gases, and the liquid product was allowed to stand over sodium fluoride. It was distilled to give 430 g. (92%) of 4-(trichloromethyl)-phenyltrifluorosilane, b.p. 95–105° (20 mm.).

Anal. Calcd. for $C_7H_4Cl_3F_3Si$: Cl, 38.1; F, 20.4; Si, 10.04. Found: Cl, 37.2, 37.4; F, 21.8, 21.9; Si, 9.89, 10.05.

4-(Trifluoromethyl)-phenyltrifluorosilane.—A mixture of 99 g. of 4-(trichloromethyl)-phenyltrichlorosilane and 10 ml. of antimony(V) chloride was stirred while 127 g. of antimony(III) fluoride was added slowly. An exothermic reaction occurred, with the formation of a black, semi-solid mass. Heat was then applied, and a colorless distillate was collected. Redistillation gave 44 g. (63%) of 4-(trifluoromethyl)-phenyltrifluorosilane, b.p. 117–119°.

This method was inconvenient on a larger scale because of difficulty in stirring. The following preparation also gave better over-all yields.

A mixture of 215 g. of powdered antimony(III) fluoride and 25 g. of antimony(V) chloride was stirred while 280 g. of 4-(trichloromethyl)-phenyltrifluorosilane was added. The mixture was light colored, and little heat was evolved. Heat was applied, and 212 g. (92%) of colorless 4-(trifluoromethyl)-phenyltrifluorosilane, b.p. 110–120°, was distilled.

Anal. Calcd. for $C_7H_4F_6Si$: F (by hydrolysis), 24.8. Found: F (by hydrolysis), 24.5, 25.1.

4-(Trifluoromethyl)-phenyltrimethylsilane.—A Grignard reagent was prepared by bubbling bromomethane into a well-stirred mixture of 12.5 g. of magnesium turnings and 200 ml. of anhydrous ethyl ether until the magnesium had dissolved. A solution of 32 g. of 4-(trifluoromethyl)-phenyltrifluorosilane in 50 ml. of ethyl ether was then added slowly, with stirring. An exothermic reaction occurred, with refluxing. Heat was then applied, and refluxing was continued for one hour. The mixture was poured over a mixture of crushed ice and hydrochloric acid. The organic layer was then separated, washed with water, dried over calcium chloride, and distilled to give 27 g. (89%) of 4-(trifluoromethyl)-phenyltrimethylsilane, b.p. 113–114° (100 mm.).

Anal. Calcd. for $C_{10}H_{13}F_3Si$: F, 26.1; Si, 12.85. Found: F, 26.8, 26.8; Si, 12.88, 12.73.

3-(Trifluoromethyl)-phenyltrimethylsilane.—A reaction was carried out, using 48.6 g. of magnesium turnings, 450 g. of 3-bromo-(trifluoromethyl)-benzene and 217 g. of chlorotrimethylsilane in one liter of anhydrous ether. The Grignard reaction was first started, using the magnesium and a portion of the bromo compound and ether. When it had started, the rest of the ingredients were mixed and added, with stirring, at a rate to maintain a moderate reflux rate. When the addition was complete, heat was applied and refluxing continued for 24 hours. During this time the coupling reaction proceeded slowly as shown by the formation of a sticky precipitate and the fading of the dark brown color the Grignard reagent. The reaction mixture was then poured over a mixture of crushed ice and hydrochloric acid. The organic layer was separated, washed with water, dried over calcium chloride and distilled to give 302 g. (69%) of 3-(trifluoromethyl)-phenyltrimethylsilane, b.p. 75–80° (25 mm.).

Anal. Calcd. for $C_{10}H_{13}F_3Si$: F, 26.1; Si, 12.85. Found: F, 26.6, 26.9; Si, 12.76, 12.95.

3-(Trifluoromethyl)-benzyltrimethylsilane.—A reaction was carried out with 195 g. of 3-(trifluoromethyl)-benzyl chloride, 130 g. of chlorotrimethylsilane and 36 g. of magnesium turnings in 500 ml. of anhydrous ether. After the Grignard reaction was started with the magnesium and part of the benzyl chloride, the remaining ingredients were mixed and added with stirring at such a rate that reflux was maintained. Stirring was continued for one hour after the addition was complete. The mixture was filtered and the filtrate was washed with water, dried over sodium sulfate, and distilled to give 151 g. (65%) of 3-(trifluoromethyl)-benzyltrimethylsilane, b.p. 90–95° (25 mm.).

