stant and log median lethal concentration to the greenhouse thrips. A similar plot with ethyl *p*-nitrophenyl alkylphosphonates of log LD_{50} (house fly) against log K_e is presented in Fig. 2. It can be seen that the compounds which showed the highest enzyme inhibition rates were most toxic.

Since it is apparent that some phosphonate esters are probably equally as effective as insecticides as phosphate esters of similar structure (compare I, II and III with XVII) it was decided to prepare and study the properties of two phosphonate analogs of the well-known systemic insecticide isoSystox (O,O-diethyl 2-(ethylthio)-ethyl phosphorothiolate). The two compounds prepared were ethyl 2-(ethylthio)-ethyl *n*-propylphosphonothiolate (XVIII) and ethyl 2-(ethylthio)-ethyl methylphosphonothiolate (XIX).[27] Compound XIX was selected because its corresponding *p*-nitrophenyl ester (I) showed the highest toxicity to the house fly, and compound XVIII was selected because its corresponding *p*-nitrophenyl ester III showed relatively high insect toxicity and was more stable to alkaline hydrolysis than I or II. Both XVIII and XIX were examined for their systemic activity in young cotton plants and were found to be extremely active. This work is still in progress, but the preliminary data show that XVIII may be even better as a systemic insecticide than isoSystox. Insect toxicological studies of these compounds will be reported in detail elsewhere.

(27) During the preparation of this manuscript the synthesis of ethyl 2-(ethylthio)-ethyl ethylphosphonothiolate was reported by H. S. Aaron, T. M. Shryne and J. J. Miller, THIS JOURNAL, **80**, 456 (1958).

Acknowledgments.—The authors thank Miss Marianne Y. Winton, Miss Patricia A. Roberts and Mr. John C. Bagger for valuable technical assistance. Semi-microanalyses were carried out by Mr. C. F. Geiger, Ontario, Calif.

RIVERSIDE, CALIF.

[CONTRIBUTION FROM THE DOW CHEMICAL CO., MIDLAND DIVISION]

Synthesis of Some Amino Acid Derivatives of Styrene[1]

BY L. R. MORRIS, R. A. MOCK, C. A. MARSHALL AND J. H. HOWE

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Several vinyl-substituted amino acids have been prepared as intermediates in the synthesis of chelating polymers. Most of the syntheses started with vinylbenzyl chloride and its derivatives. These products retain the polymerizability of styrene as well as the capacity to chelate metal ions. Polymers, both soluble and crosslinked, have been prepared and show interesting properties as chelating resins.

It has often been proposed that introduction of chelating groups into resins would give more selective exchange of various ions than possible with presently available ion exchange resins. Several experimental approaches to synthesis of such chelating resins have given qualitative success, but apparently suffered from poor physical form or indefinite chemical structure of the products. Many of these explorations were made on chemically modified or condensation polymers, wherein crosslinking and homogeneity of structure are difficult to control. Some of the most promising work thus far reported is that by Hale and co-workers in the Teddington Laboratories,[2] who have modified a polystyrene starting material *via* the chloromethylated intermediate commonly used for anion exchange resin synthesis. Although the possibilities and properties of this structure were qualitatively described, the resins did not appear to give practical rates of reaction. A good general review of chelating resins literature is found in the reference by Millar.[3]

In order to avoid many problems exposed in this early work, the synthesis of the requisite monomeric structures, followed by polymerization, was an attractive course. Since exchange resins based on polystyrene have wide-spread applications, the synthesis of some styrene derivatives containing chelating groups was initiated. Also, since amino acids are well known as complexing agents for a number of metal ions, these seemed a logical choice to introduce into a resin.

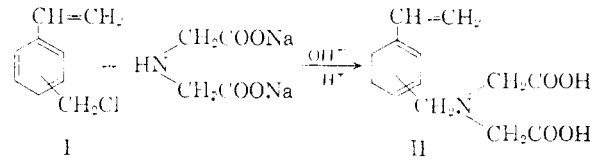
Vinylbenzyl chloride (I) was a key starting material and was supplied for this work by the Dow Laboratories. This was an attractive intermediate because of the variety of reactions which the benzyl halide structure offered. It has been shown that many reactions of benzyl chloride may be conducted with the vinylbenzyl chloride, provided conditions are not too drastic. Inhibitors against free-radical polymerization are occasionally found necessary to minimize this side reaction. It should be noted here that the starting material is a mixture of isomers, about 80% *para* and 20% *ortho*, and that derivatives therefrom will likely be of similar orientation unless the isomer ratio is altered by purification procedures. In a few cases, pure *p*-vinylbenzyl chloride has been used, but the yields and products were not distinguishable from an isomer mixture in regard to reactions and properties. This was especially true of the amino acid derivatives which did not possess discrete melting points.

Direct alkylation of several amino acids was successfully accomplished in aqueous or partly alcoholic solutions, using alkaline solutions of the amino acids. This may be illustrated by the reaction with iminodiacetic acid. Although this was in part a heterogeneous reaction, the conversion measured by ionic halide was more than 95% com-

(1) Presented in part before the Division of Polymer Chemistry at the 134th National Meeting of the American Chemical Society, Chicago, Ill., September, 1958.

