tion). Purification by distillation *in vacuo* furnished a 60% yield of α-diacetone-D-fructose, m.p. and mixed m.p. 119° (after recrystallization from petroleum ether).

(c) Preliminary experiments indicated that "Dowex 50" cation exchange resin could be used in the condensation of acetone with methyl α-D-galactopyranoside and with methyl α-D-mannopyranoside.

ST. PAUL, MINNESOTA RECEIVED SEPTEMBER 21, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DE PAUL UNIVERSITY]

Preparation of *l*-2-Aminomethyltetrahydropyran[1]

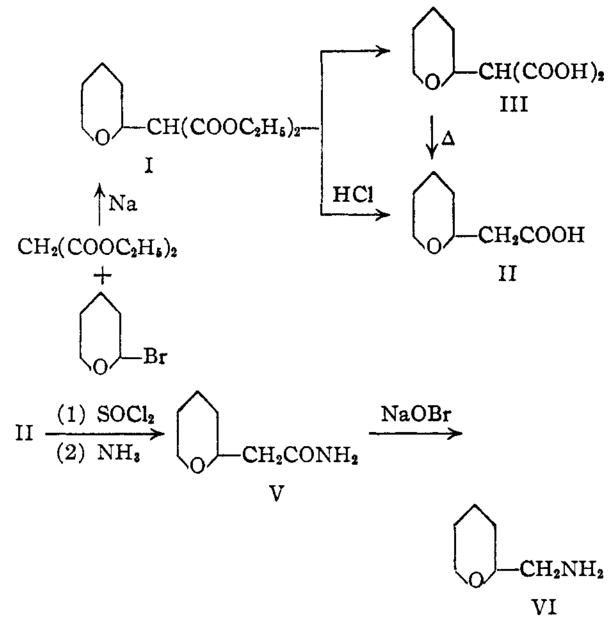
BY ROBERT P. ZELINSKI, NORMAN G. PETERSON[2] AND HOPE R. WALLNER[2]

2-Aminomethyltetrahydropyran has been prepared from 2-tetrahydropyranylacetic acid. Both have been obtained in optically active form and related stereochemically.

As part of a program to relate substituted tetrahydropyrans to carbohydrates, it was of interest to prepare and resolve some 2-substituted tetrahydropyrans. A search of the literature indicates that the only other resolution of non-carbohydrate pyran compounds has been that of 2,6-dimethyl-5,6-dihydro-2H-pyran-3-carboxylic acid.[3]

When this investigation was begun a number of analogous 4-substituted tetrahydropyrans were known. Thus 4-bromotetrahydropyran, ethyl 4-tetrahydropyranylmalonate, 4-tetrahydropyranylacetic acid and 4-aminomethyltetrahydropyran had been prepared by methods simlar to ours.[4-6] The 4-aminomethyl- compound had also been obtained by reduction of 4-cyanotetrahydropyran[5,7] and by the Gabriel synthesis with 4-bromomethyltetrahydropyran.[5] Recently the preparation of ethyl 2-tetrahydropyranylmalonate (I) by a method analogous to ours has been reported.[8] *dl*-2-Aminomethyltetrahydropyran (VI) has been prepared by the reduction of 2-tetrahydropyranylcyanide,[9] and by the hydrogenation of the cyclic, trimeric aldimine formed by the action of ammonia on 3,4-dihydro-2H-pyran-2-carboxyaldehyde.[10-12]

In the syntheses reported here, ethyl malonate has been alkylated by 2-chloro- and 2-bromotetrahydropyran[13,14] to yield ethyl *dl*-2-tetrahydropyranylmalonate (I) which was in turn hydrolyzed in acid and decarboxylated to yield *dl*-2-tetrahydropyranylacetic acid (II). Alternatively, careful saponification of I yielded *dl*-2-tetrahydropyranylmalonic acid (III) which was thermally decarboxylated to II.