Anal. Calcd. for $C_{11}H_{15}F_3Si$: F, 24.5; Si, 12.08. Found: F, 24.9, 25.0; Si, 12.04, 12.07.

4-Chloro-3-(trifluoromethyl)-phenyltrimethylsilane.—A reaction was carried out with 1038 g. of 4-bromo-2-(trifluoromethyl)-chlorobenzene, 98 g. of magnesium turnings and 490 g. of chlorotrimethylsilane in two liters of anhydrous ether, following the procedure of the preceding run except that the mixture was refluxed for 20 hours after the addition was complete. Distillation of the product gave 774 g. of 4-chloro-3-(trifluoromethyl)-phenyltrimethylsilane, b.p. 65–75° (5 mm.).

Anal. Calcd. for $C_{10}H_{12}ClF_3Si$: Cl, 14.05; F, 22.6; Si, 11.12. Found: Cl, 14.17, 14.18; F, 22.3, 22.8; Si, 10.89, 11.05.

Bis-[4-chloro-3-(trifluoromethyl)-phenyl]-dimethylsilane.—A reaction was carried out with 1038 g. of 4-bromo-2-(trifluoromethyl)-chlorobenzene, 258 g. of dichlorodimethylsilane and 100 g. of magnesium turnings in three liters of anhydrous ether, following the procedure of the preceding run except that the period of reflux was 12 hours. The dried product was distilled to give 590 g. (71%) of bis-[4-chloro-3-(trifluoromethyl)-phenyl]-dimethylsilane, b.p. 140–150° (1 mm.). This product later crystallized. A portion of it was recrystallized three times from methanol to give transparent rods, m.p. 45.8–46.2°.

Anal. Calcd. for $C_{16}H_{12}Cl_2F_6Si$: Cl, 17.00; F, 27.3; Si, 6.73. Found: Cl, 16.59, 16.65; F, 27.9, 28.1; Si, 6.99, 7.01.

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COMMUNICATIONS TO THE EDITOR

POLYPEPTIDES. IX. THE KINETICS OF STRONG-BASE INITIATED POLYMERIZATIONS OF AMINO ACID-N-CARBOXYANHYDRIDES

Sir:

It has been shown previously[1,2] that NaOH or $NaOCH_3$ initiation of γ-benzyl-L-glutamate-N-carboxyanhydride (BLGA) makes possible the preparation of very high molecular weight poly-γ-benzyl-L-glutamate (PBLG). In this communication, we report the results of kinetic measurements on this new polymerization method which indicate that base initiated polymerizations (a) proceed by a mechanism which does not require a proton in the initiator, (b) exhibit propagation constants many times those of primary amine initiated

(1) E. R. Blout, R. H. Karlson, P. Doty and B. Hargitay, THIS JOURNAL, **76**, 4492 (1954).

(2) E. R. Blout and R. H. Karlson, *ibid.*, **78**, 941 (1956).

reactions,[3,4,5] and (c) show strong molecular weight and rate dependence on the optical isomer composition of the anhydride.

The reaction rates were determined at 4% anhydride concentration in dioxane solution at 31 ± 1° by measuring the disappearance of the 1860 and 1790 cm.$^{-1}$ anhydride carbonyl frequencies during the polymerization.[5] Four BLGA rate curves were obtained for anhydride:initiator (A/I) mole ratios of 40, 100, 400 and 1000. At each A/I the initial portion of the reaction is autocatalytic but, after the reaction is about one-third completed, it becomes first order in anhydride concentration. The times for 90% completion of the reactions for the above A/I's are 30, 53, 108 and 180 minutes, respectively. Similar data have been obtained with other amino acid anhydrides and other solvents. The propagation rate constants, k_p, were calculated from the first order portion of the curves using the equation

$$k_p = \frac{\ln \frac{OD_2}{OD_1} \times DP_w}{(t_2 - t_1)A_0}$$

where OD = optical density of the anhydride carbonyl band, t = time in seconds, A_0 = initial anhydride concentration, and DP_w = weight average degree of polymerization of the final polymer. It is necessary to employ the degree of polymerization since only a fraction of the anions start growing chains. This is shown by the fact that, in the range of A/I's between 50 and 1000, the DP_w is always much higher than the A/I.[2] Inasmuch as the polydispersity of PBLG prepared in this manner has been shown to be less than 2,[6] the use of A_0/DP_w is a reasonable approximation of the actual growing chain concentration. The experimental results indicate that, over a twenty-five fold range of A/I, k_p = 6.2 ± 0.6 liter/mole/sec. This rate constant is about 100 times that found for amine initiation.

