Pyrrolo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-diones. Part I. Synthesis from 1,3,5-Triazine-2,4(1*H*,3*H*)-diones

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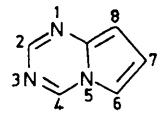
Reaction of ethyl bromopyruvate (4) with 6-methyl- (2) and 6-benzyl-1,3,5-triazine-2,4(1*H*,3*H*)-diones (3) gave moderate yields of 1,2,3,4-tetrahydro-2,4-dioxopyrrolo[1,2-*a*][1,3,5]triazine-7-carboxylate esters, (10) and (11), respectively. Other bromocarbonyl compounds failed to react or gave low yields of product. Pyrrolo[1,2-*a*]-[1,3,5]triazine-2,4(1*H*,3*H*)-dione (14) has been synthesised from the 7-ester and a bromination is shown to yield 8-mono- (17) and 6,8-di-bromo-derivatives (18). 6-Methyl-1,3-diphenacyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione (19) yields 3-phenacyl-7-phenylpyrrolo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-dione (20) with acetic acid.

THE pyrrolo[1,2-*a*][1,3,5]triazine system has been little studied and the literature contains only one reference to the synthesis of tetrahydro-derivatives,[1] and one to the synthesis of benzo-derivatives.[2] The fully aromatic system (1) is unknown. The chemotherapeutic importance of the 1,3,5-triazines[3] and our continued interest in the chemistry of *N*-bridgehead compounds led us to investigate the preparation of the pyrrolo-[1,2-*a*][1,3,5]triazines.

The synthetic route envisaged was an extension of the Tschitschibabin indolizine synthesis in which α-picoline or a derivative is quaternised with α-halogeno-ketones and then treated with aqueous alkali. This type of

[1] R. Richter, *Chem. Ber.*, 1968, **101**, 3002.
[2] R. Huisgen, K. Herbig, and M. Morikawa, *Chem. Ber.*, 1967, **100**, 1107.
[3] J. Škoda, *Progr. Nucleic Acid Res.*, 1963, **2**, 197; G. H. Hitchings and J. J Burchenal, *Adv Enzymol.*, 1965, **27**, 417; B. R. Baker, 'The Design of Active-Site-Directed Irreversible Enzyme Inhibitors,' Wiley, New York, 1967.

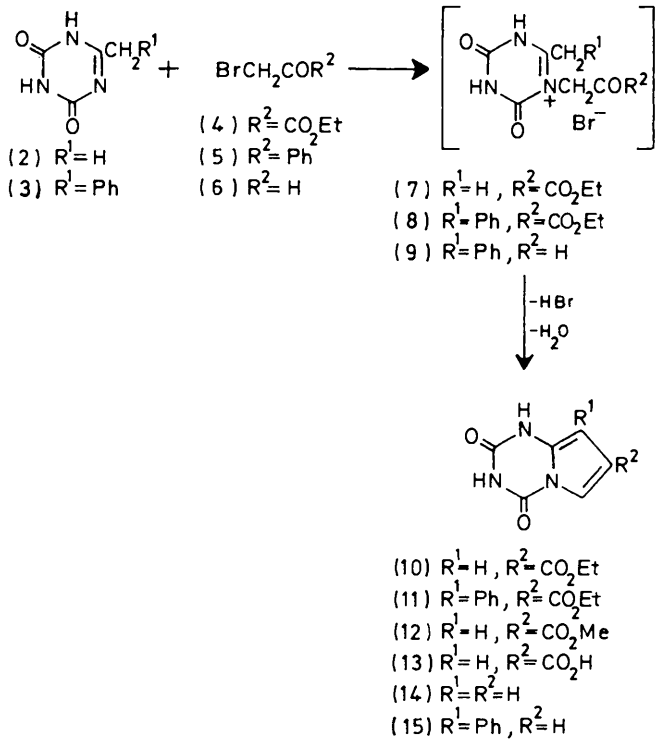
reaction has thus far been extended to the preparation of several bicyclic systems, derived from pyrimidines [4,5] and pyridazines [6] in which the pyrrole nitrogen is situated at a bridgehead position. A preliminary



(1)

investigation showed 6-methyl(or substituted methyl)-1,3,5-triazine-2,4(1*H*,3*H*)-diones to be the most suitable starting materials.

