was stirred vigorously at room temperature with 25 ml of a 1% solution of potassium permanganate in water for 3 hr. Evaporation of the dried benzene layer left 220 mg (94.4%) of dark red α-phenyl-β-phenylazoacrylonitrile, identical (infrared, mixture melting point) with the substance obtained[8] by thermolysis of 5-azido-1,4-diphenylpyrazole. The same product was formed in traces upon long exposure to the air of solutions of the phenylhydrazone in organic solvents and could be isolated by careful concentration, mp 95–96°.

5-Amino-1-(*o*-nitrophenyl)-4-arylpyrazoles (III).—The corresponding *o*-nitrophenylhydrazones (II) (generally 10 mmol) were boiled for 3 hr in 20 ml of glacial acetic acid containing 2 drops of concentrated sulfuric acid. The solvent was then removed *in vacuo*, the residue was triturated with ice water until it solidified, and a few drops of aqueous ammonia were added. The yellow solids so produced were washed with water, dried, and recrystallized from ethyl acetate. The results are collected in Table I. All of the substances so obtained were free of infrared absorption in the 2100–2300-cm^{-1} region, and all showed absorption at 3248–3300 and 3370–3410 cm^{-1} attributable to NH.

Some of the pyrazoles were also prepared directly from the aldehyde and arylhydrazine by refluxing them in ethanol solution for 48 hr, and in some cases ethanol was used as the recrystallizing solvent; yields were similar. When refluxing of the ethanolic reaction mixtures was discontinued as soon as clear solutions were obtained, the products were found to be the arylhydrazones contaminated with only small amounts of the isomeric pyrazoles.

Pyrazolo[5,1-*c*]benzo-1,2,4-triazine 5-Oxides (IV).—Solutions of the 5-aminopyrazoles (III, 5 mmol) in 10 ml of pyridine were mixed with 10 ml of 5% aqueous potassium hydroxide at room temperature; the mixtures soon became deep red. After heating on a steam bath for 3 hr, the mixtures were poured on ice slurried with enough dilute sulfuric acid to make the resulting mixture slightly acidic. The orange precipitates that separated were collected, washed with cold water, and dried. Analytical samples were obtained by recrystallization from ethyl acetate or dimethylformamide. The results are collected in Table I. None of the examples had infrared absorption above 3200 cm^{-1}, and all of them had a strong absorption peak at 1222–1226 cm^{-1}.

Pyrazolo[5,1-*c*]benzo-1,2,4-triazines (VI).—Compounds VIa and VIc were obtained by adding 1 ml of 90% hydrazine hydrate to a hot solution of 5 mmol of IVa or IVc in 200 ml of ethanol to which 100 mg of 5% palladium on charcoal had been added. After 16 hr of refluxing, the catalyst was filtered off, the filtrate was evaporated *in vacuo*, and the residue was recrystallized from ethyl acetate. When the foregoing procedure was applied to IVb, the unsubstituted product VIa was obtained in 69% yield.

3-Phenylpyrazolo[5,1-*c*]benzo-1,2,4-triazine (VIa) was obtained in 73% yield, mp 166–167°, yellow-orange.

Anal. Calcd for $C_{15}H_{10}N_4$: C, 73.15; H, 4.09; N, 22.75. Found: C, 73.22; H, 4.13; N, 22.86.

3-*p*-Methoxyphenylpyrazolo[5,1-*c*]benzo-1,2,4-triazine (VIc) was obtained in 76% yield, mp 152–153°, orange-red.

Anal. Calcd for $C_{16}H_{12}N_4O$: C, 69.55; H, 4.38; N, 20.28. Found: C, 69.53; H, 4.23; N, 20.32.

Preparation of VIa from VII.—A solution of 0.52 g (7.5 mmol) of sodium nitrite in 10 ml of water was added dropwise to a stirred and chilled solution of 1.18 g (5 mmol) of 5-amino-1,4-diphenylpyrazole (VII)[8] in 50 ml of 10% hydrochloric acid. After 15 min, 0.2 g of urea was added, and the mixture was allowed to stand in an ice bath for 3 hr and at room temperature overnight. The mixture was then brought to a boil, whereupon the flocculent, yellow precipitate coagulated to a brown mass. The product was filtered off, washed with cold water, and repeatedly recrystallized from ethanol with the aid of charcoal. A final recrystallization from ethyl acetate gave 0.40 g (32.5%) of yellow needles, mp 166–167°, identical in infrared spectrum and mixture melting point with VIa prepared from IVa.

Registry No.—IIa, 30953-09-4; IIb, 30885-17-7; IIc, 30885-18-8; IId, 30885-19-9; IIe, 30885-20-2; IIf, 30885-21-3; IIIa, 30885-22-4; IIIb, 30885-23-5; IIIc, 30885-24-6; IIId, 30885-25-7; IIIe, 30885-26-8; IIIf, 30885-27-9; IVa, 30885-28-0; IVb, 30885-29-1; IVc, 30885-30-4; IVd, 30885-31-5; IVe, 30885-32-6; IVf, 30885-33-7; VIa, 30885-34-8; VIc, 30885-35-9; α-cyanophenylacetaldehyde phenylhydrazone, 30885-36-0; α-phenyl-β-phenylazoacrylonitrile, 30885-37-1.

