[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

The Preparation of Polymers and Copolymers from Vinylpyrimidines and Triazines[*]

BY C. G. OVERBERGER AND FRANCIS W. MICHELOTTI

RECEIVED SEPTEMBER 17, 1957

The preparation of a new monomer, 4,6-diamino-2-vinyl-*s*-triazine has been described. The homopolymerization and copolymerization of this monomer with methyl vinyl ketone, 2-N,N-dimethylamino-4-vinylpyrimidine and 4-vinylpyrimidine by radical catalysis is described. The homopolymerization and copolymerization with styrene of these latter two monomers have also been carried out. The introduction of another nitrogen into the ring when compared with α-vinylpyridine increases the positive character of the double bond and brings greater alternation in the copolymer. The resonance stabilization of the radical derived from these pyrimidine monomers is greater than that derived from α-vinylpyridines. Many of these polymers and copolymers were screened for biological activity but no outstanding activity was noted.

By use of the copolymer composition equation one can obtain useful information relating to the reactivity of double bonds toward free radicals[1a–f] in radical addition reactions. In particular, we were interested in obtaining a quantitative measure of the positive nature of double bonds in the α-positions of new pyrimidine and triazine monomers and comparing their reactivity with the known values of α-vinylpyridine. In addition, the biological, particularly the antibiotic, activity was of interest.

This paper describes the preparation of a new monomer, 4,6-diamino-2-vinyl-*s*-triazine (IV), its homopolymerization and its copolymerization with methyl vinyl ketone. In addition, copolymers of IV with two recently prepared monomers,[2] 2-N,N-dimethylamine-4-vinylpyrimidine (VI, X = N-$(CH_3)_2$) and 4-vinylpyrimidine (VI, X = H) as well as a copolymer from the two pyrimidines were prepared primarily for biological screening. Homopolymerization of these pyrimidine monomers was also reinvestigated.[2] The relative reactivities of these monomers in the copolymerization reaction was of prime interest.

Experimental

Materials.—Commercial styrene was purified by washing with 5% sodium hydroxide three to four times, washing with water until neutral, drying over anhydrous magnesium sulfate, and distillation under reduced pressure, b.p. 47–48° (20 mm.), $n^{25}\text{D}$ 1.5442 (b.p. 46° (20 mm.), $n^{25}\text{D}$ 1.5439[3]). Methyl vinyl ketone (Borden Co.) was dried over anhydrous sodium sulfate, *p*-*t*-butylcatechol was added, followed by distillation at atmospheric pressure. The fraction boiling at 81.4°, $n^{25}\text{D}$ 1.4086 (b.p. 81.4°, $n^{25}\text{D}$ 1.4086[4]) was collected.

The monomers 4-vinylpyrimidine and 2-N,N-dimethylamino-4-vinylpyrimidine were prepared essentially according to the procedure of Overberger and Kogon.[2]

Synthesis of 4,6-Diamino-2-vinyl-*s*-triazine.—To a suspension of 30 g. (0.15 mole) of biguanide sulfate in 250 ml. of water was added simultaneously 20.5 g. (0.23 mole) of freshly distilled acrylyl chloride[5] and a solution of 21.5 g. (0.54 mole) of sodium hydroxide in 100 ml. of water over a half-hour period with stirring and ice-cooling. The mixture was then stirred for 0.5 hour longer followed by filtration of the crude product, 4.95 g. (24.8%). The product was recrystallized from water and decomposed without melting, 300–310°. Addition of ammoniacal copper sulfate to the filtrate precipitated the characteristic biguanide–copper sulfate complex and the odor of acrylic acid was easily discerned. An infrared spectrum of the above compound showed double bond frequencies at 7.0, 7.75, 10.15 and 10.4 μ. The double bond stretching at 6.2 μ is masked by a broad band characteristic of guanamines.

Anal. Calcd. for $C_5H_7N_5$: C, 43.78; H, 5.14; N, 51.07. Found: C, 43.75; H, 5.09; N, 50.87.