Treatment of 6-methyl- (2) and 6-benzyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione (3) with ethyl bromopyruvate



(2) R^1=H
(3) R^1=Ph
(4) R^2=CO_2Et
(5) R^2=Ph
(6) R^2=H
(7) R^1=H, R^2=CO_2Et
(8) R^1=Ph, R^2=CO_2Et
(9) R^1=Ph, R^2=H
(10) R^1=H, R^2=CO_2Et
(11) R^1=Ph, R^2=CO_2Et
(12) R^1=H, R^2=CO_2Me
(13) R^1=H, R^2=CO_2H
(14) R^1=R^2=H
(15) R^1=Ph, R^2=H

(4) in refluxing ethanol, or 1,2-dimethoxyethane respectively, afforded ethyl 1,2,3,4-tetrahydro-2,4-dioxopyrrolo[1,2-*a*][1,3,5]triazine-7-carboxylate (10) and its 8-phenyl derivative (11). The reaction proceeded in one step and the intermediate quaternary salts [(7) (8)] were not isolated; a second molecule of the triazine itself was sufficiently basic to act as a catalyst in the removal of HBr from the quaternary salt. Similarly quaternary salts were not isolated in the synthesis of indolizines from ethyl 2-pyridylacetate and ethyl bromopyruvate where a second molecule of the picolyl base was an adequate catalyst.[4]

The triazinediones [(2) and (3)] did not react with phenacyl bromide under similar conditions but in dimethylformamide (6 h) the 6-methyltriazinedione afforded a poor yield of a product which, although not fully purified, appeared to be 3- or 1-phenacyl-7-phenylpyrrolo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-dione. Treatment of the 6-benzyltriazinedione with bromoacetaldehyde (6) gave 8-phenylpyrrolo[1,2-*a*][1,3,5]triazine-2,4-(1*H*,3*H*)-dione (15) as an unstable purple solid and again no quaternary salt (9) could be isolated. The instability of the ring system and the need for the stabilising influence of strong electron-withdrawing groups in the pyrrole ring was further demonstrated by the rapid decomposition of the pyrrolotriazinedione (14) on contact with air and organic solvents. This compound (14), in fact, could not be prepared by the above method [from (2) and (6)] but was formed on decarboxylation of the acid (13) with copper-bronze.

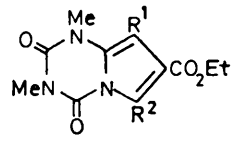
2,4-Dimethoxy-6-methyl-1,3,5-triazine, on treatment with ethyl bromopyruvate in refluxing ethanol, gave the ester (10) in 11% yield, with no evidence of any ethyl 2,4-dimethoxypyrrolo[1,2-*a*][1,3,5]triazine-7-carboxylate. The mother liquors afforded 6-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione hydrobromide. Use of the non-hydrolytic 1,2-dimethoxyethane as solvent gave only a 3% yield of the ester (10) and the mother liquors showed no evidence of any 6-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione. These facts suggest that hydrolysis of the methoxy-groups occurred prior to quaternisation by the ethyl bromopyruvate and that the triazinedione is more reactive toward electrophilic substitution at the nitrogen atom than is the 2,4-dimethoxy-compound.

