N alcoholic sodium hydroxide for 15 hours at room temperature. The material was recovered by the use of an IR-120 column and the resulting white powder was assayed using an *Escherichia coli* mutant 81–3 which requires shikimic acid and it was found to be active. The infrared spectra of *dl*-shikimic acid and natural *l*-shikimic acid taken in KBr were compared and found to be almost identical. The melting point of *dl*-shikimic acid was found to be 193–195° and *l*-shikimic 190–191°. On mixed melt of the *dl* and *l* acids the melting point was 188–190°.

Acknowledgment.—We are indebted to Dr. Max E. Rafelson, Department of Biochemistry, University of Illinois Medical School, for the biological assays and comparison of our final product with natural shikimic acid.

(7) Department of Chemistry, College of Pharmacy, University of Illinois.

DEPARTMENT OF PHARMACEUTICAL CHEMISTRY
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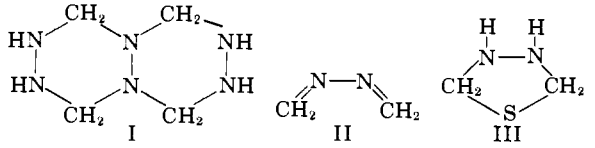
RECEIVED DECEMBER 6, 1958

MONOMERIC FORMALDAZINE—SYNTHESIS OF 1,3,4-THIADIAZOLIDINE—A NEW HETEROCYCLE

Sir:

The reaction of aqueous formaldehyde with hydrazine leads only to "tetraformaltrisazine" I[1] or a white amorphous polymer[2] instead of the expected formaldazine II.



I II III

However, by thermally decomposing[3] the polymer over a small flame in a nitrogen atmosphere (5–20 mm. pressure) and collecting the distillate in a Dry Ice trap we have isolated (50% yield), purified by low temperature distillation and characterized monomeric formaldazine II.

The redistilled product collected as large colorless or white crystals, m.p. $-48 \pm 3°$, soluble in the cold in common polar organic solvents. On warming to room temperature (either neat or in solution) the material polymerized spontaneously, first to a viscous liquid and eventually to a white solid, *anal.*[4] Found: C, 42.61; H, 7.40; N, 50.06.

From the ratio of the intensities of the isotopic 57 to the parent 56 peak in the mass spectrometer (observed 3.05), the molecular formula was determined to be $C_2H_4N_2$ (theoretical 3.04).[5]

Of the many possible structures, the infrared spectrum in the vapor phase (52 mm., 10-cm. cell) was compatible only with structure II (bands at 3.26(m), 3.41(ms), 4.93(mw), 6.04(w), 6.12(w), 7.08(w), 7.16(m), 8.47(m), 8.64(w) and 9.81(s) microns). The n.m.r. spectrum (in carbon tetrachloride) showed four peaks (two doublets) centered at about +1 parts per ten million from benzene. Using the shift charts[6] one predicts +3 p.p.t.m. for the terminal methylene hydrogens.

The only non-polymeric derivative prepared to date has been assigned the interesting 1,3,4-thiadiazolidine structure III. Mixing ether solutions of an excess of hydrogen sulfide and formaldazine at −70° gave a precipitate which was sublimed at room temperature yielding beautiful white crystals with a slight sulfide-like odor, m.p. 86–91° (dependent on rate of heating, slight decomposition), *anal.* Found: C, 26.93; H, 6.85; N, 31.09; S, 35.63; mol. wt. 90 (mass spectrometer); 117 (Menzies).[4] The infrared spectrum showed the N–H band; the n.m.r. spectrum (in deuterated chloroform) showed two types of hydrogens in the ratio of 2.25 to 1 (theory 2 to 1). The methylene hydrogen resonance was at +30 p.p.t.m. from benzene (predicted[6] +33) and the amine hydrogen resonance was a broad band centered at +37.5 p.p.t.m. The material was stable in the cold under nitrogen, but decomposed slowly at room temperature with the release of hydrogen sulfide (odor). Other reactions of formaldazine are under investigation.

The kind assistance of F. C. Stehling, D. E. Nicholson, N. F. Chamberlain and O. G. Weir of the Humble Oil and Refining Company is gratefully acknowledged.

(1) K. A. Hofmann and D. Storm, *Ber.*, **45**, 1728 (1912).

