

was obtained by a final recrystallization from methanol. The infrared curve of this material was identical with that of pure 11-ketoprogesterone. Paper chromatography of the crude reaction product showed the presence of less than 5% of 1-dehydro-5 α -pregnane-3,11,20-trione.

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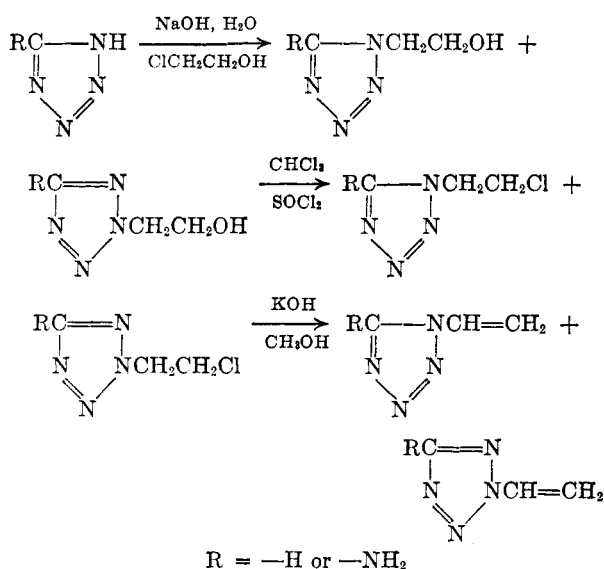
N-Vinyltetrazoles

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As part of a continuing program on the synthesis of new *N*-alkyl substituted tetrazoles,¹ the syntheses and polymerizations of the *N*-vinyltetrazoles, their 5-amino derivatives, and the *N*-allyltetrazoles were investigated.

The following sequence of reactions was employed for the syntheses of the *N*-vinyltetrazoles:



When tetrazole was employed as the starting material, the sequence of reactions was carried out as indicated and the 1- and 2-vinyltetrazoles were separated by distillation at reduced pressure. With 5-aminotetrazole, it was convenient to separate the isomers by crystallization at the hydroxyethyl stage¹ and convert these to the vinyl derivatives independently.

1- and 2-Allyltetrazoles were readily synthesized in moderate yields by direct alkylation of sodium tetrazole with allyl bromide in refluxing aqueous ethanol solution.

No attempts were made to bring the syntheses of the vinyl derivatives to optimum yields. It is an-

anticipated, however, that vinylation with acetylene² would be the preferred approach.

In preliminary polymerization studies, the vinyltetrazoles and the vinyl-5-aminotetrazoles gave only insoluble-infusible homopolymers, regardless of whether solution or emulsion techniques were employed. The possibility of di-vinyl derivatives of tetrazole as impurities appears to be remote since di-*N*-alkylation of the tetrazole ring results in the formation of undistillable tetrazolium salts.³ The insolubility of the vinyltetrazole polymers must be due either to strong molecular interactions between polymer chains, to ring involvement during free radical propagation, or possibly to involvement of the proton in the 5-position in the case of the 1- and 2-vinyltetrazoles. Limited attempts using chain transfer agents in solution polymerizations were more successful; initially soluble polymers were obtained with 1- and 2-vinyltetrazoles, but re-resolution of the freshly precipitated and undried polymers gave solutions which jelled in a short time. The 1- and 2-allyltetrazoles could not be induced to homopolymerize, but would copolymerize with styrene and methyl methacrylate.⁴

Refractive indices and densities were measured and the molar refractivity of the tetrazole ring was calculated for each of the liquid tetrazoles. These data are shown in Table I.

TABLE I
INDICES AND DENSITIES OF LIQUID TETRAZOLES

Tetrazole	η_D^{25}	D_4^{25}	M_k Tetrazole Ring
1-Ethyltetrazole ^a	1.4602 ²⁵	1.12 ²⁵	12.7
2-Ethyltetrazole ^a	1.4366 ²⁵	1.07 ²⁵	12.7
1-Allyltetrazole	1.4854 ²⁰	1.12 ²⁰	12.6
2-Allyltetrazole	1.4670 ²⁰	1.08 ²⁰	12.7
1-Vinyltetrazole	1.5000 ²⁰	1.18 ²⁰	13.1
2-Vinyltetrazole	1.4850 ²⁰	1.13 ²⁰	13.4

^a Synthesized for comparison by the method used for the syntheses of 1- and 2-allyltetrazoles. Cf. ref. (9) for physical constants.