The tetrahydropyranylacetic acid (II) was converted to *dl*-2-tetrahydropyranylacetamide (V) through the intermediate *dl*-2-tetrahydropyranylacetyl chloride (IV). The amide, V, was in turn converted to *dl*-2-aminomethyltetrahydropyran (VI) by means of the Hofmann reaction. Efforts to apply the Schmidt reaction or the Curtius method to the preparation of VI were unsuccessful.

The partial resolution of II was effected through the quinine salt, and *l*-2-tetrahydropyranylacetic acid (IIa) $[\alpha]^{20}\text{D}$ −5.7° (95% ethanol, *c* 15) was obtained. A product of lesser purity resulted through resolution *via* D-desoxyephedrine. Compound IIa was then converted to the amide, *d*-2-tetrahydropyranylacetamide (Va), $[\alpha]^{24}\text{D}$ +12.5° (95% ethanol, *c* 1.6). Application of the Hofmann reaction to Va yielded *d*-2-aminomethyltetrahydropyran (VIa), $\alpha^{24}\text{D}$ +6.5 (homogeneous, l = 1 dm.). The direct resolution of *dl*-2-aminomethyltetrahydropyran *via* the tartaric acid salt gave a product having a somewhat higher rotation, $\alpha^{24}\text{D}$ +8.3 (homogeneous, l = 1 dm.).

The lower rotation of the pyranylamine formed *via* the Hofmann degradation from the optically active acid, IIa, is undoubtedly the result of still incomplete resolution of the *dl*-acid, II. For the stereospecificity of the Hofmann degradation has been convincingly demonstrated in instances where

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[1] We gratefully acknowledge that this investigation was made possible by a grant-in-aid from the Research Corporation.

[2] Abstracted from theses, submitted in partial fulfillment of the requirements for the degree of Master of Science, by Norman G. Peterson, 1950, and Hope R. Wallner, 1951.

[3] M. Delepine and A. Willemart, *Compt. rend.*, **211**, 153, 313 (1940); M. Delepine and G. Amiard, *ibid.*, **215**, 309 (1942); **219**, 265 (1944).

[4] V. Prelog, D. Kohlbach, E. Cerkovnikov, A. Rezek and M. Piantanida, *Ann.*, **532**, 69 (1937).

[5] V. Prelog, E. Cerkovnikov and G. Ustricev, *ibid.*, **535**, 37 (1938).

[6] V. Prelog, S. Heimbach and A. Rezek, *ibid.*, **545**, 231 (1940).

[7] C. S. Gibson and J. D. A. Johnson, *J. Chem. Soc.*, 2525 (1930).

[8] J. G. Schudel and R. V. Rice, U. S. Patent 2,522,966 (1950); *C. A.*, **45**, 6223*i* (1951).

[9] Report PB 823, U. S. Department of Commerce, Office of Technical Services.

[10] Report PB 85174, FIAT final 1157.

[11] Report PB 73508, fr. 6957–6960.

[12] Report PB 73508, fr. 6983–6987.

[13] R. Paul, *Bull. soc. chim.*, [1] **5**, 1397 (1934).

[14] R. Paul, *Compt. rend.*, **198**, 1246 (1934).

the carboxamide group is directly attached to the asymmetric carbon.[15]

Experimental[16,17]

Ethyl *dl*-2-Tetrahydropyranylmalonate (I).—By essentially duplicating the directions of Schudel and Rice[8] there was obtained a 78% yield of I, b.p. 118–128° (2 mm.), $n^{20}\mathrm{D}$ 1.4491. Redistillation gave b.p. 120–122° (1–2 mm.), $n^{20}\mathrm{D}$ 1.4480, d^{20} 1.075 (lit.[8] b.p. 134–140° (7 mm.), $n^{20}\mathrm{D}$ 1.4463).

Anal.[18] Calcd. for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.94; H, 8.57.