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Pyrimido[5,4-*e*]-*as*-triazines. V. The Preparation of Alkyl 6-Amino-*as*-triazine-5-carboxylates from Some 5-Chloro-1,2-dihydropyrimido[5,4-*e*]-*as*-triazines[1]

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The reaction of 5-amino-4-chloro-6-hydrazinopyrimidine (**1**) with ethyl ortho(methoxy)acetate, ethyl ortho(chloromethyl)acetate, and ethyl ortho(ethoxycarbonyl)acetate gave, respectively, the corresponding 3-substituted 5-chloro-1,2-dihydropyrimido[5,4-*e*]-*as*-triazines (**3–5**). Oxidative 5-methoxydechlorination of 5-chloro-1,2-dihydropyrimido[5,4-*e*]-*as*-triazine (**2**), **3**, and **4** with silver oxide in MeOH gave the heteroaromatic 5-methoxy compounds **7–9**. The pyrimidine ring of **7** was opened with methanolic HCl to give methyl 6-amino-*as*-triazine-5-carboxylate (**17**). The formation of **17** and some 3-substituted derivatives was also effected by treatment of **2–5** with Br_2 in alcohol.

In previous papers, we described some replacement reactions of the chloro group of 5-chloro-1,2-dihydropyrimido[5,4-*e*]-*as*-triazine (**2**) with various nucleophiles.[2,3] We now report the preparation and conversion of this and related type compounds to the esters of 6-amino-*as*-triazine-5-carboxylate (*i.e.*, **17**). Previously, the preparation of derivatives of **17** from simple reactants was unsuccessful.[4]

The condensation of **1** with ethyl orthoformate in the presence of hydrochloric acid was shown to give **2**.[5] Similarly, the reaction of **1** with ethyl ortho(methoxy)-acetate,[6] ethyl ortho(chloromethyl)acetate,[7] and ethyl

(1) This investigation was supported by funds from the C. F. Kettering Foundation and Chemotherapy, National Cancer Institute, National Institutes of Health, Contract NIH-71-2021.

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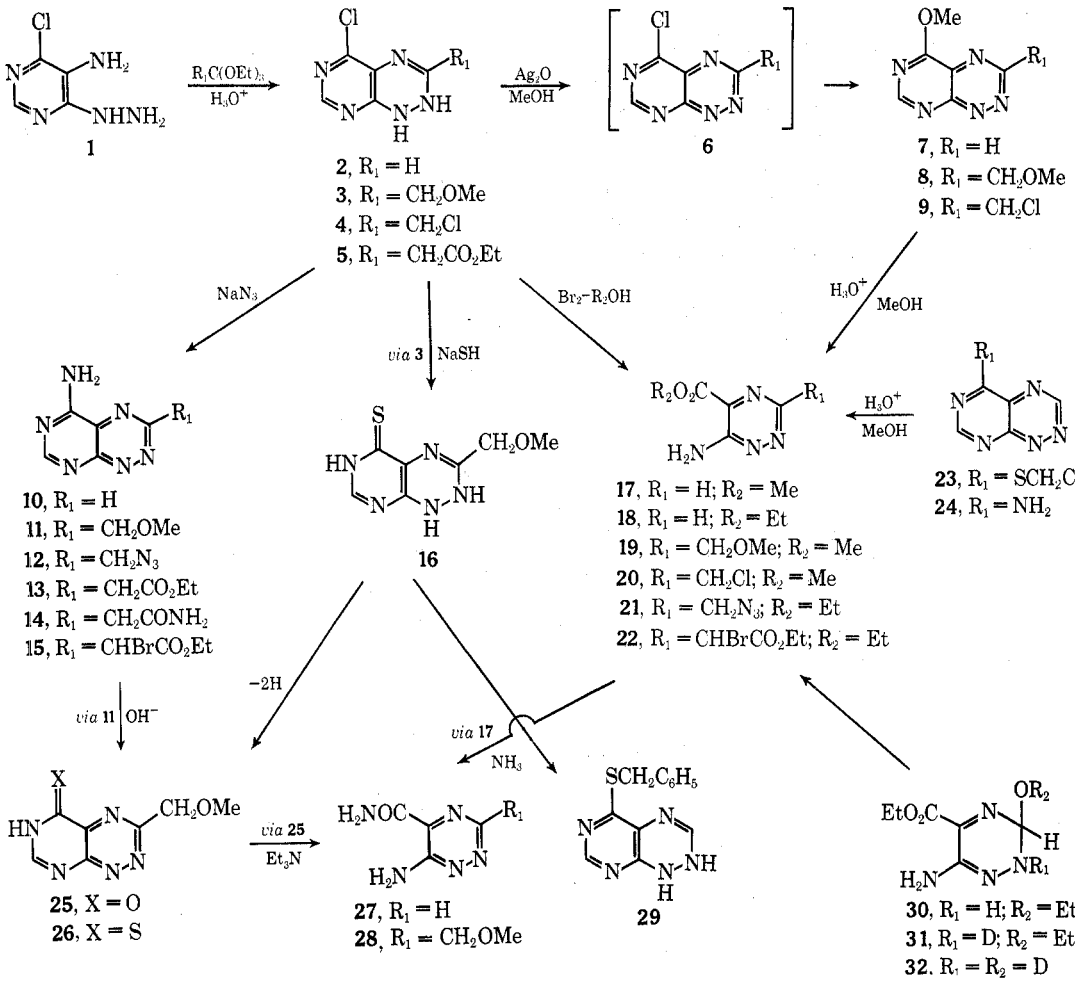