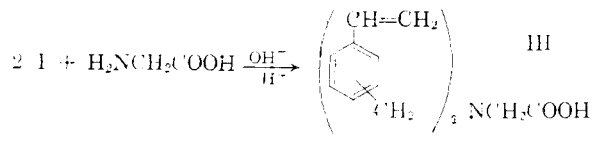
(2) D. K. Hale, *Research*, **9**, 104 (1956).

(3) J. R. Millar, *Chem. Ind.*, **20**, 606 (1957).



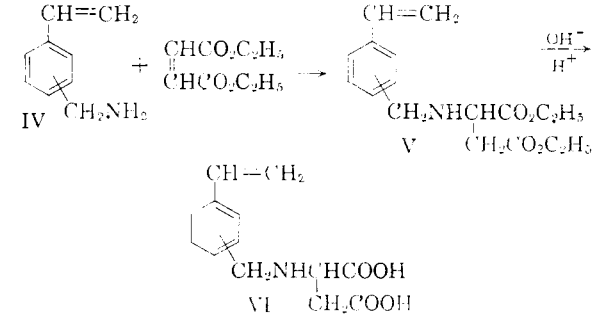
plete under the conditions employed. Isolation of the product by acidification to the isoelectric point (about *p*H 3 in this case or *p*H 5 for a monocarboxylic amino acid) gave 40–80% yields of N-(*ar*-vinylbenzylimino)-diacetic acid (II). Minor amounts of vinylbenzyl alcohol or the methyl ether in methanolic systems were obtained as side products. In a few cases polymer, as residues or gels, lowered the yields. In this manner other primary or secondary amino acids were found to be monoalkylated in yields of 20–80%. For example, isovaline, DL- and L-leucine each gave the N-vinylbenzyl derivative.

Glycine gave anomalous results when used in this reaction, since the only product isolated was the dialkylated amino acid. Yields of 40–80% of the N,N-bis-(*ar*-vinylbenzyl)-glycine (III) were isolated, even when an excess of glycine as much as five times theoretical was used and the chloride added slowly to the amino acid. One possible explanation of these results may lie in the fact that



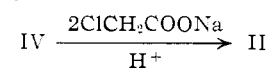
the reaction became two-phase, with the bottom layer solubilizing the benzyl halide and probably promoting the dialkylation. The second phase proved to be the sodium salt of the disubstituted glycine, sparingly soluble in the concentrated salt solution. This phase was soluble in chloroform and in excess water. This difunctional monomer was found useful as a crosslinking agent in resin formation.

A sequence of reactions shown gave a 60% over-all yield of N-(*ar*-vinylbenzyl)-aspartic acid (VI). Vinylbenzylamine (IV), available by amination of I, was added to the double bond of diethyl maleate



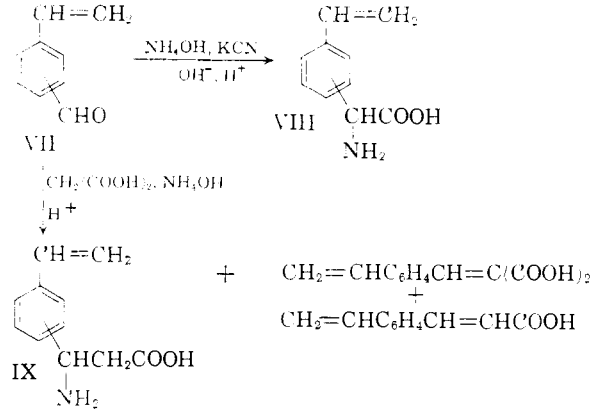
at room temperature. The resultant diethyl N-(*ar*-vinylbenzyl)-aspartate (V) then was hydrolyzed by alkali to yield VI, the substituted aspartic acid. This intermediate ester (V) was valuable as an oil-soluble monomer in that oil-phase polymerizations could be employed, with subsequent hydrolysis to liberate the free acid.

It also was shown that carboxymethylation of vinylbenzylamine (IV) with sodium chloroacetate gave another synthesis of II.



Some further examples of vinylphenyl-substituted amino acids were prepared starting with vinylbenzaldehyde (VII), shown below. 2-(*ar*-Vinylphenyl)-glycine (VIII) was isolated in 20% yield by the Strecker reaction using potassium cyanide and ammonium hydroxide, with subsequent hydrolysis of the unpurified nitrile. Best results were obtained when an excess of ammonia over the cyanide was used, but even then considerable side-reaction, including polymerization, lowered the product yield.

