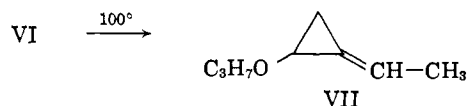
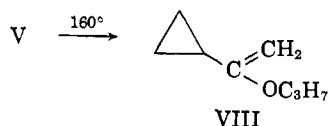


The isomerization of VI proceeds smoothly below 100° to give VII as a mixture of *syn* and *anti* isomers.^{4,7,9}



The rearrangement of V requires temperatures of the order of 160° and affords a single product (VIII, 95%) *via* a transient intermediate detectable by vapor-liquid chromatography. The n.m.r. spectrum of VIII exhibits two sets of doublets centered at τ 6.13 and 6.32



($J = 1.9$ c.p.s., terminal methylene, two protons).⁷

The elimination-addition sequences described have been extended to several other substituted dichlorocyclopropanes with similar results. Nucleophiles examined thus far include isopropoxide ion, methoxide ion, and methylmercaptide ion. These studies as well as details regarding the thermal rearrangement of substituted methylenecyclopropanes will be described in the full paper.

(8) Another mechanism which warrants consideration is that involving initial formation of 1,3-dimethyl-3-isopropoxycyclopropane followed by an $\text{S}_{\text{N}}2'$ attack by isopropoxide and rearrangement to VI. Although the product ratios observed (methoxide *vs.* isopropoxide) are not in the order expected for such a sequence, it cannot be unequivocally ruled out on the basis of these data.

(9) This type of rearrangement has been studied with other methylenecyclopropanes at much higher temperatures: E. F. Ullman and W. J. Fanshaw, *J. Am. Chem. Soc.*, **83**, 2379 (1961); J. P. Chesick, *ibid.*, **85**, 2720 (1963).

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Zeeman Effect of the Nuclear Quadrupole Resonance of Chlorine-35 in 3,5- and 2,6-Dichloropyridine

Sir:

Working on single crystals of 3,5- and 2,6-dichloropyridine, we determined the so-called "zero-splitting" cones¹ corresponding to the C-Cl bonds and the asymmetry parameters of the relative electric field gradients at the chlorine nuclei: $\eta = (V_{XX} - V_{YY})/V_{ZZ}$.² The value of η often depends largely on the extent of π -bond character between the Cl atom and the atom to which it is bonded.

The measurements were made by using a super-regenerative spectrometer and a magnetic field generated by a coil capable of orienting around a vertical and a

(1) T. H. Das and P. L. Hahn, "Solid State Physics," Supplement 1, "Nuclear Quadrupole Resonance Spectroscopy," Academic Press Inc., New York, N. Y., 1958.

(2) We follow the Das-Hahn convention: $|V_{XX}| < |V_{YY}| < |V_{ZZ}|$.

horizontal axis, according to a technique which has been already described.³

The cones were first referred to a laboratory reference system, x, y, z (in the origin of which there was the crystal). Their principal axes, X, Y, Z , were then determined by calculating their eulerian angles with respect to the former system. From these, we determined the angles between the two C-Cl bonds existing in each of these molecules. The working temperature was $26 \pm 1^\circ$.

Some common features of these two substances are listed. In the single crystal there appear to be only two C-Cl directions. This means that the molecules lie in the crystal all parallel to the same plane and with the same direction, N-C₄. The X axes of the two cones are substantially parallel: the small angles resulting are probably within the limits of the experimental error in the orientation of the X and Y axes (about 2°). The two C-Cl bonds are then coplanar (or "quasi"-coplanar) and probably lie in the plane of the ring, while the X axes are perpendicular to it. Other results are collected in Table I.

Table I

	Dichloropyridine	
	3,5-	2,6-
Frequency, ^a Mc.p.s.	34.773	33.850
η	0.086 ± 0.002	0.118 ± 0.002
Angle between the two C-Cl bonds	$122^\circ 23' \pm 10'$	$113^\circ 50' \pm 10'$

^a Frequency measurements were made with a BC 221 frequency meter.