All distillations were accompanied by the formation of considerable quantities of gelatinous residue. When anhydrous dioxane was used as the reaction solvent, the yield was only 48%.

***dl*-2-Tetrahydropyranylmalonic Acid** (III).—A solution of 48.8 g. of ethyl 2-tetrahydropyranylmalonate (I) and 40.0 g. of sodium hydroxide in 300 cc. of 33% ethyl alcohol was boiled for 1.5 hours. It was then titrated to the phenolphthalein end-point with 0.59 mole of 4 *N* hydrochloric acid. After concentration of the aqueous solution to a volume of about 150 cc., an additional 0.39 mole of 4 *N* acid was added and the resultant solution was extracted with ether for five hours in a liquid–liquid extractor. Evaporation of the ether left 35.2 g. of crude 2-tetrahydropyranylmalonic acid, m.p. 135–136° dec. An additional five hour extraction gave 1.6 g. more for a total yield of 36.8 g. (98%). Recrystallization from a solution of isopropyl ether and petroleum ether, b.p. 60–70°, gave a pure product, m.p. 140–141° dec.

Anal. Calcd. for $C_8H_{12}O_5$: C, 51.05; H, 6.54. Found: C, 50.92; H, 6.58.

***dl*-2-Tetrahydropyranylacetic Acid** (II). **Acid Hydrolysis.**—A mixture of 29.7 g. of I and 366 cc. of 2 *N* hydrochloric acid was boiled for two hours and then distilled to remove the mineral acid. Distillation of the residue *in vacuo* gave *dl*-2-tetrahydropyranylacetic acid (II), b.p. 110–112° (2 mm.). After two recrystallizations from petroleum ether, b.p. 90–120°, the yield was 9.0 g. (52%), m.p. 55–57°, K_a 4.1 × 10^{-5}.[19]

Anal. Calcd. for $C_7H_{12}O_3$: C, 58.31; H, 8.39; neut. equiv., 144.6. Found: C, 57.90; H, 8.51; neut. equiv., 144.1.

In larger scale operations, the yield was considerably less. When the hydrolysis was of six hours duration with 1 *N* hydrochloric acid, the yield was 48%. Boiling two hours with 4 *N* acid gave 47% yield.

Thermal Decarboxylation.—Thirty-six and eight-tenths grams of the crude *dl*-2-tetrahydropyranylmalonic acid (III) was heated in an oil-bath at 140–150° until vigorous ebullition ceased. The residue was then distilled *in vacuo* to yield 21.6 g. (77%) of liquid *dl*-2-tetrahydropyranylacetic acid (II) which spontaneously crystallized to a solid, m.p. 52–53°.

***dl*-2-Tetrahydropyranylacetyl Chloride** (IV).—A solution of 10 g. of *dl*-2-tetrahydropyranylacetic acid (II) in 25 cc. of purified thionyl chloride was heated on a steam-bath for one hour. Distillation *in vacuo* gave 8.4 g. (93%) of *dl*-2-tetrahydropyranylacetyl chloride (IV), b.p. 60–65° (3 mm.).

Anal. Calcd. for $C_7H_{11}O_2Cl$: C, 51.70; H, 6.82. Found: C, 51.57; H, 6.87.

The acid chloride (III) was also characterized as the **anilide**. A solution of 0.88 g. of III, 3 cc. of aniline and 25 cc. of dry benzene was warmed on a steam-bath for three minutes. Work up and two recrystallizations from petroleum ether gave 0.58 g. (49%) of *dl*-2-tetrahydropyranylacetanilide, m.p. 83–84°.

Anal. Calcd. for $C_{13}H_{17}O_2N$: C, 71.20; H, 7.82. Found: C, 71.23; H, 7.73.

***dl*-2-Tetrahydropyranylacetamide** (V).—A solution of 2.3 g. of IV in 60 cc. of petroleum ether, b.p. 90–120°, was cooled in an ice-bath while gaseous anhydrous ammonia was introduced. After precipitation was complete, the mixture was boiled and filtered while hot. Upon cooling, 1.7 g. (83%) of the crude amide, V, was obtained. Three recrystallizations from petroleum ether gave a pure product, m.p. 99–101°.

