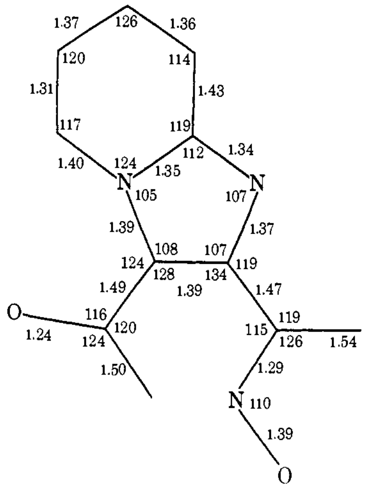
From the spectroscopic data and chemical transformations described so far a unique structure for **4** cannot be defined. We therefore undertook a single-crystal X-ray analysis of **6** which secures the structure shown in Figure 1 and Chart I.[10,11] Now the structures of **4**[11] and **7**[11] follow unambiguously.

Chart I. Bond Lengths (Ångstroms) and Bond Angles (Degrees)[a]



[a] R = 0.089. The nine atoms of the ring system form a least-squares plane with standard deviation 0.011 Å. The nonhydrogen atoms of the CH_3CO–C group form a plane with standard deviation 0.009 Å; torsional angle with the ring system, 12.4°. The five nonhydrogen atoms of the $CH_3C(NOH)$–C group form a plane with standard deviation 0.002 Å; torsional angle with the ring system, 60.0°.

A distinguishing feature of the nmr spectra of **4** and **6** is the low-field resonance due to H-5, deshielded by the peri carbonyl[12] [in the X-ray structure (Figure 1 and Chart I) this is oriented as shown, almost in the plane of the ring system (φ = 12.4°), and we assume that this situation persists for solutions of **4** and **6** in chloroform]. In **7** the deshielding is markedly lowered, because the bulky 1,1-dinitroethyl group (relative to $CH_3C{=}NO$– in **4** and **6**) causes the planar rotamer to be less populated. In support of this argument, carbonyl stretching frequencies indicate less conjugation of the carbonyl group with the heteroaromatic system of **7** (ν 1656 cm^{-1}) compared with **4** and **6** (ν 1640 cm^{-1} for both compounds).

The formation of compound **4** is probably a general reaction of alkyl(pyridine)cobaloximes since **1** and **2** behaved similarly to **3** on treatment with acetic anhydride in pyridine, although they react more slowly. A homolog (**8**) of **4** is obtained (16% yield) by reacting 2-hydroxypropyl(4-methylpyridine)cobaloxime with acetic anhydride in 4-methylpyridine for 2 days at 60°. Compound **4** is not formed from bromo(pyridine)-cobaloxime under similar conditions, nor is it produced from dimethylglyoxime and acetic anhydride in pyridine containing cobaltous acetate.[13] The production of compounds **4** and **8** involves an oxidation of a dimethylglyoxime unit; the yield of **4** obtained from **3** is insensitive to the presence or absence of oxygen and the oxidant must therefore be the cobaltic ion of the complex. Exposure of reaction mixtures to light does not increase the yield of **4**. We are investigating the mechanism of formation of **4** from alkyl(base)cobaloximes, with particular reference to the role and fate of the alkylcobalt group of the substrate and to possible template effects around cobalt.

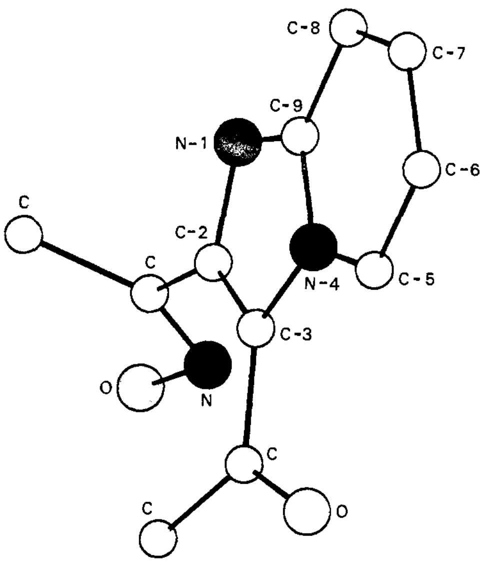


Figure 1.