(2) G. Pulvermacher, *ibid.*, **26**, 2360 (1893).

(3) The conversion was later found to be similar in principle to the method for preparing N-alkylmethylenimines, J. L. Anderson, U. S. Patent No. 2,729,679; see *C. A.*, **50**, P12097d (1956).

(4) Schwarzkopf Microanalytical Laboratories, Woodside, N. Y.

(5) Method described by H. E. Lumpkin, Meeting of Gulf Coast Spectroscopic Group, Corpus Christi, March, 1959.

(6) See N. F. Chamberlain, *Anal. Chem.*, **31**, 56 (1959).

RESEARCH AND DEVELOPMENT DIVISION
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RECEIVED MARCH 25, 1959

IONIC POLYMERIZATION. THE EFFECT OF SOLVENTS ON THE COPOLYMER COMPOSITION IN CATIONIC CATALYZED POLYMERIZATION

Sir:

We wish to report an interesting and new observation in homogeneous cationic catalyzed polymerization. The object of this work was to study the effects of some reaction variables, particularly catalyst and solvent, on the monomer reactivity ratios in the *p*-chlorostyrene-isobutylene copolymer system catalyzed by cationic initiators. Such studies offer an effective method of obtaining the relative reactivities of monomers toward carbonium ions, and the system studied in this work is of particular value in this respect because of the differences in the reactivity and structure of the carbonium ions derived from the two monomers, and of the monomers themselves. This might be expected to lead to changes in reactivity ratios as the polarity of the solvent changes. In previous work,[1] only minor effects on monomer reactivity ratios were observed with monomer pairs of similar types (styrene, *p*-chlorostyrene) in homogeneous cases with mixed solvent system (CCl_4, $C_6H_5NO_2$). Here localized solvent effects from one of the solvents may play a role. With styrene and 3,4-

(1) C. G. Overberger, R. J. Ehrig and D. Tanner, THIS JOURNAL, **76**, 772 (1954).

dichlorostyrene[2] as the monomer pair, some variations in monomer reactivity ratios *have* been observed with different Lewis acid catalysts, although, since most of these polymerizations were heterogeneous, some of the variations may be due to surface effects.

Stannic chloride and aluminum bromide were used as catalysts for homogeneous copolymerizations carried out in *n*-hexane, nitrobenzene and nitromethane at 0°. The monomers were mixed in predetermined proportions and added to the solvent, then after cooling, the catalyst. The total concentration of monomer was 20 mole % in all cases. Polymerization times varied from 3 to 15 minutes, preliminary experiments with each system having indicated the times required for conversions to reach roughly 7%. The copolymer was precipitated by addition of methanol and purified by repeatedly dissolving in methyl ethyl ketone and precipitating by addition of methanol. The compositions of the copolymers were determined by analytical determination of their chlorine contents.

For each system studied, the monomer reactivities r_1 and r_2 (isobutylene = monomer 1; *p*-chlorostyrene = monomer 2) were calculated. The values obtained were: $r_1 = 1.01$, $r_2 = 1.02$ for copolymerization in *n*-hexane using $AlBr_3$ (0.5 mole %) as catalyst; $r_1 = 14.7$, $r_2 = 0.15$ in nitrobenzene using $AlBr_3$ (0.1 mole %); $r_1 = 22.5$, $r_2 = 0.7$ in nitromethane using $AlBr_3$ (0.5 mole %) and $r_1 = 8.6$, $r_2 = 1.2$ in nitrobenzene using $SnCl_4$ (0.3 mole %). No polymerization took place in *n*-hexane when $SnCl_4$ was used as a catalyst.

From these results it can be seen that, in the systems studied, the monomer reactivities in the non-polar solvent differ very greatly from those in the polar solvents. Although several explanations can be offered for these results, it is best to await further data. Such large variations have not been observed previously in ionic copolymerization systems in which homogeneity is retained during polymerization. Further work in this unique system is in progress.

Acknowledgment.—We gratefully acknowledge the support given by a "Grant-in-Aid" from the Shell Development Company.

(2) R. E. Florin, THIS JOURNAL, **71**, 1867 (1949); **73**, 4468 (1951).