The n.m.r. spectra of the pyrrolo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-diones exhibit two doublets attributable to 6-H and 8-H; *e.g.*, the pyrrole protons of ethyl 1,2,3,4-tetrahydro-2,4-dioxo-1,3-dimethylpyrrolo[1,2-*a*]-[1,3,5]triazine-7-carboxylate occur at τ ($CDCl_3$) 2·24 and 4·00 respectively. The lower of the two resonances is assigned to the 6-proton because of the deshielding effect of the adjacent pyrrolic nitrogen, an observation confirmed by the presence of a singlet at τ 1·96 in the 8-phenyl compound (15). It is noteworthy that the coupling constant between 6-H and 8-H ($J_{6,8}$ 2 Hz) is larger than the expected coupling constant between the 2- and 4-protons of similarly substituted pyrroles ($J_{2,4}$ 1·35 Hz),[7] thus suggesting a lower degree of electron delocalisation in the bicyclic compound. Previous workers have stated that it is impossible to predict coupling constants between ring nuclei in condensed pyrroles from a knowledge of the values in similarly substituted pyrroles.[7]

Treatment of the dipotassium salt of the ester (10) with methyl iodide in dimethylformamide afforded the dimethyl derivative (16), which gave a mixture of the 8-monobromo- (17) and 6,8-dibromo- (18) derivatives on treatment with *N*-bromosuccinimide in chloroform. Comparison of the n.m.r. spectrum of the starting

[4] J. Taylor and D. G. Wibberley, *J. Chem. Soc.* (*C*), 1968, 2693.
[5] E. Ochiai and M. Yanai, *J. Pharm. Soc. Japan*, 1939, **59**, 18.
[6] R. L. Letsinger and R. Lasco, *J. Org. Chem.*, 1956, **21**, 765.
[7] J. W. Emsley, J. Feeney, and C. H. Sutcliffe, ' High Resolution Nuclear Magnetic Resonance Spectroscopy,' Pergamon Press, Oxford, 1966, vol. 2.

material with that of the products proved the position of substitution. Thus the removal and decoupling of the resonances attributable to the 6- and 8-protons enabled the compounds to be readily identified. A



(16) $R^1=R^2=H$
(17) $R^1=Br, R^2=H$
(18) $R^1=R^2=Br$

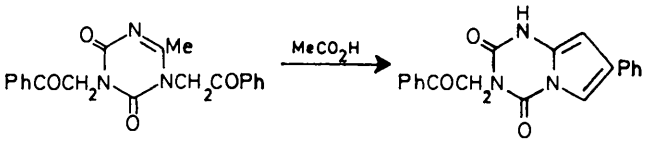
diagnostic feature in the ^1H n.m.r. spectra of the 8-bromopyrrolotriazines was the pronounced deshielding of the *N*-1 methyl protons (τ 6·55 in the starting material; 6·14 in the 8-bromo-compounds).

The pyrrolo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-diones, like the simpler 1,3,5-triazine-2,4(1*H*,3*H*)-diones,[8] exhibit two carbonyl stretching vibrations in their i.r. spectra. Conjugation with the lone pair of the bridgehead nitrogen atom causes the carbonyl functions at the 7-position of compounds (10)—(13) and (16) to absorb at lower than expected values. The i.r. spectrum of the *NN'*-dimethyl compound (16) was closely similar to that of the ester (10) in the carbonyl stretching region, as would be expected if the latter existed largely in the dione form.

The mass spectra of the pyrrolo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-diones, which exhibit intense molecular ion peaks (base peaks), were also helpful in structure determination although the expected loss of neutral isocyanate from M^+ is not observed.[9] Such a loss is of major importance in the mass spectra of the 1,3,5-triazine-2,4(1*H*,3*H*)-dione precursors (2) and (3) and related compounds,[9] the pyrimidinediones,[10] and bicyclic systems containing the NHCONHCO system.[10,11] The stability of the pyrrolotriazinediones to decomposition by this route can be explained by the lack of a suitably placed double bond, necessary to initiate ejection of RNCO by retro-Diels–Alder reaction.

A report that treatment of the silver salt of 6-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione with methyl iodide affords the *N*-1 methyl compound [12] led us to investigate a second route to the ring system *via* ring closure of 6-methyl-1,3,5-triazinediones phenacylated at position 1.

