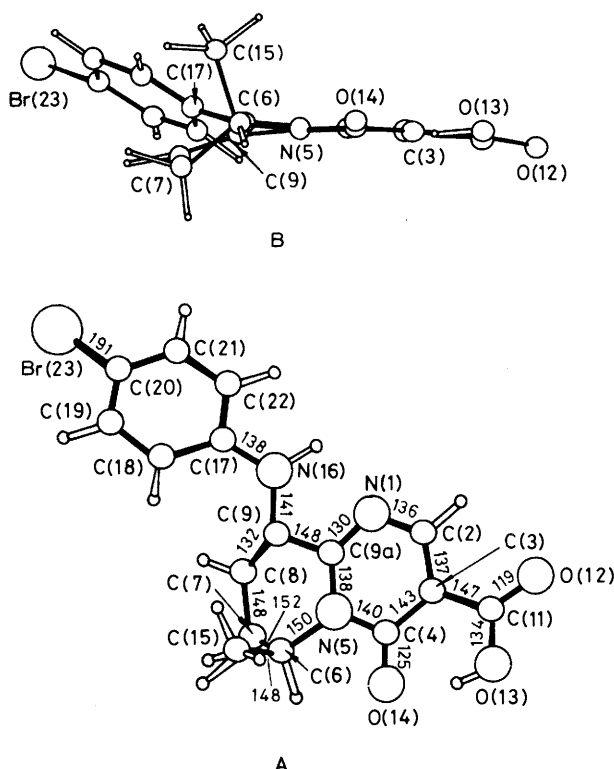
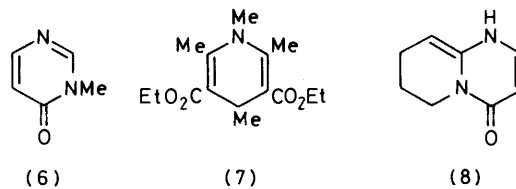


Figure 1. Molecular diagram of (-)-(S)-(5) with atomic numbering and bond lengths (pm), showing the absolute configuration. E.s.d.s are ca. 1 pm for bond lengths. A: C(3), N(5), and C(9a) lie in the plane of the drawing. B: The N(5)-C(9a) bond is perpendicular to the projection

After refinement for both enantiomers, the Hamilton test<sup>10</sup> showed unambiguously that the absolute configuration at C(6) in (-)-(5), and therefore in (+)-(1b), is *S*. From their relationship with (+)-(1b), all enantiomers in Scheme 1 are also *S* in configuration.

**Analysis of Experimental U.v. and C.d. Spectra.**—The u.v. spectra of tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones (1) were studied by Horváth *et al.*<sup>11</sup> with the aim of establishing the chemical constitution. Our new experimental and theoretical investigations are focused primarily on the characterization of the chromophoric systems in these molecules and on the correlation between their chiroptical properties and known absolute stereochemistry.

On the basis of their u.v. and c.d. spectroscopic properties (Table 1), the compounds studied can be divided into two distinct groups, compounds of types (1) and (2), and those of type (3).



**U.v. spectra and chromophoric systems.** The u.v. spectra of (1a) in different solvents above 200 nm exhibit two well separated absorption maxima of medium intensity (*cf.* ref. 11). That at 276 nm in water shows a bathochromic shift with decreasing solvent polarity. The relatively high intensity of this band ( $\epsilon$  5 400), however, precludes its  $n \rightarrow \pi^*$  parentage. It must therefore be assigned to a  $\pi \rightarrow \pi^*$  transition, with the excited state less polar than the ground state. The spectral position of the band at 227 nm, also  $\pi \rightarrow \pi^*$  in origin, is almost independent of the nature of the solvent.

The u.v. spectrum of (1a) in water is very similar to that of 3-methylpyrimidin-4(3*H*)-one (6),  $\lambda_{\text{max}}$  269, ( $\epsilon$  3 900) and 221 nm (6 810),<sup>12</sup> indicating the analogous structures of the chromophoric systems.

Protonation of (1a) or of (6) causes a strong hypsochromic shift in the first band and a weak bathochromic shift in the second [for (6) in 1*M*-HCl,  $\lambda_{\text{max}}$  258 ( $\epsilon$  2 940) and 226 nm ( $\epsilon$  9 080)<sup>12</sup>]. The spectra of (1a) and of (6) in 1*M*-HCl are almost identical to that of (2a) in water, indicating that protonation of (1a) and (6) occurs at N(1). The somewhat higher wavelengths of the maxima in the spectrum of (2a) can be ascribed to the additional methyl substituent at N(1).

The extension of the chromophoric system in the 3-substituted derivatives of (1a) and (2a) results in appreciable increases in both wavelength and intensity for the first maximum, whereas the second remains almost unchanged, while a third maximum appears at ca. 207 nm (*cf.* Table 1).

The above spectroscopic properties mean that the chromophoric system in 6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones of types (1) and (2) is analogous to the cyclically conjugated system of 3-methylpyrimidin-4(3*H*)-one (6), which is a heteroatomic derivative of the benzyl anion.<sup>13</sup>

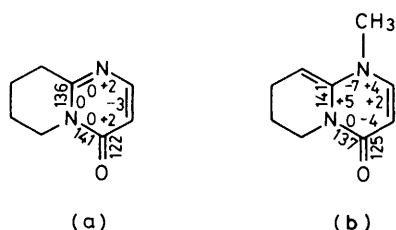
1,6,7,8-Tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones (3) have spectroscopic properties significantly different from those of their 6,7,8,9-tetrahydro-isomers. In the u.v. spectrum of (3e) in ethanol a very broad, medium intensity band is found between 450 and 300 nm, with a maximum at 361 nm ( $\epsilon$  3 100). This band is followed by a very intense one at 260 nm ( $\epsilon$  25 000) with a shoulder at 225 nm, and by a third band of medium intensity ( $\epsilon$  8 000) at 205 nm. With decreasing solvent polarity, the first band shows a hypsochromic shift. Thus, we may conclude that all bands in the spectrum of (3e) originate from  $\pi \rightarrow \pi^*$  transitions of an extended conjugated system.