ortho(ethoxycarbonyl)acetate[8] gave, respectively, **3**, **4**, and **5**. Recently the oxidative 5-methoxylation of 1,2-dihydropyrimido[5,4-*e*]-*as*-triazine and its *C*-methyl derivatives with silver oxide in MeOH gave the corresponding 5-methoxypyrimido[5,4-*e*]-*as*-triazines (two oxidation steps).[9] Treatment of **2** with the reagent at room temperature resulted in oxidative 5-methoxydechlorination to give **7**. Similarly, treatment of the dihydro compounds **3** and **4** gave, respectively, the 3-methoxymethyl- and 3-chloromethyl-5-methoxy compounds **8** and **9**. Apparently the pyrimidotriazine **6** is an intermediate in which the reactivity of the chloro group is increased by the increase in the electron-withdrawing ability of the heteroaromatic *as*-triazine ring. The pyrimidine ring of **7** was opened in methanolic HCl to give the triazine-5-carboxylate **17**, presumably formed *via* an imino ether intermediate. Similarly, the pyrimidine ring of the heteroaromatic 5-benzylthio[2] and 5-amino[3] compounds **23** and **24** was opened in hot methanolic HCl to give **17**. The preparation of **17** was also effected by treatment of a methanolic solution of **2** with Br_2. Presumably **7** is an intermediate, which undergoes acidic ring cleavage by the HBr generated in the oxidation step. In the reaction of **2** with Br_2 in EtOH, the product was identified as the hydrobromide of either the 3-ethoxy-2,3-dihydro-*as*-triazine **30** or the corresponding 5-ethoxy-4,5-dihydro compound by its pmr spectrum in deuterated DMSO. This spectrum also showed that the product disassociated with time to give **18**, and the addition of D_2O to this solution gave another form, presumably (from **30**) either **31** or **32**. Structure **30** is favored by steric considerations but protonation of **18** might result in addition across the 4,5[10a] double bond. The corresponding 3-ethoxy-3,4-dihydro-*as*-triazine is a possible addition product, but this compound is probably less stable than **30**.[10b]

The uv spectrum of **17** in HCl changed with time from three peaks to one peak, indicating that this compound also undergoes covalent hydration readily. Neutralization of an aqueous solution of **30** not only removed the HBr but also the covalently bound EtOH to give **18**. Proof of the structure of the latter was provided by its reaction with refluxing NH_3 to give the known amide **27**.[3] These and previous results indicate that in an acidic medium the triazine ring of a dihydropyrimidotriazine is opened to give a pyrimidine, whereas the pyrimidine ring of a heteroaromatic pyrimidotriazine is opened to give an *as*-triazine.[2,3,11]

The dihydropyrimidotriazines **3**–**5** were also treated with Br_2 in MeOH. Compound **3** gave **19**, **4** gave a 4:1 mixture of **20** and the corresponding 3-bromomethyl compound, and **5** gave the 3-bromoacetic acid derivative **22**. The mixture of **20** and the bromomethyl compound was identified by elemental analyses, by its pmr spectrum and by reaction with NaN_3 in EtOH to give **21**, transesterification occurring during the reaction.

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Previously, the reaction of **2** with NaN_3 gave directly the heteroaromatic 5-aminopyrimidotriazine **10**.[3] Similarly, **3–5** gave **11–13**. In **4** azidodechlorination of both the 5-chloro- and 3-chloromethyl groups occurred, but only the 5-azido group was converted to an amino group. Treatment of **13** with refluxing NH_3, and Br_2 in $CHCl_3$, gave the acetamide **14** and the α-bromoacetate **15**, respectively. Reaction of **11** with aqueous NaOH gave **25**, and reaction of **3** with hydrated NaSH gave **16**. The latter was oxidized with diethyl azodicarboxylate to give **26** and alkylated with benzyl chloride to give **29**. The pyrimidine ring of **25** was opened with aqueous ethanolic triethylamine to give **28**.

Experimental Section

Melting points were determined on a Kofler–Heizbank apparatus. The uv absorption spectra of solutions were determined with Cary Model 14 and 17 spectrophotometers, whereas the ir absorption spectra were determined in pressed KBr disks with Perkin–Elmer Models 521 and 621 spectrophotometers. The pmr spectra were obtained on DMSO-d_6 solutions (5–10% w/v) with a Varian A-60A spectrometer at a probe temperature of about 37° with tetramethylsilane as an internal reference. Chemical shifts quoted in the case of multiplets are measured from the approximate center, and the relative peak areas are given to the nearest whole number.

Condensation of Ortho Esters with 5-Amino-4-chloro-6-hydrazinopyrimidine (1).—Ethyl ortho(chloro)acetate (50 ml)[7] was added with vigorous stirring to a mixture of **1** (5.0 g) and concentrated HCl (2.5 ml). After 1.5 hr, the hydrochloride of **4** was collected by filtration, washed with EtOAc (800 ml), and dried *in vacuo* over P_2O_5: yield 6.1 g (76%); mp 180–181° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12a] 0.1 *N* HCl, 335 (5.50); pmr δ 3.87 (2, CH_2), 7.46 (1, CH), ~9.3 (NH, HCl, H_2O).

Anal. Calcd for $C_6H_5Cl_2N_5 \cdot HCl$: C, 28.32; H, 2.38; N, 27.82. Found: C, 28.52; H, 2.53; N, 27.87.

Similarly, ethyl ortho(methoxy)acetate[6] was added with stirring to a mixture of **1** (5.0 g) and concentrated HCl (3.0 ml). After 2 hr, the resulting solution deposited a mixture of **3** and its hydrochloride, which was collected by filtration and washed with petroleum ether, yield 4.5 g. The combined filtrate and wash deposited an additional 1.4 g. The total yield was 5.9 g (75%), mp 143–145° with presoftening. Recrystallization of this material from THF gave the hygroscopic hydrochloride salt of **3**: yield 2.9 g; mp 147–149° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] 0.1 *N* HCl, 224 (14.4), 337 (5.03).

