bonds. The possibility that linkages other than disulfide bonds are involved has not been excluded.

THE ROCKEFELLER INSTITUTE
NEW YORK, N. Y. GERALD M. EDELMAN

RECEIVED APRIL 24, 1959

THE HOMOPOLYMERIZATION OF MONOISOCYANATES

Sir:

Beyond the formation of cyclic dimers[1] and trimers[2] from monoisocyanates (Reactions I and II in Fig. 1) and the suggestion that cyamelide[3] is a linear polyisocyanic acid, there has been no evidence to indicate the possibility of obtaining addition polymers from monofunctional compounds containing >C=N– groups. I have recently found that monoisocyanates can be polymerized to linear high molecular weight polymers in a manner similar to vinyl compounds in accordance with the Reaction III in Fig. 1. These polymers may be regarded as N-substituted "1-nylons."

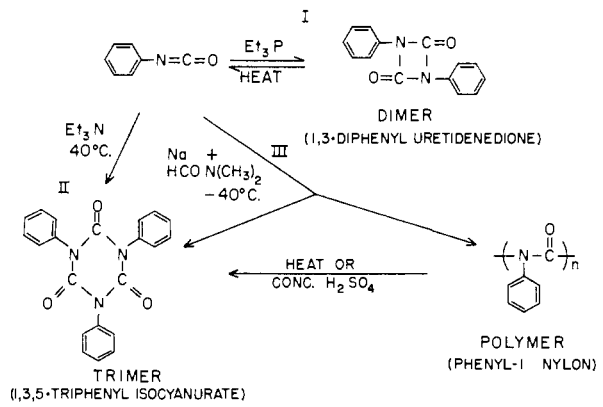


Fig. 1.—Reactions of phenyl isocyanate.

The polymerization takes place at low temperatures (−20° to −100°) in polar solvents, such as N,N-dimethylformamide, N,N-dimethylacetamide and triethylamine, through the use of anionic initiators. Ethyl isocyanate and phenyl isocyanate, examples of an aliphatic and aromatic isocyanate, were polymerized in the manner to be described.

Ethyl isocyanate, 25 ml., and dry triethylamine, 25 ml., both previously cooled to −40°, were stirred together rapidly under dry nitrogen, and further cooled to −100° with liquid nitrogen. Next 10 ml. of a sodium catalyst solution in N,N-dimethylformamide[4] was added to the rapidly stirring solution during about 30 seconds. A white, fibrous solid precipitated immediately upon contact of the catalyst with the monomer solution. The solid was filtered off, washed with methanol and dried to give 8.5 g. (39%) of ethyl 1-Nylon polymer (m.p. 250° with decomposition; found: C, 50.76; H, 6.88; N, 19.34). From the filtrate the cyclic trimer, 1,3,5-triethyl isocyanurate, was isolated and identified by its solubility and melting (m.p. 94°) characteristics.

Ethyl 1-Nylon was soluble in trifluoroacetic acid (TFA) and concentrated sulfuric acid. Clear films were obtained when TFA solutions were air dried and extracted with methanol at room temperature. Prolonged standing of the polymer in TFA resulted in degradation: a change in the inherent viscosity at 0.5% concentration from 0.3 to 0.04 occurred in two days. Light scattering studies on the aged solution gave a molecular weight value of 1600–3000 (*i.e.*, a D.P. of 23 to 42).[5] The polymer was further characterized by its distinct infrared spectrum where the only significant bands were those corresponding to carbonyl at 5.85μ, N,N-disubstituted amide at 7.4μ and a conspicuous absence of isocyanate and NH bands.[5]

With phenyl isocyanate, a polymer (m.p. 197° with decomposition) was obtained in 86% yield in N,N-dimethylformamide using the sodium catalyst[4a] at −40°. The polymer was soluble in concentrated sulfuric acid, but insoluble in TFA and chlorinated hydrocarbons. Its infrared spectrum was consistent with a phenyl 1-Nylon structure and quite distinct from either the dimer or trimer of phenyl isocyanate.

(1) A. W. Hofmann, *Ber.*, **3**, 765 (1870).

(2) D. H. Chadwick and T. C. Allen, U. S. Patent 2,733,254 (1956).

(3) W. Kern, H. Paul and W. Mehren, *Makromol. Chem.*, **14**, 146 (1954).

(4) (a) The catalyst solution was prepared by adding 10 drops of a 50% sodium dispersion in xylene (du Pont Electrochemicals Department) to 50 ml. of dry N,N-dimethylformamide. The mixture was stirred for 1 hour before use. (b) The use of this combination as a catalyst for the anionic polymerization for vinyl compounds was demonstrated by L. Grandine, E. I. du Pont de Nemours & Company (private communication).

(5) The author wishes to thank Drs. D. Akeley and R. Zbinden for the light scattering data and infrared analysis, respectively.