Synthesis of 4,6-Diamino-2-ethyl-*s*-triazine from 4,6-Diamino-2-vinyl-*s*-triazine.—4,6-Diamino-2-vinyl-*s*-triazine (1 g., 0.007 mole) was suspended in 200 ml. of water followed by the addition of 1 ml. of concentrated hydrochloric acid and 0.5 g. of platinum oxide. The mixture was then reduced in a Parr apparatus until no more hydrogen was absorbed. The catalyst was removed by filtration and to the filtrate was added 0.48 g. of sodium hydroxide in 10 ml. of water slowly with stirring. A powdery material separated which was removed by filtration and dried, 0.4 g. (40%). Recrystallization was achieved from water, m.p. 308° (m.p. 293–295°[6]). Carbon–carbon double bond frequencies were absent in the infrared spectrum.

Synthesis of 4,6-Diamino-2-ethyl-*s*-triazine from Ethyl Propionate and Biguanide.—To 2 g. of biguanide (0.02 mole) dissolved in 50 ml. of absolute methanol was added 2.1 g. (0.02 mole) of ethyl propionate and the reaction mixture heated gently for one hour. The solution was cooled and the solid removed by filtration and dried, 0.7 g. (25%). Recrystallization was achieved from water, m.p. 306–308°. A mixed melting point with a sample obtained from the catalytic reduction of 4,6-diamino-2-vinyl-*s*-triazine, m.p. 308°, was not depressed, m.p. 307–308°. The infrared spectrum of this compound was identical to that obtained in the previous synthesis.

Polymerization of 4,6-Diamino-2-vinyl-*s*-triazine.—In 75 ml. of distilled water at 90° under a nitrogen atmosphere was dissolved 0.85 g. (0.006 mole) of 4,6-diamino-2-vinyl-*s*-triazine. Polymerization was then initiated by adding 0.002 g. (0.5 mole %) of potassium peroxydisulfuric acid, and heating continued for another 5 minutes. The precipitated polymer was removed by filtration, washed with absolute ethanol and dried in vacuum. A white powder, 0.75 g. (88% conversion), was obtained, insoluble in all solvents except dilute mineral acids. An intrinsic viscosity of 2.05 was obtained for this polymer dissolved in 0.1 *N* solution of hydrochloric acid and potassium chloride.

Anal. Calcd. for $(C_5H_7N_5)_x$: C, 43.78; H, 5.14; N, 51.07. Found: C, 43.84; H, 5.32; N, 50.92.

Polymerization of 4-Vinylpyrimidine.—4-Vinylpyrimidine (0.50 g., 0.005 mole) was dissolved in 5 ml. of dry toluene followed by the addition of 0.0035 g. of 2,2'-azobisisobutyronitrile (0.5 mole %). The solution was then transferred to a

---

[*] (a) This is the 14th in a series of papers on new monomers and polymers. For the previous paper in this series, see C. G. Overberger, F. W. Michelotti and P. M. Carabateas, THIS JOURNAL, **79**, 941 (1957). (b) This paper comprises a portion of a thesis submitted by F. W. Michelotti in partial fulfillment of the requirements of the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

(1) (a) F. M. Lewis, F. R. Mayo and W. F. Hulse, THIS JOURNAL, **67**, 1701 (1945); (b) T. Alfrey, E. Merz and H. Mark, *J. Polymer Sci.*, **1**, 37 (1946); (c) F. M. Lewis, C. Walling, W. Cummings, E. R. Briggs and F. R. Mayo, THIS JOURNAL, **70**, 1519 (1948); and succeeding papers, among which are F. R. Mayo, F. M. Lewis and C. Walling, *ibid.*, **70**, 1529 (1948); (d) C. Walling, E. R. Briggs, K. B. Wolfstirn and F. R. Mayo, *ibid.*, **70**, 1537 (1948); (e) T. Alfrey and C. C. Price, *J. Polymer Sci.*, **2**, 101 (1947); (f) C. C. Price, *ibid.*, **3**, 772 (1948).

(2) C. G. Overberger and I. C. Kogon, THIS JOURNAL, **76**, 1879 (1954).

(3) C. E. Schildknecht, "Vinyl and Related Polymers," John Wiley and Sons, Inc., New York, N. Y., 1952, p. 8.

(4) Reference 3, p. 686.

(5) G. H. Stempel, R. P. Gross and R. P. Mariella, THIS JOURNAL, **72**, 2299 (1950).