Anal. Calcd for $C_7H_8ClN_5O \cdot HCl$: C, 33.62; H, 3.63; N, 28.00. Found: C, 33.61; H, 4.43; N, 27.96.

The filtrate from above was evaporated to dryness *in vacuo*, and the resulting residue was recrystallized from petroleum ether (bp 85–105°) to give **3**: yield 0.84 g; mp 148–150° dec; pmr δ 3.27 (3, CH_3), 3.59 (2, CH_2), 7.43 (1, CH), ~7.6, ~9.2 (1, 1, NH).

Anal. Calcd for $C_7H_8ClN_5O$: C, 39.36; H, 3.77; Cl, 16.6; N, 32.78. Found: C, 39.53; H, 3.68; Cl, 16.7; N, 32.84.

Similarly, a mixture of **1** (18.5 g), concentrated HCl (9.8 ml), and ethyl ortho(ethoxycarbonyl)acetate (93 ml)[8] was stirred with cooling for 45 min. The solid (30.9 g) was collected by filtration and added with stirring to a 4.2% (w/v) solution of $NaHCO_3$ (310 ml) to give **5**: yield 17 g (57%); mp 177° dec with presoftening from 171° (recrystallization from petroleum ether did not change the melting point); λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] 0.1 *N* HCl, 224 (15.5), 337 (5.49); ν_{max}, cm^{-1}, 1735, 1710 (CO); pmr δ 1.21 (t, 3, CH_3), 3.98 (2, CH_2CO_2), 4.12 (q, 2, CH_2O), 7.45 (1, CH), 7.88, 9.13 (1, 1, NH).

Anal. Calcd for $C_9H_{10}ClN_5O_2$: C, 42.28; H, 3.94; N, 27.39. Found: C, 42.49; H, 4.10; N, 27.21.

Preparation of 5-Methoxypyrimido[5,4-*e*]-*as*-triazines (7–9).—A mixture of **2** (2.0 g)[5] and Ag_2O (5.4 g) in MeOH (400 ml) was stirred at room temperature for 40 hr. The residue was removed by filtration, the filtrate was evaporated to dryness, and the resulting product was recrystallized from petroleum ether to give **7**: yield 0.82 g (43%); mp 99–100° (lit.[9] mp 100°); λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] pH 7, 227 (16.4),255 sh (2.12), 326 (5.72).

Similarly, treatment of **3**·HCl (2.0 g) gave a solid that was recrystallized from hexane to give **8**: yield 0.84 g (51%); mp 91°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12a] pH 7, 257 sh (3.12), 332 (5.68); pmr δ 3.45 (3, 3-CH_3O), 4.25 (3, 5-CH_3O), 5.10 (2, CH_2), 9.12 (1, CH).

Anal. Calcd for $C_8H_9N_5O_2$: C, 46.38; H, 4.38; N, 33.80. Found: C, 46.20; H, 4.69; N, 33.95.

Similarly, treatment of **4**·HCl (5.0 g) gave a residue that was extracted with ether. Removal of ether *in vacuo* gave an oil that was triturated with H_2O to give solid **9**, yield 2.1 g, mp ~67°. Recrystallization of this sample from hexane gave pure **9**: yield 0.70 g (17%); mp 79–81°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12a] pH 7, 258 sh (3.35), 332 (5.73); pmr δ 4.25 (3, CH_3), 5.38 (2, CH_2), 9.18 (1, CH).

Anal. Calcd for $C_7H_6ClN_5O$: C, 39.73; H, 2.86; N, 33.10. Found: C, 39.69; H, 2.92; N, 33.32.

The hexane and H_2O filtrates from above gave an additional 1.5 g of crude **9**, mp ~69° with presoftening. The infrared spectrum (ν_{max} 1710 cm^{-1}) indicated that this material was contaminated with the corresponding 5(6H)-oxy compound.

5-Amino-3-methoxymethylpyrimido[5,4-*e*]-*as*-triazine (11).—A mixture of **3** HCl (5.0 g) and NaN_3 (3.3 g) in 1:1 EtOH–H_2O (100 ml) was refluxed for 2 hr. The resulting solution was evaporated to dryness *in vacuo*, and the residue was extracted with hot THF. Removal of the solvent gave a solid which was recrystallized from EtOAc to give **11** in two crops: yield 3.0 g (78%); mp 178–180°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] pH 7, 222 (11.1), 253 (12.3), 283 sh (2.35), 373 (5.33); pmr δ 3.52 (3, CH_3), 5.05 (2, CH_2), 8.70, ~8.8 (3, CH, NH_2).

Anal. Calcd for $C_7H_8N_6O$: C, 43.75; H, 4.20; N, 43.73. Found: C, 43.77; H, 4.16; N, 43.90.

5-Amino-3-azidomethylpyrimido[5,4-*e*]-*as*-triazine (12).—A solution of NaN_3 (4.0 g) in H_2O (40 ml) was added to a solution of **4** HCl (2.0 g) in EtOH (130 ml). The mixture was stirred at room temperature for 18 hr and evaporated to dryness *in vacuo* at ~50°. The resulting residue was extracted with $CHCl_3$ (three 200-ml portions), and the combined extracts were evaporated to dryness, yield 1.2 g (75%), mp 177° dec. Recrystallization of a portion of this sample (0.2 g) from C_6H_6 gave pure **12**: yield 0.1 g; mp 179–180° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12a] pH 7, 254 (13.0), 284 sh (2.78), 376 (5.44); ν_{max}, cm^{-1}, 2110 (N_3); pmr δ 5.05 (2, CH_2), 8.67, ~8.7 (3, CH, NH_2).