Acknowledgment. We gratefully acknowledge a Royal Society European Exchange Fellowship (to U. H.) and a Science Research Council Studentship (to. D. R. H.).

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(10) Crystal data: orthorhombic; space group $Pbca$; a = 16.402, b = 13.463, and c = 9.735 Å; Z = 8. Observed reflections (520) ($I/\sigma(I) > 5.0$) were collected on a Stoe two-circle diffractometer, with Mo $K\alpha$ radiation and graphite monochromator. The structure was solved by direct methods and refined to a current R factor of 0.089 with anisotropic temperature factors for all nonhydrogen atoms and isotropic temperature factors for hydrogen atoms.

(11) **4**, 2-(1-(*E*)-acetoxyiminoethyl)-3-acetylimidazo[1,2-*a*]pyridine; **6**, 2-(1-(*E*)-hydroxyiminoethyl)-3-acetylimidazo[1,2-*a*]pyridine; **7**, 2-(1,1-dinitroethyl)-3-acetylimidazo[1,2-*a*]pyridine.

(12) For analogous examples see R. M. Acheson and D. A. Robinson, *J. Chem. Soc. C*, 1633 (1968) and W. K. Anderson and A. E. Friedman, *Can. J. Chem.*, **49**, 668 (1971).

(13) Dimethylglyoxime di-*O*-acetate is produced in these reactions and is also a by-product in the formation of 4.

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Structural Index for Elemental Solids

Sir:

We have discovered an index for s–p bonded elemental solids which separates covalent, fcc, hcp, and bcc structures. The index is based on the pseudopotential of an atomic core in a solid, which may be approximated by the Pauli-force model potential[1–3]

$$V = -Z/r + \sum_l [\hat{l}(\hat{l} + 1) - l(l + 1)]P_l/2r^2 \quad (1)$$

Here Z is the net core charge, l is the angular momentum quantum number of a valence orbital, $\hat{l} = \hat{l}(l)$ is an l-dependent parameter obtained from atomic spectral data,[1,2] and P_l is the l-projection operator. A physical interpretation of (1) and a tabulation of $\hat{l}$ values for

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(1) G. Simons and A. Bloch, submitted to *Phys. Rev.*

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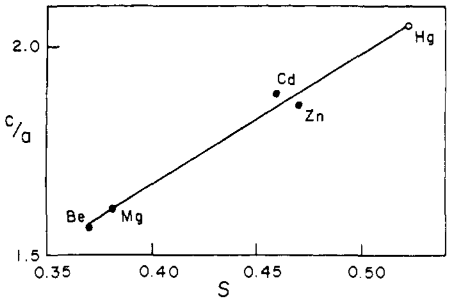

Figure 1. *c/a vs. S* for divalent hcp metals, including hypothetical hcp Hg.[4]

various elements are given elsewhere.[1] The potential has simple analytic eigenfunctions and eigenvalues, and has proved useful in studies of atoms,[3] molecules,[2] and solids.[1]

For many elements *d* and higher *l* components in the valence wave function are unimportant. In those cases bonding is dominated by s and p orbitals and the structure of the solid must be determined by Z, $\hat{l}(0)$, and $\hat{l}(1)$.

For given *l*, the radial maximum of the (unscreened) lowest valence eigenfunctions of (1) is[2]

$$r_l = \hat{l}(l)[\hat{l}(l) + 1]/Z \tag{2}$$

We define a structural index *S* as the fractional difference between the maxima of the s and p radial functions

$$S \equiv \frac{r_1 - r_0}{r_1} = \frac{\hat{l}(1)[\hat{l}(1) + 1] - \hat{l}(0)[\hat{l}(0) + 1]}{\hat{l}(1)[\hat{l}(1) + 1]} \tag{3}$$

In Table I we show how *S* partitions the s–p bonded portion of the periodic table. At zero temperature and pressure, elements with *S* less than 0.30 possess open structures resembling the bonding in molecules. Indices between 0.30 and 0.36 correspond to fcc or distorted fcc structures, while values between 0.36 and 0.57 are found for hcp or distorted hcp. Since lithium and sodium are hcp at zero temperature but bcc at room temperature, we infer that elements with *S* somewhat higher than 0.57 would be bcc. Among other borderline cases, thallium is hcp at zero pressure but fcc at 1 atm, and covalent gray tin is more stable at low temperature than fcc metallic white tin. We know of no other scale or rule which divides the periodic table in this fashion.

