s-TRIAZINE DERIVATIVES.

4.* SOME PECULIARITIES OF THE REACTIONS OF DICARBETHOXYMETHYLENETRIAZINE DERIVATIVES

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2-(Carbethoxycyanomethylene)-4,6-dimethoxy-1,2-dihydro-s-triazine reacts with hydrochloric acid to give 2-(carbethoxycyanomethylene)-4,6-dioxohexahydro-s-triazine (I) and with boric acid to give a mixture of the first compound with 2-(carbethoxycyanomethylene)-4-oxo-6-methoxy-1,2,3,4-tetrahydro-s-triazine. The products of the reaction of 2,4,6-tris(dicarbethoxymethylene)hexahydro-s-triazine with aniline are 2-(dicarbanilidomethylene)-4-methyl-6-phenylamino-1,2-dihydro-s-triazine (43%), N,N'-diphenylurea (18%), and malonic acid dianilide (18%). In aqueous dioxane in the presence of Al_2O_3 this compound is converted to 2,4-bis(dicarbethoxymethylene)-6-methyl-1,2,3,4-tetrahydro-s-triazine, which reacts with liquid ammonia to give 2-(dicarbethoxymethyl)-4-amino-6-methyl-s-triazine.

A study of the chemical properties of 2-(dicarbethoxymethyl)-4,6-dimethoxy-s-triazine (I) [2] enabled us to uncover some peculiarities of the reactions of compounds of this type. The methoxy groups in the triazine ring of I proved to be more reactive than the ester residues of malonic ester. Treatment of I at room temperature with hydrochloric acid or an alcohol solution of ammonia leads to replacement of the methoxy groups by a hydroxy or amino group to give, respectively 2-(dicarbethoxymethylene)-4,6-dioxohexahydro-s-triazine (II) and 2-(dicarbethoxymethyl)-4-amino-6-methoxy-s-triazine (III). The methoxy groups in 2-(carbethoxycyanomethylene)-4,6-di-methoxy-1,2-dihydro-s-triazine (IV) display similar high reactivity; whereas I undergoes 58% hydrolysis only after 3 days, both methoxy residues in IV undergo virtually quantitative conversion to oxo groups in 3 h. Even under milder conditions, viz., upon heating with boric acid, IV is converted in 2 h to a mixture of 2-(carbethoxycyanomethylene)-4,6-dioxohexahydro-s-triazine (V) (25%) and 2-(carbethoxycyanomethylene)-4-oxo-6-methoxy-1,2,3,4-tetrahydro-s-triazine (VI) (48%). The existence of IV, in contrast to I, in the methylene form with an exocyclic orientation of the double bond evidently creates a definite advantage in the hydrolysis of the methoxy groups to give V and VI.

An exocyclic orientation of the double bonds has an even greater effect on the reactivity of 2,4,6-tris(dicarbethoxymethylene)hexahydro-s-triazine (VII).

Splitting out of two carbethoxy groups from one carbon atom, which due to reaction with aniline form N,N'-diphenylurea (VIII), and replacement of one of the malonic ester residues by a phenylamino group with conversion of the cleaved malonic ester to malonic acid dianiline (IX) occur in the reaction of VII with aniline. As a result of these reactions, 2-(dicarbanilidomethylene)-4-methyl-6-phenylamino-1,2-dihydro-s-triazine (X) is formed from triazine VII. All three substances, viz., VIII, IX, and X, were isolated preparatively from the reaction mixture. Compounds VIII and IX were identified by comparison with authentic samples prepared by alternative synthesis. The structure of X was confirmed by the results of elementary analysis and by the mass spectrum.

The reaction of VII with benzylamine evidently proceeds similarly. However, in this case we were able to isolate preparatively from the reaction products only malonic acid dibenzylamide (XI), which was identified by comparison with a compound prepared by alternative synthesis. When VII is refluxed in aqueous dioxane in the presence of aluminum oxide it undergoes splitting out of two carbethoxy groups attached to one carbon atom to

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*See [1] for Communication 3.