EXPERIMENTAL⁵

Tetrazole. Tetrazole was prepared by diazotization of 5-aminotetrazole in the presence of hypophosphorous acid.⁶ An improvement was made in the procedure⁷ by extracting the tetrazole with ethyl acetate directly from the reaction

(2) J. W. Copenhaver and M. H. Bigelow, *Acetylene and Carbon Monoxide Chemistry*, Reinhold Publishing Corp., New York, N. Y., 1949, p. 66.

(3) G. F. Duffin, J. D. Kendall, and H. R. J. Waddington, *Chemistry and Industry*, **42**, 1355 (1955).

(4) Charles J. Thelen, this laboratory, unpublished results.

(5) The melting points were determined in capillary tubes and are uncorrected.

(6) R. A. Henry and W. G. Finnegan, *J. Am. Chem. Soc.*, **76**, 290 (1954).

(7) This improvement is a variation of one suggested by James Moffat, University of Louisville, Louisville, Ky.

(1) R. A. Henry and W. G. Finnegan, *J. Am. Chem. Soc.*, **76**, 923 (1954).

solution after neutralization to pH 3.5. A continuous extraction was used with an efficient stirrer to ensure thorough mixing of the two phases; and an efficient condenser to permit rapid cycling of the ethyl acetate. The yields of high purity tetrazole recovered from the ethyl acetate approached 98%.

1- and 2-(2-Hydroxyethyl)tetrazoles. A suspension of 140 g. (2.0 moles) of tetrazole in 300 ml. of distilled water was neutralized to a phenolphthalein end point with a solution of 82.5 g. (2.0 moles) of 97% sodium hydroxide in 300 ml. of water. The solution of sodium tetrazole was heated to reflux and 201 g. (2.5 moles) of 2-chloroethanol was added from an addition funnel over a 15-min. period. The resulting solution was refluxed for 18 hr. and then concentrated *in vacuo* on a steam bath to a sirupy mixture of products and sodium chloride.

The hydroxyethylated products were extracted from the sodium chloride with one 300-ml. and three 100-ml. portions of boiling acetone. Concentration of the acetone extracts *in vacuo* on a steam bath yielded 236 g. (theory 228 g.) of a mixture of 1- and 2-(2-hydroxyethyl)tetrazoles and other alkylated products. Attempts to separate the mixture by distillation at 1 mm. pressure were unsuccessful due to decomposition.

1- and 2-(2-Chloroethyl)tetrazoles. The mixture of 2-hydroxyethyltetrazoles (236 g.) from the preceding section was slurried with 250 ml. of chloroform in a 2-liter, 3-necked flask. Thionyl chloride (300 g., 2.5 moles) was added dropwise with stirring while the temperature of the reaction mixture was maintained below 20° by immersing the flask in an ice bath. The cooling bath was then removed and the mixture was allowed to stir at room temperature for 24 hr. The reaction mixture became homogeneous during this time. The mixture was refluxed for 2 hr. to drive off hydrogen chloride and sulfur dioxide and then concentrated to a sirup at reduced pressure on a steam bath. After cooling to 5°, the sirup was treated with 100 g. of crushed ice, with stirring, to decompose thionyl chloride complexed with the tetrazoles. When the exothermic reaction was over, the excess ice was melted by warming the mixture on a steam bath and the chloroethyltetrazoles were extracted with three 100-ml. portions of chloroform. Evaporation of the chloroform solution left 265 g. of 1- and 2-(2-chloroethyl)tetrazoles as a yellow viscous oil. Separation of the isomers was possible at this point by distillation. Distillation of the chloroethyltetrazoles obtained from 3.8 moles of tetrazole yielded 154.3 g. (30.7%) of 2-(2-chloroethyl)tetrazole, b.p. 76° at 1 mm. The 1-(2-chloroethyl)tetrazole was not distilled, but could be using molecular distillation techniques.

1- and 2-Vinyltetrazoles. The 265 g. (ca. 2.0 moles) of chloroethyltetrazoles from the preceding chlorination and 1 g. of hydroquinone were dissolved in 200 ml. of methanol in a 2-liter, 3-necked flask and the solution was heated to reflux.