Difficulties were, however, encountered in the preparation of suitable *N*-substituted intermediates. Thus 6-methyl-1,3-diphenacyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione (19) was obtained by treatment of the monopotassium salt of the triazinedione (2) with 1 mol. equiv. of phenacyl bromide in dimethylformamide, and not the expected 1-monophenacylated derivative. The major constituent of the reaction mixture was the 6-methyltriazinedione (2). A third, very minor component was unidentified but when 2 mol. equiv. of phenacyl bromide were used the minor component, in this case, was identified as 6-methyl-1-phenacyl-1,3,5-triazin-2,4(1*H*,3*H*)-dione hydrobromide; the major products were the same. Treatment of the diphenacyl derivative (19) with boiling acetic acid afforded 3-phenacyl-7-phenylpyrrolo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-dione (20).



(19) (20)

EXPERIMENTAL

I.r. spectra were determined, unless otherwise stated, as Nujol mulls, with a Unicam SP 200, n.m.r. spectra with a Varian A60-A, and mass spectra with an A.E.I. MS9 spectrometer. The term light petroleum refers to the fraction of boiling range 60—80°. An asterisk after a chemical shift value indicates that the signal disappeared on deuteriation.

1,3,5-*Triazine*-2,4(1H,3H)-*diones*.— 6-Methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione (2) was prepared by adaptation of the method of Necki.[13] 2,4-Diamino-6-methyl-1,3,5-triazine (30 g) was added slowly to a mixture of concentrated sulphuric acid (134 cm^3) and water (40 cm^3) below 30°. The mixture was then heated at 150° for 2 h with stirring, cooled, poured into water, and neutralised with calcium carbonate. After removal of the precipitated calcium sulphate the aqueous filtrate was taken to dryness to give a solid, which was extracted with hot methanol. The extract was evaporated to dryness and the residue re-extracted with methanol. This procedure was repeated several times until all the inorganic material had been removed. The final methanolic extract gave the triazine (2) (60%), needles, m.p. 273—275° (decomp.) (lit.,[13] 276—277°) (from methanol), $\nu_{max.}$ 1760 and 1705 (C=O) and 1600 (C=N) cm^{-1}, τ (CF_3CO_2H) 7·10 (3H, s, Me), τ [$(CD_3)_2SO$] (dimethyl sulphoxide, τ 7·38, internal standard) —1·85br* (2H, s, 1- and 3-NH) and 7·75 (3H, s, Me). Potassium hydroxide (0·23 g), in the minimum amount of ethanol, was added to a solution of the triazinedione (0·51 g) in ethanol (50 cm^3). The precipitate was collected and dried *in vacuo* to give the potassium salt of (2) (0·56 g, 85%), $\nu_{max.}$ 3180 (N–H) and 1660 and 1640 (C=O) cm^{-1}.

6-Benzyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione (3) was prepared by the method of Ostrogovich and Tanislav,[14] as lustrous plates, m.p. 254—255° (lit.,[14] 251—252°) (from ethanol) (Found: M^+, 203·069202. Calc. for $C_{10}H_9N_3O_2$: *M*, 203·069472), $\nu_{max.}$ 1750 and 1670 (C=O), and 1605 (C=N) cm^{-1}, τ (CF_3CO_2H) 2·54 (5H, s, $PhCH_2$) and 5·58 (2H, s, $PhCH_2$).

o-Chlorophenylacetyl chloride (1·9 g) and biuret (0·7 g)

[8] J. Jonáš, M. Horák, A. Píškala, and J. Gut, *Coll. Czech. Chem. Comm.*, 1962, **27**, 2754.
[9] J. R. Traynor, Ph.D. Thesis, University of Aston in Birmingham, 1973.
[10] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Mass Spectrometry of Organic Compounds,' Holden-Day, San Francisco, 1967.
[11] T. Goto, A. Tatematsu, and S. Matsuura, *J. Org. Chem.*, 1965, **30**, 1844; T. J. Batterham, A. C. K. Triffett, and J. H. Wunderlich, *J. Chem. Soc.* (*B*), 1967, 892; I. R. Gelling, W. J. Irwin, and D. G. Wibberley, *J. Chem. Soc.* (*B*), 1969, 513.
[12] A. Píškala, *Coll. Czech. Chem. Comm.*, 1963, **28**, 2365.
[13] M. Necki, *Ber.*, 1874, **7**, 755.
[14] A. Ostrogovich and I. Tanislav, *Gazzetta*, 1934, **64**, 824.