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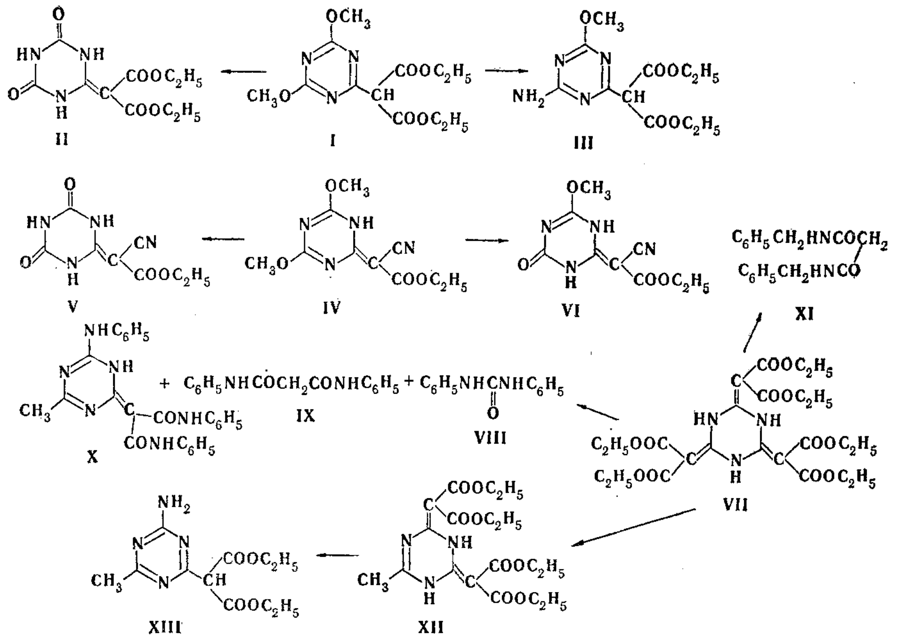

give 2,4-bis(dicarbethoxymethylene)-6-methyl-1,2,3,4-tetrahydro-s-triazine (XII), which on treatment with liquid ammonia gives 2-(dicarbethoxymethyl)-4-amino-6-methyl-s-triazine (XIII). Thus the action of various nucleophilic reagents on 2,4,6-tris(dicarbethoxymethylene)hexahydro-s-triazine (VII) leads to facile splitting out of two carbethoxy groups attached to one carbon atom to give the corresponding methyl derivative of s-triazine in which further replacement of one of the dicarbethoxymethylene residues by a nucleophilic reagent is possible.

EXPERIMENTAL

The IR spectra of the compounds in mineral oil were recorded with a Perkin–Elmer 457 spectrometer. The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Varian XL-100A spectrometer with tetramethylsilane as the internal standard on the δ scale. The mass spectra were obtained with a Varian MAT-112 spectrometer (direct introduction of the samples) at 70 eV and an ionization-chamber temperature of 180°C. Thin-layer chromatography (TLC) was carried out on Silufol-254 plates in a benzene–ethyl acetate system (3:1). Column chromatography (650 by 30 mm) was realized on L 40/100 μm silica gel.

2-(Carbethoxycyanomethylene)-4,6-dioxohexahydro-s-triazine (V). A suspension of 0.5 g (1.98 mmole) sample of 2-(carbethoxycyanomethylene)-4,6-dimethoxy-1,2-dihydro-s-triazine (IV) in 10 ml of hydrochloric acid was stirred at 20°C for 3 h, after which the precipitated V was removed by filtration and washed to neutrality with water to give 0.42 g (94%) of dioxo derivative V as colorless crystals that decomposed at 284°C [3] (from ethanol). The product was insoluble in ether, heptane, benzene, and chloroform but soluble in acetone, dimethylformamide (DMF), and hot alcohol, water, and ethyl acetate. IR spectrum: 1712 (CONH), 1759 ($COOC_2H_5$), and 2210 cm^{-1} (CN). PMR spectrum (in d_6-DMSO): 1.24 (3H, t, $CH_3{-}CH_2$); 4.21 (2H, q, $CH_2{-}CH_3$); 11.45, 11.75 ppm (broad NH signals). Mass spectrum: 224 ($M^{+\cdot}$), 196 [$(M{-}C_2H_4)^{+\cdot}$], 179 [$(M{-}C_2H_5O)^{+}$], 178 [$(M{-}C_2H_5OH)^{+\cdot}$], 152 [$(M{-}CO_2{-}C_2H_4)^{+:}$], 136 [$(M{-}C_2H_5O{-}CONH)^{+}$], 135 [$(M{-}C_2H_5OH{-}CONH)^{+\cdot}$], 110 [$(M{-}CONH{-}C_2H_5O{-}CN)^{+}$], 93 [$(M{-}C_2H_5O{-}2CONH)^{+}$]. Found: C 42.7; H 3.6; N 25.2%. $C_8H_8N_4O_4$. Calculated: C 42.9; H 3.6; N 25.0%.