Though the 3-unsubstituted compound (3a) cannot be isolated in crystalline form, it can be prepared in acetonitrile from (2a) by treatment with a strong base (*e.g.* *N*-methylmorpholine). The first maximum in this solution is at 344 nm, *i.e.* a shorter wavelength, than for (3e). This means that the free or functionalized 3-carboxy-substituent (CO<sub>2</sub>H, CONH<sub>2</sub>) also causes a bathochromic shift in the first band of type (3) compounds.

The common chromophoric system in molecules of type (3) is a divinylamine moiety conjugated with an amide group. The divinylamine chromophore is present in 1,4-dihydropyridine,<sup>14</sup> the 1,2,4,6-tetramethyl-3,5-bisethoxycarbonyl derivative of which (7) exhibits a u.v. spectrum with positions of the maxima,  $\lambda_{\text{max}}$  (EtOH) 355 ( $\epsilon$  7 000), 263 (10 000), and 228 nm (16 000),<sup>15</sup> which are very similar to those in the

**Table 1.** Experimental u.v. and c.d. data for the (*R*)-enantiomers of 6-methyl-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one derivatives (1)–(3)

| Compound | $[\alpha]_D^{20}$ (°) (c 2, MeOH) | M.p. (°C) | Solvent          | U.v. $\lambda$ /nm ( $\epsilon$ )        | C.d. $\lambda$ /nm ( $\Delta\epsilon$ )           |
|----------|-----------------------------------|-----------|------------------|--|---|
| (1a)     | -136                              | 77        | 1M-HCl           | 259 (3 900), 231 (8 070)                 | 260 (-2.50), 228 (-5.81)                          |
|          |                                   |           | H <sub>2</sub> O | 276 (5 400), 227 (6 840)                 | 273 (-3.63), 222 (-4.53)                          |
|          |                                   |           | EtOH             | 279 (5 000), 227 (6 750)                 | 277 (-3.49), 224 (-3.83), 194 (+5.3)              |
|          |                                   |           | dioxane          | 284 (4 700), 228 (6 100)                 | 282 (-3.64), 224 (-3.09)                          |
| (1b)     | -116                              | 121       | EtOH             | 303 (8 230), 230 (5 510), 207 (5 510)    | 300 (-3.03), 243 (+0.73), 230 (-1.43), 195 (+3.0) |
| (1c)     | -129                              | 92        | EtOH             | 305 (8 180), 231 (5 690), 207 (5 780)    | 300 (-3.76), 242 (+2.33), 229 (-1.53), 211 (+1.2) |
| (1d)     | -140                              | oil       | EtOH             | 304 (8 120), 231 (5 650), 207 (5 700)    | 300 (-2.65), 243 (+1.11), 230 (-0.93), 210 (+0.4) |
| (1e)     | -138                              | 214       | 1M-HCl           | 280 (6 800), 232 (7 600), 207 (6 600)    | 278 (-3.46), 246 (+0.85), 227 (-3.46)             |
|          |                                   |           | EtOH             | 303 (8 650), 231 (6 700), 206 (6 650)    | 298 (-3.64), 242 (+1.01), 228 (-1.62), 200 (+1.8) |
| (2a)     | -28                               | 142       | H <sub>2</sub> O | 265 (4 090), 234 (9 550), 201 (4 000)    | 266 (-2.41), 230 (-6.81), 195 (+4.24)             |
| (2b)     | -31                               | 177       | H <sub>2</sub> O | 282 (5 740), 238 (7 540), 204 (7 110)    | 282 (-3.16), 249 (+1.15), 232 (-3.25), 200 (+5.1) |
| (2d)     | -31                               | 164       | H <sub>2</sub> O | 281 (5 680), 238 (7 510), 204 (7 200)    | 282 (-3.56), 248 (+1.48), 232 (-3.76), 200 (+3.2) |
| (2e)     | -38                               | 218       | H <sub>2</sub> O | 287 (6 600), 235 (8 500), 208 (8 000)    | 283 (-3.78), 249 (+1.46), 231 (-4.51), 200 (+2.5) |
| (3a)     |                                   |           | MeCN             | 344 (1 550)                              | 347 (+2.81)                                       |
| (3b)     | +110                              | 134       | EtOH             | 365 (2 960) (in MeCN)                    | 372 (+1.90), 257 (-6.02), 215 (+0.93), 200 (-4.5) |
| (3e)     | +103                              | 176       | EtOH             | 361 (3 100), 260 (25 000), 225sh (6 500) | 367 (+2.15), 260 (-6.00), 228 (-2.60), 205 (-7.8) |
|          |                                   |           | dioxane          | 205 (8 000)                              | 360 (+1.89), 259 (-3.35), 224 (-2.49)             |

**Figure 2.** Selected bond lengths and torsion angles of the pyrimidine moiety in compounds of type (1) (a) and type (3) (b)

spectrum of (3e). [The intensity differences in the spectra of (7) and (3e) are ascribed mainly to the different modes of conjugation of the divinylamine moiety with the two carbonyl groups.] According to this picture, the bond between C(9a) and N(5) does not belong to the 'open-chain' conjugated system of the chromophore in molecules of type (3). This idea is supported by MO calculations (see below).

The different natures of the chromophoric systems in the two groups of isomeric tetrahydro-derivatives are also reflected in *X*-ray geometries.<sup>16,17</sup> In this respect, the C(9a)-N(5)-C(4)-O(14) moiety is the most significant. The C(9a)-N(5) bond is shorter in (1d) (136 pm) than in (3b) (141 pm), whereas the N(5)-C(4) bond is longer in (1d) (141 pm) than in (3b) (137 pm) (Figure 2). These significant bond length differences are due to the different electronic structures of the two molecules.