were heated slowly to 140° and this temperature was maintained for 1 h. The mixture was then cooled and washed with ethanol to give 1-(*o*-chlorophenylacetyl)-biuret (1·2 g, 69%), as a solid, m.p. 228—232°. The crude biuret was added to an aqueous potassium hydroxide solution (25 cm³; containing 0·8 g KOH) and the mixture stirred for 6 h. Acetic acid was then added to precipitate 1-(*2-chlorobenzyl*)-1,3,5-*triazine*-2,4(1H,3H)-*dione* (0·5 g, 45%), needles, m.p. 268—269° (decomp.) (Found: C, 50·3; H, 3·4; N, 17·7. $C_{10}H_8ClN_3O_2$ requires C, 50·5; H, 3·4; N, 17·7%), $\nu_{max.}$ 3120 (N–H) and 1750 and 1670 (C=O) cm⁻¹, τ (CF_3CO_2H) 2·51 (4H, s, $ClC_6H_4CH_2$) and 5·43 (2H, s, $ClC_6H_4CH_2$).

The potassium salt of the 6-methyltriazinedione (2) (0·56 g) and phenacyl bromide (0·7 g) were stirred at room temperature in dimethylformamide (10 cm³) for 15 h. The mixture was then poured into water to give 6-*methyl*-1,3-*diphenacyl*-1,3,5-*triazine*-2,4(1H,3H)-*dione* (0·4 g, 32·5%), prisms, m.p. 103—105° (efferves.) (from carbon tetrachloride–chloroform) [Found: C, 60·7; H, 4·7; N, 10·25%; M^+ ($-2H_2O$), 363. $C_{20}H_{17}N_3O_4,2H_2O$ requires C, 60·15; H, 5·3; N, 10·5%; *M* ($-2H_2O$), 363], τ ($CDCl_3$) 2·05 (4H, m, 1- and 3-CH_2COPh, *o*-protons), 2·52 (6H, m, 1- and 3-CH_2COPh, *m*- and *p*-protons), 4·60 (2H, s, 3-CH_2COPh), 5·03 (2H, s, 1-CH_2COPh), and 7·69 (3H, s, Me). On standing, the aqueous mother liquors afforded an unidentified compound (0·07 g), prisms, m.p. 234·5—235·5° (decomp.) (from aqueous dimethyl sulphoxide) (Found: C, 54·1; H, 4·9; N, 15·5%), $\nu_{max.}$ 1695 (C=O) cm⁻¹, τ [(CD_3)SO] (dimethyl sulphoxide, τ 7·38, internal standard) 1·90 (2H, m), 2·28 (3H, m), 5·08 (1H, s), 5·15 (1H, s), 6·58 (3H, s), and 7·75 (3H, s). Evaporation of the remaining mother liquors to dryness gave the 6-methyltriazinedione (2).