(6) J. K. Simons, U. S. Patent 2,684,266 (1954).

polymerization tube, degassed and sealed under vacuum. The tube was then placed in a constant temperature bath at 59.9° for 9 hours. After opening the tube, the precipitated solid was removed by filtration and washed with a few ml. of toluene and dried in vacuum. The yield of crude polymer was 0.368 g.

Purification of the polymer was achieved by dissolving it in methanol–dimethylformamide and precipitating with anhydrous ether. After two such precipitations, the polymer was dissolved in 10 ml. of distilled water, filtered through a medium sintered glass filter and subjected to freeze-drying. A fluffy white solid was obtained, 0.35 g. (70% conversion). This polar polymer held traces of water tenaciously.

Anal. Calcd. for $(C_6H_6N_2)_x$: C, 67.90; H, 5.70; N, 26.40. Found: C, 66.38; H, 6.26; N, 25.71.

If a correction for water is applied, assuming 0.084 mg. still present after drying: C, 67.90; H, 6.04; N, 26.44. An infrared spectrum of poly-4-vinylpyrimidine which had been dried in vacuum over phosphorus pentoxide at 56° for 48 hours still indicated the presence of water. An intrinsic viscosity of 1.18 was obtained for this polymer dissolved in water.

Polymerization of 2-N,N-Dimethylamino-4-vinylpyrimidine.—2-N,N-dimethylamino-4-vinylpyrimidine (0.51 g., 0.003 mole) was dissolved in 5 ml. of dry toluene, followed by the addition of 0.002 g. (0.5 mole %) of 2,2′-azobisisobutyronitrile. The solution was transferred to a polymerization tube, degassed, sealed under vacuum and placed in a bath at 59.9° for 9 hours. The tube was opened, the contents transferred to a 50-ml. beaker, and 30 ml. of anhydrous ether added dropwise with stirring. The gummy polymer which precipitated was then washed with a few ml. of fresh ether, dissolved in 15 ml. of redistilled benzene and precipitated again with anhydrous ether. After a further precipitation, the polymer was subjected to freeze-drying from benzene. An intrinsic viscosity of 1.28 was obtained for this polymer dissolved in benzene.

Anal. Calcd. for $(C_8H_{11}N_3)_x$: C, 64.39; H, 7.43; N, 28.17. Found: C, 63.67; H, 7.11; N, 27.83.

Copolymerization of Heterocyclic Monomers.—A solution of 0.494 g. (0.004 mole) of 4-vinylpyrimidine and 0.663 g. (0.004 mole, 50 mole %) of 2-N,N-dimethylamino-4-vinylpyrimidine was prepared in 5 ml. of dry toluene with subsequent addition of 0.0075 g. (0.5 mole %) of 2,2′-azobisisobutyronitrile. After transferring it to a polymerization tube, it was degassed, sealed and polymerized at 59.9° for 20 hours. As polymerization progressed no polymer precipitated from solution. The tube was opened, the viscous contents poured out, and the copolymer precipitated with anhydrous ether. After dissolving it in 8 ml. of benzene it was precipitated again with anhydrous ether. Two more precipitations were then carried out before final purification by freeze-drying from benzene, yielding 0.85 g. (74% conversion) of product. It was not possible to analyze accurately for copolymer composition since both monomers contained nitrogen.

In a similar manner, 4-vinylpyrimidine was copolymerized with 4,6-diamino-2-vinyl-*s*-triazine in dimethylformamide solution and 2-N,N-dimethylamino-4-vinylpyrimidine with 4,6-diamino-2-vinyl-*s*-triazine.

2-N,N-Dimethylamino-4-vinylpyrimidine–Styrene (System I).—Pairs of monomer mixtures dissolved in dry toluene and placed in polymerization tubes were prepared over the entire range of composition, degassed twice under a nitrogen atmosphere and sealed under vacuum. The tubes were placed in a constant temperature bath at 59.9°.

All monomer mixtures contained 0.5 mole % of 2,2′-azobisisobutyronitrile as initiator and the copolymerizations were stopped below 10% conversion (Table I) by immersing the tubes in a Dry Ice–acetone-bath. The copolymers were precipitated with anhydrous ether, then dissolved in benzene and precipitated again with ether. Since all samples precipitated as gums, the technique of freeze-drying was employed. The copolymers were analyzed quantitatively for nitrogen. The results are given in Table I.