In a Knoevenagel reaction of vinylbenzaldehyde (VII) with malonic acid under ammoniacal conditions, a small yield of 3-(*ar*-vinylphenyl)-β-alanine (IX) was obtained, with the majority of the products appearing as the vinylbenzylidenemalonic



and the vinylcinnamic acids. However, a search for the optimum conditions for this synthesis was not pursued. This addition of amines to the cinnamic acid structure has been previously well described.[4]

By the reactions indicated below some further derivatives of the substituted amino acids already described were isolated. Carboxymethylation of VI and VIII gave the corresponding tricarboxylic acids, N-carboxymethyl-N-(*ar*-vinylbenzyl)-aspartic acid (X) and 2-(*ar*-vinylphenylnitrilo)-triacetic acid (XI). Another divinyl monomer, N-(*ar*-vinylbenzyl)-2-(*ar*-vinylphenyl)-glycine (XII), was prepared by the reaction of VIII with vinylbenzyl chloride (I).

Each of the isolated amino acids was found to be amphoteric, being more soluble in base than in acid, and having limited solubility at the isoelectric point. Purification was accomplished by both reprecipitation and recrystallization from water or aqueous alcohol. In a few cases, for example the leucines, a nickel salt was formed and purified readily because of its alcohol solubility. These amino acids were all white powders or crystals with indefinite decomposition points, usually above 200°. Infrared and ultraviolet spectra were nor-

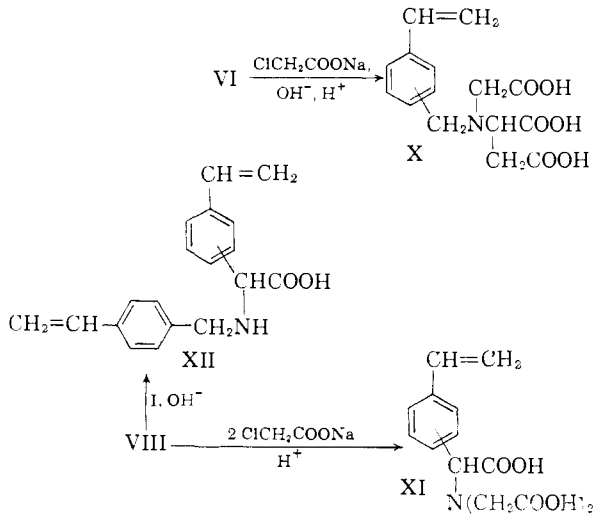
(4) (a) W. M. Rodionov and E. A. Postovskaja, THIS JOURNAL, **51**, 841 (1929); (b) J. R. Johnson, "Organic Reactions," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 249.

TABLE I

VINYL SUBSTITUTED AMINO ACIDS

Compound	Nitrogen, % Found	Nitrogen, % Calcd.	Unsaturation, mmoles Br_2/g. Found	Unsaturation, mmoles Br_2/g. Calcd.	Titration, meq./g. Found	Titration, meq./g. Calcd.
N-(Vinylbenzylimino)-diacetic acid	5.36	5.62	3.6	4.0	3.9	4.0
N-(Vinylbenzyl)-isovaline	5.87	6.39	4.5	4.6	3.7	4.6
N-Vinylbenzyl-D,L-isoleucine	5.43	5.67	3.9	4.1	..	..
N-Vinylbenzyl-L-isoleucine	5.75	5.67	4.1	4.1	..	..
N,N-Bis-(vinylbenzyl)-glycine	4.33	4.56	6.3	6.5	3.4	3.3
N-(Vinylbenzyl)-aspartic acid	..	..	3.6	4.0	3.7	4.0
2-(Vinylphenyl)-glycine	7.43	7.90	5.5	5.6	5.5	5.6
3-Vinylphenyl-β-alanine	7.56	7.33	5.0	5.2	5.3	5.2
2-(Vinylphenylnitrilo)-triacetic acid	4.89	4.78	3.5	3.4	2.9	3.3
N-Carboxymethyl-N-(vinylbenzyl)-aspartic acid	..	..	..	..	3.6	3.4
N-Vinylbenzyl-2-(vinylphenyl)-glycine	4.09	4.78	6.3	6.8	3.4	3.4

mal for the zwitterionic form of the amino acid and for the styrene portion of the structure.



Further characterization of these products involved elemental analysis, unsaturation analysis and potentiometric titration with acid or base. The data are summarized in Table I. A modified bromate–bromide unsaturation test involving 50% acetic acid gave satisfactory results with all the monomers. The titration values are those obtained at the high *p*H end-point, measuring the amino group.

Titration curves of the monomer amino acids were used to study the ability of the products to chelate metals, as well as to determine purity. In Fig. 1 is the titration curve for N-(vinylbenzylimino)-diacetic acid (II). As can be seen, from the starting point, or isoelectric point, to the first end-point requires one equivalent of base and is titrating the undissociated carboxyl group. A second equivalent of base titrates the proton of the ammonium nitrogen with an end-point at two moles of base per mole of amino acid.

Addition of one mole of cupric salt per mole of amino acid forms a 1:1 chelate, shifting the end-point to 2 on the abscissa. If only one-half this amount of copper is added, the first end-point occurs at 1.5 equivalents of base per mole of amino acid. As shown by the classical work of Schwarzenbach,[5] these data may be used to determine chelate stability constants. This has been done with a number of the amino acids described in this report and is the subject of another paper.