The potassium salt of the 6-methyltriazinedione (2) (3·3 g) and phenacyl bromide (8 g) were stirred in dimethylformamide (30 cm³) for 96 h and the mixture was then poured into water. Extraction of the aqueous solution with chloroform gave a yellow oil, which after being triturated with the minimum of chloroform gave 6-*methyl*-1-*phenacyl*-1,3,5-*triazine*-2,4(1H,3H)-*dione hydrobromide* (0·08 g, 1·6%), pale yellow solid, m.p. 281—283° (decomp.) [Found: M^+, 245, M^+ ($-H_2O$), 227·068941. $C_{12}H_{11}N_3O_3,H_2O$ requires *M*, 245, *M* ($-H_2O$), 227·069472], $\nu_{max.}$ 1780 and 1700 (C=O) and 1600 (C=N) cm⁻¹, τ (CF_3CO_2H) 1·92 (2H, CH_2COPh, *o*-protons), 2·33 (3H, CH_2COPh, *m*- and *p*-protons), 4·12 (2H, s, 1-CH_2COPh), and 7·02 (3H, s, Me). The chloroform washings, after removal of the solvent, yielded 6-methyl-1,3-diphenacyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione (0·62 g, 8·6%), identical with the previous sample.

Pyrrolo[1,2-a][1,3,5]*triazine*-2,4(1H,3H)-*diones*.— The 6-methyltriazinedione (2) (1·3 g) was heated under reflux with ethyl bromopyruvate (0·9 g) and ethanol (100 cm³) for 70 h. Removal of the solvent under reduced pressure gave a yellow solid which was washed with 2N-hydrochloric acid to yield *ethyl* 1,2,3,4-*tetrahydro*-2,4-*dioxopyrrolo*[1,2-a][1,3,5]*triazine*-7-*carboxylate* (10). Extraction of the acidic washings with ether yielded a further quantity of the pyrrolotriazine, total yield (0·5 g, 48%), fawn needles, m.p. 260—261° (decomp.) (from ethanol) (Found: C, 48·6; H, 4·2; N, 18·7%; M^+, 223·059300. $C_9H_9N_3O_4$ requires C, 48·4; H, 4·1; N, 18·8%; *M*, 223·059071), $\nu_{max.}$ 3450 and 3250 (N–H), 1740 and 1700 (C=O), 1630 (C=C), and 1230 (C–O) cm⁻¹, τ (CF_3CO_2H) 1·94 (1H, d, *J* 2 Hz, 5-H), 3·52 (1H, d, *J* 2 Hz, 8-H), 5·48 (2H, q, *J* 2 Hz, CO_2CH_2Me), and 8·53 (3H, t, *J* 6 Hz, CO_2CH_2Me).

In a similar manner the 6-benzyltriazinedione (3) (2·03 g), ethyl bromopyruvate (1·95 g), and 1,2-dimethoxyethane (50 cm³) were refluxed together for 24 h to give *ethyl* 1,2,3,4-*tetrahydro*-2,4-*dioxo*-8-*phenylpyrrolo*[1,2-a][1,3,5]*triazine*-7-*carboxylate* (11) (1·4 g, 47%), needles, m.p. 277—278° (decomp.) (from methanol) (Found: C, 60·1; H, 4·2; N, 13·8%; M^+, 299·091534. $C_{15}H_{13}N_3O_4$ requires C, 60·2; H, 4·3; N, 14·1%; *M*, 299·090598), $\nu_{max.}$ 3200 and 3100 (N–H), 1745 and 1720 (C=O), 1620 (C=C), and 1200 (C–O) cm⁻¹, τ (CF_3CO_2H) 1·96 (1H, s, 6-H), 2·60 (5H, s, 8-Ph), 5·62 (2H, q, *J* 7 Hz, CO_2CH_2Me), and 8·73 (3H, t, *J* 7 Hz, CO_2CH_2Me).

Bromoacetaldehyde [from bromoacetaldehyde diethyl acetal (1·3 g)] and the 6-methyltriazinedione (2) (0·64 g) were heated under reflux in ethanol for 30 h. Removal of the solvent afforded a quantitative recovery of the starting material (2).