Anal. Calcd for $C_6H_5N_9$: C, 35.47; H, 2.48; N, 62.05. Found: C, 35.63; H, 2.56; N, 62.03.

Ethyl 5-Aminopyrimido[5,4-*e*]-*as*-triazine-3-acetate (13).—A mixture of **5** (1.0 g) and NaN_3 (0.6 g) in 1:1 EtOH–H_2O (40 ml) was stirred at room temperature for 18 hr and evaporated to dryness *in vacuo*. The residue was extracted with THF, the extract was evaporated to dryness, and the resulting solid was recrystallized from C_6H_6: yield 0.43 g (47%); mp 175°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] pH 7, 218 (11.0), 255 (13.5), 284 sh (3.05), 374 (5.48); ν_{max}, cm^{-1}, 1730 (CO); pmr δ 1.22 (t, 3, CH_3), 4.20 (q, 2, CH_2O), 4.46 (2, CH_2CO_2), 8.68, ~8.8 (3, CH, NH_2).

Anal. Calcd for $C_9H_{10}N_6O_2$: C, 46.15; H, 4.30; N, 35.89. Found: C, 46.27; H, 4.40; N, 35.68.

5-Aminopyrimido[5,4-*e*]-*as*-triazine-3-acetamide (14).—A mixture of **13** (0.90 g) and liquid NH_3 (~30 ml) was confined in a Parr bomb for 18 hr at room temperature. The contents of the bomb were evaporated to dryness, and the residue was recrystallized from H_2O: yield 0.24 g (30%); mp >264°; λ_{max}, nm,[12a] pH 7, 263, 395 unstable; ν_{max}, cm^{-1}, 1670 sh (CO), 1615 (NH_2).

Anal. Calcd for $C_7H_7N_7O$: C, 40.97; H, 3.44; N, 47.79. Found; C, 40.87; H, 3.45; N, 47.49.

An additional amount of crude **14** (0.4 g) was obtained from H_2O filtrate. The total yield was 0.64 g (81%).

Ethyl α-Bromo-5-aminopyrimido[5,4-*e*]-*as*-triazine-3-acetate Hydrobromide (15).—A mixture of **13** (400 mg) and Br_2 (0.1 ml) in $CHCl_3$ (70 ml) was stirred at room temperature for 24 hr followed by the addition of a solution of Br_2 (0.1 ml) in $CHCl_3$ (10 ml). After 90 hr, the solid was collected by filtration and recrystallized from CH_3CN: yield 81 mg (12%); mp ~187° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] pH 7, 260 (13.0), 294 sh (3.51), 379 (5.45); ν_{max}, cm^{-1}, 1740 (CO); pmr δ 1.20 (t, 3, CH_3), 4.25 (q, 2, CH_2), 6.53 (1, CHBr), 8.82 (1, CH), ~7.2, ~9.7 (3, NH_2, HBr).

Anal. Calcd for $C_9H_9BrN_6O_2 \cdot HBr$: C, 27.43; H, 2.56; N, 21.33. Found: C, 27.61; H, 2.55; N, 21.44.

(12) Each solution contains 10% dissolving solvent and 90% appropriate aqueous solvent: (a) 8% methanolic DMSO; (b) MeOH; (c) 0.1 *N* NaOH.

Concentration of recrystallization filtrate deposited an additional amount (292 mg) of crude **15**. The total yield was 373 mg (55%).

1,2-Dihydro-3-methoxymethylpyrimido[5,4-*e*]-*as*-triazine-5-(6*H*)-thione (16).—A mixture of **3** (5.2 g), EtOH (650 ml), and hydrated NaSH (26 g) was refluxed for 1 hr, cooled to room temperature, and filtered. The filtrate was evaporated to dryness *in vacuo*, and the residue was dissolved in H_2O and acidified with HOAc. The solid that deposited was collected by filtration, washed with C_6H_6, and reprecipitated from a dilute NaOH solution by the addition of dilute HCl: yield 3.3 g (64%); mp ~253–254° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12c] 0.1 *N* HCl, 234 (7.04), 260 (5.68), 336 (2.94), 406 (2.15); pmr δ 3.25 (3, CH_3), 3.68 (2, CH_2), 6.20, 8.95, ~12.7 (1, 1, 1, NH), 7.57 (1, CH).

Anal. Calcd for $C_7H_9N_5OS$: C, 39.79; H, 4.30; N, 33.15; S, 15.18. Found: C, 39.90; H, 4.31; N, 33.10; S, 15.05.

Methyl 6-Amino-*as*-triazine-5-carboxylate (17). Acidic Cleavage of 7.—A solution of **7** (300 mg) in MeOH (10 ml) containing 1 *N* HCl (2.0 ml) was stirred at room temperature for 18 hr. The product that deposited was collected by filtration: yield 127 mg (45%); mp 186–187° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] 0.1 *N* HCl, 233, 282, 366 changing to 282 (4.36), pH 7, 240 (10.8), 363 (4.17); ν_{max}, cm^{-1}, 1710 (CO); pmr δ 3.90 (3, CH_3), ~7.5 (2, NH_2), 9.15 (1, CH).

Anal. Calcd for $C_5H_6N_4O_2$: C, 38.96; H, 3.92; N, 36.35. Found: C, 38.84; H, 4.12; N, 36.38.

The MeOH filtrate was evaporated to dryness *in vacuo*, and the resulting residue was extracted with $CHCl_3$ to give an additional 79 mg of **17**. The total yield was 206 mg (73%).

Similarly, a solution of **23**[2] was heated at 60° for 2 hr to give a 90% crude yield of **17**. Also, treatment of **24**[3] at 75° for 5 hr gave a 29% crude yield of **17**.