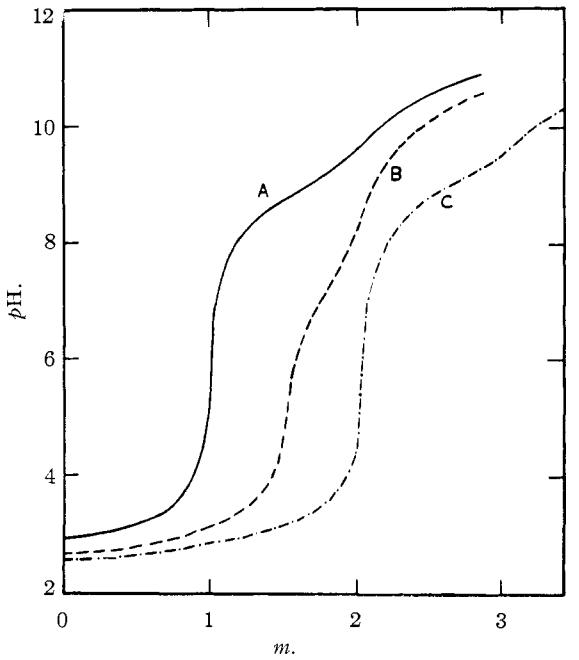


Fig. 1.—Potentiometric titration of II at 30°: A, [II] = 10^{-3} *M*; B, [II]/[$CuCl_2$] = 2: C, [II]/[$CuCl_2$] = 1: *m* = moles OH^-/mole amino acid.

In Fig. 2 is the titration curve for a monocarboxylic amino acid, 2-(vinylphenyl)-glycine (VIII). In this case a 2:1 chelate forms upon addition of one-half mole of copper ion per mole of amino acid, causing loss of the first end-point.

A reaction of particular interest was the polymerization of these vinyl monomers. Various free-radical catalysts such as sodium persulfate, azobisisobutyronitrile or ultraviolet light readily formed polymers under conditions illustrated in Table II. Generally, alkaline aqueous solutions were employed so as to obtain 5–50% concentrations of the amino acids. Conversions were followed by unsaturation tests. Many of the monovinyl structures are seen to give alkali-soluble polymers. One possible exception to this was the N-(vinylbenzylimino)-diacetic acid, which gave at least some gel formation. If the purity of the monomer may be accepted as precluding difunctional

(5) G. Schwarzenbach and H. Ackermann, *Helv. Chim. Acta*, **30**, 1029 (1948).

TABLE II

AQUEOUS SOLUTION POLYMERIZATION OF SOME AMINO ACID MONOMERS

Monomer	Concn., %	Catalyst conditions		Polymer
N-(Vinylbenzylimino)-diacetic acid	1.75	U.v. light	90°, 3 days	Partially gel, some sol
N-(Vinylbenzylimino)-diacetic acid	35	0.5% $Na_2S_2O_8$	80°, 12 hr.	All gel
N,N-Bis-(vinylbenzyl)-glycine	10	0.5% $Na_2S_2O_8$	Refl., 2 days	All gel, containing 27% unsatn.
N-(Vinylbenzyl)-isovaline	10	1% ABIN[a]	80°, 3 days	Soluble polymer, viscous soln.
2-(Vinylphenyl)-glycine	10	1% $Na_2S_2O_8$	80°, 6 days	Sol. at alk. *p*H, gelatinous at *p*H 5
3-Vinylphenyl-β-alanine	10	1% ABIN[a]	80°, 3 days	Soluble polymer
2-(Vinylphenylnitrilo)-triacetic acid	10	1% ABIN[a]	80°, 3 days	Soluble polymer over wide *p*H range

[a] Azobisisobutyronitrile.

contaminants, two other possible explanations for the formation of gels may be suggested. Either a crosslinking due to chain-transfer, or some interchain salt formation could explain these results.

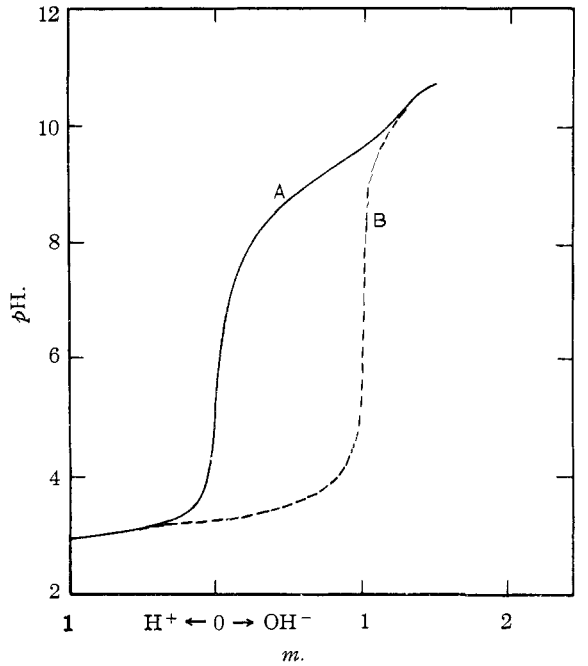


Fig. 2.—Potentiometric titration of III at 30°: A, [III] = 2×10^{-3} *M*; B, [III]/[$CuCl_2$] = 2; *m* = moles OH^- or H^+/mole amino acid.