In (1d), containing a formal double bond between N(1) and C(9a), *i.e.* inside the pyrimidine ring, the  $\pi$ -system is cyclically delocalized, and the pyrimidine moiety is quasi-aromatic, favouring equalization of the bond lengths. The formal C(9a)-N(5) single bond is therefore nearly as short as in pyrimidine itself,<sup>18</sup> while the N(5)-C(4) bond is longer [and the C(4)-O(14) double bond is shorter] than in the N=C=O

system of simple amides and lactams.<sup>19</sup> Hence, the N(5)-C(4)-O(14) fragment of (1d) cannot be considered a separate amide group, but rather as part [with its N(5)-C(4) bond] of a cyclic aromatic system. The relatively short C(4)-O(14) bond indicates that conjugation of the carbonyl group with N(5) or with the whole ring is of minor importance.

In contrast to the situation in (1d), in (3b) there is a normal amide group with a relatively short N(5)-C(4) and a relatively long C(4)-O(14) bond. It is separated from the rest of the molecule by the relatively long C(9a)-N(5) bond. Thus, the bond length data for (3b) also suggest an open-chain conjugated system composed of a divinylamine and an amide moiety.

The torsion angles too lend support to the different natures of the chromophoric systems in the two classes of molecules. As the very small torsion angles show (*cf.* Figure 2), the pyrimidine ring of (1d) is nearly planar, in accord with its presumed quasiaromatic character. In the analogous moiety of (3b), however, the torsion angles deviate significantly from zero, accounting for an inherently chiral chromophoric system in this type of tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones.

*C.d. spectra.* The wavelength and intensity data of the maxima in the c.d. spectra of (1a) in various solvents are well correlated with those of the corresponding u.v. bands (Table 1). In the c.d. spectra of (*R*)-(1a) both maxima are negative in sign and of about the same intensity. That at *ca.* 280 nm exhibits a definite fine structure, which appears most clearly in the apolar solvent dioxane. This feature of the band is characteristic of the vibrational nature of the first aromatic transition. In the c.d. spectrum of protonated (*R*)-(1a) the intensity of the first band is somewhat diminished and that of the second increased, as found in the u.v. spectrum. The anisotropy ( $g \Delta\epsilon/\epsilon$ ) is about the same ( $0.7 \times 10^{-3}$ ) for both c.d. bands, indicating the analogous nature of the corresponding electronic transitions ( $\pi \rightarrow \pi^*$ ) and of the origin of their optical activity.

Two further features of the c.d. spectra are worth mentioning. The first band is not symmetrical but has a convex hump in its low wavelength half. Though not a definite shoulder, this is an indication of a hidden negative band at *ca.* 250 nm. Below 208 nm the c.d. becomes positive in sign, pointing to a positive band at lower wavelengths.

The c.d. spectra of the *R*-enantiomers of the 3-substituted derivatives (1b—e) are somewhat similar to that of (*R*)-(1a). However, the first band is red-shifted by *ca.* 20 nm, allowing the hidden band to appear as a shoulder at *ca.* 260 nm. The band corresponding to the second band of (1a) remains at nearly the same wavelength, but its intensity is strongly reduced. The seemingly most striking difference between the spectra of (1a and e) is a weak positive band between the two negative ones, at 242 nm for (*R*)-(1e). This band is apparently missing from the c.d. spectrum of (1a), but the sharp minimum with a  $\Delta\epsilon$  of nearly zero at 237 nm suggests the presence of a weak positive band hidden by the two neighbouring intense negative ones in this spectrum as well. In the u.v. curve of (1e) a not too definite shoulder is found at *ca.* 240 nm, corresponding to the weak positive maximum in the c.d. At 218 nm the CD curve of (*R*)-(1e) crosses the zero line and at 206 nm, where a maximum appears in the u.v. spectrum, the c.d. of (*R*)-(1e) is positive.

All the bands are also present in the c.d. spectra of the protonated forms of compounds (1) and their quaternary salts (2), with the hypsochromic shift of the first band. However, no shoulder or asymmetry of the first band is observed at *ca.* 260 nm in the c.d. curves of the cationic derivatives. Thus the 'hidden' band is in fact missing in these spectra. This can be considered as an indication of the  $n \rightarrow \pi^*$  parentage of the corresponding transition in the free bases.

The u.v. and c.d. spectra of (1a and e) in ethanol are presented in Figure 3.

The striking differences in chiroptical properties between 1,6,7,8-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones (3) and their 6,7,8,9-tetrahydro-isomers (1) are apparent from the opposite signs of the optical rotations at the  $\text{Na}_D$  line for homochiral analogous derivatives of types (1) and (3) (*cf.* Table 1). In accord with the positive optical rotation of (*R*)-(3e), the 367 nm maximum in its c.d. spectrum in ethanol is also positive. This band is very broad and, like the corresponding one in the u.v. spectrum, shows a hypsochromic shift with solvent polarity decrease. The anisotropy of this band ( $0.7 \times 10^{-3}$ ) is of about the same magnitude as that of the first c.d. band in (1e), pointing to its  $\pi \rightarrow \pi^*$  origin. At lower wavelengths, three further c.d. bands are found, all of them negative. The first and third, at 260 and 205 nm, are relatively strong; that at 228 nm is weaker. The spectral positions of these bands coincide with the two maxima and the shoulder in the u.v. spectrum of (3e) (*cf.* Figure 4). The first c.d. maximum of (3a) shows a hypsochromic shift with respect to that of (1e), indicating that the substituent at C(3) causes a bathochromic shift in this c.d. band.

**Theoretical Studies.—General remarks.** Through the determination of the absolute geometry of (5) by anomalous *X*-ray scattering, the absolute configuration at C(6) of all compounds of types (1)—(3) has become known (*cf.* Schemes 1 and 2). Thus, it has become possible to establish a phenomenological correlation between the chiroptical properties and stereochemistry of the molecules. However, to gain better insight into the nature of the electronic transitions and the origin of their optical activity, a theoretical study was also performed.