Oxidation and Ring Opening of 5-Chloro-1,2-dihydropyrimido[5,4-*e*]-*as*-triazines (2–5).—A solution of Br_2 (6.1 ml) in MeOH (100 ml) was added slowly with stirring to a suspension of **2**[5] (10 g) in MeOH (100 ml). After 15 min, the resulting warm solution was diluted with H_2O (10 ml), stirred at room temperature for an additional 3 hr, and evaporated to dryness *in vacuo*. The residue was dissolved in H_2O (300 ml); the solution was neutralized with $NaHCO_3$ and extracted with $CHCl_3$ (three 1000-ml portions). The extracts were dried ($MgSO_4$) and evaporated to dryness to give **17**, yield 4.3 g (47%), mp 181° dec. Recrystallization of a small sample from hexane gave a product identical with that described above, mp 185–186° dec.

Similarly, **3** (2.0 g) and Br_2 (0.82 ml) in MeOH (40 ml) and H_2O (2.0 ml) gave **19**, yield 0.93 g (59%), mp 144–145°. Recrystallization of a sample (0.20 g) from C_6H_6 gave the analytical sample (0.13 g): mp 149–150°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] pH 7, 245 (14.1), 368 (4.2); ν_{max}, cm^{-1}, 1715 (CO); pmr δ 3.33 (3, CH_3O), 3.91 (3, CH_3O_2C), 4.58 (2, CH_2), 7.5 (2, NH_2).

Anal. Calcd for $C_7H_{10}N_4O_3$: C, 42.42; H, 5.09; N, 28.27. Found: C, 42.45; H, 4.91; N, 28.11.

In the reaction of **4** (1.0 g) with Br_2 in MeOH (20 ml) and H_2O (1.0 ml), the residue obtained by evaporation of the reaction mixture was dissolved in H_2O (20 ml) and neutralized with $NaHCO_3$ to deposit a 4:1 mixture of **20** and the corresponding 3-bromomethyl compound: yield 0.58 g (70%); mp ~163° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12a,13] pH 7, 252 (14.0), 370 (3.99); ν_{max}, cm^{-1}, 1715 (CO); pmr δ 3.94 (3, CH_3), 4.83, 4.93 (2, CH_2Cl, CH_2Br), ~7.7 (2, NH_2).

Anal. Calcd for $(C_6H_7ClN_4O_2)_4 \cdot C_6H_7BrN_4O_2$: C, 34.29; H, 3.35; N, 26.65. Found: C, 33.97; H, 3.30; N, 26.30.

Similarly, **5** (1.0 g) and Br_2 (0.40 ml) in EtOH (20 ml) and H_2O (1.0 ml) gave an H_2O-insoluble residue that was extracted into $CHCl_3$. The residue obtained from the dried extract ($MgSO_4$) was washed with hexane to give **22**: yield 0.34 g (26%); mp ~115° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12a] pH 7, 254 (9.75), 366 (3.13); ν_{max}, cm^{-1}, 1740, 1710 (CO); pmr (DMSO-d_6–D_2O), δ 1.27 (m, CH_3), 4.32 (m, CH_2), 6.24 (CHBr).

Anal. Calcd for $C_{10}H_{13}BrN_4O_4$: C, 36.05; H, 3.93; Br, 23.99; N, 16.82. Found: C, 35.93; H, 4.00; Br, 24.26; N, 17.09.

Ethyl 6-Amino-*as*-triazine-5-carboxylate (18) and Ethyl 6-Amino-3-ethoxy-2,3-dihydro-*as*-triazine-5-carboxylate Hydrobromide (30).—A solution of Br_2 (0.61 ml) in EtOH (50 ml) was added with stirring over a 10-min period to a suspension of **2**[5] (2.0 g) in EtOH (120 ml). After 1 hr, this solution was concentrated *in vacuo* to half-volume and allowed to stand at room temperature for 18 hr. The solid that deposited was collected by filtration, washed with Et_2O, and recrystallized from ethanol to give **30**: yield 1.3 g (37%); mp 191° dec with presublimation; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] 0.1 *N* HCl, 284 (4.72), pH 7, 241 (11.5), 364 (4.58); ν_{max} cm^{-1}, 1760 (CO); pmr δ 1.20 (m, CH_3 of **30**, **18**, and EtOH), 3.44, 4.32 (m, CH_2 of **30**, **18**, and EtOH), ~8.6 (br, CH of **30**), 9.16 (CH of **18**), ~7.7, ~11 (NH, HBr, OH). Addition of D_2O gave a new peak at δ 8.45 (CH).

Anal. Calcd for $C_6H_8N_4O_2 \cdot C_2H_6O \cdot HBr$: C, 32.56; H, 5.12; N, 18.98. Found: C, 32.67; H, 5.08; N, 19.18.

A sample of **30** (200 mg) was dissolved in H_2O (10 ml); this solution was neutralized with NaOAc (56 mg) and evaporated to dryness. The residue was extracted with hot petroleum ether, and the extract was cooled to deposit **18**: yield 63 mg (55%); mp 119°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] 0.1 *N* HCl, 237, 282, 364 unstable; pH 7, 241 (11.3), 363 (4.48); ν_{max}, cm^{-1}, 1705; pmr δ 1.33 (t, 3, CH_3), 4.38 (q, 2, CH_2), 7.5 (2, NH_2), 9.17 (1, CH).

Anal. Calcd for $C_6H_8N_4O_2$: C, 42.86; H, 4.80; N, 33.32. Found: C, 42.87; H, 4.85; N, 33.19.