4-Vinylpyrimidine–Styrene (System II).—The copolymerizations were conducted essentially in the same manner as described for the substituted pyrimidine (system I). The copolymers were analyzed quantitatively for nitrogen. The results are presented in Table II.

TABLE I

COPOLYMERIZATION OF PYRIMIDINES AND TRIAZINES

M_2 in monomer mixt. (mole %)	Reaction time, min.	Conversion, %	N,[a] %	m_2[b] in copolymer
Styrene (M_1)–2-N,N-dimethylamino-4-vinylpyrimidine (M_2) (system I)				
0.0087 (10)	60	0.4	8.04	0.216
.0134 (25)	60	3.0	14.43	.423
.0134 (50)	80	9.4	20.28	.642
.0168 (65)	38	6.1	23.02	.756
.0275 (75)	18	2.0	24.50	.823
.0470 (85)	12	1.3	25.96	.891
Styrene (M_1)–4–vinylpyrimidine (M_2) (system II)				
0.0094 (10)	58	3.0	8.09	0.302
.0188 (25)	32	3.2	13.00	.488
.0283 (50)	15	0.51	20.04	.755
.0471 (65)	27	5.3	20.02	.820
.0665 (75)	20	4.3	21.71	
Methyl vinyl ketone (M_1)–4,6-diamino-2-vinyl-*s*-triazine (M_2) (system III)				
0.0073 (10)	5.5	2.2	18.88	0.300
.0146 (34)	3.3	0.2	36.02	.550
.0146 (53)	3.5	4.3	42.30	.712
.0146 (75)	3.0	3.0	45.75	.813
.0218 (90)	5.3	6.6	46.06	.824

[a] Analyses by Dr. K. Ritter, Basel, Switzerland. [b] Mole fraction of pyrimidine or triazine in copolymer.

4,6-Diamino-2-vinyl-*s*-triazine–Methyl Vinyl Ketone.—Pairs of monomer mixtures dissolved in distilled water under a nitrogen atmosphere at 80° were prepared over the entire range of composition.

All monomer mixtures contained 0.5 mole % of potassium peroxydisulfuric acid initiator and the copolymerizations probably were stopped well below 10% conversion by immersing the reaction mixture in a Dry Ice–acetone-bath until room temperature was reached. In most cases it was not possible to obtain quantitatively the copolymer formed even after prolonged centrifugation because of the colloidal nature of the resultant solution. Purification of the copolymer was achieved by dissolving in 1 *N* hydrochloric acid, precipitating with 5% sodium hydroxide under a nitrogen atmosphere and finally drying in vacuum. The copolymers were analyzed quantitatively for nitrogen. The results are shown in Table II.

Results and Discussion

In a previous paper,[7] biguanide (II) was condensed with methyl acrylate in the absence of sodium methoxide catalyst in methanol in an effort to prepare 4,6-diamino-2-vinyl-*s*-triazine (I, R = CH$=CH_2$). We reported that only the 2-β-methoxyethylguanamine (I, R = $CH_2CH_2OCH_3$) was isolable with this technique. This monomer has now been prepared successfully from the reaction of biguanide sulfate with aqueous acrylyl chloride in the presence of three equivalents of sodium hydroxide in 25% yield. Catalytic hydrogenation of this material over Adams catalyst in an acidic medium yielded the corresponding ethyl derivative III in 40% yield which was unequivocally synthesized in 25% yield from ethyl propionate and biguanide in the absence of catalysts. A mixed melting point of these materials was not depressed and comparison of their infrared spectra substantiated their similarity.

Since it was desirable to study the reactivity of this new monomer toward free radicals, it was neces-

---

[7] C. G. Overberger, F. W. Michelotti and P. M. Carabateas, THIS JOURNAL, **79**, 941 (1957).