Anal. Calcd. for $C_7H_{13}O_2N$: C, 58.72; H, 9.15. Found: C, 58.83; H, 8.96.

Alternatively the amide was prepared by means of aqueous ammonium hydroxide. The undistilled acid chloride prepared from 10 g. of II, 47 g. of thionyl chloride and 4 cc. of pyridine was dissolved in 20 cc. of dioxane and added slowly to 150 cc. of ice-cold, 15 *N* ammonium hydroxide. This solution of the water-soluble amide was evaporated to dryness on a steam-bath, and the residue was extracted with benzene in a soxhlet extractor for ten hours. Addition of petroleum ether, b.p. 60–70°, to the hot benzene solution until precipitation started was followed by cooling. A second crop was obtained by evaporating the mother liquor to 10 cc. The total yield of V was 8.0 g. (81%), m.p. 99–100°.

***dl*-2-Aminomethyltetrahydropyran** (VI). **Hofmann Reaction.**—To the ice-cold sodium hypobromite prepared by addition of 24 g. of bromine to 23 g. of sodium hydroxide in 193 cc. of water there was rapidly added with stirring 14.0 g. of V. After three hours at 0°, the mixture was heated to 90°. Then 300 cc. of water was added and the solution was distilled into 100 cc. of 3 *N* hydrochloric acid until bumping occurred. Another 300 cc. of water was added and distillation was resumed until bumping occurred again. The acid solution of the amine was then evaporated to near dryness.

The crude amine hydrochloride (hygroscopic) was added to 8.0 g. of sodium hydroxide dissolved in 200 cc. of water. This solution was then extracted with benzene in a liquid–liquid extractor for eight hours. The benzene solution was finally dried over solid sodium hydroxide and then distilled through a short unpacked column. The 5.5 g. (48%) of colorless material collected at 167–169° was *dl*-2-aminomethyltetrahydropyran (VI), $n^{20}\mathrm{D}$ 1.4589, d^{20} 0.987.

Anal. Calcd. for $C_6H_{13}ON$: C, 62.57; H, 11.37. Found: C, 62.62; H, 11.20.

The identity of VI was substantiated by reaction of 0.53 g. with 2 cc. of benzoyl chloride and 20 cc. of 10% potassium hydroxide to give 0.44 g. (43%) of **N-benzoyl-2-aminomethyltetrahydropyran**, m.p. 116–118°, after recrystallization from 95% ethanol.

Anal. Calcd. for $C_{13}H_{17}O_2N$: C, 71.18; H, 7.81. Found: C, 71.38; H, 7.76.

In a similar fashion 0.59 g. of VI was treated with 1.0 g. of III, followed by slow addition of 10 cc. of 10% potassium hydroxide. Evaporation and extraction of the water-soluble derivative from the residue with petroleum ether gave **N-(2-tetrahydropyranylacetyl)-2-aminomethyltetrahydropyran**, m.p. 67–69° after recrystallization from petroleum ether, b.p. 38–47°.

Anal. Calcd. for $C_{13}H_{23}O_2N$: C, 64.69; H, 9.61. Found: C, 64.91; H, 9.64.

Schmidt Reaction.—The directions[5] given for the preparation of 4-aminomethyltetrahydropyran were followed, using 5.3 g. of *dl*-2-tetrahydropyranylacetic acid (II) and 2.8 g. of activated sodium azide. None of the desired amine could be obtained.