The geometries of the molecules are derived from *X*-ray data<sup>16,17</sup> with some simplifications (see below). For calculation of the appropriate wave functions, the CNDO/S method<sup>20</sup> in the parametrization of Ellis *et al.*<sup>21</sup> was used.

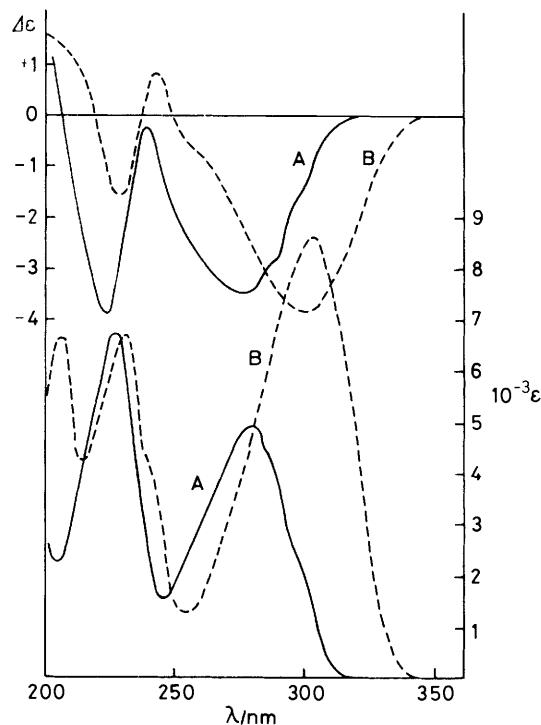


Figure 3. C.d. (above) and u.v. (below) spectra of (*R*)-(1a) (A) and (*R*)-(1e) (B) in ethanol

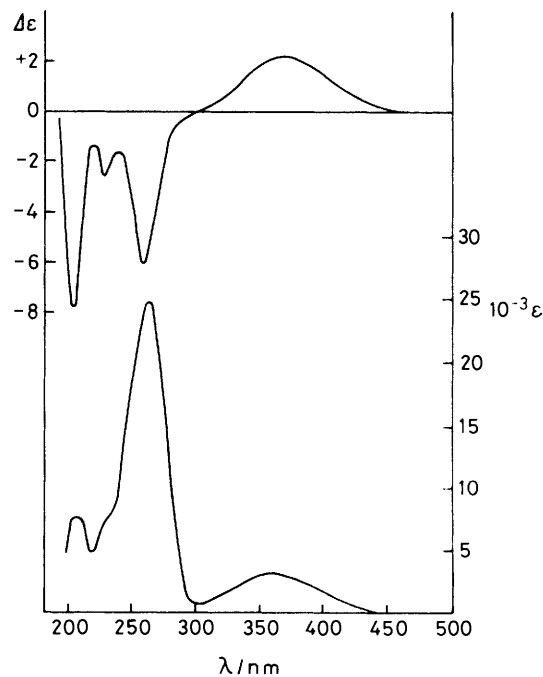


Figure 4. C.d. (above) and u.v. (below) spectra of (*R*)-(3e) in ethanol

To determine excited states, after obtaining the SCF MOs one should also perform a configuration interaction (CI) calculation. In our case, however, the size of the molecules allowed us to perform only a rather limited CI calculation, which in itself may sometimes be worse than to employ the simple single transition approximation (STA), particularly if

the aim of the calculation is to obtain realistic rotational strength data. It is known that the rotational strength is very sensitive to the size of the CI.<sup>22,23</sup> This means that the sign obtained without any CI may in some cases be more reliable than that resulting from a truncated CI calculation. The reliability of a restricted CI calculation can only be judged by contrasting its results with the experimental ones. We therefore performed calculations at both the STA and the limited CI levels.

Having the appropriate ground and excited state wave functions, one can calculate rotational strengths in different approximations for the matrix elements over atomic orbitals.<sup>24-28</sup> To make sure of the stability of their signs, we always calculated the rotational strengths by several of these different approximations. Since reliably accurate numerical values of the rotational strengths can by no means be expected from semiempirical methods, in the assignment of the c.d. bands we confined ourselves to the signs and orders of magnitude of the calculated rotational strengths as the only significant data.

*U.v. and c.d. spectroscopic properties of type (1) compounds.* We performed calculations for the simplest member of this series, *i.e.* the 3-unsubstituted molecule (1a). Its geometry was generated from that of (1d) (determined by X-ray crystallography<sup>16</sup>) by substituting the ethoxycarbonyl group of the latter with a hydrogen atom 100 pm from C(3) in the direction of the C(3)-C(11) bond. The X-ray data show the pyrimidinone ring of (1d) to deviate only slightly from planarity. However, this insignificant deviation, which may be considered as arising from experimental errors in the determination, will make the chromophoric system 'inherently chiral' and may therefore falsify the whole picture of the origin of the optical activity of these compounds, as well as the results of the rotational strength calculations. To avoid this danger, we made small corrections in the X-ray coordinates of (1d), to make the atoms forming the pyrimidinone ring of (1a) geometrically coplanar, and performed the calculations for this geometry.

The MOs involved in the lower energy transitions of (1a) are depicted in Figure 5, where the calculated orbital energies in eV are also given. (Due to the CNDO/S parametrization, the latter cannot be considered reliable approximations to ionization potentials.)

The determination of the transitions of molecule (1a) having a planar, 'aromatoid' chromophore, could not be made except on the basis of a (limited) CI calculation. For this purpose 15 configurations formed by single excitations from the five highest occupied to the three lowest vacant MOs were selected. The correlation diagram of the energy levels of excited states resulting from the STA and the CI calculations are shown in Figure 6.