2-(Carbethoxycyanomethylene)-4-methoxy-6-oxo-1,2,3,4-tetrahydro-s-triazine (VI). A mixture of 1 g (4 mmole) of 2-(carbethoxycyanomethylene)-4,6-dimethoxy-1,2-dihydro-s-triazine and 0.5 g (8 mmole) of boric acid was heated on an oil bath at 160°C for 2 h, after which it was cooled and treated with chloroform, and the unchanged boric acid was removed by filtration. The chloroform mother liquor was evaporated, 15 ml of ether was added, and 0.45 g (48%) of VI was removed by filtration. The product was obtained as colorless crystals with mp 239-239.5°C (from ethanol). It was quite soluble in ordinary organic solvents but insoluble in water and ether and had R_f 0.63 [in a chloroform–methanol system (15:2)]. IR spectrum: 1710 (CONH), 1770 ($COOC_2H_5$), and 2220 cm^{-1} (CN). PMR spectrum: 1.27 (6H, t, $CH_3{-}CH_2$), 3.34 (3H, s, OCH_3), 4.30 (4H, q, $CH_2{-}CH_3$), and 11.68 ppm (broad NH signal). Mass spectrum: 238 ($M^{+\cdot}$), 210 [$(M-C_2H_4)^{+\cdot}$], 193 [$(M-OC_2H_5)^+$], 181 [$(M-CO-C_2H_5)^+$], 166 [$(M-CO_2-C_2H_4)^{+\cdot}$], 136 [$(M-C_2H_5O-CONCH_3)^+$], 135 [$(M-C_2H_5OH-CONCH_3)^{+\cdot}$], 110 [$(M-C_2H_5O-CN-CONCH_3)^+$], 93 [$(M-C_2H_5O-CONH-CONCH_3)^+$]. Found: C 45.0; H 4.2; N 23.7%. $C_9H_{10}N_4O_4$. Calculated: C 45.4; H 4.2; N 23.5%.

The ether mother liquor after separation of VI was evaporated to give 0.32 g of a mixture of substances, which, according to the TLC data, contained $\sim$25% of V with R_f 0.43.

Reaction of 2,4,6-Tris(dicarbethoxymethylene)hexahydro-s-triazine (VII) with Aniline. A solution of 0.55 g (1 mmole) of VII in 7 ml of aniline was heated at 110°C for 5 h and at 165°C for 1 h until the spot of the starting VII with R_f 0.57 disappeared on the thin-layer chromatogram. The unchanged aniline was removed by vacuum distillation, 20 ml of ether was added, and 0.84 g of a precipitate was removed by filtration. Ethanol (30 ml) was added to the precipitate, and the mixture was refluxed for 5 min. It was then filtered to give 0.19 g (43.4%) of 2-(dicarbanilidomethylene)-4-methyl-6-phenylamino-1,2-dihydro-s-triazine (X) as colorless crystals with mp 243-244°C (from dioxane). The product was quite soluble in acetone, chloroform, and benzene but only slightly soluble in alcohol. IR spectrum: 1660 ($CONHC_6H_5$) and 3030-3300 cm^{-1} (NHC_6H_5). Mass spectrum: 438 ($M^{+\cdot}$), 319 [$(M-C_6H_5-N{=}C{=}O)^{+\cdot}$], 200 [$(M-2C_6H_5-NCO)^{+\cdot}$], 119 [$(C_6H_5N{=}C{=}O)^{+\cdot}$], 93 [$(C_6H_5NH_2)^{+\cdot}$]. Found: C 68.1; H 5.2; N 18.9%. $C_{25}H_{22}N_6O_2$. Calculated: C 68.5; H 5.0; N 19.2%.