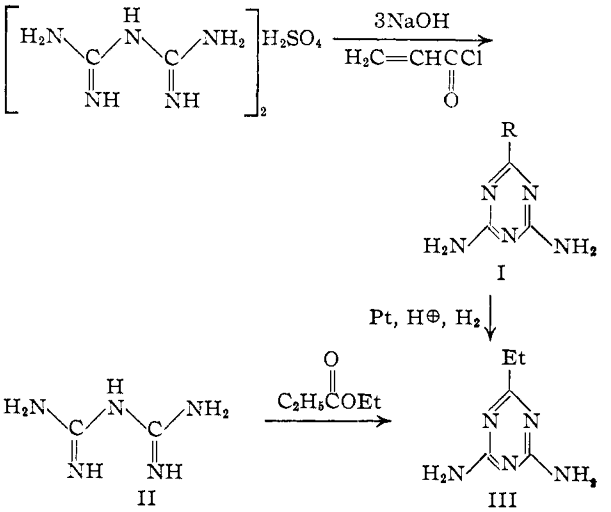
TABLE II

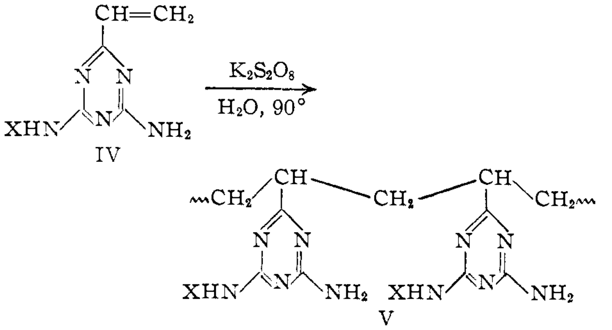
MONOMER REACTIVITY RATIOS FOR PYRIMIDINES AND TRIAZINE

M_2	M_1	r_1	r_2	r_1r_2	e'^a	Q'^a
2-Vinylpyridine	Styrene	0.55	1.14	0.62	−0.1	1.07
2-N,N-Dimethylamino-4-vinylpyrimidine	Styrene	.35 ± 0.02	1.4 ± 0.1	.49	.045	1.34
4-Vinylpyrimidine	Styrene	.17 ± .02	1.2 ± .1	.20	.46	2.15
4,6-Diamino-2-vinyl-*s*-triazine	Methyl vinyl ketone	.26 ± .04	1.2 ± .15	.31	1.78	8.2

[a] Adjusted values of *Q* and *e* after C. C. Price, *J. Polymer Sci.*, **3**, 722 (1948).

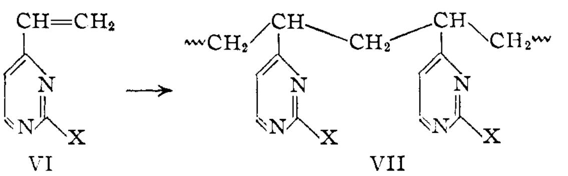
sary to characterize the homopolymer. It was found that polymerization of IV, X = H, under a nitrogen atmosphere with potassium peroxydisulfuric acid in water at 90° gave a white polymer (V, X = H) analytically pure. Because of apparent extensive hydrogen bonding along the polymer chain, V, X = H, was insoluble in all solvents except dilute mineral acids. Intrinsic viscosity measurements gave a value of 2.05 from which one may estimate a molecular weight of the order of 100,000 to 500,000. When 4-amino-6-anilino-2-vinyl-*s*-triazine[8] (IV, X = C_6H_5) was polymerized under these conditions, a polymer was obtained which was insoluble in all solvents including hot mineral acids. This insolubility indicates cross-linked polymer chains brought about perhaps by chain transfer of the growing polymer with the N-substituted hydrogen of the 6-anilino substituent.





The polymerization of 4-vinylpyrimidine (VI, X = H) and 2-N,N-dimethylamino-4-vinylpyrimidine (VI, X = $N(CH_3)_2$) required reinvestigation. Since the temperature previously employed for polymerization was too high,[2] these polymerizations were now carried out at 59.9°. The initiator concentration, 2,2′-azobisisobutyronitrile, was also reduced to 0.55 mole per cent. Under these conditions, using dry toluene as a solvent, 4-vinylpyrimidine was polymerized successfully to give a high molecular weight polymer. As polymerization progressed, the polymer (VII, X = H) precipitated from the toluene solution and surprisingly it was found to be water soluble. The intrinsic viscosity was found to be 1.18 indicating a molecular weight of the order of 10,000 to 100,000.