Table I. Index *S* for Elemental Solids

Li	Be	B	C	N	O	F
0.533	0.370	0.284	0.231	0.195	0.168	0.149
Na	Mg	Al	Si	P	S	Cl
0.568	0.381	0.314	0.261	0.220	0.197	0.176
	Zn	Ga	Ge	As	Se	
	0.472	0.347	0.297	0.255	0.226	
	Cd	In	Sn	Sb	Te	
	0.460	0.351	0.290	0.245	0.218	
	Hg	Tl	Pb	Bi		
	0.522	0.404	0.338	0.296		

The index also monitors certain structural trends within a given class. For example, in Figure 1 we plot as a function of *S* the axial ratios *c/a*[4] for the divalent hcp series Be, Mg, Zn, Cd. We find a linear correlation. Extrapolation to Hg confirms the very large *c/a* deduced for hypothetical hcp mercury by Heine and Weaire.[4] This value represents so extreme a distortion of the hcp structure that it is hardly surprising to find Hg an exception to our simple partitioning scheme. As an alternative to hcp, however, the high value of *S*(Hg) does suggest the distorted bcc structure actually observed[5] at low temperatures.

The connection between these observations and conventional band theory is tenuous, but the behavior of *S* can be rationalized in terms reminiscent of the valence-bond theory of solids proposed by Pauling.[6] Valence-bond theory provides a conceptual basis for discussing crystal structure in terms of the hybridization of atomic bonding orbitals. If these orbitals were strictly s-like, bonds would be weak and nondirectional; the structure of minimum energy would be metallic with many bonding neighbors to allow for resonance stabilization.[7] If the bonding orbitals were strictly p, we might expect an open structure with fewer, stronger bonds—a "covalent" structure. In intermediate cases structural trends should be related to the relative amounts of s and p character in the hybrid bonding orbitals.

Now the index *S* describes the coextension of the s and p pseudoorbitals and should be at least a rough measure of the degree of hybridization. When $r_1 = r_0$, p orbitals should be preferred due to their directional properties; when $r_1 \gg r_0$, s orbitals should be preferred due to their compactness. In the latter case the screened p orbitals may be too diffuse to form strong bonds. This interpretation of *S* is supported for first-row elemental solids, at least, by the hybridizations estimated by Pauling.[6] Pauling suggests that Li should have 59% s character and Be somewhat more than 33%; *S*(Li) is 0.53 and *S*(Be) is 0.37. Carbon in the sp^3 diamond structure has 25% s character, and *S*(C) is 0.23. The bonding in fluorine should certainly be almost entirely p, as *S*(F) = 0.15 attests.

In contrast to trends in molecular hybridization,[8] the *S* values *increase* down columns of the periodic table. According to our discussion, this implies that the heavier elements are more metallic due to greater s participation in bonding.

The index *S* is not necessarily a unique measure of the structural information contained in the pseudopotential. For example, the index

$$S' \equiv k_F(r_1 - r_0) \tag{4}$$

where k_F is the Fermi wave number, provides a more dramatic partitioning of the periodic table and a more accurate indication of fourth-column trends, although its correlation with *c/a* ratios in divalent metals is less satisfactory.

More detailed studies, including extensions of (3) and (4) to binary solids and to elements having signifi-

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(6) L. Pauling, *Proc. Roy. Soc., Ser. A*, **196**, 343 (1949).

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cant amounts of d or f bonding (such as the heavy alkalies and alkaline earths), are in progress.

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Synthesis of Some DE and CDE Ring Analogs of Camptothecin

Sir:

Since the isolation and structure determination of the antitumor alkaloid camptothecin (**1**) in 1966,[1] several syntheses have been developed.[2a–d] The α-hydroxylactone functionality present in the E ring is an absolute requirement[3] for antitumor activity, and at present only one synthetic analog of camptothecin containing this E ring structure is known.[4] We now present the synthesis of several DE and CDE ring analogs.