As a result of the CI, the nearly degenerate pairs of the two  $n_O \rightarrow \pi^*$  and the two  $n_N \rightarrow \pi^*$  STA states mix and separate to a great extent. In the CI picture of the excited states, the first  $\pi \rightarrow \pi^*$  transition and the lower energy combinations of the  $n \rightarrow \pi^*$  pairs come close to each other in energy. Thus, it seems very probable that the broad first experimental band is composed of three transitions: the  $\pi \rightarrow \pi^*$  transition responsible for the high oscillator strength of the u.v. band, and the two  $n \rightarrow \pi^*$  components contributing to the rotational strength of the c.d. band. The asymmetry of the c.d. band of (1a) and the shoulder on that of (1e) (see above) can be correlated with the higher energy  $n \rightarrow \pi^*$  component of the first group of transitions.

The spectroscopic properties calculated for the first composite band of (R)-(1a) agree surprisingly well with the experimental data (Table 2).

The calculations show the second band too in the experimental u.v. spectrum to be of a mixed nature, originating from

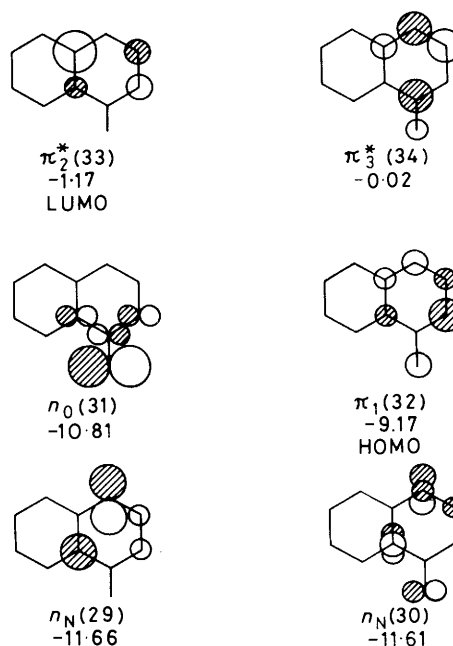


Figure 5. Selected MOs of (1a). Figures in parentheses are serial numbers of the MOs. Orbital energies in eV are also indicated. The areas of the circles are roughly proportional to the coefficients of the component atomic 2p-orbitals (AO components with coefficients lower than 0.2 are omitted)

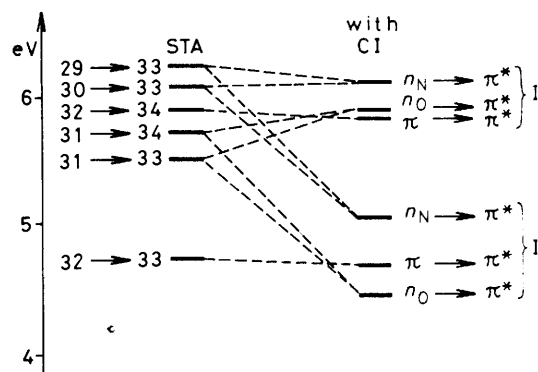


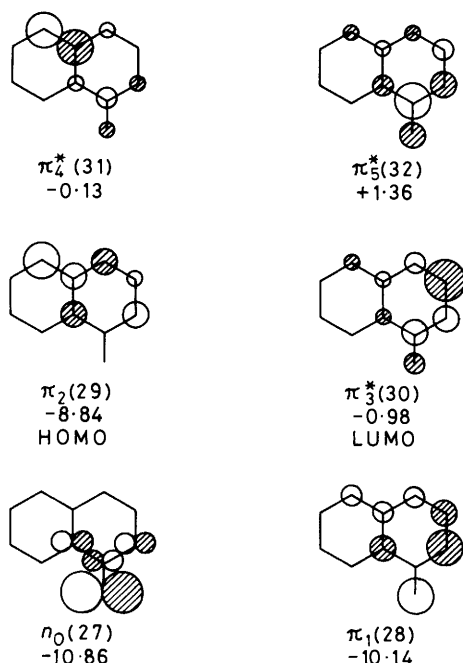
Figure 6. Correlation diagram of the transitions of (1a) calculated in STA and with CI

the higher energy  $\pi \rightarrow \pi^*$  transition of high oscillator strength, and from the higher energy combinations of the two  $n_O \rightarrow \pi^*$  and the two  $n_N \rightarrow \pi^*$  single transitions. In this case, however, there is a discrepancy between calculation and experiment in the order of the component transitions. The calculated  $\pi \rightarrow \pi^*$  transition with negative rotational strength is of somewhat lower energy than the  $n_O \rightarrow \pi^*$  transition with positive rotational strength, while the order of the sign of the two experimental c.d. bands is just the opposite. The latter appear with rather low intensity in the c.d. spectrum of (1e), and the longer wavelength one is even missing from that of (1a) (see above). This points to the strongly overlapping character of the component bands and the degeneracy of the corresponding transitions. That the energy order of the two nearly degenerate states does not reproduce the experimental situation may probably be attributed either to the truncated character of the CI calculation or to the approximate nature of the MOs.

**Table 2.** Theoretical and experimental spectroscopic data for (*R*)-(1a) with CI calculation

| Expt. band | Transition Type         | Energy (eV) |                  | Oscillator strength ( <i>f</i> ) |       | Reduced rotational strength [ <i>R</i> ] |                  |          |          |
|------------|-------------------------|-------------|------------------|----------------------------------|-------|--|------------------|----------|----------|
|            |                         | Expt.       | Calc.            | Expt. <sup>d</sup>               | Calc. | Expt. <sup>e</sup>                       | Calc.            |          |          |
|            |                         |             |                  |                                  |       |  | <i>a</i>         | <i>b</i> | <i>c</i> |
| I          | $n_O \rightarrow \pi^*$ | 4.4         | 4.3              | 0.12                             | 0.01  | -13                                      | -10              | -14      | -6       |
|            | $\pi \rightarrow \pi^*$ |             | 4.6              |                                  | 0.11  |  | 0                | -2       | -3       |
|            | $n_N \rightarrow \pi^*$ |             | 4.95             |                                  | 0.02  |  | -9               | -8       | -6       |
| II         | $n_O \rightarrow \pi^*$ | 5.5         | 5.8 <sup>f</sup> | 0.15                             | 0.00  | (+) <sup>g</sup>                         | +6               | +8       | +6       |
|            | $\pi \rightarrow \pi^*$ |             | 5.7 <sup>f</sup> |                                  | 0.14  |  | -8               | -6       | -7       |
|            | $n_N \rightarrow \pi^*$ |             | 6.0              |                                  | 0.02  |  | (+) <sup>g</sup> | +4       | +3       |