The polymerization of 2-N,N-dimethylamino-4-vinylpyrimidine under the same conditions gave a polymer (VII, X = $N(CH_3)_2$) which was benzene or toluene soluble and water insoluble. A measurement of its intrinsic viscosity in benzene gave a value of 1.28 also indicating an approximate molecular weight in the range of 10,000 to 100,000.



Reactivity Ratios.—Reference to Table II shows the experimental results obtained for all systems. The curve-fitting method and the method of intersection were employed to calculate the reactivity ratios in all cases.

System I. 2-N,N-Dimethylamino-4-vinylpyrimidine–Styrene.—The copolymers analyzed were stable, non-hygroscopic, white solids. The theoretical curve for $r_1 = 0.35$, $r_2 = 1.4$ gave an almost perfect fit to the experimental points (Fig. 1). The curves for $r_1 = 0.35$ and $r_2 = 1.3$ and $r_1 = 0.35$ and $r_2 = 1.5$ (not shown) were found to be the limits of the possible values and therefore are an indication of the precision of the reported values. In a curve of this type, the copolymer composition is determined mainly by r_2 over practically the whole composition range. The above values for this system indicate that both the styrene and pyrimidine radicals prefer to attack the pyrimidine monomer. Since the product r_1r_2 (0.49), is less than one, there is a tendency for alternation along the polymer chain.

By means of the Alfrey–Price equation the polarity (*e*) and the resonance stabilization (*Q*) of the double bond in copolymerization has been calculated (Table II).

System II. 4-Vinylpyrimidine–Styrene.—The copolymers analyzed were stable, though somewhat hygroscopic, white solids. At 65 and 75 mole % pyrimidine in the monomer feed, the copolymers separated from solution as polymerization progressed.

---

[8] C. G. Overberger and S. L. Shapiro, THIS JOURNAL, **76**, 1061 (1954)

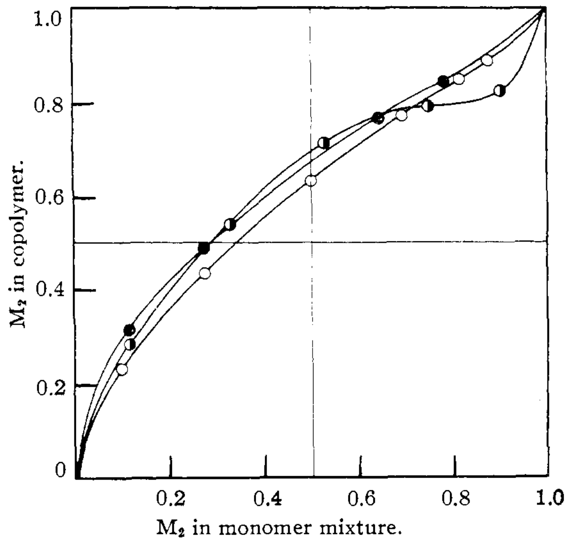


Fig. 1.—Copolymerization of nitrogen containing heterocyclic monomers: ○, 2-N,N'-dimethylamino-4-vinylpyrimidine (M_2) and styrene (M_1); ●, 4-vinylpyrimidine (M_2) and styrene (M_1); ◐, 4,6-diamino-2-vinyl-*s*-styrene (M_2) with methyl vinyl ketone (M_1).

The theoretical curve for $r_1 = 0.17$, $r_2 = 1.2$ gave an excellent fit to the experimental curve (Fig. 1). From the intersection method (Fig. 2) it can be seen that the lines intersect at almost the same point. The area of the small triangle is a measure of the errors involved in the values of r_1 and r_2. As in the case of the substituted pyrimidine, the copolymer composition is determined mainly by r_2 over practically the whole composition range, and both styrene and pyrimidine radicals prefer to attack the pyrimidine monomer. Since the product r_1r_2 (0.20) is considerably less than one, there is greater tendency for alternation along the polymer chain than in the case of the substituted pyrimidine.

The *Q* and *e* values also have been calculated from the above results (Table II).