PIONEERING RESEARCH LABORATORY
TEXTILE FIBERS DEPARTMENT VICTOR E. SHASHOUA
E. I. DU PONT DE NEMOURS & CO., INC.
WILMINGTON, DELAWARE

RECEIVED APRIL 28, 1959

STEROIDS. CXXII.[1] 6α-FLUORO-16α-METHYLCORTICOIDS—SYNTHESIS AND BIOLOGICAL ACTIVITY

Sir:

Among the most recent chemical modifications of the hydrocortisone and prednisolone molecule—resulting in increased anti-inflammatory activity and diminution of salt retention—have been introduction of a 6α-fluorine atom[1,2,3] *or* addition of a methyl group in the 16α-position.[4,5] We now wish to report the synthesis and preliminary biological evaluation of analogs of the most important cortical hormones combining *both* of these structural features.

The preparation in this Laboratory of 6α-fluoro-16α-methylhydrocortisone acetate (I) *via* 6α-fluoro-16α-methyl "Substance S" already has been recorded.[6] Dehydration of I with mesyl chloride in

(1) Paper CXXI, A. Bowers, E. Denot, M. B. Sánchez and H. J. Ringold, *Tetrahedron*, in press.

(2) A. Bowers and H. J. Ringold, THIS JOURNAL, **80**, 4423 (1958).

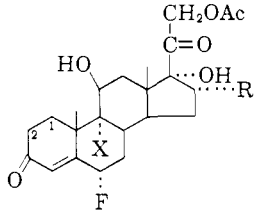
(3) J. A. Hogg, G. B. Spero, J. L. Thompson, B. J. Magerlein, W. P. Schneider, D. H. Peterson, O. K. Sebek, H. C. Murray, J. C. Babcock, R. L. Pederson and J. A. Campbell, *Chemistry and Industry*, 1002 (1958).

(4) G. E. Arth, J. Fried, D. B. R. Johnston, D. R. Hoff, L. H. Sarett, R. H. Silber, H. C. Stoerk and C. A. Winter, THIS JOURNAL, **80**, 3161 (1958).

(5) E. P. Oliveto, R. Rausser, L. Weber, A. L. Nussbaum, W. Gebert, C. T. Coniglio, E. B. Hershberg, S. Tolksdorf, M. Eisler, P. L. Perlman and M. M. Pechet, *ibid.*, **80**, 4431 (1958).

(6) J. A. Edwards, A. Zaffaroni, H. J. Ringold and C. Djerassi, *Proc. Chem. Soc.*, 87 (1959). All intermediates in that synthesis were

pyridine–dimethylformamide provided 6α-fluoro-16α-methyl-$\Delta^{4,9(11)}$-pregnadiene-3,20-dione-17α,21-diol 21-acetate (m.p. 188–190°, $[\alpha]D$ +74° (all rotations in $CHCl_3$), λ_{max}^{EtOH} 235, log ε 4.17; *Anal.* found for $C_{24}H_{31}O_5F$: C, 69.28, H, 7.24, F, 3.99), which was treated with N-bromoacetamide in aqueous dioxane in the presence of perchloric acid[7] and the bromohydrin cyclized directly with potassium acetate in acetone to afford 6α-fluoro-16α-methyl-9β,11β-oxido-Δ^4-pregnene-3,20-dione-17,21-diol 21-acetate (m.p. 188–191°). Opening of the epoxide with hydrogen fluoride in methylene chloride–tetrahydrofuran[8] led to 6α,9α-difluoro-16α-methylhydrocortisone acetate (II) (m.p. 255–260°, $[\alpha]D$ +113°, λ_{max}^{EtOH} 234 mμ, log ε 4.22; *Anal.* found for $C_{24}H_{32}O_6F_2$: C, 63.15; H, 6.96; F, 8.01), while oxidation of II with selenium dioxide[9] provided 6α,-



I, X = H, R = CH_3
II, X = F, R = CH_3
III, X = F, R = CH_3 with 1-2-double bond
IV, X = F, R = H
V, X = F, R = H with 1-2 double bond

9α-difluoro-16α-methylprednisolone acetate (III) (m.p. 260–264°, $[\alpha]D$ +91°, λ_{max}^{EtOH} 237 mμ, log ε 4.16; *Anal.* found for $C_{24}H_{30}O_6F_2 \cdot CH_3COCH_3$: C, 63.90, H, 7.40). This latter substance combines in one molecule four substituents (Δ^1-double bond,[10] 6α-fluorine,[1,2,3] 9α-fluorine,[7] 16α-methyl group[4,5]) known to increase individually anti-inflammatory activity.

