m.p. 157–159, $[\alpha]^{25}D$ +0.54° (1.9% in glacial acetic acid), $[\alpha]^{31}D$ −13.5° (1.9% in 95% alcohol).

Anal. Calcd. for $C_{25}H_{29}O_8N_3$ (499.5): N, 8.4. Found: N, 8.3.

(2) H·Glu·OH (LL).—This was obtained by the hydrogenation of compound I in 60% methanol in the usual manner.[9] It was recrystallized from water–ethanol; yield 80–90%, $[\alpha]^{23}D$ +8.7° (1.0% in 0.5 *N* HCl).

Anal. Calcd. for $C_{10}H_{17}O_6N_3$ (275.2): N, 15.3; amide N, 5.1; amino N, 5.1; carboxyl N, 5.1. Found: N, 15.2; amide N, 5.0; amino N, 14.2; carboxyl N, 4.4.

Stability of γ-L-Glutamyl-L-glutamic Acid in 0.5 *N* HCl.—The γ-peptide (0.0265 g.) was dissolved in 5 ml. of 0.5 *N* HCl at 25°. Aliquots (1 ml.) were then removed at suitable time intervals and carboxyl N analysis performed (ninhydrin, 7 minutes, *p*H 2.5).

Anal. Calcd. for $C_{10}H_{16}O_7N_2$ (276.2): carboxyl N, 5.1.

Time, hours	0	6	24
Found: % carboxyl N	5.3	5.3	5.3

Estimation of Lactone.—L-Glutamic acid was used as a standard for the colorimetric estimation of the lactone formed. The procedure consisted of treating the test substance with nitrous acid under the usual Van Slyke conditions (with respect to *p*H and HNO_2 concentration) decomposing the excess HNO_2 with $NH_2OH·HCl$ and then preparing and estimating the hydroxamic acid–iron complex in the usual manner.[13]

Approximately 35–45 μmoles of glutamic acid (or amount of test substance which would yield 35–45 μmoles of lactone) was weighed into a 15-cc. volumetric flask. The following reagents were added in the order: 2.5 ml. of H_2O, 0.5 ml. of glacial acetic acid, 1.0 ml. of $NaNO_2$ solution (800 g. of $NaNO_2$ per liter of H_2O). After ten minutes at 25°, the solution was cooled (0°), and 5 ml. of 2 *M* $NH_2OH·HCl$ solution added dropwise. The solution was permitted to stand for 3 minutes at 25°, and enough H_2O was then added to bring the volume to 15 ml. Aliquots (3.0 ml.) of this solution were then added to a solution containing 1.0 ml. of 2 *M* $NH_2OH·HCl$ and 2 ml. of 3.5 *N* NaOH. The reaction mixture was allowed to stand for four minutes (25°), and then 1.65 ml. of HCl (HCl, sp. gr. 1.18 diluted with 2 parts by volume of H_2O) and enough $FeCl_3$ solution (0.37 *M* in 0.1 *N* HCl) were added to bring the final volume to 10 cc. (final *p*H 1.2). The optical density of the colored solution was determined with the aid of a Klett–Summerson photoelectric colorimeter (number 54 filter).

The glutamic acid standard showed an approximately linear relationship of concentration to optical density in the region 3–9 μmoles. Under these experimental conditions the absorption spectrum of the colored hydroxamic acid complex (measured in the Beckman model DU spectrophotometer) exhibited a broad maximum at about 540–500 mμ (using either glutamic acid or γ-glutamylglutamic acid as starting material).

Optical Configuration of the α-Hydroxy Acid Formed.—L-Glutamic acid (0.1225 g.), L-glutamine (0.1230 g.), γ-L-glutamylglutamic acid (0.114 g.) and L-alanine (0.1219 g.) were each treated with nitrous acid for ten minutes as described above. The solutions were then taken down to dryness in a stream of air, 5 ml. of H_2O added to each and the solvent was again evaporated. This was repeated twice more; then the residues were each taken up in 0.5 ml. of 2 *N* NaOH and the volume adjusted to 3 ml. with H_2O. The optical rotations were measured and the specific rotations calculated on the basis of complete conversion to the hydroxy acid.

Starting materials	$[\alpha]^{26}D$	Concn., %
H·Gl·OH (L)[17]	−11.1°	3.6
H·Glu·OH (LL) (L-Glu·OH)	−10.3	3.5
H·Glu·OH (L) (L-NH_2)	−10.8	3.6
H·Ala·OH (L)	− 9.2	4.1

(17) E. Fischer and A. Moreschi (*Ber.*, **45**, 2447 (1912)) prepared the disodium salt of L-α-hydroxyglutaric acid; $[\alpha]^{19}D$ −8.65° (1.6% in H_2O).

