Anal. Calcd. for $C_{19}H_{24}N_2O_2$: C, 73.0; H, 7.7. Found: C, 73.4; H, 7.8.

In a similar manner were prepared the following carbamates.

2-Diethylaminomethyl-6-benzylphenyl N,N-dimethylcarbamate, b.p. 196–201° (1 mm.), 84% yield, n^{20}D 1.5494. *Anal.* Calcd. for $C_{21}H_{28}N_2O_2$: C, 74.1; H, 8.3. Found: C, 74.5; H, 8.2.

4-Chloro-2-dimethylaminoethyl-6-benzylphenyl N,N-dimethylcarbamate, b.p. 197–201° (2 mm.), 38% yield, n^{20}D 1.5704. *Anal.* Calcd. for $C_{19}H_{23}ClN_2O_2$: C, 65.8; H, 6.7. Found: C, 66.4; H, 6.7.

2-Dimethylaminomethyl-4-benzylphenyl N,N-dimethylcarbamate, b.p. 196–197° (1 mm.), 57% yield, n^{20}D 1.5548. *Anal.* Calcd. for $C_{19}H_{24}N_2O_2$: C, 73.0; H, 7.7. Found: C, 73.3; H, 7.9.

2-Diethylaminomethyl-4-benzylphenyl N,N-dimethylcarbamate, b.p. 200–205° (0.5 mm.), 93% yield, n^{20}D 1.5456. *Anal.* Calcd. for $C_{21}H_{28}N_2O_2$: C, 74.1; H, 8.3. Found: C, 74.2; H, 8.2; hydrochloride, m.p. 148.5–150.0° (recrystallized from isopropyl alcohol–Skellysolve B). *Anal.* Calcd. for $C_{21}H_{28}N_2O_2 \cdot HCl$: C, 66.9; H, 7.8. Found: C, 67.2; H, 8.0.

2-Diethylaminomethyl-4-benzylphenyl N,N-diethylcarbamate, b.p. 202–206° (1 mm.), 56% yield, n^{20}D 1.5358. *Anal.* Calcd. for $C_{23}H_{32}N_2O_2$: C, 75.0; H, 8.8. Found: C, 75.0; H, 8.8.

Quaternary Ammonium Compounds.—The compounds listed in Tables I and II were prepared by addition of an excess of alkyl halide to an isopropyl alcohol solution of the carbamate. With methyl iodide, the reaction proceeded rapidly at room temperature so that the product could be collected by filtration after a few hours. With ethyl iodide, the reaction mixture was refluxed for a few hours, then cooled and diluted with ether or ethyl acetate if necessary to cause crystallization. Compound 11 of Table II was obtained instead of the desired bisquaternary when ethylene bromide was used as the alkyl halide.

Carbamates of Benzylphenols.—Typical examples are given for the preparation of disubstituted carbamates (method A) and monosubstituted carbamates (method B). The properties of these compounds are summarized in Table III.

Method A.—A solution of 46.0 g. (0.25 mole) of 2-benzylphenol and 28.0 g. (0.26 mole) of N,N-dimethylcarbamyl chloride in 80 ml. of pyridine was heated overnight on the steam-bath. The cooled solution was poured into 500 ml. of water and extracted three times with benzene. The combined benzene extracts were washed in turn with Claisen alkali, dilute sodium hydroxide and water, then dried and distilled. 2-Benzylphenyl N,N-dimethylcarbamate was obtained as an oil, b.p. 177–179° (1.4 mm.).

Method B.—One mole each of 4-benzylphenol (184 g.) and phenyl isocyanate (119 g.) were stirred together in one liter of cyclohexane and 100 ml. of benzene for one hour at reflux. The solid which formed on cooling amounted to 220 g. and melted from 75–194°. Since this was obviously a mixture, the mother liquor was concentrated to an oil which was taken up in ether and combined with the crude solid. This ether solution was extracted three times with 10% potassium hydroxide (on acidification of these extracts 93 g. (53%) of unreacted 4-benzylphenol were recovered). Two successive concentrations of the ether solution gave a total of 115 g. of 4-benzylphenyl N-phenylcarbamate.

SYRACUSE 1, N.Y.