TABLE I

Compound	Anti-inflammatory[a] activity
6α-Fluoro-16α-methylhydrocortisone acetate (I)	5[b]
6α,9α-Difluoro-16α-methylhydrocortisone acetate (II)	50[c]
6α,9α-Difluoro-16α-methylprednisolone acetate (III)	120[c]
6α,9α-Difluorohydrocortisone acetate (IV)	100[b]
6α,9α-Difluoroprednisolone acetate (V)	200[b]

[a] Assays in immature adrenalectomized rats, cotton pellet implant, hydrocortisone acetate = 1. [b] Assays by Dr. R. I. Dorfman, The Worcester Foundation for Experimental Biology; oral route. [c] Assays by the Endocrine Laboratories, Madison, Wisconsin; subcutaneous route.

Preliminary biological data covering these three substances (I, II, III) as well as 6α,9α-difluorohydrocortisone acetate (IV)[1,3] and 6α,9α-difluoroprednisolone acetate (V)[1,3] are summarized in the accompanying table. Pronounced sodium excretion was exhibited by I, II and III in the rat.[11]

fully characterized and analyzed, but the data were not included for reasons of editorial policy.

(7) J. Fried and E. F. Sabo, THIS JOURNAL, **79**, 1130 (1957).

(8) R. F. Hirschmann, R. Miller, J. Wood and R. F. Jones, *ibid.*, **78**, 4956 (1956).

(9) H. J. Ringold, G. Rosenkranz and F. Sondheimer, *J. Org. Chem.*, **21**, 239 (1956); C. Meystre, H. Frey, W. Voser and A. Wettstein, *Helv. Chim. Acta*, **39**, 734 (1956); S. A. Szpilfogel, T. A. P. Posthumus, M. S. De Winter and D. A. Van Dorp., *Rec. Trav. Chim.*, **75**, 475 (1956); K. Florey and A. R. Restivo, *J. Org. Chem.*, **22**, 406 (1957).

(10) H. L. Herzog, A. Nobile, S. Tolksdorf, W. Charney, F. B. Hershberg, P. L. Perman and M. M. Pechet, *Science*, **121**, 176 (1955).

(11) Salt assays in adrenalectomized rats without sodium chloride load, subcutaneous route. We are indebted to Dr. E. Rosemberg and Dr. R. I. Dorfman, Worcester Foundation for Experimental Biology, for these assays.

RESEARCH LABORATORIES
SYNTEX, S.A.
APDO. POSTAL 2679
MEXICO, D.F.
J. A. EDWARDS
H. J. RINGOLD
CARL DJERASSI

RECEIVED MARCH 20, 1959

MASS SPECTROMETRIC EVIDENCE FOR HEPTABORANE

Sir:

In mass spectrometric examination of tetraborane prepared by the method of Klein, Harrison and Solomon[1] mass number *versus* intensity patterns were found corresponding to B_6H_{10}, B_5H_9 and B_5H_{11}, B_4H_{10} and B_2H_6 with the B_4H_{10} pattern accounting for 94 to 97% of the total pressure. In addition, a new group of peaks was observed from mass numbers 77 through 89 with the principal peak at 83. In 5 of 6 samples examined there was no evidence of higher boranes up to mass number 150. In the sixth sample, a small amount of octaborane was found. The samples were obtained from three separate preparations of tetraborane.

Spectra were obtained using a Model 21–620 Consolidated Electrodynamics Corporation mass spectrometer with a modified d.c. amplifier circuit for greater sensitivity. The patterns from mass 77 through 89 for the 5 samples and the sixth with the octaborane subtracted were identical within the limits of instrument reproducibility. The height of the peak at mass 83 was over 80 recorder units read to ± 0.3 for each sample. The representative pattern obtained is shown in Fig. 1.

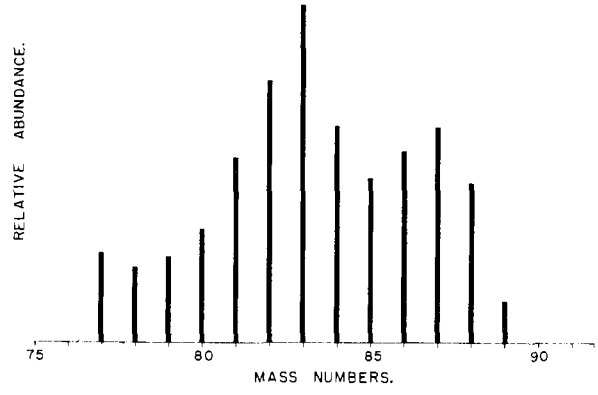


Fig. 1.

The range of mass numbers would necessitate a β_7^- compound and the sharp cutoff at mass 89 would indicate a minimum formula of B_7H_{12}. This formula does not fit either the stable B_nH_{n+4} series or the less stable B_nH_{n+6} series proposed by Wiberg.[2] The parent peak of the proposed B_7H_{13} compound from Wiberg's B_nH_{n+6} series

(1) M. J. Klein, B. C. Harrison and I. J. Solomon, THIS JOURNAL, **80**, 4149 (1958).

(2) E. Wiberg, *Ber.*, **69B**, 2816 (1936).