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Contribution of the Cyclopropyl Ring to Molar Refraction[1]

BY VERNON A. SLABEY

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In 1900, Tschugaeff[2] reported that the observed molar refractions of cyclopropane derivatives were higher than those calculated by summation of atomic and group refractivities. This difference between observed and calculated refractions was attributed by Tschugaeff to the cyclopropyl ring, and from the average difference for a number of compounds he concluded that the magnitude of this ring contribution was about 0.7. Östling[3] reported on a larger number of compounds, and his average difference agreed well with Tschugaeff's value. Consequently, the value 0.7 has generally been accepted as the contribution of the cyclopropyl ring to the molar refraction of cyclopropane derivatives.

More recently, Jeffery and Vogel[4] determined the contribution of the cyclopropyl ring by a different procedure: from the observed molar refraction of the cyclopropane derivative is subtracted the observed molar refraction of a structurally similar acyclic compound, two hydrogen atomic refractivities being added to the result to make up for the two additional hydrogens in the acyclic structure. From data obtained principally with alkyl cyclopropane mono- and dicarboxylates, the authors assigned the value 0.614 to the ring contribution.

In each of the previous investigations the number of individual cyclopropane compounds and also, the number of derivative types were limited; consequently, it was uncertain: (1) whether any one value adequately expresses for all cyclopropane derivatives the contribution of the ring to the molar refraction, and (2) which of the methods proposed for determining the ring contribution is most likely to give such a "constant" value. The physical properties of 30 cyclopropane derivatives, were available from previous work[5]; these data were used in the present effort to answer these questions.

Results and Discussion

In Table I are presented the observed molar refractions of the 30 cyclopropane derivatives, the dif-

(1) Presented before the Organic Division at the 124th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 6–11, 1953.

(2) L. Tschugaeff, *Ber.*, **33**, 3118 (1900).

(3) G. Östling, *J. Chem. Soc.*, **101**, 457 (1912).

(4) G. Jeffery and A. Vogel, *ibid.*, 1804 (1948).

(5) (a) V. A. Slabey and P. H. Wise, THIS JOURNAL, **71**, 3252 (1949); (b) **74**, 1473 (1952); (c) **74**, 3887 (1952); (d) V. A. Slabey, *ibid.*, **68**, 1335 (1946); (e) **74**, 4928 (1952); (f) **74**, 4930 (1952); (g) **74**, 4963 (1952); (h) V. A. Slabey, P. H. Wise and L. C. Gibbons, "Hydrocarbon and Nonhydrocarbon Derivatives of Cyclopropane," National Advisory Committee for Aeronautics, Technical Report 1112.

ference, ΔM_r, between the observed and calculated refractions and values for ring contribution determined by Vogel's procedure. It can be seen from the ΔM_r values that a ring contribution determined by the method of reference 2 would have little, if any, meaning. Even if the averaging process were confined to an homologous series, and if the value so obtained were used only for members of that series, the calculated molar refraction would only approximate the observed refraction.

TABLE I

CONTRIBUTION OF THE CYCLOPROPYL RING TO THE MOLECULAR REFRACTION

Cyclopropane derivatives	M_r (obsd.)[a]	ΔM_r[b]	Ring contribution[c]
2-Cyclopropylpropane	28.33	0.45	0.44
2-Cyclopropylbutane	32.85	.32	.44
2-Cyclopropylpentane	37.51	.33	.45
2-Cyclopropylhexane	42.15	.33	.44
2-Cyclopropyl-3-methylbutane	37.37	.19	.44
Dicyclopropyl	26.53	.70	.37
Spiropentane	22.45	1.27	
Vinylcyclopropane	23.60	0.85	.83
2-Cyclopropylpropene	27.98	.58	.62
2-Cyclopropyl-1-butene	32.46	.41	.5
2-Cyclopropyl-1-pentene	37.12	.42	
2-Cyclopropyl-1-hexene	41.75	.41	
2-Cyclopropyl-3-methyl-1-butene	37.06	.36	
2-Cyclopropyl-2-butene, L.B.	32.63	.58	
2-Cyclopropyl-2-pentene, L.B.	37.47	.77	
2-Cyclopropyl-2-hexene, L.B.	42.11	.77	
2-Cyclopropyl-2-butene, H.B.	32.66	.61	
2-Cyclopropyl-2-pentene, H.B.	37.45	.75	
2-Cyclopropyl-2-hexene, H.B.	42.13	.79	
Methylcyclopropylcarbinol	25.12	.37	
Dimethylcyclopropylcarbinol	29.65	.25	
Methylethylcyclopropylcarbinol	34.25	.20	
Methylpropylcyclopropylcarbinol	38.85	.16	
Methylbutylcyclopropylcarbinol	43.48	.14	
Methylisopropylcyclopropylcarbinol	38.64	−.05	
Methyl cyclopropyl ketone	23.94	.60	.75[d]
Diethyl cyclopropane-1,1-dicarboxylate	45.77	.84	.76[e]
Cyclopropyl chloride	19.07	.31	
1,1-Dichlorocyclopropane	24.06	.49	
trans-1,2-Dichlorocyclopropane	24.06	.49	