COMMUNICATIONS TO THE EDITOR

POLYPEPTIDES. XII. THE OPTICAL ROTATION AND CONFIGURATIONAL STABILITY OF α-HELICES[1]

Sir:

In view of the interest in the configuration of synthetic polypeptides and proteins, it is pertinent to record now some work that has been done in our laboratories on the configurational stability of such molecules. Rotatory dispersion studies of poly-γ-benzyl-L-glutamate[2] and poly-L-glutamic acid[3] have shown that in solvents where the α-helical configuration is known to exist, the specific rotation, $[\alpha]_D$, has small, positive values and the dispersion is abnormal. In contrast when the configuration is that of a random coil $[\alpha]_D$ is negative and the dispersion is normal. These results suggested that the helix is of a single screw-sense. Recent theories of the optical properties of helices[4,5,6,7] have confirmed this view and appear to have established the absolute configuration as being right-handed. Similar conclusions have been reached tentatively by Elliott and Malcolm[8] from X-ray diffraction data.

The specific rotation which the helical configuration confers on the polypeptide chain cannot, however, be rigorously determined by subtracting the rotation in the randomly coiled form from that in the helical form because the environmental effects on the peptide bonds in the two configurations are sufficiently different as to alter substantially the intrinsic residue rotations on going from one form to the other. An alternative approach is possible, however, upon recognizing that copolymers of D and L-residues should exhibit an increase in $[\alpha]_D$ as a result of the cancellation of the intrinsic residue rotations of matched D and L residues, thereby revealing the positive contribution made to the rotation by the helix itself.[9,10] The specific rotations of a number of copolymers of γ-benzyl-D and L-glutamate[11] in chloroform, a solvent in which the helical form is known to be the stable one, are

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[1] For the last paper in this series see ref. 13.

[2] P. Doty and J. T. Yang, THIS JOURNAL, **78**, 498 (1956).

[3] P. Doty, A. Wada, J. T. Yang and E. R. Blout, paper presented at International Symposium on Macromolecules, Rehovot, Israel, April 4, 1956. To be published January 1957 in *Journal of Polymer Science*.

[4] W. Moffitt, *J. Chem. Phys.*, **25**, 467 (1956).

[5] W. Moffitt and J. T. Yang, *Proc. Nat. Acad. Sci., U. S.*, **42**, 596 (1956).

[6] W. Moffitt, *ibid.*, **42**, 736 (1956).

[7] D. D. Fitts and J. G. Kirkwood, THIS JOURNAL, **78**, 2650 (1956).

[8] A. Elliott and B. R. Malcolm, *Nature*, **178**, 912 (1956).

[9] This effect already has been reported and a preliminary value given in footnote 8 of P. Doty and R. D. Lundberg, THIS JOURNAL, **78**, 4810 (1956).

[10] A. Elliott, W. E. Hanby and B. R. Malcolm, *Nature*, **178**, 1170 (1956).

[11] Prepared by Mr. R. H. Karlson.

shown as the points on the left-hand abscissa in the figure. When small amounts of the D-residues are present the rotation is seen to increase linearly. Extrapolation of these data to the composition of a racemic mixture permits the estimation of the specific rotation of a right-handed helix free of any residue contribution. This estimated value is +48° for $[\alpha]_D$ and +105° for the residue rotation. The latter figure is the value that should be compared with the prediction of +68° by Fitts and Kirkwood[4] instead of the differences between the rotations of helical and randomly coiled configurations which has been employed. The agreement is well within the uncertainties of the two figures. The value recently published for polyleucine[10] is 31% higher than that reported here.

It has been pointed out that the steric hindrance between β-carbon atoms may be sufficient to prevent or weaken the α-helical configuration when both D and L residues are present. The copolymers used for the above measurements provide an opportunity to test this suggestion by making use of the transition that can be observed when the ratio of a solvent favoring the helical configuration to one favoring the random coil configuration is gradually changed. The sharpness of this transition and its similarities to a melting process have been discussed already.[2] This transition is conveniently detected by measuring the rotation as dichloroacetic acid is added to a chlororform solution of the polypeptide.[12] The results of this kind of experiment are shown in the figure. The pure L-polypeptide helix "melts out" sharply at about 68% dichloroacetic acid. However, with increasing D-residue content the melting out of the helical structure occurs at successively lower dichloroacetic acid concentrations and the range over which the melting occurs is broadened. Since the molecular weights of these polymers were of the same order of magnitude (~100,000) it is clear that the introduction of optical isomers brings about a proportionate weakening of the helix. Inasmuch as the helical configuration of L-polypeptides and proteins possesses only a rather marginal stability in aqueous media[3,12] it is apparent that these structures would not be maintained if significant amounts of D-residues were present.[13]