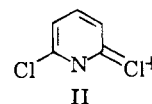
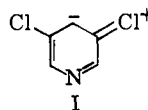
The directions of the C-Cl bonds were assumed, as usual, to be coincident with the directions of the Z axes of the zero-splitting cones. The obtained angles are slightly smaller than those given for the corresponding C-H directions in pyridine⁴: $124^\circ 8'$ and $114^\circ 46'$ for the 3,5- and 2,6-positions, respectively.

If we make the calculation concerning the double bond and the ionic character of the C-Cl bonds according to the approximate theory of C. H. Townes and B. P. Dailey,¹ we obtain the results shown in Table II

Table II

	Dichloropyridine	
	3,5-	2,6-
Double-bond character, %	3.72	5.05
Ionic character, %	18.3	19.3

The strong relative change of the π -bond character is probably due to the greater weight of the resonance structures of type II with respect to that of the structures of type I.



(3) (a) P. Bucci, P. Cecchi, and E. Scrocco, *Ric. Sci.*, **34** (IIA), 129 (1964); (b) P. Bucci and P. Cecchi, *ibid.*, **34** (IIA), 543 (1964).

(4) B. Bak, L. Hansen, and J. Rastrup-Andersen, *J. Chem. Phys.*, **22**, 2013 (1954).

It should be noted that the resonance frequencies are in the same order as those of the corresponding mono-substituted pyridines and differ by about the same quantity. All this would agree with Bray and co-workers' opinion⁵⁻⁷ that the decrease of the frequency of a chlorine attached to a carbon atom which is adjacent in the ring to a nitrogen atom is due to the increase of the double-bond character of the C-Cl bond.

While writing this paper, we had been informed that a communication concerning the same study was to be given by E. A. C. Lucken and C. Mazeline of the Cyanamid European Research Institute, Geneva, Switzerland, at the XIIIth Colloque Ampère, to be held in Leuven, Belgium, on September 1-5, 1964. We report their results for comparison in Table III.⁸

Table III

	Dichloropyridine	
	3,5-	2,6-
Frequency, Mc.p.s.	34.79	33.86
η	0.07 \pm 0.02	0.09 \pm 0.02
Angle between the two C-Cl bonds	122° 30' \pm 30'	113° \pm 30'

Acknowledgment. We are indebted to Dr. Margherita Landucci for help in preparing the single crystals, to Professor Eolo Scrocco for encouragement, and to the C.N.R. for sponsoring this research.

(5) P. J. Bray, *et al.*, *J. Chem. Phys.*, **25**, 1286 (1956).

(6) P. J. Bray, *et al.*, *ibid.*, **28**, 99 (1958).

(7) H. O. Hooper and P. J. Bray, *ibid.*, **30**, 957 (1959).

(8) On this subject we have contacted Drs. Lucken and Mazeline. Considering the respective techniques, we all feel that there is not a real disagreement between the two sets of results. On the other hand, on the basis of our experience, it seems to us that the error indicated in Table I is a fair estimate of the standard error in the present case.

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Optically Active Peptide Oxazolones. Preliminary Racemization Studies under Peptide-Coupling Conditions

Sir:

There is ample evidence in the literature to indicate the importance of oxazolone intermediates in racemization processes during peptide synthesis.^{1,2} In our laboratory we isolated and studied the racemization of the amino acid oxazolone, 2-phenyl-L-4-benzyl-5-oxazolone.³

We now wish to report the isolation of the first optically active, crystalline peptide oxazolones, namely, 2-(1'-benzyloxycarbonylamino-1'-methyl)ethyl-L-4-benzyloxazolone (I) and 2-(1'-benzyloxycarbonylamino-1'-methyl)ethyl-L-4-methyloxazolone (II).