These homopolymers exhibited titration and chelation behavior analogous to that of the monomers. Details of solution properties, chelating properties and applications are to be described in subsequent communications.

A variety of copolymers of these monomers have been prepared. These chelate resin beads having small amounts of crosslinking gave good rates of reaction and good selectivity for certain metal ions.

As a brief example of these properties, the separation of copper from zinc ions in a saturated potassium sulfate solution is illustrated in Fig. 3. A column was filled with chelate resin beads containing the crosslinked polyvinylbenzylaspartic acid structure. Then a solution about 0.1 *M* in each Cu^{++} and Zn^{++} was passed through the column at a rate of about 2 ml./min. A chromatographic-like separation of the metals occurred, the copper being held most tightly and the zinc preceding the blue copper chelate front. On the graph of effluent volume *vs.* metal ion concentration it is noticed that the Zn^{++} becomes concentrated to twice the original value, with the Cu^{++} finally appearing as the column becomes saturated. After a water rinse, the pure Cu^{++} held by the resin bed readily was eluted with dilute mineral acid.

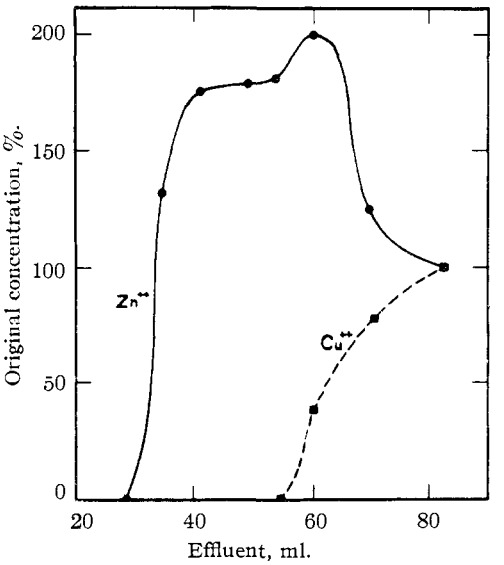


Fig. 3.—Effluent analysis of column separation of Zn^{++} and Cu^{++} by a chelating resin: 4 g. (dry) of crosslinked polyvinylbenzylaspartic acid resin, equilibrated with satd. K_2SO_4 solution in a column $^1/_2'' \times 15''$; metal solution, 0.1 *M* $ZnSO_4$, 0.07 *M* $CuSO_4$ in satd. K_2SO_4 solution; flow-rate, 2 ml./min.

Further discussion of the applications and unit processes developed for chelate resin separation of the ions of metals such as Cu, Ni and Co will be presented in the near future.

Acknowledgment.—The authors wish to thank R. C. Calkins, T. C. Hampton and E. C. Gyarfus for the assistance given this work.

Experimental

Materials.—*ar*-Vinylbenzyl chloride[6] (I) and *ar*-vinylbenzylamine[7] (IV) were supplied by S. C. Stowe and E. L. McMaster of the Dow Research Laboratories. The vinylbenzyl chloride had a b.p. of 87° (5 mm.), $n^{25}D$ 1.5725 and d^{25}_4 1.088. Infrared analysis indicated about 20% *ortho* and 80% *para* isomers. Vinylbenzylamine was received as the hydrochloride, m.p. 160–172° dec., and was neutralized

(6) J. T. Clarke, N. Highlands and L. Hamerschlag, U. S. Patent 2,780,604 (1956).

(7) This amine was prepared in about 70% yield by a reaction of vinylbenzyl chloride with liquid ammonia, analogous to the procedure of J. v. Braun, R. Lotz, K. C. Warne, W. Pinkernelle, W. Rohland, A. Pohl, D. Dengel and H. Arnold, *Ber.*, **70B**, 979 (1937). After removal of the excess ammonia the product was isolated as the hydrochloride by recrystallization from ethanol.

with aqueous caustic before use to liberate free base. Approximately equal amounts of *o*- and *p*-isomers were present. *ar*-Vinylbenzaldehyde[5] (VII) was prepared by the Sommelet reaction of *ar*-vinylbenzyl chloride and had a b.p. of 70–80° (1 mm.), $n^{25}D$ 1.586–1.589, d^{30}_4 1.037.

All amino acid starting materials were from commercial sources.

Analyses.—Unsaturation was determined by a standard bromate–bromide method, modified by use of 50% acetic acid as solvent. Potentiometric titrations were made with glass electrodes and a Beckman model G *p*H meter, using a nitrogen atmosphere and about 10^{-3} molar solutions of the amino acids in 1 *N* potassium chloride.

