The molecular weights obtained with ultraviolet optics on solutions that are effectively infinitely dilute (c = 0.0025 g./dl.) are M_w = 26,300 ± 300 (D.P.$_w$ = 76) and M_z = 27,400 ± 600 (D.P.$_z$ = 79). Figure 2 shows the data from an ultraviolet optics experiment plotted as ln c *vs.* r^2. The resulting line shows a very slight but distinct curvature from the meniscus to the cell bottom, where the point M_w values are 25,600 ± 300 (D.P.$_w$ = 74) and 26,800 ± 300 (D.P.$_w$ = 78), respectively. A similar direct analysis of polydispersity from the equilibrium distribution plots derived from schlieren optics experiments was not possible because of the strong concentration dependence of equilibrium distribution.

The determined M_n and M_w values (Table I) are indistinguishable, and when corrected for the missing terminal adenosine residue are seen to be coincident with the known molecular weight of one member of the population, an alanyl s-RNA for which M = 26,600 (D.P. = 77).[15] These findings cannot, however, be taken as valid evidence that all the s-RNA's contain the same number of nucleotides. M_n and M_w values, identical within experimental error, could result from a variety of narrow molecular weight distributions which would also lead to the observed M_z. Furthermore, the slight concavity in Figure 2 and the M_w values at the extremes of the curve indicate a real, but very small heterogeneity in the s-RNA samples examined. Of course, the possibility cannot now be discounted that the molecular weight distribution is even narrower than that suggested by Figure 2, since the true distribution might have superimposed on it a contribution from trace ultraviolet-absorbing contaminants. Differences in nucleotide composition among the different s-RNA molecules could only account for a part (<1 nucleotide) of the observed heterogeneity. The close proximity of the M_n, M_w, and M_z values shows that dimers or higher aggregates of s-RNA molecules, if at all present, account for <0.2% of the total material. It should be noted that the higher M_z value from schlieren optics indicates minor contamination (<1%) with nonnucleic acid material, not observable with the selective ultraviolet optics.

Table I. Molecular Weight Data on Yeast s-RNA[a]

	Osmotic pressure	Sedimentation equilibrium — Schlieren optics	Sedimentation equilibrium — Ultraviolet optics
M_n	26,500 ± 300	...	...
M_w	...	26,000 ± 300	26,300 ± 300
M_z	...	29,800 ± 600	27,400 ± 600

[a] These data are for s-RNA essentially devoid of the terminal adenosine residue.

The foregoing observations make it appear that the vast majority of s-RNA species from yeast differ by no more than a very few nucleotides from 77. This narrow molecular weight distribution suggests that the function of this class of RNA molecules has placed a severe restriction on their evolutionary development.

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Structures of Leurocristine (Vincristine) and Vincaleukoblastine.[1] X-Ray Analysis of Leurocristine Methiodide

Sir:

Leurocristine (LCR), also known as vincristine (VCR), and vincaleukoblastine (VLB) are alkaloids which have been isolated from *Vinca rosea* Linn (Madagascar periwinkle) and which are known to have antitumor activity.[2] Molecular structures for LCR and VLB have been proposed,[3] along with some tentative assignments of a few of the steric arrangements at asymmetric centers. We wish to report the complete molecular structure, stereochemistry, and absolute configuration from an X-ray diffraction study of single crystals of leurocristine methiodide. The structures of VLB and LCR follow from the known relationships[4] among these molecules.