Resolution of *dl*-2-Aminomethyltetrahydropyran.—A solution of 8.0 g. of *dl*-2-aminomethyltetrahydropyran (VI) in 10 cc. of hot methanol was added to 10.5 g. of *d*-tartaric acid in 25 cc. of hot methanol and the solution was filtered while hot. After standing at +5° for two days, the crystals were washed three times with 5-cc. portions of cold methanol. The product weighed 14 g. (78%), m.p. 114–120°, $[\alpha]^{27}\mathrm{D}$ +18.6° (water, *c* 1.5). After six recrystallizations from methanol, the physical properties of the *d*-2-aminomethyltetrahydropyran *d*-tartrate were essentially constant. After ten, the yield was 3.7 g. (40%), m.p. 160–161°, $[\alpha]^{27}\mathrm{D}$ +40.3° (water, *c* 1.35).

Anal. Calcd. for $C_{10}H_{19}O_7N$: N, 5.28. Found: N, 5.01.

The free amine was obtained by dissolving the 3.7 g. of salt in 20 cc. of 10% sodium hydroxide solution and extract-

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[15] E. S. Wallis and J. F. Lane, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 270.

[16] Except for compound I, analyses were performed by Micro-Tech Laboratories, Skokie, Illinois.

[17] Part of the dihydropyran used in these experiments was kindly supplied by the Electrochemicals Department of E. I. du Pont de Nemours and Company, Inc., Wilmington 98, Delaware.

[18] Analysis by John A. Cella, De Paul University.

[19] Acid strength was determined potentiometrically as described by Newman, Taylor, Hodgson and Garrett, THIS JOURNAL, **69**, 1784 (1947). In our hands the ionization constant of benzoic acid determined by this method was 6.9 × 10^{-5} (lit. value 6.6 × 10^{-5}).

ing with benzene in a liquid–liquid extractor for six hours. After having been dried 24 hours over solid potassium hydroxide, the benzene was removed by fractional distillation through a column 30 cm. long packed with glass helices. The *d*-2-aminomethyltetrahydropyran was then distilled through a short unpacked column, redried and redistilled to give 0.8 g. (50%), b.p. 167–169°, $\alpha^{24}\text{D}$ +8.3° (homogeneous, *l* = 1 dm.).

The resolved *d*-amine was also characterized by converting 0.10 g. to 0.06 g. (45%) of **N-benzoyl-*d*-2-aminomethyltetrahydropyran**, m.p. 112–113°, $[\alpha]^{24}\text{D}$ +28.3° (chloroform, *c* 2.9).

Resolution of *dl*-2-Tetrahydropyranylacetic Acid.—To 52.6 g. of quinine in 450 cc. of hot benzene there was added 23.3 g. of II in 15 cc. of the same solvent. The hot solution was filtered, allowed to crystallize at 20°, and cooled to 5° for two days. The crystals were washed with three 10-cc. portions of cold benzene to yield 59.0 g. (79%) of mixed quinine 2-tetrahydropyranylacetates, m.p. 140–150°, $[\alpha]^{26}\text{D}$ −133.2° (ethanol, *c* 0.4). A second crop of 9.9 g., m.p. 130–135°, $[\alpha]^{26}\text{D}$ −123.7° (ethanol, *c* 0.4) was not further purified. After eight recrystallizations from benzene, the physical properties were essentially constant, m.p. 162–163°, $[\alpha]^{27}\text{D}$ −136.3° (ethanol, *c* 0.7). The yield of quinine *l*-2-tetrahydropyranylacetate was 10.1 g. (28%).

Anal. Calcd. for $C_{27}H_{36}O_5N_2$: C, 69.23; H, 7.69; N, 5.90. Found: C, 69.00; H, 7.72; N, 6.10.

The salt was hydrolyzed by dissolving 10.0 g. in 50 cc. of chloroform and shaking with 60 cc. of 2 *N* aqueous sodium hydroxide. The chloroform layer was washed with two 20-cc. portions of water. The combined aqueous phase was then extracted with chloroform in a liquid–liquid extractor for four hours. The basic solution was finally neutralized to methyl orange indicator with 1.5 *N* hydrochloric acid and extracted with fresh chloroform for six hours. Distillation of the chloroform solution gave 3.4 g. (74%) of *l*-2-tetrahydropyranylacetic acid (IIa), b.p. 120–125° (4 mm.). One recrystallization from petroleum ether, b.p. 60–90°, gave a product melting at 37–38°, $[\alpha]^{27}\text{D}$ −5.67° (ethanol, *c* 15).