Alkylations with Vinylbenzyl Chloride. Iminodiacetic Acid.—A solution containing 133 g. (1.0 mole) of iminodiacetic acid and 66 g. (1.65 moles) of sodium hydroxide in 2 l. of 50% methanol was heated to 60° while 153 g. (1.0 mole) of vinylbenzyl chloride was added dropwise with stirring. After one-half the chloride had been added in 30 min., another 66 g. of sodium hydroxide was introduced and the addition continued. Heating was continued for 30 min. after addition was complete, at which time the methanol was distilled under vacuum until two-thirds the original volume remained. Extraction of solution with ether removed about 20 g. of thick oil, consisting of vinylbenzyl alcohol and methyl vinylbenzyl ether. Acidification of the aqueous phase to *p*H 2.5 with hydrochloric acid then gave a white precipitate which became thick after standing overnight. Filtration of the solid and vacuum drying gave 405 g. of crude product containing considerable sodium chloride. Recrystallization of this material from 10% aqueous solution gave 70.7 g. (28%) of **N-(*ar*-vinylbenzylimino)-diacetic acid** (II), as white clusters of needles, m.p. >200° dec. Analyses are listed in Table I.

By similar procedures, monoalkylated derivatives of isovaline, DL- and L-leucine were prepared, with the analyses as shown in Table I.

Glycine.—A solution of 150 g. (2.0 moles) of glycine in 800 ml. of water was heated to 75° with stirring. Concurrent addition of 152 g. (1.0 mole) of vinylbenzyl chloride and 300 ml. of 9.8 *N* sodium hydroxide was maintained, so that a *p*H of 8–10 existed in the reaction mixture during the 3-hr. period. After a further 30 min. of heating the two-phase system was cooled, 3 l. of water added, and the separated layers each extracted with ether. Concentration of the ether extract gave 13.5 g. of yellow oil, $n^{25}D$ 1.5954, a mixture of unreacted vinylbenzyl chloride and vinylbenzyl alcohol.

Neutralization of the combined aqueous layers with hydrochloric acid to *p*H 5 gave an oily solid which was filtered, washed with water and ether, and vacuum-dried to a tan powder, weighing 115.5 g. (75%).

Anal. Calcd. for $C_{20}H_{21}O_2N$: unsatn., 6.52 mmoles Br_2/g. Found: unsatn., 5.70.

Recrystallization of the above product in 40% yield from 95% ethanol provided a sample of **N,N-bis-(*ar*-vinylbenzyl)-glycine** (III) with the analyses listed in Table I.

N-(*ar*-Vinylbenzyl)-aspartic Acid (VI).—A solution of 26.5 g. (0.2 mole) of vinylbenzylamine in 100 ml. of ether was added to 68.8 g. (0.4 mole) of diethyl maleate. A slight warming occurred, but the mixture was allowed to stand at room temperature for six days. Then the oil was extracted with 20 ml. of water containing 16 ml. of concd. hydrochloric acid. After the aqueous phase was re-extracted with ether, it was made strongly basic with caustic and the dark red oil then ether extracted. Following drying with sodium sulfate, removal of the ether gave 49.1 g. (81%) of **diethyl N-(*ar*-vinylbenzyl)-aspartate** (V), $n^{24}D$ 1.5144.

Anal. Calcd. for $C_{17}H_{23}O_4N$: N, 4.59; unsatn. 3.28 mmoles Br_2/g.; neut. equiv., 305. Found: N, 4.73; unsatn. 2.89; neut. equiv., 325.

The entire sample of ester was then refluxed for 3 hr. with 150 ml. of water containing 16.1 (0.4 mole) of sodium hydroxide until the oil disappeared. Upon acidification to *p*H 2.5, the N-vinylbenzylaspartate precipitated and was filtered and dried to give 30.0 g. (75%) of VI, m.p. 200° dec. Analyses are listed in Table I.

2-(*ar*-Vinylphenyl)-glycine (VIII).—To a solution of 132 g. (1 mole) of vinylbenzaldehyde in 250 ml. of methanol was added 53.5 g. (1.15 moles) of ammonium chloride, 51.0 g. (1.05 moles) of sodium cyanide, 100 ml. concd. ammonium hydroxide and 300 ml. of water. After addition of 1 g. of *t*-butylcatechol, the mixture was heated at 40–50° for 1 hr. with the solution becoming red. Then a solution of 160 g. (4 moles) of sodium hydroxide in 250 ml. of methanol and 1 l. of water was added and the mixture refluxed for one hour more. After extraction of the system with benzene, the aqueous layer was neutralized to *p*H 6 with dil. hydrochloric acid. A yellow precipitate formed and was filtered, washed with water, and then redissolved in dil. acid. After warming with Norite, filtration and neutralization gave a gray solid. This was water-washed and dried to give 37.9 g. (21%) of crude VIII.

Reprecipitation of 17.2 g. of the above product by solution in 5% sodium hydroxide and neutralization gave 10.8 g. of VIII with analyses given in Table I.