A solution of 132 g. (2.0 moles) of 85% potassium hydroxide in 500 ml. of methanol was added dropwise with stirring over a 1-hr. period. Precipitation of potassium chloride began immediately. The reaction mixture was maintained at reflux temperature for 30 min. after the addition was complete. The methanol was then distilled at atmospheric pressure; stirring was continued to prevent bumping. After cooling the residue of vinyltetrazoles, water, and potassium chloride to room temperature, the vinyltetrazoles were extracted with three 100-ml. portions of methylene chloride. The methylene chloride solution was dried with anhydrous magnesium sulfate and an additional gram of hydroquinone was added to prevent polymerization. Distillation of the methylene chloride at atmospheric pressure left a residue of 1- and 2-vinyltetrazoles which was distilled at reduced pressure to yield: 38.6 g. (20.1%) of 2-vinyltetrazole, b.p. 66–68° at 60 mm.

Anal. Calcd. for $C_2H_4N_4$: C, 37.49; H, 4.19; N, 58.31. Found: C, 37.62; H, 4.60; N, 57.82. and 70.6 g. (36.8%) of 1-vinyltetrazole, b.p. 94° at 1 mm.

Anal. Calcd. for $C_3H_4N_4$: C, 37.49; H, 4.19; N, 58.31. Found: C, 37.52; H, 4.42; N, 58.12.

Dehydrohalogenation of 154.3 g. (1.17 moles) of distilled 2-(2-chloroethyl)tetrazole by the same procedure yielded 78.0 g. (70%) of 2-vinyltetrazole. *Caution:* 2-Vinyltetrazole is capable of detonation by cavity impact at a drop height only slightly greater than that required for the detonation of nitroglycerin.⁸

The structure assignment of the lower boiling vinyltetrazole was established by catalytic dehalogenation of the preceding 2-chloroethyltetrazole.

2-Ethyltetrazole. A mixture of 13.25 g. (0.1 mole) of 2-(2-chloroethyl)tetrazole, b.p. 76° at 1 mm., 13.8 g. (0.1 mole) of potassium carbonate, and 50 ml. of methanol was hydrogenated at 50 p.s.i. with 0.2 g. of 5% platinum-on-charcoal and 1 ml. of aqueous 5% palladium chloride for 18 hr. After filtration to remove solids, the solvent was removed by distillation leaving 9.48 g. of fluid oily residue. Distillation of the residue at reduced pressure yielded 6.42 g. (65.6%) of 2-ethyltetrazole, b.p. 72° at 37 mm. An authentic sample of 2-ethyltetrazole⁹ was purified by distillation in the same apparatus, b.p. 72° at 37 mm. Comparison of the two samples using infrared and nuclear magnetic resonance spectroscopy confirmed their identity.

1-(2-Chloroethyl)-5-aminotetrazole. Thionyl chloride (150 ml.) was placed in a 500-ml. flask and cooled to 5° in an ice bath. 1-(2-Hydroxyethyl)-5-aminotetrazole¹ (45.4 g., 0.352 mole) was added portionwise with shaking and cooling to maintain the temperature below 20°. The mixture was then heated to reflux for 4 hr. Hydrogen chloride and sulfur dioxide were evolved and the mixture became homogeneous. The excess thionyl chloride was then removed *in vacuo* on a steam bath and the residue was treated (after cooling to room temperature) with 50 ml. of 95% ethanol to decompose complexed thionyl chloride. When the exothermic reaction had subsided, 50 ml. of water was added and the mixture was stripped to dryness at reduced pressure on a steam bath. The solid residue was dissolved in 250 ml. of boiling water, decolorized with charcoal, and the solution was cooled to 5° overnight. The yield of 1-(2-chloroethyl)-5-aminotetrazole amounted to 39.24 g. (75.7%), m.p. 150–151.5°.

Anal. Calcd. for $C_3H_6N_5Cl$: N, 47.46; Cl, 24.03. Found: N, 47.43; Cl, 24.40.

2-(2-Chloroethyl)-5-aminotetrazole. The chlorination of 78.5 g. (0.069 mole) of 2-(2-hydroxyethyl)-5-aminotetrazole¹ was accomplished in the same manner as that described for the 1-isomer. Recrystallization of the crude final product from benzene yielded 55.4 g. (61.8%) of 2-(2-chloroethyl)-5-aminotetrazole, m.p. 51–52°.