<sup>a</sup> Method of ref. 25 for dipole velocity formalism. <sup>b</sup> Method of ref. 28 for dipole velocity formalism. <sup>c</sup> Method of ref. 28 for dipole length formalism. <sup>d</sup>  $f_{\text{exp.}} = 4.32 \times 10^{-9} \epsilon_{\text{max}} \Delta_{\frac{1}{2}} (\Delta_{\frac{1}{2}} \text{ in } \text{cm}^{-1})$ . <sup>e</sup>  $[R]_{\text{exp.}} = 26.5 \Delta \epsilon_{\text{max}} \Delta_{\frac{1}{2}} (\text{nm}) / \lambda_{\text{max.}} (\text{nm})$ . <sup>f</sup> The order of the two almost degenerate transitions is changed. <sup>g</sup> Measured only in the c.d. spectra of (1b - e) (see Table 1).

**Figure 7.** Selected MOs of (8) (for explanation see caption to Figure 5. AO components with coefficients lower than 0.1 are omitted)

The sign of the last c.d. band detectable in the experimental spectrum of (1e) can be correlated with that of the third component ( $n_N \rightarrow \pi^*$ ) of the second group of calculated transitions.

The results of the CI calculation are thus in satisfactory agreement with the experimental spectra as regards both the energies and the signs and intensities of the bands. However, the composite character of the latter does not allow us to formulate a rule correlating the signs of the CD bands with the absolute geometry of the molecules. The  $n_O$  and especially the  $n_N$  MOs mostly involved in the transitions responsible for the optical activity are of a mixed nature, with non-negligible contributions from atomic orbitals localized on the chiral tetrahydropyridine ring, primarily the C(6)-CH<sub>3</sub> moiety. Since the chromophoric fragment of the molecule is inherently achiral, the optical activity of the transitions can only originate from the small contributions of the chiral second sphere, mainly the axial methyl group, to the MOs taking part in the excitation process.

*U.v. and c.d. spectroscopic properties of type (3) compounds.* Our theoretical calculations were made for a relatively simple

**Table 3.** Theoretical and experimental spectroscopic data for (*R*)-(8) and (*R*)-(3e), respectively (STA calculation)

| Expt. band | Transition Type             | Energy (eV)        |       | Oscillator strength ( <i>f</i> ) |       | Reduced rotational strength [ <i>R</i> ] |                    |
|------------|-----------------------------|--------------------|-------|----------------------------------|-------|--|--------------------|
|            |                             | Expt.              | Calc. | Expt.                            | Calc. | Expt.                                    | Calc. <sup>a</sup> |
| I          | $\pi_2 \rightarrow \pi_3^*$ | 3.4                | 4.5   | 0.09                             | 0.07  | +10                                      | +3                 |
|            |                             | (3.6) <sup>b</sup> |       |                                  |       |  |                    |
| II         | $n_O \rightarrow \pi_3^*$   | 4.8                | 5.57  | 0.54                             | 0.01  | -15                                      | -9                 |
|            | $\pi_2 \rightarrow \pi_4^*$ |                    | 5.65  |                                  | 0.26  | -9                                       | -9                 |
| III        | $\pi_1 \rightarrow \pi_3^*$ | 5.5                | 6.1   |                                  | 0.25  | -4                                       | -5                 |
| IV         | $\pi_1 \rightarrow \pi_4^*$ | 6.0                | 6.7   |                                  | 0.07  | -9                                       | -6                 |
| V          | $\pi_2 \rightarrow \pi_5^*$ | 6.5                | 6.8   |                                  | 0.02  | (+)                                      | +2                 |

<sup>a</sup> Method of ref. 5 for dipole velocity formalism. <sup>b</sup> For (*R*)-(3a).

model molecule (8) having identical geometry to that determined by X-ray diffraction<sup>17</sup> for (*R*)-(3b), with the modification that the two methyl and the carboxy-substituents in positions 1, 6, and 3 of (3b), respectively, were replaced by hydrogen atoms 100 pm from the ring atoms in the original bond directions. Control calculations showed that the presence of these groups does not significantly influence the chiroptical properties, their role being only to fix the chromophoric fragment of the molecule in its inherently chiral conformation.

The three highest energy occupied and the three lowest energy vacant MOs of (8) are represented in Figure 7.

The results of the simple STA calculations for the model molecule (8) together with the experimental u.v. and c.d. spectral data for (*R*)-(3e) are given in Table 3.

The first calculated transition of (8) is  $\pi \rightarrow \pi^*$  in nature. The calculated excitation energy is ca. 1 eV higher than that corresponding to the maxima of the first u.v. and c.d. bands. The sign of the calculated rotational strength, however, is in agreement with that of the first experimental c.d. band of (*R*)-(3e).

The calculations suggest that the second band of the experimental spectra can be assigned to two transitions of nearly equal energy, one being  $n \rightarrow \pi^*$  and the other  $\pi \rightarrow \pi^*$  in nature. The excitation energies are again overestimated by ca. 0.8 eV by calculation. The oscillator strength of the electrically forbidden  $n \rightarrow \pi^*$  transition is nearly zero, but its contribution to the rotational strength of the second experimental band is substantial. The calculated rotational strengths of both transitions are negative in sign, in full agreement with the intense negative band in the experimental c.d. spectrum of (*R*)-(3e).

