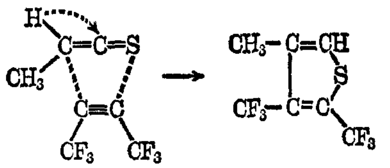
pected to lead to 2,3-bis(trifluoromethyl)-4-methylthiophene formation.



A more detailed account of these studies will be forthcoming.

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Epimerization of 2,4-Diphenylpentane, an Oligomer of Polystyrene

Sir:

The frequency of incidence of the various conformations of a chain molecule such as a vinyl polymer HCH_2CHRCH_2CHR–, etc., or an oligomer thereof, is determined by bond torsional potentials and by interactions between nonbonded atoms. These interactions occur in profusion if R is a group as large as or larger than CH_3. The same factors must determine the equilibrium distribution among the various diastereoisomers generated by racemization of the asymmetric centers CHR. A statistical mechanical theory of stereochemical equilibrium in chain molecules containing asymmetric centers has been developed recently on this basis.[1] The same parameters that serve to describe the relative proportions of various conformers for a given stereoisomer also define the equilibrium distribution over the various diastereomeric species. Methods for racemization of the asymmetric centers in molecules of the type considered, and for accurate analysis of the equilibrated mixture, are therefore of immediate relevance to investigation of the incidence of various conformations which a given species may assume.

In pursuit of this objective we have succeeded in establishing conditions for equilibration of the *meso* and *dl* isomers of 2,4-diphenylpentane in dimethyl sulfoxide (DMSO) containing potassium *t*-butoxide. The ready occurrence of proton transfer reactions between hydrocarbons under these conditions has been demonstrated in a number of instances.[2,3] By analogy to these investigations, racemization of the asymmetric centers of 2,4-diphenylpentane may be presumed to occur *via* the formation of a planar alkyl-substituted benzyl anion.[2]

meso- and *dl*-2,4-diphenylpentanes were synthesized by the method of Overberger and Bonsignore.[4] The diastereoisomers were partially separated[5] and quantitatively determined[6] by gas chromatography. Nmr spectra[7] of the compounds agreed with published results.[8,9] The equilibrium ratios shown in the final column of Table I represent averages of triplicate analyses[10] which were in mutual agreement within ±0.5%; other values reported are the means of duplicate measurements.

Table I. Epimerization of *meso*- and *dl*-2,4-Diphenylpentane

Sample	Initial % *meso*	Equilibration Time, days	% *meso*
1	70.0	7	56.5[a]
2	45.0	14	48.4
3	29.5	14	48.4
4	84.5	28	48.5

[a] Not fully equilibrated.

The compounds were epimerized by layering the reagents in a narrow tube in the following order: potassium *t*-butoxide, DMSO, and a mixture of the hydrocarbon with DMSO. The contents were immediately frozen, then degassed, and the tube was sealed. Mixing of the different layers upon gradual warming to room temperature produced a pink color which persisted until the tube was opened and the base destroyed by the addition of water. The color, which disappears rapidly on exposure to air, is indicative of a benzyl anion.[11] The hydrocarbon was extracted with pentane, a poor solvent for DMSO, and analyzed. From the final values of the % *meso* given in the last column of Table I, it is evident that the epimerization has reached equilibrium after 14 days and that the same final composition, 48.4% *meso*, is attained from both directions.

In order to confirm that the response of the flame ionization detector used for the gas chromatographic analysis was directly proportional to the concentration of the two isomers, an equilibrated mixture was independently analyzed by taking its nmr spectrum in CCl_4 using the Varian HR-100 spectrometer, the instrument being tuned with special care. The proportions of the two isomers were calculated from the areas of the respective methyl peaks[12] as determined by the triangle approximation. They were also computed from the peak heights. The latter method has been shown to be valid for a series of diastereomeric esters.[13] Both methods gave 47 ± 1% *meso* for the composition of the equilib-

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(1) P. J. Flory, *J. Am. Chem. Soc.*, **89**, 1798 (1967).

(2) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965.