Anal. Calcd. for $C_3H_6N_5Cl$: N, 47.46; Cl, 24.03. Found: N, 47.71; Cl, 24.0.

1-Vinyl-5-aminotetrazole. A solution of 39.79 g. (0.27 mole) of 1-(2-chloroethyl)-5-aminotetrazole and 0.1 g. of hydroquinone in 150 ml. of methanol was heated to reflux. A solution of 18 g. (0.27 mole) of 85% potassium hydroxide in 100 ml. of methanol was then added dropwise with stirring over a period of 30 min. The reaction was refluxed for 1 hr. after the addition was complete and then cooled to 20°. After the precipitated potassium chloride was removed by filtration the solution was evaporated to dryness at reduced pressure on a steam bath. The residue of impure 1-vinyl-5-aminotetrazole was dissolved in a minimum of hot water and cooled, yielding 22.75 g. (0.247 mole) of 1-vinyl-5-aminotetrazole, m.p. 157–158°. An additional 2.30 g. was recovered by concentrating and cooling the mother liquors. The total of 26.05 g. represents an 86.8% yield.

(8) See F. P. Bowden, M. F. R. Culcahy, R. G. Vines, and A. Yoffee, *Proc. Roy. Soc. London*, **188**, 306 (1947) for a detailed discussion of the detonation of liquid explosives by cavity impacts.

(9) E. Oliveri-Mandala and T. Passalacqua, *Gass. Chim. Ital.*, **43**, II, 468 (1913).

Anal. Calcd. for $C_8H_8N_4$: C, 32.42; H, 4.54; N, 63.04. Found: C, 32.7, 32.5; H, 4.50, 4.72; N, 62.86.

Hydrogenation of 2.72 g. (0.098 mole) of 1-vinyl-5-aminotetrazole in glacial acetic acid at 50 p.s.i. using Adams platinum oxide as catalyst gave 2.70 g. (97.7%) of 1-ethyl-5-aminotetrazole, m.p. 149–150.5° after recrystallization from water. A mixture melting point with an authentic sample of 1-ethyl-5-aminotetrazole¹⁰ was not depressed.

2-Vinyl-5-aminotetrazoles. The dehydrohalogenation of 40.47 g. (0.274 mole) of 2-(2-chloroethyl)-5-aminotetrazole was accomplished in the same manner as for the 1-isomer using potassium hydroxide in methanol. After evaporation of the methanol at reduced pressure, the crude product was extracted with three 50-ml. portions of methylene chloride. Distillation of the methylene chloride left 30 g. of oil which on distillation gave 23.39 g. (77.7%) of 2-vinyl-5-aminotetrazole, b.p. 75–77° at 0.8 mm., m.p. 47–49° after recrystallization from carbon tetrachloride. The melting point of a sample was unchanged by sublimation at reduced pressure.

Anal. Calcd. for $C_8H_8N_4$: C, 32.42; H, 4.54; N, 63.04. Found: C, 32.29; H, 4.65; N, 63.05.

1- and 2-Allyltetrazoles. A suspension of 70 g. (1.0 mole) of tetrazole in 400 ml. of 95% ethanol was neutralized to a phenolphthalein end point with a 50% aqueous solution of 41.2 g. (1.0 mole) of 97% sodium hydroxide. The suspension was heated to reflux, 121 g. (1.1 moles) of allyl bromide was added dropwise with stirring over a 10-min. period and the solution was refluxed overnight. The ethanol was then removed by distillation at atmospheric pressure and the residue was extracted with three 100-ml. portions of cold benzene. After drying the solution with anhydrous magnesium sulfate, the benzene was distilled at atmospheric pressure. The residue of mixed 1- and 2-allyltetrazoles was distilled at reduced pressures, yielding 36.3 g. (28.96%) of 2-allyltetrazole, b.p. 80–81° at 20 mm.

Anal. Calcd. for $C_8H_8N_4$: C, 43.62; H, 5.49; N, 50.89. Found: C, 43.51; H, 5.62; N, 51.22.

and 41.52 g. (37.36%) of 1-allyltetrazole, b.p. 101° at 1 mm.

Anal. Calcd. for $C_8H_8N_4$: C, 43.61; H, 5.49; N, 50.89. Found: C, 44.23; H, 5.45; N, 50.71.