3-(*ar*-Vinylphenyl)-β-alanine (IX).—A procedure similar to that described for anisaldehyde[4b] was used. A solution of 12.6 g. (0.12 mole) of malonic acid in 6.0 g. of concd. ammonium hydroxide was mixed with 13.2 g. (0.1 mole) of vinylbenzaldehyde and 50 ml. of absolute ethanol. After warming gently on the steam-bath, most of the ethanol was distilled and the residue dissolved in warm water by addition of some sodium carbonate. This solution then was poured into 200 ml. of cold dilute hydrochloric acid, giving a slightly gummy solid which was filtered and dried to give 7.3 g. of mixed acids, m.p. 170–180°.

Anal. Calcd. for $C_{11}H_{10}O_2$: neut. equiv., 174. Calcd. for $C_{12}H_{10}O_4$: neut. equiv., 109. Found: neut. equiv., 117.

Recrystallization of 1 g. of this mixture from 50% alcohol gave 0.6 g. of white crystals, m.p. 208–209° (decomposing and resolidifying on further heating), of ***ar*-vinylbenzylidenemalonic acid**, probably chiefly the *p*-isomer.

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 66.05; H, 4.62; neut. equiv., 109. Found: C, 66.17; H, 4.34; neut. equiv., 110.

The aqueous acidic filtrate from the initial separation was then carefully adjusted to *p*H 5 and concentrated to one-third its original volume by an air stream. Cooling then gave a slow precipitation of a white solid, the crude IX. Recrystallization from hot water gave the analytical sample of IX listed in Table I.

A copper complex of this amino acid was isolated from aqueous solution at *p*H 11 as a pale blue powder.

Anal. Calcd. for $(C_{11}H_{12}O_4N)_2Cu$: N, 6.32. Found: N, 5.81.

Carboxymethylations.—The following procedure is typical of the several reactions of amino acids with sodium chloroacetate.

2-(*ar*-Vinylphenylnitrilo)-triacetic Acid (XI).—A mixture of 3.0 g. (0.017 mole) of VIII, 4.5 g. (0.04 mole) of chloroacetic acid and 3.0 g. of sodium carbonate in 35 ml. of water containing a trace of hydroquinone was heated to 70–80° for 8 hours. Another 3 g. of sodium carbonate was added at the end of five hours of reaction. A small amount of insoluble material was filtered and the filtrate adjusted to *p*H 2.0 before concentrating the solution to about 15 ml. by an air stream. The precipitate thus formed was separated (4.2 g., 84%) and recrystallized from hot water to yield two fractions. The least soluble material was a mixture of mono- and dicarboxymethylated products.

Anal. Calcd. for $C_{14}H_{15}O_6N$: N, 4.78; unsatn., 3.41 mmoles Br_2/g. Found: N, 5.06; unsatn., 3.59.

The more soluble fraction was essentially pure tricarboxylic acid XI, with analyses shown in Table I.

Polymerization of Amino Acid Monomers. Homopolymers.—Results of several aqueous solution polymerizations of the vinyl-substituted amino acids are summarized in Table II. Usually a nitrogen atmosphere was maintained during the reaction, but in several cases no special precaution was found necessary. In many cases, polymerization was essentially complete in a few hours, but the reactions were allowed to proceed for the longer times indicated to ensure high conversion to polymer.

Copolymers.—Copolymers of some of these unsaturated amino acids with vinyl acetate, acrylamide, sodium acrylate and sodium *p*-styrene sulfonate have been prepared in aqueous or alcoholic solutions. Furthermore, oil-soluble

(8) R. H. Wiley and P. H. Hobson, THIS JOURNAL, **71**, 2424 (1949); *J. Polymer Sci.*, **5**, 483 (1950).

derivatives of these monomers, such as the diethyl N-(vinylbenzyl)-aspartate, have been copolymerized with 0–10% divinylbenzene and the resulting beads hydrolyzed by base or acid. Details of these reactions and descriptions of the resins are subjects of forthcoming publications.

MIDLAND, MICH.

[CONTRIBUTION FROM THE AGRICULTURAL RESEARCH DIVISION, SHELL DEVELOPMENT CO.]

The Preparation of Some Insecticidal Chlorinated Bridged Phthalazines[1,2]

BY J. G. KUDERNA, J. W. SIMS, J. F. WIKSTROM AND S. B. SOLOWAY

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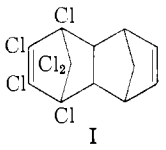
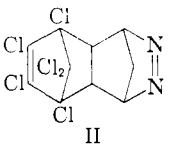
A number of bridged phthalazines, many of which are highly toxic to insects, have been prepared. Synthesis was effected *via* the Diels–Alder reaction of hexachlorocyclopentadiene, cyclopentadiene and tetrachlorocyclopentadienone dimethyl acetal with a 2,3-diazabicyclo[2.2.1]hept-5-ene obtained by known methods from cyclopentadiene and an azodiformic ester. Decarbalkoxylation of these adducts was effected under both acidic and basic conditions. In this way 5,6,7,8,9,9-hexachloro-1,2,3,4,4a,5,8,8a-octahydro-1,4,5,8-dimethanophthalazine (VI) was made. A series of salts of VI was prepared. Oxidation of VI gave the azo derivative II, a nitrogen analog of the insecticide aldrin (I) in which the unchlorinated olefinic grouping is formally replaced by the isoelectronic azo group. Oxidation of II provided a stable N-oxide XIV. Thermal decomposition of II occurs with liberation of nitrogen and formation of 1,7,8,9,10,10-hexachlorotetracyclo[5.2.1.$0^{2,6}$.$0^{3,5}$]-dec-8-ene (XIII).