Crystals of leurocristine methiodide, $(C_{47}H_{59}O_{10}N_4)^+I^-$, hydrate are monoclinic in the space group $P2_1$. There are two molecules in the unit cell, which has parameters a = 10.96 Å., b = 21.89 Å., c = 12.68 Å., and β = 124° 53′. Because of slow decomposition of the material in the X-ray beam, the data (about 800 reflections/crystal) were taken from five different single crystals. Anomalous dispersion pairs were recorded with the use of the Buerger automated diffractometer, and data from the crystals were correlated after the usual corrections were made for Lorentz and polarization factors. The structure was solved from a Fourier synthesis based partly upon phases for the I atoms and upon phases as given by the differences ($\Delta|F|^2$) between anomalous dispersion pairs.[5] This synthesis, which showed as a clearly recognizable feature only one of the two indole rings, was then compared with the weighted (by b) sum function, $P_c + bP_s$,[6] which combines the mirror plane of P_c with the antimirror plane of P_s. This comparison yielded 36 peaks which formed the starting point for several Fourier and least-squares cycles of refinement. The value of $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ is 0.12 for the 1378 observed reflections.

The molecular structure, stereochemistry, and absolute configuration, which was preserved in the X-ray

(1) American Medical Association approved generic names are Vincristine (VCR) for leurocristine and vinblastine (VLB) for vincaleukoblastine. VLB is supplied as Velban® and VCR as Oncovin® (Lilly).

(2) (a) R. L. Noble, *Canadian Cancer Conf.*, **4**, 333 (1961); (b) I. S. Johnson, J. Vlantic, B. Mattus, and H. F. Wright, *ibid.*, **4** 339 (1961); (c) C. T. Beer, *ibid.*, **4**, 355 (1961); (d) J. H. Cutts, *ibid.*, **4**, 363 (1961); (e) R. Hertz, *ibid.*, **4**, 383 (1961); (f) M. E. Hodes, R. J. Rohn, and W. H. Bond, *ibid.*, **4**, 389 (1961); (g) I. S. Johnson, H. F. Wright, G. H. Svoboda, and J. Vlantis, *Cancer Res.*, **20**, 1016 (1960); (h) also see the symposium in *Lloydia*, **27**, 275 (1964).

(3) N. Neuss, M. Gorman, W. Hargrove, N. J. Cone, K. Biemann, G. Büchi, and R. E. Manning, *J. Am. Chem. Soc.*, **86**, 1440 (1964).

(4) N. Neuss, M. Gorman, H. E. Boaz, and N. J. Cone, *J. Am. Chem. Soc.*, **84**, 1509 (1962).

(5) (a) A. F. Peerdeman and J. M. Bijvoet, *Acta Cryst.*, **9**, 1012 (1956); (b) G. N. Ramachandran and S. Raman, *Current Sci* (India), **25**, 348 (1956).

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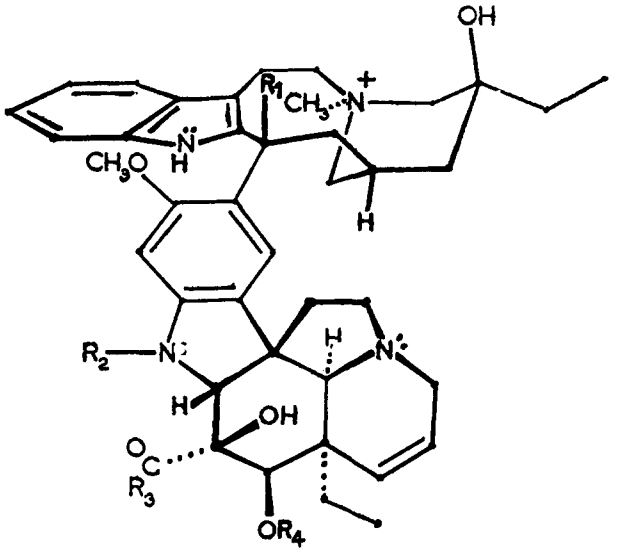

Figure 1. The conformational structure of leurocristine methiodide. Attached are R_1 = $COOCH_3$, R_2 = CHO, R_3 = OCH_3 and R_4 = $COCH_3$.