(3) J. E. Hoffman, R. J. Muller, and A. Schriesheim, *J. Am. Chem. Soc.*, **85**, 3002 (1963).

(4) C. G. Overberger and P. V. Bonsignore, *ibid.*, **80**, 5427 (1958).

(5) Aerograph Model A90-P3 chromatograph, Varian Aerograph Inc., Walnut Creek, Calif. A column, 20 ft × 3/8 in., packed with 20% by weight FFAP on Chromosorb W operated at 240° with helium as the carrier gas was used.

(6) Aerograph Model 600-D chromatograph with flame ionization detector. A column, 12 ft × 1/8 in., filled with 20% Apiezon-L on acid-washed Firebrick was used. Optimum separation was achieved at 230° with a helium flow rate of 75 cc/min.

(7) Varian A-60 spectrometer operated at room temperature with approximately 20% (w/v) solutions in CCl_4 and tetramethylsilane as reference.

(8) F. A. Bovey, F. P. Hood III, E. W. Anderson, and L. C. Snyder, *J. Chem. Phys.*, 42, 3900 (1965).

(9) D. Lím, B. Obereigner, and D. Doskočilová, *J. Polymer Sci.*, **B3**, 893 (1965).

(10) Calculations of the two isomers based on the areas of the respective peaks measured with a planimeter.

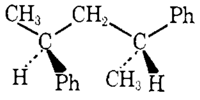
(11) G. A. Russell and A. G. Bemis, *J. Am. Chem. Soc.*, **88**, 5491 (1966).

(12) The methyl doublets of *meso*- and *dl*-2,4-diphenylpentane are centered respectively at δ 1.20 and 1.15.

(13) J. A. Dale and H. S. Mosher, to be published.

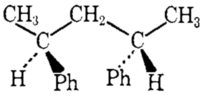
rium mixture, a result which agrees with the analysis by gas chromatography within the combined experimental errors. Gas chromatographic analysis is believed to be the more reliable method.

The only conformers of the *meso* isomer not precluded by severe steric overlaps are the *trans,gauche* (*tg*), *i.e.*



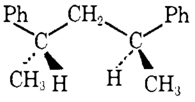
tg

and its analog (*gt*) of opposite screw sense. The eligible conformations of the racemic isomer are *tt* and *gg*, *i.e.*,



tt

and



gg

Let η denote the statistical weight for a conformation in which phenyl is *gauche* with respect to a CH group separated from it by three skeletal bonds. This statistical weight is to be assigned relative to a statistical weight of unity for a CH_3 group similarly situated with respect to CH. On this basis the combined statistical weight for the two equivalent *meso* conformers is 2η; the statistical weights for the *tt* and *gg* conformers of the racemic form are η^2 and 1, respectively. Hence, the fraction of *meso* at equilibrium[1] is $f_{meso} = 2\eta/(1 + \eta)^2$. Taking $f_{meso} = 0.48$ as a weighted mean of the experiments here reported, $\eta = 1.5$ at 25°.[14] The *tt* conformer of the racemic isomer is predicted to be favored over the *gg* by the factor $\eta^2 = 2.25$. At the same temperature the ratio of these two conformers deduced from nmr spectra interpreted in terms of coupling constants is *ca.* 3.0 according to Bovey[8] and Doskočilová[15] and their co-workers, in satisfactory agreement with our deductions.

At least one additional parameter is required for the interpretation of the stereochemical equilibrium and the distribution among conformers for any higher homolog.[1] Analysis of the epimerization equilibrium for the next homolog, namely, 2,4,6-triphenylheptane, should yield this parameter and also test the validity of the scheme presented elsewhere.[1] Experiments directed to this end are in progress, along with investigation of the epimerization of polystyrene. These results and their implications concerning the conformations of vinyl chain molecules will be subjects of future publications.

Acknowledgment. This work was supported by the Directorate of Chemical Sciences, Air Force Office of Scientific Research Contract No. AF49(638)1341.