DEPARTMENT OF CHEMISTRY C. G. OVERBERGER
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BROOKLYN, N. Y. V. G. KAMATH

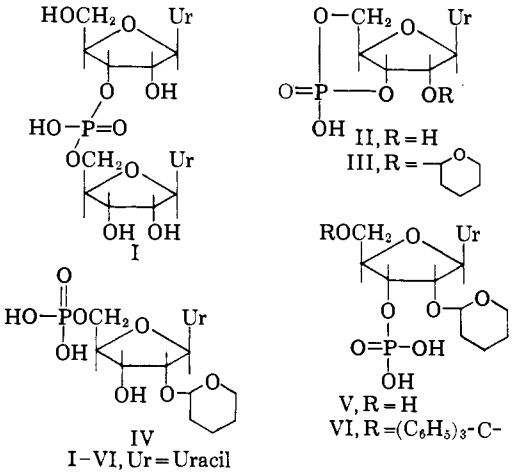
RECEIVED APRIL 14, 1959

SPECIFIC SYNTHESIS OF THE C_5'–C_3' INTER-RIBONUCLEOTIDE LINKAGE: THE SYNTHESIS OF URIDYLYL-(5′ → 3′)-URIDINE[1,2]

Sir:

The problem of the synthesis of ribo-polynucleotides containing the naturally occurring (C_5'–C_3') inter-ribonucleotide linkage is seriously complicated by the presence of the 2′-hydroxyl group in ribonucleosides. Consequently, while considerable progress recently has been made in the synthesis of deoxyribo-oligonucleotides containing C_5'–C_3' internucleotide bonds,[3] no specific synthesis of corresponding compounds in the ribonucleoside series has hitherto been reported. The present communication outlines an approach which has been used successfully in the synthesis of uridylyl-(5′→3′)-uridine (I) and offers promise for the synthesis of other ribo-oligonucleotides.

Uridine-5′ phosphate was treated with dicyclohexylcarbodiimide under high dilution conditions to yield uridine-3′,5′ cyclic phosphate (II), R_f 0.29,[4] which was isolated after chromatography as the ammonium salt in 60% yield. The cyclic phosphate (II) as the free acid was treated with dihydropyran in anhydrous dioxane to give the 2′-*O*-tetrahydropyranyl derivative (III), R_f 0.55,[4] quantitatively. Hydrolysis of III with sodium hydroxide gave a mixture of IV and V, which was treated directly in anhydrous pyridine with an excess of triphenylmethyl chloride. The resulting derivative (VI, R_f 0.68[4] isolated in 30% yield based on II) and unreacted IV, R_f 0.30[4], (10% yield from II) were separated by partition chromatography. Both IV and V, as well as VI are suitable intermediates for diester synthesis by procedures already applied in the deoxyribonucleotide field.[3a] In the present work, VI was treated with two molar equivalents of 2′,3′-di-*O*-acetyluridine[5] and dicyclohexylcarbodiimide under the standard conditions used earlier.[3a] After work-up, which included successive treatments with aqueous acetic acid to remove triphenylmethyl and tetrahydropyranyl groups, and ammonium hydroxide to remove acetyl groups, the desired uridylyl-(5′→3′)-uridine (I), R_f 0.19,[4] and uridine were found to be the only products and were readily separated. The synthetic dinucleoside phosphate was characterized in a variety of ways; it was degraded completely to uridine-3′ phosphate and uridine by a spleen diesterase preparation[6] and also by pan-



(3) (a) P. T. Gilham and H. G. Khorana, THIS JOURNAL, **80**, 6212 (1958); *ibid.*, **81**, in press; (b) G. M. Tener, H. G. Khorana, R. Markham and E. H. Pol, *ibid.*, **80**, 6223 (1958); (c) A. F. Turner and H. G. Khorana, *ibid.*, in press.

(4) Determined in isopropyl alcohol, ammonium hydroxide, water (7:1:2).

(5) G. W. Kenner, A. R. Todd, R. F. Webb and F. J. Weymouth, *J. Chem. Soc.*, 2288 (1954).

(6) L. A. Heppel and R. J. Hilmoe, "Methods in Enzymology," Vol. II, Academic Press, Inc., New York, N. Y., 1955, p. 565.

(1) For nomenclature system see ref. 3a.

(2) This work has been supported by a grant from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.