D-Desoxyephedrine was somewhat less satisfactory as a resolving agent. After preparation in, and five recrystallizations from butanone, the physical properties of the salt were essentially constant. At the end of seven, the yield of D-desoxyephedrine *l*-2-tetrahydropyranylacetate was 30%, m.p. 103–104°, $[\alpha]^{25}\text{D}$ +2.00° (ethanol, *c* 6.5).

Anal. Calcd. for $C_{17}H_{27}O_3N$: C, 69.62; H, 9.21; N, 4.78. Found: C, 69.63; H, 9.28; N, 4.68.

Hydrolysis of 4.5 g. of salt gave 0.13 g. (3%) of impure IIa, m.p. 36–37°, $[\alpha]^{25}_{\text{D}}$ −4.54° (ethanol, *c* 6).

***d*-2-Aminomethyltetrahydropyran (VIa) by the Hofmann Reaction.**—By means of the procedure outlined for the conversions of the racemic mixtures, 3.0 g. of IIa was converted to 2.0 g. (74%) of *d*-2-tetrahydropyranylacetamide (Va), m.p. 84–85°, $[\alpha]^{24}\text{D}$ +12.5° (ethanol, *c* 1.6).

Anal. Calcd. for $C_7H_{13}O_2N$: C, 58.74; H, 9.09; N, 9.79. Found: C, 58.90; H, 9.30; N, 9.30.

Application of the Hofmann reaction to 2.0 g. of Va gave 1.0 g. of VIa, b.p. 167–169°, $\alpha^{24}\text{D}$ +6.40° (homogeneous, *l* = 1 dm.).

The N-benzoyl derivative was also formed, m.p. 111–113°, $[\alpha]^{25}\text{D}$ +25.4° (chloroform, *c* 1.75).

CHICAGO 14, ILLINOIS RECEIVED SEPTEMBER 13, 1951

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

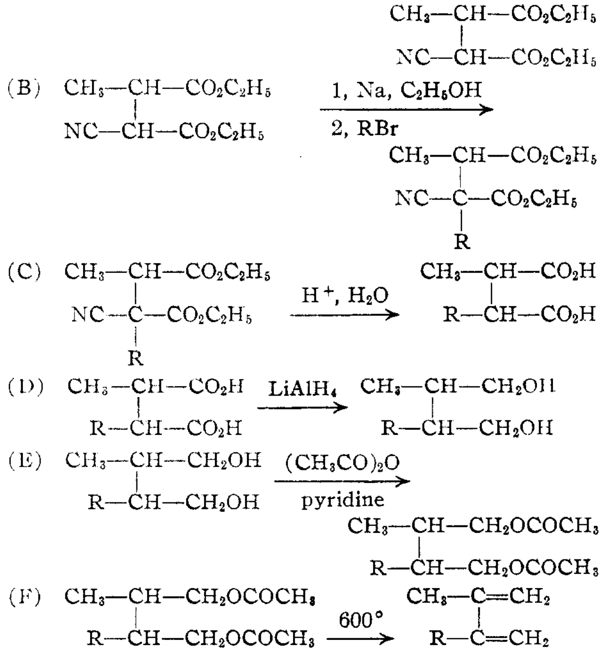
The Synthesis and Polymerization of Some 2-Methyl-3-alkyl-1,3-butadienes[1]

BY C. S. MARVEL AND J. A. FULLER

Three new 2-methyl-3-alkyl-1,3-butadienes have been prepared and polymerized in an emulsion system. Polymerization rates of the new dienes are lower than that of dimethylbutadiene. Determination of 1,4-addition in the polymers by the perbenzoic acid method indicates a value of 95% for poly-2-methyl-3-*n*-butyl-1,3-butadiene.