The alcohol solution remaining after separation of X was evaporated *in vacuo*, and the residue was dissolved in the minimum amount of benzene and chromatographed with a column filled with 30 g of silica gel. Elution with benzene—ethyl acetate (3:1) gave 0.23 g (18%) of N,N'-diphenylurea (VIII) as colorless crystals with mp 240°C (from ethanol) and R_f 0.48. No melting-point depression was observed for a mixture with a genuine sample of N,N'-diphenylurea, and the IR spectra of the two samples were identical.

Further elution from the column with the same mixture of solvents gave 0.14 g (18%) of malonic acid dianilide (IX) as colorless crystals with mp 232°C (from ethanol) and R_f 0.14. No melting-point depression was observed for a mixture with a genuine sample of malonic acid dianilide [4], and the IR spectra of the two samples were identical.

Reaction of 2,4,6-Tris(dicarbethoxymethylene)hexahydro-s-triazine (VII) with Benzylamine. A solution of 0.55 g (1 mmole) of VII in 5 ml of benzylamine was heated at a temperature in the reaction mixture of 125-130°C for 1 h until the spot of starting VII with R_f 0.57 disappeared on the chromatogram; the unchanged benzylamine was removed by vacuum distillation, and 15 ml of benzene—ether (1:1) was added to the residue. The resulting precipitate was removed by filtration to give 0.18 g (21.3%) of malonic acid dibenzylamide (XI) as colorless crystals with mp 144-145°C (from ethanol). No melting-point depression was observed for a mixture with a genuine sample of malonic acid dibenzylamide [5], and the IR spectra of the two samples were identical.

2,4-Bis(dicarbethoxymethylene)-6-methyl-1,2,3,4-tetrahydro-s-triazine (XII). A 24-g sample of Al_2O_3 and 0.9 ml of water were added to a solution of 1.67 g (3 mmole) of VII in 60 ml of dioxane, and the mixture was refluxed with stirring for 30 h. The aluminum oxide was removed by filtration and washed in 50 ml of dioxane, and the combined dioxane solutions were evaporated *in vacuo*. The residue was dissolved in 3 ml of benzene and chromatographed with a column filled with 75 g of silica gel by elution with benzene—ethyl acetate (9:1) to give successively 0.28 g (17%) of starting VII, with R_f 0.57 (no melting-point depression was observed for a mixture with a genuine sample), and 0.2 g (16.5%) of XII, with R_f 0.49, as light-yellow crystals with mp 144-145°C (from heptane). The product was quite soluble in ordinary organic solvents. IR spectrum: 1730 cm^{-1} ($COOC_2H_5$). PMR spectrum: 1.26-1.33 (overlapped t, CH_3-CH_2); 2.25 (3H, s, CH_3); 4.20-4.37 (overlapped q, CH_2-CH_3); 13.0, 13.7 ppm (broad NH signals). Mass spectrum: 411 [$(M)^{+\cdot}$], 366 [$(M-OC_2H_5)^+$], 365 [$(M-C_2H_5OH)^{+\cdot}$], 339 [$(M-CO_2-C_2H_4)^{+\cdot}$], 320 [$(M-C_2H_5OH-C_2H_5O)^+$], 294 [$(M-CO_2-C_2H_4-C_2H_5O)^+$], 293, [$(M-CO_2-C_2H_4-C_2H_5OH)^{+\cdot}$], 267 [$(M-2CO_2-2C_2H_4)^{+\cdot}$], 221 [$(M-2CO_2-2C_2H_4-C_2H_5OH)^{+\cdot}$], 195 [$(M-3CO_2-3C_2H_4)^{+\cdot}$]. 149 [$(M-3CO_2-3C_2H_4-C_2H_5OH)^{+\cdot}$]. Found: C 52.3; H 6.2; N 10.2%. $C_{18}H_{25}N_3O_8$. Calculated: C 52.6; H 6.1; N 10.4%.