The next two calculated transitions are  $\pi \rightarrow \pi^*$  too, with

somewhat overestimated energies compared to those of the corresponding experimental bands. The rotational strengths are negative for both calculated transitions, the absolute value of the first being smaller. This feature of the calculations is nicely mirrored in the experimental c.d. spectrum.

The sixth calculated transition ( $\pi_2 \rightarrow \pi_5^*$ ) is nearly degenerate with the fifth ( $\pi_1 \rightarrow \pi_4^*$ ). Because of the opposite signs of their rotational strengths, however, they appear well separated in the experimental c.d. spectrum. Though the maximum of the highest energy band could not be measured experimentally, its presence is apparent in the sign change of the c.d. curve at the low wavelength end.

The above calculations were performed at the STA level. A limited CI calculation including 15 singly excited configurations failed to predict the experimental results. The CI makes the energy of the first  $n \rightarrow \pi^*$  state with negative rotational strength to decrease to such an extent that it lies below that of the first  $\pi \rightarrow \pi^*$  transition with positive rotational strength. These results are in contradiction with the experimental spectra, the first band being positive in the c.d. and, at the same time, of fairly high intensity in the u.v.

On the basis of these findings it may be concluded that, for an inherently chiral chromophore like that in compounds (3), the simple STA calculation furnishes a more realistic picture of the spectroscopic properties than a limited version of the more sophisticated CI. It is therefore very important to make a qualitative assignment, based on the u.v. spectrum, of the  $n \rightarrow \pi^*$  or  $\pi \rightarrow \pi^*$  nature of at least the first experimental c.d. band, before coming to a decision concerning the reliability of the results of the STA *versus* the limited CI calculations.

From our calculations relating to two basically different chromophoric systems, the general conclusion might be drawn that in the case of the intense  $\pi \rightarrow \pi^*$  transitions of an extended, 'open-chain' chromophoric system with inherently chiral geometry, even the simplest STA calculation affords the possibility of reliably assigning the c.d. bands to the chirality of the chromophore. For inherently achiral heteroaromatic chromophores with transitions of mixed  $n \rightarrow \pi^*$  and  $\pi \rightarrow \pi^*$  character, however, the results of simple calculations are much more questionable, and a reliable theo-

retical assignment of the c.d. spectrum cannot be made without performing a CI calculation, the more extended the better.

### Experimental

M.p.s are uncorrected. N.m.r. spectra were recorded on a JEOL-FX spectrometer, in  $\text{CDCl}_3$  solutions, using tetramethylsilane as internal standard. U.v. and c.d. spectra were measured on a SPECORD (Zeiss) spectrophotometer and on a Roussel-Jouan dichrograph (No. III Jobin-Yvon), respectively.

(6*S*)-9-Bromo-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine-3-carboxylic Acid. (6*S*)-(4).—A solution of bromine (1.59 g, 10 mmol) in acetic acid (2 ml) was added dropwise at 25 °C to a stirred solution of carboxylic acid (+)-(S)-(1b) {2.08 g, 10 mmol;  $[\alpha]_D^{20} +116.2^\circ$  (*c* 2, MeOH)} in acetic acid (8 ml). After stirring for 0.5 h at 60 °C the mixture was poured into water (50 ml) and the pH of the solution was adjusted to 3 with 20% NaOH solution. The mixture was extracted with  $\text{CHCl}_3$ , the organic layer was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated, and the crude (6*S*)-(4) (2.25 g, 78%) was crystallized from methanol, m.p. 153–154 °C (*ca.* 4:1 mixture of *trans*- and *cis*-isomers);  $[\alpha]_D^{20} -40^\circ$  (*c* 1; MeOH) (Found: C, 41.65; H, 3.75; N, 10.4; Br, 28.0. Calc. for  $\text{C}_{10}\text{H}_{11}\text{BrN}_2\text{O}_3$ : C, 41.85; H, 3.85; N, 9.75; Br, 27.85%).

(-)-(S)-9-p-Bromoanilino-6-methyl-4-oxo-6,7-dihydro-4H-pyrido[1,2-a]pyrimidine-3-carboxylic Acid (-)-(S)-(5).—A solution of (6*S*)-(4) (2.9 g, 10 mmol) and 4-bromoaniline (3.8 g, 22 mmol) in dimethyl sulphoxide (5 ml) was left to stand at ambient temperature for 3 days in an open Erlenmeyer flask. Methanol (20 ml) was added to the mixture and the precipitated (-)-(S)-(5) (2.8 g, 74.4%) was filtered and recrystallized from acetonitrile, m.p. 214–215 °C,  $[\alpha]_D^{20} -85^\circ$  (*c* 1,  $\text{CHCl}_3$ ) (Found: C, 51.15; H, 4.1; N, 10.9; Br, 21.2. Calc. for  $\text{C}_{16}\text{H}_{14}\text{BrN}_3\text{O}_3$ : C, 50.8; H, 4.25; N, 11.1; Br, 21.15%).

Table 4. Bond angles (°) and torsion angles (°) for (-)-(S)-(5)