Two factors which may account for the superiority of natural rubber in several of its properties are the regularity of the 1,4-structure of the chain and the slight dissymmetry of the individual isoprene units. Emulsion polybutadiene is composed of approximately 80% 1,4-units[2] while emulsion poly-2-alkylbutadienes contain 85% 1,4-units.[3] Emulsion polydimethylbutadiene also has 85% of its units linked in the 1,4-manner but the greater symmetry of the units apparently results in a rise in the brittle point[4] of the material. This study was undertaken to see whether the amount of 1,4-addition could be increased by the presence of larger alkyl substituents on the monomer. The two substituents on each monomer prepared were unlike in order to avoid properties associated with symmetry.

The preparation of the monomers by the following reactions presented no special difficulties.



$$\text{(A)}\quad NCCH_2CO_2C_2H_5 \xrightarrow[2,\ CH_3CHBrCO_2C_2H_5]{1,\ Na,\ C_2H_5OH} \begin{array}{l} CH_3-CH-CO_2C_2H_5 \\ \qquad\;| \\ NC-CH-CO_2C_2H_5 \end{array}$$

$$\text{(B)}\quad \begin{array}{l} CH_3-CH-CO_2C_2H_5 \\ \qquad\;| \\ NC-CH-CO_2C_2H_5 \end{array} \xrightarrow[2,\ RBr]{1,\ Na,\ C_2H_5OH} \begin{array}{l} CH_3-CH-CO_2C_2H_5 \\ \qquad\;| \\ NC-C-CO_2C_2H_5 \\ \qquad\;| \\ \qquad\;R \end{array}$$

$$\text{(C)}\quad \begin{array}{l} CH_3-CH-CO_2C_2H_5 \\ \qquad\;| \\ NC-C-CO_2C_2H_5 \\ \qquad\;| \\ \qquad\;R \end{array} \xrightarrow{H^+,\ H_2O} \begin{array}{l} CH_3-CH-CO_2H \\ \qquad\;| \\ R-CH-CO_2H \end{array}$$

$$\text{(D)}\quad \begin{array}{l} CH_3-CH-CO_2H \\ \qquad\;| \\ R-CH-CO_2H \end{array} \xrightarrow{LiAlH_4} \begin{array}{l} CH_3-CH-CH_2OH \\ \qquad\;| \\ R-CH-CH_2OH \end{array}$$

$$\text{(E)}\quad \begin{array}{l} CH_3-CH-CH_2OH \\ \qquad\;| \\ R-CH-CH_2OH \end{array} \xrightarrow[\text{pyridine}]{(CH_3CO)_2O} \begin{array}{l} CH_3-CH-CH_2OCOCH_3 \\ \qquad\;| \\ R-CH-CH_2OCOCH_3 \end{array}$$

$$\text{(F)}\quad \begin{array}{l} CH_3-CH-CH_2OCOCH_3 \\ \qquad\;| \\ R-CH-CH_2OCOCH_3 \end{array} \xrightarrow{600^\circ} \begin{array}{l} CH_3-C=CH_2 \\ \qquad\;| \\ R-C=CH_2 \end{array}$$

Each monomer contained a methyl substituent to make possible a closer comparison with known polymers. The R groups selected for the alkylating agents were ethyl, isopropyl and *n*-butyl.

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[1] This investigation was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the U. S. Government Synthetic Rubber Program.

[2] I. M. Kolthoff, T. S. Lee and M. A. Mairs, *J. Polymer Sci.*, **2**, 220 (1947).

[3] C. S. Marvel, J. L. R. Williams and H. E. Baumgarten, *ibid.*, **4**, 583 (1949).

[4] G. Salomon and C. Koningsberger, *ibid.*, **2**, 522 (1947).