2-(Dicarbethoxymethyl)-4-amino-6-methyl-s-triazine (XIII). Liquid ammonia (20 ml) was added to 0.6 g (1.08 mmole) of XII, and the mixture was allowed to stand until the ammonia had evaporated completely. This operation was repeated three times. The residue remaining after evaporation of the last portion of ammonia was dissolved in 3 ml of benzene and chromatographed with a column filled with 75 g of silica gel by elution with benzene—ethyl acetate (9:1). As a result, we obtained successively, 0.18 g (30%) of starting XII with Rf 0.49 (23%) (identified from a mixed melting-point determination) and 0.09 g (23%) of XIII as light-yellow crystals with mp 118-119°C (from ether). The product was quite soluble in ordinary organic solvents. IR spectrum: 1725 ($COOC_2H_5$) and 3380 cm^{-1} (NH_2). PMR spectrum: 1.28 (6H, t, CH_3-CH_2), 2.43 (3H, s, CH_3), 4.27 (4H, q, CH_2-CH_3), 4.72 (1H, s, CH), and 5.82 ppm (broad NH signal). Mass spectrum: 268 ($M^{+\cdot}$), 223 [$(M-OC_2H_5)^+$], 196 [$(M-CO_2-C_2H_4)^{+\cdot}$], 179 [$(M-OC_2H_5-OC_2H_4)^+$], 151 [$(M-CO_2-C_2H_4-OC_2H_5)^+$], 150 [$(M-CO_2-C_2H_4-C_2H_5OH)^{+\cdot}$], 124 [$(M-2CO_2-2C_2H_4)^{+\cdot}$]. Found: C 49.3; H 6.3; N 21.0%. $C_{11}H_{16}N_4O_4$. Calculated: C 49.3; H 6.0; N 20.9%.

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SYNTHESIS OF POLYNUCLEAR UNCONDENSED TRI- AND TETRAZOLES

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A number of the corresponding 1- and 2-propargylazoles were obtained by propargylation of 5-substituted tetrazoles and 1,2,3-triazoles with various degrees of substitution. Polyazole structures with a system of two to five uncondensed azole rings were synthesized by the reaction of the 1- and 2-propargylazoles with organic azides, diazides, and azoles, as well as by oxidative dimerization.

It is known that uncondensed polynitrogenous heterocyclic compounds have pesticidal activity [1-3]. In our search for new substances in the polyazole series that regulate plant growth we accomplished the synthesis of polynuclear uncondensed azoles with two or more heterocycles connected by methylene links. The cycloaddition of organic azides to the triple bond of propargylazoles may serve as one of the variants of this synthesis.

N-Substituted propargyltetrazoles (III, IV) and 1,2,3-triazoles (V, VI) are obtained rather smoothly and in high yields as a result of the direct action of propargyl bromide on tetrazoles (I) and 1,2,3-triazoles (II) in the presence of triethylamine or potassium hydroxide; in this case one generally observes the formation of a mixture of two isomeric propargylazoles (IIIa, b and VIa, b), the IR spectra of which contain bands of vibrations of a terminal acetylenic bond with frequencies of 2100-2140 and 3300-3320 cm^{-1}. The use of sodium ethoxide as a catalyst in the case of the reaction with 1,2,3-triazole promotes a secondary reaction of nucleophilic addition of alcohol to the triple bond and the formation of 1-(2-ethoxy-2-propen-1-yl)-1,2,3-triazole (VIIa). It is possible that an acetylene-allene rearrangement of the propargyl substituent of triazole V precedes the addition reaction. The same VIIa was obtained by treatment of 1-propargyltriazole Va with sodium ethoxide in ethanol. The IR spectrum of ethoxypropenyltriazole VIIa is characterized by the presence of a band of the vibration of a terminal vinyl group (1645-1660 cm^{-1}) and overlapped bands of the vibrations of the multiple bonds of the triazole ring and the ether bond (910, 1076, 1180, 1470, and 1600 cm^{-1}).

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