Aldrin (I), a commercially produced insecticide,[3–5] is the product of the Diels–Alder reaction of hexachlorocyclopentadiene with bicyclo[2.2.1]-hepta-2,5-diene and thus has a 1,4,5,8-dimethanonaphthalene structure. In considering analogs of aldrin it appeared feasible to prepare the corresponding dimethanophthalazine II wherein the unchlorinated olefinic grouping is formally replaced by the isoelectronic azo group.



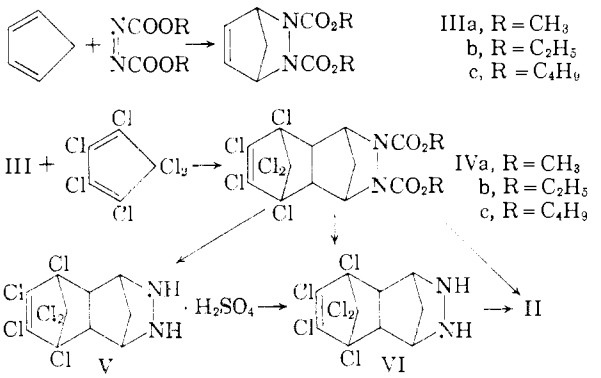
I



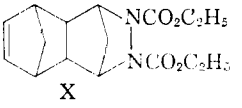
II

This view was supported by the knowledge that an intermediate which would be needed was available in the form of a bicyclo[2.2.1]hept-2-ene containing nitrogen atoms in positions 5 and 6. Accordingly, diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate[6] was prepared by the reaction of cyclopentadiene with diethyl azodiformate. This adduct, as well as others of the same type, reacted with hexachlorocyclopentadiene to give dimethanophthalazines in which the azo group readily was generated. The reaction sequences which led to the desired nitrogen analog of aldrin, II, are

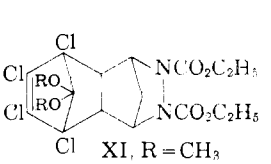
The cyclopentadiene adducts IIIa and b involved in the first step were prepared following described procedures[6]; the dibutyl ester IIIc and its precursor, dibutyl azodiformate, are new. In addition to the cyclopentadiene adduct IIIb, adducts of diethyl azodiformate with furan (VII) and butadiene[6b,7] (VIII) were also made (Table I).



The reaction of these adducts with dienic components such as cyclopentadiene, hexachlorocyclopentadiene and tetrachlorocyclopentadienone dimethyl acetal then was carried out to yield a number of phthalazinedicarboxylic esters (Table II). Diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate[6] (IIIb), for example, reacted smoothly with hexachlorocyclopentadiene at 130° to give the adduct IVb in 95% yield as a stable, colorless, crystalline solid melting at 110–111°, freely soluble in common organic solvents. Adducts IVa and IVc were obtained similarly from compounds IIIa and IIIc. Three other phthalazinedicarboxylic esters were obtained *via* this route; IX was prepared by reaction of hexachlorocyclopentadiene with VIII; X and XI from IIIb with cyclopentadiene and tetrachlorocyclopentadienone dimethyl acetal, respectively. An attempt to isolate a product from the reaction of hexachlorocyclopentadiene with VII was unsuccessful.



X



XI, R = CH_3

(1) Paper presented in part before the Division of Agricultural and Food Chemistry at the 133rd Meeting of the American Chemical Society in San Francisco, Calif., April, 1958.

(2) J. G. Kuderna, U. S. Patent 2,802,012 (to Shell Development Co.), August 6, 1957.

(3) For the purpose of this paper aldrin is considered to be the pure compound 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4-*endo*, *exo*-5,8-dimethanonaphthalene.

(4) R. E. Lidov, H. Bluestone, S. B. Soloway and C. W. Kearns, *Adv. in Chem. Ser.*, **1**, 175 (1950); R. E. Lidov, U. S. Patent 2,635,977 (to Shell Development Co.), April 21, 1953.

(5) S. B. Soloway, Ph.D. Thesis, Univ. of Colorado, 1955.

(6) (a) O. Diels, J. H. Blum and W. Koll, *Ann.*, **443**, 242 (1925); (b) J. C. J. MacKenzie, A. Rodgman and G. F. Wright, *J. Org. Chem.*, **17**, 1666 (1952); (c) A. Rodgman and G. F. Wright, *ibid.*, **18**, 465 (1953).

(7) K. Alder, H. Niklas, R. Ammüller and B. Olson, *Ann.*, **585**, 81 (1954).