1-Vinyl-4-methyl-5-aminotetrazole hydrochloride. 1-Vinyl-5-aminotetrazole (5.55 g., 0.05 mole) and 9.5 g. (0.055 mole) of redistilled methyl benzenesulfonate were mixed and heated on a hot plate in a small beaker. An exothermic reaction occurred when the temperature of the mixture reached about 100° and the beaker was removed from the hot plate. The reaction temperature rose spontaneously to 165°. After cooling, the mixture solidified. The product was dissolved in 50 ml. of methanol and made basic by the addition of 3.62 g. (0.055 mole) of potassium hydroxide in 25 ml. of methanol. The solution was then evaporated to dryness. The free base was extracted from the residue with three 50-ml. portions of chloroform and the insoluble potassium benzenesulfonate discarded. Evaporation of the chloroform solution yielded an oily yellow residue of 1-vinyl-4-methyl-5-aminotetrazole,¹¹ which was acidified with 5 ml. of concentrated hydrochloric acid. After the water was removed *in vacuo* on a steam bath, the 1-vinyl-4-methyl-5-aminotetrazole hydrochloride was recrystallized twice from 98% 2-propanol, yielding 2.56 g. (31.7%) of product, m.p. 214–215° (dec.).

Anal. Calcd. for $C_8H_8N_4Cl$: C, 29.73; H, 4.99; N, 43.35; Cl, 21.94. Found: C, 29.74; H, 5.73; N, 42.79; Cl, 21.73.

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Lucernic Acid, A New Triterpene from Alfalfa

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Interest in the possible toxic physiological activity of alfalfa (*Medicago sativa*) saponins in poultry and animal feeds has led to further investigation of these saponins and their aglycones. Recent manuscripts have described the isolation and characterization of medicagenic acid from the "cholesteride" saponins of alfalfa.^{1,2} Further examination of the fractions obtained during the isolation of medicagenic diacetate has led to the isolation of a new triterpene, $C_{30}H_{46}O_7$, which is shown to be a trihydroxy, monolactone, monocarboxylic acid.

Characterization studies of this triterpene—now named lucernic acid³—demonstrated the presence of 3 easily acylable hydroxyl groups, as shown by the formation of the triacetate (II) at room temperature with pyridine-acetic anhydride. The infrared spectrum (KBr pellet) of II shows bands at 1775, 1730, and 1250 cm^{-1} , corresponding to a 5-membered lactone, acetate, and C—O stretching adsorption. The presence of lactone was confirmed by the consumption of 5 equivalents (3 acetyls, a lactone, and a carboxyl) of alkali during saponification of II with 0.1*N* KOH in methanol; upon neutralization of the salt the lactone ring closed. II gives no color with tetranitromethane in glacial acetic acid or with the Liebermann-Burchard reagent and shows no high terminal ultraviolet adsorption.

Periodic acid oxidation of the methyl ester (III) resulted in the consumption of one equivalent of the reagent, thus demonstrating the existence of a 1,2-glycol moiety in lucernic acid.

Biogenetic relationship of I to triterpenes previously isolated from alfalfa^{2,4} might lead one to expect a β -amyryn structure; present information, however, gives only very limited clues as to the location of the functional groups.

Final characterization of I will necessitate correlation with the structure of a known triterpene.

(1) C. Djerassi, D. B. Thomas, A. L. Livingston, and C. Ray Thompson, *J. Am. Chem. Soc.*, **79**, 5292 (1957).

(2) E. D. Walter, G. R. Van Atta, C. R. Thompson, and W. D. Maclay, *J. Am. Chem. Soc.*, **76**, 2271 (1954).

(3) Taken from the English term, lucerne, a common name for alfalfa.

(4) E. D. Walter, E. M. Bickoff, C. R. Thompson, C. H. Robinson, and C. Djerassi, *J. Am. Chem. Soc.*, **77**, 4936 (1955).

(10) W. G. Finnegan, R. A. Henry, and Eugene Lieber, *J. Org. Chem.*, **18**, 779 (1953).

(11) See R. A. Henry, W. G. Finnegan, and Eugene Lieber, *J. Am. Chem. Soc.*, **76**, 2894 (1954) and R. M. Herbst and D. F. Percival, *J. Org. Chem.*, **19**, 439 (1954) for proof of structures of analogous compounds.