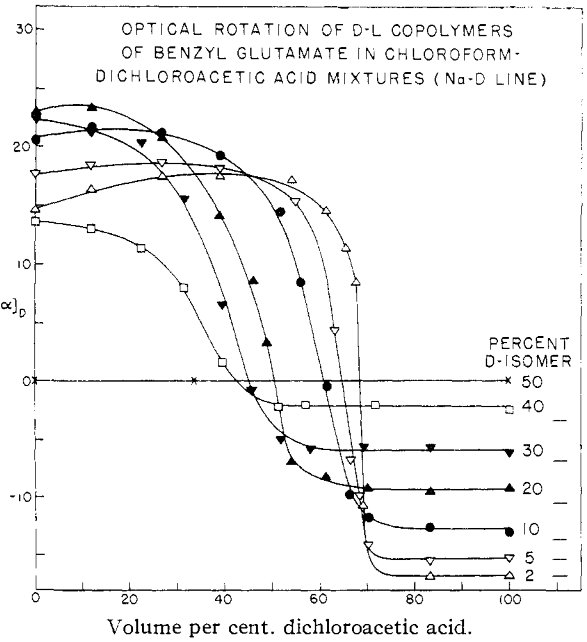

Fig. 1.—The specific rotation (sodium D-line) of poly-γ-benzyl glutamate as a function of the amount of dichloroacetic acid added to chloroform solutions. The lines on the right indicate the rotation expected if rotations of D and L-residues are additive. The data for the pure L-polypeptide ($[\alpha]_D$ 13.8° in $CHCl_3$) have been omitted because they fall so close to the polymer containing 2% D-residues.

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(12) J. T. Yang and P. Doty, THIS JOURNAL, in press.

(13) We wish to acknowledge support of this work by the Office of the Surgeon General, Department of the Army and the Office of Naval Research (N5ori-07654).

(14) Chemical Research Laboratory, Polaroid Corporation, Cambridge 39, Massachusetts.

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RECEIVED DECEMBER 5, 1956

THE RING FISSION OF CYCLOPROPANES: THE CONSTITUTION OF MAALIOL

Sir:

Acid catalyzed cleavages of cyclopropanes obey the rule of Markownikoff. In other words, opening occurs between the carbon atoms holding the smallest and largest number of alkyl groups.[1] We now would like to suggest that derivatives of bicyclo[4,1,0]heptane lead to diaxial cyclohexanes or monoaxial cyclohexenes. Such a mechanism accounts readily for the acid catalyzed isomerizations of cycloartenol,[2,3] cyclolaudenol,[4] phyllanthol[2] and carene.[5] In the course of structural studies on maaliol (I), $C_{15}H_{26}O$, m.p. 103–104°,[6] which turns out to be a sequiterpene homolog of carane, we have now observed a non-Markownikoff cleavage of a cyclopropane. On treatment with anhydrous hydrogen chloride at 20° maaliane (II) was transformed to an olefin (IV or VI), b.p. 115° (7 mm.), found: C, 87.39; H, 12.52; 3.33, 6.14, 11.36 μ. Osmylation followed by glycol cleavage with lead tetraacetate gave formaldehyde and a norketone (V or VII), m.p. 33°, found: C, 81.17; H, 11.81; 5.88, μ, *negative* iodoform test, 2.98 *D* introduced with NaOD in EtOD. The operation of the mechanism discussed above for acid cleavage of cyclopropanes is handicapped in this case by the instability of the intermediate (III). Examination of III reveals that such a structure would be unduly strained because of the three bulky *cis*-1,3-triaxial groups. The molecule being a *trans*-decalin cannot undergo ring transformation to the

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(1) R. A. Raphael in E. H. Rodd, "The Chemistry of Carbon Compounds," Vol. IIA, Elsevier, Amsterdam, 1953, p. 26.

(2) D. H. R. Barton, E. W. Warnhoff and J. E. Page, *J. Chem. Soc.*, 2715 (1954).

(3) D. S. Irvine, J. A. Henry and F. S. Spring, *ibid.*, 1316 (1955).

(4) J. A. Henry, D. S. Irvine and F. S. Spring, *ibid.*, 1607 (1955).

(5) Ref. 1, Vol. IIB, p. 558.

(6) *Schimmel Reports*, 137 (1908).