Our synthetic procedure is broadly applicable and consists essentially of three stages. First, a nipecotic acid is subjected to the methylene lactam rearrangement,[5] giving the corresponding 3-methylene-2-piperidone. Second, this methylene lactam is converted to the dihydropyridone–primary allylic alcohol, and the acetic acid residue is introduced *via* Claisen rearrangement. Third, this 4-substituted 3-methylene-2-piperidone is again converted to a primary allylic alcohol, dehydrogenated, lactonized, and oxidized to give the fused pyridone–hydroxylactone. Examples of this overall process, with variations, are given below.

Nicotinic acid was converted to glycol **5a** (82%) *via* **2a**, **3a**, and **4a** as described.[5] Acetylation with acetic anhydride–pyridine at room temperature gave the monoacetate **6a** (mp 105–106°, 95%)[6] from which the 5,6-dihydropyridone **7a** (70%) was obtained by successive dehydration ($SOCl_2$–pyridine) and deacetylation (K_2CO_3–aqueous CH_3OH). Introduction of the lactone ring carbon atoms was accomplished by Claisen rearrangement.[7] Thus, allylic alcohol **7a**, excess trimethyl orthobutyrate,[8] and a catalytic amount of propionic acid at 145°, 3 hr, led to methylene lactam **9a** (96%) as a mixture of diastereomers. Allylic oxidation of **9a** with selenium dioxide[9] in refluxing toluene gave a mixture of tertiary alcohols which was converted into dihydropyridone **10a** (69%) by heating in acetic acid–acetic anhydride (catalytic H_2SO_4, 135–140°, 3 hr).

Although dehydrogenation of **10a** proceeded poorly with both lead tetraacetate in acetic acid[2a] and DDQ in boiling *p*-dioxane,[4] bromopyridone **11a** was prepared in 96% yield from **10a** with 200 mol % of NBS in CCl_4 (AIBN initiation, 8 min). Lactonization of **11a** in 2 *N* H_2SO_4–monoglyme at 50° (20 hr) gave lactone **13a** (100%). Removal of the bromine was cleanly effected (97%) by dehalogenation with H_2–Pd/C–Et_3N.[10] The resulting lactone **14a** (mp 91–92°) was converted to the camptothecin analog **15a** (mp 176–177°, 68%) by oxidation[11] with oxygen and alkali in the presence of triethyl phosphite.

6-Methoxycarbonylnicotinic acid,[12] successively treated with $SOCl_2$ (reflux, 2 hr) and benzyl alcohol (benzene–pyridine, 15 hr), gave the 2-methyl 5-benzyl diester[13] which on hydrogenation as hydrochloride in ethanol over PtO_2 followed by substitution of 10% Pd/C and addition of excess formaldehyde gave the hydrochloride of ester acid **2b** (62% overall). Rearrangement[5] of **2b** in acetic anhydride–K_2CO_3 gave methylene lactam **3b** (85%). Treatment of **3b** with MCPA[5] gave epoxide **4b** (98%) which was converted in refluxing HOAc, 24 hr, to the hydroxy acetate **6b** (60%).[14] Dehydration with $SOCl_2$–pyridine (55%) followed by deacetylation (K_2CO_3–CH_3OH) gave the allylic alcohol **7b** which was subjected to Claisen rearrangement and selenium dioxide oxidation as described above to effect the transformation to **10b**. NBS–CCl_4 converted **10b** directly to pyridone **12b** (60%). The desired camptothecin analog **15b** (mp 152–153°) was obtained by one-step lactonization–oxidation of **12b** with K_2CO_3 in oxygenated methanol, while deoxylactone **14b** resulted when oxygen was excluded.

3-Cyano-6-phenyl-2-pyridone,[15] heated with $C_6H_5POCl_2$[16] at 180°, 4 hr, gave 2-chloro-3-cyano-6-phenylpyridine which was dehalogenated (71%) in DMF with H_2–Pd/C–Et_3N. Hydrolysis[17] to the acid[18] and esterification gave methyl 6-phenylnicotinate[19] in 83%

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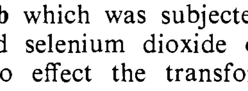

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