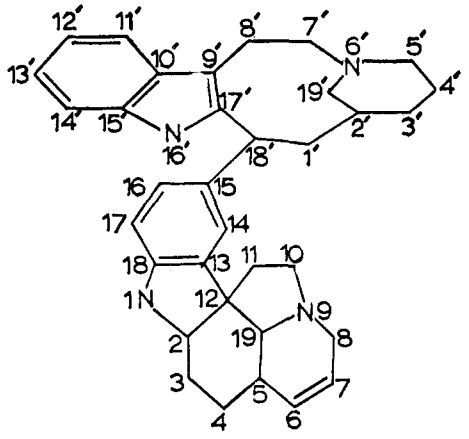

Fig. 2. The numbering system for the rings of leurocristine methiodide, LCR and VLB.

analysis, are indicated in Figure 1a. A reorientation by 180° about the bond between atoms 15 and 18′ (Figure 2) has been made in order to facilitate comparison with the structure proposed in ref. 3. If the CH_3^+ on the nitrogen at position 6′ is removed, then VLB has R_1 = $COOCH_3$, R_2 = CH_3, R_3 = OCH_3, and R_4 = $COCH_3$, while LCR has R_1 = $COOCH_3$, R_2 = CHO, R_3 = OCH_3, and R_4 = $COCH_3$.[3] Of the ten asymmetric centers in the molecule, the five for which the assignment was made in ref. 3 are mirror images of those of the actual structure. The vindoline[7] ring system of the molecule has asymmetric centers at 2, 3, 4, 5, 12, and 19, while the cleavamine-like ring region has centers at 2′, 4′, 6′, and 18′. Our results for the absolute configuration of the centers 6′ and 2′ are in agreement with the absolute configuration assigned by Camerman and Trotter[8] to cleavamine. In addition, leurocristine has asymmetric centers at 4′ and 18′, not present in cleavamine. Furthermore, the conformations of the nine-membered ring are considerably different in leurocristine and cleavamine owing to the strain imposed by the attachment at the bond (15–18′) joining the two parts of the leurocristine molecule.

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Aryl Coupling by Irradiation of Lithium Aryls

Sir:

In connection with our studies of the photochemistry of ionic carbon species, we wish to report a novel, extremely specific photochemical reaction. On irradiation with a 450-w. Hanovia high-pressure mercury arc lamp, 0.04 *M* solutions of phenyllithium in ethyl ether[1] gave over 80% yield of biphenyl and metallic lithium. This coupling is specific, 2-naphthyllithium giving exclusively 2,2′-binaphthyl. Only small amounts of products resulting from radical attack on solvent were detected. In contrast, photochemical decompositions of organomercury,[3,4] -bismuth,[5] and -lead[4,6] compounds lead to products derived from radical reactions with the solvent.

Addition of deuterium oxide in the workup of the reaction resulted in no incorporation of deuterium in the biphenyl. Thus biphenyl and not biphenyllyllithium is the product of the primary reaction. Phenyl radicals generated by the thermal decomposition of phenylazotriphenylmethane in ether produced only benzene and no biphenyl. Consequently the formation of biphenyl in the photolysis reaction is probably not a "simple" free radical coupling reaction. A possible pathway leading to biphenyl may be the reaction of a phenyl radical with phenyllithium. This need not be a typical radical reaction, however, since phenyllithium has been shown to be associated as dimers in ether,[7,8] and production of a phenyl radical by homolysis of the carbon–lithium bond would probably occur in the immediate vicinity of another molecule of phenyllithium. The specificity of radical attack on the carbon–lithium bond is understandable in terms of the intermediate which would result from this reaction. Unlike the usual homolytic aromatic substitution intermediates, which are simply resonance-stabilized free radicals,[9] this intermediate is, in effect, the considerably more stable biphenyl radical anion and lithium

(1) Phenyllithium was prepared in approximately 95% yield from bromobenzene and lithium metal,[2] and the solution was filtered before irradiation. All solutions were dry, oxygen free, and maintained under nitrogen.

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