|                       |          |                       |          |                        |          |
|-----------------------|----------|-----------------------|----------|------------------------|----------|
| C(2)–N(1)–C(9a)       | 117.2(6) | C(4)–N(5)–C(9a)       | 120.5(6) | N(1)–C(9a)–N(5)        | 123.7(6) |
| N(1)–C(2)–C(3)        | 124.4(7) | C(6)–N(5)–C(9a)       | 121.0(5) | N(1)–C(9a)–C(9)        | 118.8(7) |
| C(2)–C(3)–C(4)        | 118.0(7) | N(5)–C(6)–C(7)        | 108.6(6) | N(5)–C(9a)–C(9)        | 117.5(6) |
| C(2)–C(3)–C(11)       | 120.6(7) | N(5)–C(6)–C(15)       | 111.6(7) | C(3)–C(11)–O(12)       | 123.1(7) |
| C(4)–C(3)–C(11)       | 121.4(7) | C(7)–C(6)–C(15)       | 112.8(6) | C(3)–C(11)–O(13)       | 114.6(7) |
| C(3)–C(4)–N(5)        | 115.8(6) | C(6)–C(7)–C(8)        | 113.0(6) | O(12)–C(11)–O(13)      | 122.1(8) |
| C(3)–C(4)–O(14)       | 125.2(7) | C(7)–C(8)–C(9)        | 121.6(7) | C(9)–N(16)–C(17)       | 124.6(5) |
| N(5)–C(4)–O(14)       | 119.0(6) | C(8)–C(9)–C(9a)       | 120.1(7) | N(16)–C(17)–C(18)      | 122.9(6) |
| C(4)–N(5)–C(6)        | 118.2(6) | C(8)–C(9)–N(16)       | 127.8(7) | N(16)–C(17)–C(22)      | 118.6(6) |
|                       |          | C(9a)–C(9)–N(16)      | 111.6(6) |                        |          |
| C(9a)–N(1)–C(2)–C(3)  | –4       | C(4)–C(3)–C(11)–O(13) | –3       | N(5)–C(6)–C(7)–C(8)    | –46      |
| C(2)–N(1)–C(9a)–N(5)  | +4       | C(3)–C(4)–N(5)–C(6)   | –179     | C(15)–C(6)–C(7)–C(8)   | +78      |
| C(2)–N(1)–C(9a)–C(9)  | –174     | C(3)–C(4)–N(5)–C(9a)  | –6       | C(6)–C(7)–C(8)–C(9)    | +26      |
| N(1)–C(2)–C(3)–C(4)   | –2       | O(14)–C(4)–N(5)–C(6)  | +2       | C(7)–C(8)–C(9)–C(9a)   | +7       |
| N(1)–C(2)–C(3)–C(11)  | 180      | O(14)–C(4)–N(5)–C(9a) | +175     | C(7)–C(8)–C(9)–N(16)   | +178     |
| C(2)–C(13)–C(4)–N(5)  | +6       | C(14)–N(5)–C(6)–C(7)  | –148     | C(8)–C(9)–C(9a)–N(1)   | +161     |
| C(2)–C(3)–C(4)–O(14)  | –174     | C(4)–N(5)–C(6)–C(15)  | +87      | C(8)–C(9)–C(9a)–N(5)   | –17      |
| C(11)–C(3)–C(4)–N(5)  | –175     | C(9a)–N(5)–C(6)–C(7)  | +40      | N(16)–C(9)–C(9a)–N(1)  | –11      |
| C(11)–C(3)–C(4)–O(14) | +4       | C(9a)–N(5)–C(6)–C(15) | –85      | N(16)–C(9)–C(9a)–N(5)  | +171     |
| C(2)–C(3)–C(11)–O(12) | –9       | C(4)–N(5)–C(9a)–N(1)  | 0        | C(8)–C(9)–N(16)–C(17)  | +26      |
| C(2)–C(3)–C(11)–O(13) | +175     | C(4)–N(5)–C(9a)–C(9)  | +179     | C(9a)–C(9)–N(16)–C(17) | –162     |
| C(4)–C(3)–C(11)–O(12) | +172     | C(6)–N(5)–C(9a)–N(1)  | +173     | C(9)–N(16)–C(17)–C(18) | +34      |
|                       |          | C(6)–N(5)–C(9a)–C(9)  | –9       |                        |          |

Optically active compounds (1)–(3) were prepared from the enantiomers of (1b), as for the racemic compounds.<sup>3,9,29–31</sup>

**X-Ray Investigation.**—Prismatic, yellow crystals of (–)-(S)-(5) were obtained from acetonitrile. The crystal selected for X-ray analysis measured  $0.25 \times 0.19 \times 0.14$  mm in the (100), (011), and (001) directions, respectively. Crystal data are  $a = 738.3(1)$ ,  $b = 1247.3(3)$ ,  $c = 1636.5(2)$  pm,  $Z = 4$ ,  $U = 1.507$  nm<sup>3</sup>,  $\mu(\text{Cu-K}\alpha \text{ radiation}) = 36.35$  cm<sup>-1</sup>, space group  $P2_12_12_1$  from systematic absences. Cell dimensions were determined from precession photographs. 1414 independent reflexions were collected on a Stoe-Güttinger two-circle diffractometer. After data reduction the co-ordinates of the bromine atom were obtained from Patterson synthesis ( $R$  0.39). The subsequent electron density calculation revealed the position of the remaining non-hydrogen atoms ( $R$  0.23). After one cycle of isotropic and one cycle of anisotropic refinement, the  $R$  value dropped to 0.08. Eleven hydrogen atoms were generated and were held fixed during the further two refinement cycles. The final reliability ( $R$ ) values are for the ( $R$ )-enantiomer,  $R$  5.15,  $R_w$  5.47,  $R_G$  7.78%; and for the ( $S$ )-enantiomer,  $R$  5.58,  $R_w$  6.53,  $R_G$  9.31%. The puckering parameters<sup>32</sup> for the pyrimidine ring are  $Q = 60$  pm,  $\theta = 80^\circ$ ,  $\Phi = 175^\circ$  and for the pyridine ring  $Q = 430$  pm,  $\theta = 67^\circ$ ,  $\Phi = 77^\circ$ .

In the crystal lattice one intramolecular hydrogen bond O(13)–H(13)···O(14) and one intermolecular H-bond N(16)–H(16)···O(12) ( $-1 - x$ ,  $\frac{1}{2} + y$ ,  $-\frac{1}{2} - z$ ) are present. The H(13) atom was found in the difference electron density map made after the final refinement.

Bond and torsion angles relating to the non-hydrogen atoms are given in Table 4. Observed and calculated structure factors are in Supplementary Publication No. SUP 23724 (10 pp.) (see *J. Chem. Soc., Perkin Trans. 2*, 1983, Issue 1 for details of the deposition scheme).

All calculations were carried out on an ODR-1305 computer using the SHELX-76 program system.<sup>33</sup>

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