Ethyl 6-Amino-3-azidomethyl-*as*-triazine-5-carboxylate (21).—A suspension of a 4:1 mixture of **20** and the corresponding 3-bromomethyl compound (0.40 g) and NaN_3 (1.0 g) in 5:2 EtOH–H_2O (35 ml) was stirred at room temperature for 20 hr and evaporated to dryness *in vacuo*. The residue was washed with H_2O and dissolved in ether ($MgSO_4$), and the resulting solution was evaporated to dryness *in vacuo*: yield 0.22 g (56%); mp 134–135°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12a] pH 7, 246 (14.8), 368 (4.15); ν_{max}, cm^{-1}, 2130, 2095 (N_3), 1710 (CO); pmr δ 1.35 (t, 3, CH_3), 4.41 (q, 2, CH_2), 4.67 (2, CH_2), ~7.6 (2, NH_2).

Anal. Calcd for $C_7H_9N_7O_2$: C, 37.67; H, 4.06; N, 43.93. Found: C, 37.62; H, 3.82; N, 43.61.

3-Methoxymethylpyrimido[5,4-*e*]-*as*-triazin-5(6*H*)-one (25).—A suspension of **11** (1.0 g) in H_2O (10 ml) containing 1 *N* NaOH (5.3 ml) was stirred at room temperature for 2 hr. The resulting solution was acidified with 1 *N* HCl (11 ml), and the yellow solid that deposited was collected by filtration and dried *in vacuo* over P_2O_5 at 78°: yield 0.75 g (75%); mp ~175° dec; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] 0.1 *N* NaOH, 251 (14.7), 282 sh (3.18), 372 (4.58); ν_{max}, cm^{-1}, 1715, 1700 (CO).

Anal. Calcd for $C_7H_7N_5O_2$: C, 43.52; H, 3.66; N, 36.27. Found: C, 43.78; H, 3.72; N, 36.28.

3-Methoxymethylpyrimido[5,4-*e*]-*as*-triazine-5(6*H*)-thione Hemihydrate (26).—A mixture of **16** (1.0 g), diethyl azodicarboxylate (1.5 ml), and $CHCl_3$ (100 ml) in a flask protected from light with aluminum foil was stirred at room temperature for 20 hr, then evaporated to dryness *in vacuo*. The solid was washed with MeOH (100 ml) and dried *in vacuo* over P_2O_5 to give mainly **26**, yield 0.84 g (85%), mp ~226° dec (taken rapidly). A solution of the product (0.17 g) in H_2O containing 1 *N* NaOH (0.9 ml) was neutralized with 1 *N* HCl (0.9 ml) to deposit the hemihydrate (0.07 g): mp 160–161° dec with presoftening; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12c] 0.1 *N* NaOH, 254 (11.3), 375 (2.18), 455 (2.77); pmr δ 3.58 (CH_3), 5.27 (CH_2), 9.33 (CH), ~13 (NH).

Anal. Calcd for $C_7H_7N_5OS \cdot {}^1/_2H_2O$: C, 38.51; H, 3.69; N, 32.09. Found: C, 38.43; H, 4.05; N, 32.09.

6-Amino-*as*-triazine-5-carboxamide (27).—A mixture of **18** (200 mg) and liquid NH_3 was refluxed under a Dry Ice–acetone condenser for 8 hr. The ammonia was allowed to evaporate, and the practically pure product (156 mg) was recrystallized from MeOH, yield 47 mg (28%), mp 253° (lit.[3] mp 253–254°).

6-Amino-3-methoxymethyl-*as*-triazine-5-carboxamide (28).—A mixture of **25** (4.4 g), EtOH (90 ml), H_2O (9.0 ml), and Et_3N (9.0 ml) was refluxed for 22 hr. The solid that deposited was collected by filtration and dried *in vacuo* over P_2O_5: yield 2.1 g (50%); mp 206–207°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] pH 7, 243 (14.2), 362 (3.91); ν_{max}, cm^{-1}, 1700 (CO).

Anal. Calcd for $C_5H_9N_5O_2$: C, 39.34; H, 4.95; N, 38.24. Found: C, 39.36; H, 5.04; N, 38.19.

5-(Benzylthio)-1,2-dihydro-3-methoxymethylpyrimido[5,4-*e*]-*as*-triazine (29).—A solution of **16** (1.0 g) in H_2O (25 ml) containing benzyl chloride (0.6 ml) and 1 *N* NaOH (5.0 ml) was stirred at room temperature for 5 hr. The solid that deposited (1.2 g) was extracted with hot C_6H_6, the extract was evaporated to dryness, and the resulting residue (0.91 g) was recrystallized from petroleum ether: yield 0.34 g; mp 134–135°; λ_{max}, nm ($\epsilon \times 10^{-3}$),[12b] pH 7, 242 (13.8), 265 sh (6.90), 392 (8.07); pmr δ 3.25 (3, CH_3), 3.61 (2, CH_2O), 4.33 (2, CH_2S), 7.05, 8.83 (1, 1, NH), 7.35 (5, C_6H_5), 7.71 (1, CH).

(13) The ϵ values were calculated from the molecular weight of the mixture.

Anal. Calcd for $C_{14}H_{16}N_6OS$: C, 55.79; H, 5.05; N, 23.24. Found: C, 55.84; H, 5.04; N, 23.20.