[a] $(n^2 - 1/n^2 + 2) \times (m/d) = M_r$(obsd.). [b] M_r(obsd.) − M_r(calcd.) = ΔM_r. Atomic and group refractivities of A. Vogel, *J. Chem. Soc.*, 1842 (1948), were used. [c] M_r(obsd.) $\left[\begin{array}{l}CH_2 \\ | \\ CH_2\end{array}\!\!>\!C\!<\begin{array}{l}R \\ | \\ R'\end{array}\right]$ + 2 [H_r] − M_r(obsd.) $\left[\begin{array}{l}CH_2 \\ | \\ CH \\ | \\ CH_3\end{array}\!\!>\!\begin{array}{l}R \\ | \\ R'\end{array}\right]$. Atomic refractivity of hydrogen (H_r) taken from ref. of footnote *b*. M_r(obsd.) of the acylic hydrocarbons taken from Natl. Bureau Standards Circular C461, U. S. Government Printing Office, Washington, D. C., 1947. [d] M_r(obsd.) of acyclic compound taken from D. M. Cowan, G. H. Jeffery and A. Vogel, *J. Chem. Soc.*, 175 (1940). [e] M_r(obsd.) of acyclic compound taken from A. Vogel, *ibid.*, 643 (1948).

The procedure used in reference 4 could be applied only to the 2-cyclopropylalkanes and to a few additional compounds because reliable physical data were not available for the acyclic structures similar to the remaining compounds. The 2-cyclopropylalkanes gave a "constant" ring contribution, 0.44. However, indiscriminate use of this "constant" for all types of cyclopropane derivatives would give misleading results, because the "constant" changes with the character of the substituents on the ring. This is indicated by the values obtained for the other compounds shown in Table I, and also by the fact that Vogel obtained a ring contribution of 0.614 for the compounds used in his investigation.

It must be concluded that no single value adequately expresses for all structures the contribution of the cyclopropyl ring to molar refraction. This is not entirely unexpected when one considers that the refractivity of the 3-carbon ring reflects the polarization of the electrons of the ring, and that as the substituents on the ring are changed, the degree of polarization of the ring and, hence, the refractivity of the ring, is changed. In neither of the methods of determining ring contribution is this factor taken into consideration; Tschugaeff's method disregards, in addition, the changes in the atomic and group refractivities which occur as the structure varies. Consequently, Vogel's procedure is to be preferred when reliable physical data are available for the appropriate acyclic compounds.

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Characteristic Infrared Absorption Bands of the Cyclopropyl Ring[1]

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In the course of investigating the synthesis of cyclopropane derivatives, a method of establishing the presence of the cyclopropyl ring in the synthesis products was desired. The detection of the cyclopropyl ring by chemical means is difficult, and of the physical methods, infrared spectroscopy appeared to be the most promising.

While our investigation was in progress, three papers were published in which the respective authors suggested three different regions of the spectrum between 2 and 16 μ as being useful for determining the presence of the cyclopropyl ring. Bartleson, Burk and Lankelma[2] used absorption bands at 9.75 and 11.55 μ to indicate the rings' presence in 1,1,3-trimethyl- and 1,2-dimethyl-3-ethylcyclopropane. In 1949, Derfer, Pickett and Boord[3] observed that in the infrared spectra of 14 individual cyclopropane hydrocarbons, strong absorption, apparently due to ring deformation, occurred between 9.8 and 10.0 μ, but that the absorption at 11.6 μ used by Bartleson, *et al.*, did not consistently occur in their spectra. More recently,

(1) Presented before the Organic Division at the 124th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 6-11, 1953.

(2) J. D. Bartleson, R. E. Burk and H. P. Lankelma, THIS JOURNAL, **68**, 2513 (1946).

(3) J. M. Derfer, R. E. Pickett and C. E. Boord, *ibid.*, **71**, 2482 (1949).