A comparison of the reactivity ratios of both pyrimidine monomers with each other and with 2-vinylpyridine (all copolymerized with styrene), leads one to the following interesting conclusions (Table II). The introduction of another nitrogen into the ring increases the positive character of the double bond, thereby bringing about greater alternation along the copolymer chain. The resonance stabilization (*Q*) is also seen to increase. The effect of a powerful electron-releasing group (though in the *m*-position) can be seen easily in going from 4-vinylpyrimidine to 2-dimethylamino-4-vinylpyrimidine. Here we see that the tendency to alternate, the positive character of the double bond and the resonance stabilization decrease as might be expected, though one might not have predicted such a pronounced effect for a *m*-substituent.

System III. 4,6-Diamino-2-vinyl-*s*-triazine–Methyl Vinyl Ketone.—Because of the nature of the system, the shape of the experimental curve (Fig. 1) is somewhat questionable. For all points, the system was heterogeneous—as polymerization progressed the copolymers separated from solution. In addition, since it was never possible to obtain the copolymer quantitatively (a colloidal solution invariably resulted), it is possible that an unequal distribution of the various copolymer molecules took place between the colloidal suspension and precipitated product. If such is the case, the nitrogen content of the copolymers analyzed could vary considerably from the true values, and it perhaps might explain the fact that it was not possible to obtain a good fit of the theoretical curve to the experimental one. Again, under the conditions of purification of the copolymer, methyl vinyl ketone is known to undergo aldol-type condensations either intra- or intermolecularly. The latter effect (cross-linking) was detected at 90 mole % methyl vinyl ketone.

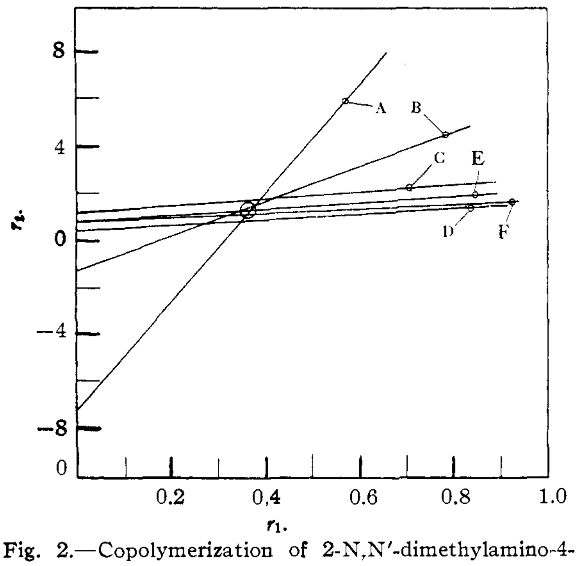


Fig. 2.—Copolymerization of 2-N,N'-dimethylamino-4-vinylpyrimidine (M_2) with styrene (M_1): A, 10 mole % M_2; B, 25 mole % M_2; C, 50 mole % M_2; D, 65 mole % M_2; E, 75 mole % M_2; F, 85 mole % M_2.

The best values for r_1 and r_2 for this system are recorded in Table II. An attempt was made to use a Fineman and Ross[9] plot, but erratic points were obtained so that no unequivocal straight line could be drawn. The errors in r_1 and r_2 were determined by the intersection method. Because of the relatively large error in r_2, it cannot be stated that the triazine monomer is more reactive with both growing free radical chains than is methyl vinyl ketone. Since the product r_1r_2 is less than one, there appears to be some tendency toward alternation along the polymer chain.

The corresponding values for *Q* and *e* are recorded in Table II. The extremely high value for *Q* is again questionable.

Pharmacological Results.—All compounds mentioned in this paper as well as those reported in reference 7 were screened by Eli Lilly Co. on a broad spectrum basis. No outstanding biological activity was noted with any of these compounds.

Acknowledgments.—We wish to gratefully acknowledge the support of this work in large part by a Grant-in-aid from Eli Lilly and Co. We thank again the American Cyanamid Co. for their generous supply of biguanide.

BROOKLYN 1, N. Y.

---

[9] M. Fineman and S. D. Ross, *J. Polymer Sci.*, **5**, 259 (1950).