[14] The other root, $\eta = 0.667$, of the quadratic equation for f_{meso} has been dismissed on the grounds that it is irreconcilable with the preference for the *tt* conformer of the racemic isomer.

[15] D. Doskočilová, S. Sýkora, H. Pivcová, B. Obereigner, and D. Lím, *J. Polymer Sci.*, in press.

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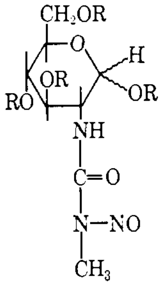
The Structure of Streptozotocin

Sir:

Streptozotocin,[1-4] an antibiotic produced by *Streptomyces achromogenes*, is a broad spectrum antibacterial agent and also has antitumor activity in both *in vitro* and *in vivo* systems. We wish to present evidence supporting the assignment of structure I to streptozotocin.



I, R = H
II, R = $COCH_3$

Streptozotocin has the molecular formula[5,6] $C_8H_{15}N_3O_7$ and decomposes with evolution of gas at *ca.* 115°. The molecular weight determined by isothermal distillation in water is 269 (calcd, 265). Potentiometric titration showed the absence of any titratable groups. The nmr spectrum[7] of streptozotocin could not be completely interpreted; however, it showed the presence of an $N-CH_3$ group (singlet, 3 H, at δ 3.15) and the absence of any $C-CH_3$ groups.

Acetylation of streptozotocin with acetic anhydride and pyridine afforded crystalline tetraacetate II, $C_8H_{11}N_3O_7$ $(COCH_3)_4$, $[\alpha]^{25}D$ +41° (*c* 0.78, 95% ethanol), mp 111–114° dec. The nmr spectrum of II showed the presence of four O-acetyl groups (12 H, δ 1.97–2.08) and the $N-CH_3$ group which is also present in streptozotocin.

Treatment of the antibiotic with alkali (2 *N* aqueous NaOH) at 0° resulted in the evolution of diazomethane,[8] and carbon chromatography of the neutralized reaction mixture resulted in the isolation of III as an amorphous colorless solid, $C_7H_{11}NO_6$, $[\alpha]^{25}D$ −40° (*c* 1, water). III exhibited infrared absorption at 1725 cm^{-1} and yielded carbon dioxide and D-glucosamine hydrochloride, $C_6H_{13}NO_5 \cdot HCl$, by treatment with 2 *N* aqueous HCl. Treatment of the alkali degradation reaction mixture with acetic anhydride and pyridine afforded IV, a crystalline colorless solid, $C_7H_7NO_6$ $(COCH_3)_4$, mp 178–180° (uncor), $[\alpha]^{25}D$ −46° (*c* 0.7, 95% ethanol). Acid hydrolysis of IV (2 *N* HCl, reflux) again yielded D-glucosamine hydrochloride and carbon dioxide. The infrared spectrum (carbonyl absorption at 1790 and 1745 cm^{-1}) and the nmr spectrum (3 H, singlet, at δ

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[1] J. J. Vavra, C. DeBoer, A. Dietz, L. J. Hanka, and W. T. Sokolski, *Antibiot. Ann.*, **1959–1960**, 230 (1960).

[2] W. T. Sokolski, J. J. Vavra, and L. J. Hanka, *ibid.*, **1959–1960,** 241 (1960).

[3] C. Lewis and A. R. Barbiers, *ibid.*, **1959–1960**, 247 (1960).

[4] R. R. Herr, T. E. Eble, M. E. Bergy, and H. K. Jahnke, *ibid.*, **1959–1960**, 236 (1960).

[5] Analytical values for all the compounds described in this paper are consistent with the indicated formulas.

[6] The molecular formula was previously reported as $C_{14}H_{27}N_5O_{12}$,[4] based on early molecular weight determinations.

[7] Nmr spectra were observed in dimethylformamide-d_7 on a Varian A-60 spectrometer using internal tetramethylsilane as a reference.

[8] Diazomethane was collected in ether and this solution was mixed with an ether solution of *p*-nitrobenzoic acid. Crystalline methyl *p*-nitrobenzoate isolated was identical with an authentic sample.