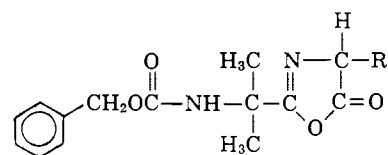
We undertook to prepare compounds I and II after noting the work of Kenner and his associates⁴ who

(1) M. W. Williams and G. T. Young, *J. Chem. Soc.*, 3701 (1964).

(2) M. Goodman and K. C. Stueben, *J. Org. Chem.*, **27**, 3409 (1962).

(3) M. Goodman and L. Levine, *J. Am. Chem. Soc.*, **86**, 2918 (1964).

(4) M. T. Leplawy, D. S. Jones, G. W. Kenner, and R. C. Sheppard, *Tetrahedron*, **11**, 39 (1960).



I, R = CH₂

II, R = CH₃

prepared the crystalline optically inactive oxazolone 2-(1'-benzyloxycarbonylamino-1'-methyl)ethyl-4,4-dimethyloxazolone. They synthesized this oxazolone by heating the peptide acid Z-Aib-Aib-OH⁵ in acetic anhydride at 110-120° for 15 min.

In order to prepare the dipeptide acids from which compounds I and II were derived we employed the technique of Mazur,⁶ who observed the acceleration of the *p*-nitrophenyl ester coupling reaction by imidazole. The amino acid derivative Z-Aib-ONp was allowed to react separately with the ester hydrochlorides HCl-Phe-OCH₃ and HCl-Ala-OCH₃ in the presence of NEt₃ and excess imidazole in DMF solvent. Excellent yields of the optically pure dipeptide esters were obtained. These esters were converted to the corresponding free acids under careful, dilute acidic hydrolysis conditions. Physical data on the key compounds are recorded in Table I.

Table I

Compound ^a	M.p., °C.	$[\alpha]^{25D}$, deg. (c, dioxane)
Z-Aib-L-Phe-OCH ₃	94.2-94.8	+27.2 (2.2)
Z-Aib-L-Phe-OH	60-65	+34.2 (2.5)
Z-Aib-L-Ala-OCH ₃	68.6-69.6	-5.5 (4.5)
Z-Aib-L-Ala-OH	139-140	+5.9 (4.5)
Oxazolone from Z-Aib-L-Phe-OH	96.0-97.4	-131.3 (2.2)
Oxazolone from Z-Aib-Ala-OH	115-119	-52.1 (1.5)

^a The microchemical analyses of C, H and N for compounds listed fall within accepted limits.

The optically active oxazolone I can be obtained from the free acid after 8-10 hr. room-temperature treatment with a 2:1 dioxane-acetic anhydride solution using a concentration of approximately 60 mg./ml. of peptide. The solvent is removed by careful distillation when the negative rotation of the solution reaches a maximum value.

The oxazolone I, which can be obtained optically pure by fractional crystallization, has m.p. 96.0-97.4°; $[\alpha]^{25D}$ -131.3° (c 2.2, dioxane) (*Anal. Calcd.* for C₂₁H₂₂N₂O₄: C, 68.85; H, 6.01; N, 7.65. *Found:* C, 68.85; H, 6.22; N, 7.72); ν_{max} 3280, 1825, 1717, 1662, 1529, 1380, 1262, 1099, 1080, 1040, and 698 cm.⁻¹. All are intense peaks. The peak at 1825 cm.⁻¹ is characteristic for the oxazolone carbonyl group.

Some difficulty was encountered in obtaining the optically active compound II. Using the dioxane-acetic anhydride treatment for 4 hr. at room temperature an optically impure oxazolone was obtained, m.p. 109-115°; $[\alpha]^{25D}$ -43.3° (c 1.0, dioxane).

(5) The residue Aib refers to the α -aminoisobutyryl residue.

(6) R. H. Mazur, *J. Org. Chem.*, **28**, 2498 (1963).