Registry No.—**3**, 30855-40-4; **3** HCl, 30855-41-5; **4** HCl, 30855-42-6; **5**, 30855-43-7; **8**, 30855-44-8; **9**, 30855-45-9; **11**, 30855-46-0; **12**, 30855-47-1; **13**, 30855-48-2; **14**, 30855-49-3; **15**, 30936-92-6; **16**, 30855-50-6; **17**, 30855-51-7; **18**, 30855-52-8; **19**, 30855-53-9; **20**, 30855-54-0; **20** (R_1 = CH_2Br), 30855-55-1; **21**, 30855-56-2; **22**, 30855-57-3; **25**, 30855-58-4; **26**, 30855-59-5; **28**, 30855-60-8; **29**, 30855-61-9; **30**, 30855-62-0.

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The Facile Isomerization in the 1,3-Dipolar Addition Reactions of Substituted 1-Alkoxycarbonyliminopyridinium Ylides with Dimethyl Acetylenedicarboxylate[1]

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The 1,3-dipolar cycloaddition of substituted 1-alkoxycarbonyliminopyridinium ylides (**1**, **2**, **6**, **7**, **10–14**, and **32–34**) with dimethyl acetylenedicarboxylate in the absence and the presence of tetracyanoethylene produced pyrazolo[1,5-*a*]pyridines (**3–5**, **8**, **9**, and **39**), dihydropyrazolo[1,5-*a*]pyridines (**15–19**), vinylpyridines (**20–24** **35–37**), and cycloadducts (**25**, **26**, and **29–31**). The dihydro compounds **22** and **23** were easily transformed into the vinylpyridines **41** and **42**. Structural elucidation of the cycloadducts and the rearranged products was accomplished by spectral means, while the structures of **45** and **46** were established by chemical degradation. Some mechanisms for the rearranged products are also discussed.

Although 1,3-dipolar cycloaddition reactions of zwitterionic ylides have been extensively studied,[2] the addition of 1-alkoxycarbonyliminopyridinium ylides (pyridinium *N*-betaines) to dipolarophiles have not yet been reported. Okamoto, *et al.*,[3] observed that *N*-iminopyridinium ylides reacted with nucleophilic reagents, but the reactions of *N*-methylimino- and *N*-acetyliminopyridinium ylides with a dipolarophile such as acetonitrile did not afford 1,3-dipolar cycloadducts; the contrasting reactivity of these compounds was attributed to the difference in basicity. The mechanism of 1,3-dipolar cycloaddition reactions of the heteroaromatic nitrogen ylides with dipolarophiles has been discussed,[3] but information concerning the detailed mechanisms and, in particular, convincing evidence for dihydro-type intermediates have not been presented. In continuation of work in this area,[4] this paper deals with the 1,3-dipolar cycloaddition of substituted 1-alkoxycarbonyliminopyridinium ylides with dimethyl acetylenedicarboxylate (DAC) in the presence and the absence of tetracyanoethylene (TCNE).

Results and Discussion

Several ring-substituted 1-alkoxycarbonyliminopyridinium ylides **1**, **2**, **6**, **10–14**, and **32–34** were prepared by the modified Gösl method.[4] The ylide **7**[5] was obtained by the modified Hafner method described by Snieckus, *et al.*, and the yield was increased to 40%.

1,3-Dipolar Cycloaddition of Substituted Pyridinium Ylides with DAC.—The 1,3-dipolar cycloaddition reactions of the 1-alkoxycarbonyliminopyridinium ylides with dimethyl acetylenedicarboxylate (DAC) were carried out both in the absence and the presence of tetracyanoethylene (TCNE) in benzene or acetonitrile. These results are summarized in Tables I and II.

TABLE I

1,3-DIPOLAR CYCLOADDITION OF THE YLIDES AND DAC IN THE ABSENCE OF TCNE

	Yields of reaction products[a]					
	Dihydropyrazolopyridine derivatives		Vinylpyridine derivatives		Pyrazolopyridine derivatives	
Ylide	Yield, %	Compd no.	Yield, %	Compd no.	Yield, %	Compd no.
1					*Ca.* 1	3
2					Trace	4 + 5
6					27	8
7					28	9
10	12	15	22	20		
11	11	16	24	21		
12	80	17	3	22		
13	68	18	17	23		
14	56	19	44	24		
32			43	35		
33			27	36		
34			5	37		

[a] C, H, and N analyses within ±0.35% for all products: Ed.

The reactions of **1** and **2** with DAC in the presence of TCNE gave the pyrazolopyridine derivative **3**[2] and an isomeric mixture of **4** and **5** (on the basis of the nmr inspection), respectively, in very low yields. In the reactions in the absence of TCNE, the pyrazolopyridine derivatives were formed in only trace amounts. On similar treatment of γ-substituted pyridinium ylides

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(2) For leading references, see (a) R. Huisgen, R. Grashey, and J. Sauer, "The Chemistry of Alkenes," S. Patai, Ed., Interscience, New York, N. Y., 1964, Chapter 11, p 739; (b) V. Boekelheide and N. A. Fedoruk, *J. Org. Chem.*, **33**, 2062 (1968).

(3) T. Okamoto, M. Hirobe, Y. Tamai, and E. Yabe, *Chem. Pharm. Bull.*, **14**, 506 (1966).

(4) (a) T. Sasaki, K. Kanematsu, and Y. Yukimoto, *J. Chem. Soc. C*, 481 (1970); (b) T. Sasaki, K. Kanematsu, A. Kakehi, I. Ichikawa, and K. Hayakawa, *J. Org. Chem.*, **35**, 426 (1970).

(5) This ylide could not be synthesized by the Gösl method. Although 4-ethoxycarbonyl-1-ethoxycarbonyliminopyridinium ylide was prepared by the Hafner method, the yield was reported as only 1%; see A. Balasubramanian, J. M. McItosh, and V. Snieckus, *ibid.*, **35**, 433 (1970).