Since it is known that sodium methoxide reacts rapidly and quantitatively with N-carboxyanhydrides to yield two products,[7,2] and since the strong base initiated polymerization is not first order during the early part of the reaction, sodium methoxide cannot be the true initiator. The autocatalytic nature of the kinetic curve suggests that one or both of the primary reaction products are subsequently and more slowly converted to the true initiating species. Support for this suggestion is obtained from the longer autocatalytic periods observed as the sodium methoxide concentration is decreased, *i.e.*, at higher A/I's. The effect of initiating with each of the two primary products of the reaction of sodium methoxide and anhydride is being investigated.

Polymerizations of BLGA have been performed using sodium triphenylmethyl in ether as the primary initiator. The reaction rate data were essentially the same as for sodium methoxide (in methanol) initiated reactions indicating that a labile proton on the initiator or the solvent is not required. Initiation by strong bases is evidently quite different from salt-initiated polymerizations described by Ballard and Bamford.[8] With base initiation the rate increases during the course of the reaction whereas in salt-initiated polymerizations the observed rate is slower and decreases further during the reaction.

When γ-benzyl-N-carboxy-D,L-glutamate anhydride is polymerized with $NaOCH_3$ initiation the reaction rate constant is 0.36—approximately $^1/_{20}$ that observed with both the pure D and L isomers. Reaction rate and molecular weight data for various mixtures of D and L anhydrides are shown in the table.

POLYMERIZATIONS OF γ-BENZYLGLUTAMATE-N-CARBOXYANHYDRIDES AT A/I = 100 IN DIOXANE

% D isomer	0	5	25	50	90	95	100
k_p	6.1	2.1	0.37	0.36	0.97	2.0	6.0
DP_w	900	580	275	200	515	525	800

It is apparent that the presence of the opposite optical isomer has an effect *far beyond* that which would be predicted on a simple *infinite preference* of a growing chain of one isomer for its own isomer, since this should only diminish the rate by $^1/_2$. Interesting possibilities that would explain the experimental rate and molecular weight results with mixtures of optical isomers are (a) the anhydride complexes strongly with its opposite isomer or with growing chains of the opposite configuration, and (b) the polypeptide helices which are formed have a preferred screw direction for each optical isomer and the rate of incorporation of the opposite isomer is lower due to steric interferences.[9]

(3) D. G. H. Ballard and C. H. Bamford, *Proc. Roy. Soc.* (*London*) **A233**, 495 (1954).

(4) P. M. Doty and R. L. Lundberg, to be published.

(5) M. Idelson and E. R. Blout, to be published.

(6) J. T. Yang and P. Doty, personal communication.

(7) A. Berger, M. Sela, and E. Katchalski, *Anal. Chem.*, **25**, 1554 (1953).

(8) D. G. H. Ballard and C. H. Bamford, Symposium of Peptide Chemistry Special Publication No. 2, The Chemical Society, London, p. 25 (1955).

(9) This work was supported by the Office of the Surgeon General, Department of the Army.

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RECEIVED JUNE 14, 1956

THE AMINO ACID SEQUENCE OF GLUCAGON

Sir:

A previous report[1] from this laboratory[2] described the isolation in crystalline form and the preliminary structure study of glucagon, the hyperglycemic-glycogenolytic hormone of the pancreas. We now wish to report the complete amino acid sequence of glucagon.[3]

Quantitative amino acid chromatography[4] and chemical analyses of tryptophan[5] and amide am-

(1) A. Staub, L. Sinn and O. K. Behrens, *J. Biol. Chem.*, **214**, 619 (1955).

(2) Biochemical Research Department, Lilly Research Laboratories, Indianapolis.

(3) We gratefully acknowledge the assistance of our associates, C. W. Pettinga, H. L. Bird, E. R. Diller, W. A. Tandy and R. Scheib.

(4) S. Moore and W. H. Stein, *J. Biol. Chem.*, **192**, 663 (1951).

(5) J. R. Spies and D. C. Chambers, *Anal. Chem.*, **20**, 30 (1948).