The 6-benzyltriazinedione (3) (1·0 g), bromoacetaldehyde [from bromoacetaldehyde diethyl acetal (1·5 g)], and 1,2-dimethoxyethane (60 cm³) were heated under reflux for 5 h. Removal of the solvent under reduced pressure gave a purple oily solid which on trituration with ethanol afforded the 8-phenylpyrrolotriazine (15) as a purple-brown solid (0·65 g, 58%), m.p. slow decomp. above 300°. On standing the compound quickly changed colour to a deep red-purple and an analytically pure sample could not be obtained but the mass and i.r. spectra indicated that 8-phenylpyrrolo[1,2-*a*][1,3,5]triazin-2,4(1*H*,3*H*)-dione was present (Found: M^+, 227·068941. Calc. for $C_{12}H_9N_3O_2$: *M*, 227·069472), $\nu_{max.}$ 3400 and 3200 (N–H), 1735—1680 (C=O), and 1630 (C=C) cm⁻¹.

2,4-Dimethoxy-6-methyl-1,3,5-triazine (0·31 g) and ethyl bromopyruvate (0·2 g) were heated under reflux in absolute ethanol (15 cm³) for 68 h. After removal of the solvent the remaining oily solid was triturated with dilute hydrochloric acid to give the ethyl dioxopyrrolotriazine-7-carboxylate (10) (0·05 g, 11%), identical with an authentic sample. A chloroform extract of the aqueous washings was dried ($MgSO_4$) and the solvent removed to afford a brown oil, the n.m.r. spectrum of which showed the presence of ethyl protons, and a small amount of starting material, but no evidence of any pyrrolotriazine. The aqueous mother liquors were taken to dryness to give 6-methyl-1,3,5-triazine-2,4(1*H*,3*H*)-dione hydrobromide (0·1 g, 25%) as a fawn solid. A similar reaction using 1,2-dimethoxyethane as solvent (68 h) gave a brown oil which was taken up in chloroform to leave the insoluble ethyl 1,2,3,4-tetrahydro-2,4-dioxopyrrolo[1,2-*a*][1,3,5]triazine-6-carboxylate (0·015 g, 3·5%). The chloroform extract was taken to dryness to yield a brown oil which consisted entirely of the starting materials.

Ethyl bromopyruvate (0·2 g), 2-methyl-4,6-diphenoxy-1,3,5-triazine (0·56 g), and ethanol (10 cm³) were refluxed for 76 h. Removal of the solvent under reduced pressure gave ethyl 1,2,3,4-tetrahydro-2,4-dioxopyrrolo[1,2-*a*]-[1,3,5]triazine-7-carboxylate, identical with an authentic sample.

The ethyl dioxopyrrolotriazine-7-carboxylate (10) (0·1 g) was warmed with 2N-hydrochloric acid (5 cm³) on a steam-bath for 2 h. 1,2,3,4-*Tetrahydro*-2,4-*dioxyopyrrolo*[1,2-a]-[1,3,5]*triazine*-7-*carboxylic acid* (13) separated from the hot solution as needles (0·06 g, 69%), m.p. 298—291° (decomp.). The acid was washed with water and purified

by dissolution in sodium hydroxide followed by precipitation with hydrochloric acid, but no suitable solvent could be found for recrystallisation (Found: M^+, 195·028001. $C_7H_5N_3O_4$ requires M, 195·026674), $\nu_{max.}$ 3300 (bonded OH), 3150 (N–H), 1725 and 1700 (C=O), and 1630 (C=C) cm^{-1}, τ [$(CD_3)_2SO$] 2·52 (1H, d, J 2 Hz, 6-H), 3·41br* (2H, s, 1- and 3-NH), and 4·25 (1H, *d*, J 2 Hz, 8-H).

The pyrrolotriazine-7-carboxylic acid (13) (0·1 g) and copper-bronze (0·05 g) were intimately mixed and heated to 280° in a closed flask fitted with a cold-finger. The flask was then evacuated (1 mmHg) and *pyrrolo*[1,2-a][1,3,5]*triazine*-2,4(1H,3H)-*dione* (14) collected on the cold-finger (0·04 g, 52%), as a powder, m.p. 208—210° (decomp.). The pyrrolotriazine rapidly decomposed on contact with air and organic solvents (Found: M^+, 151·038092. $C_6H_5N_3O_2$ requires M, 151·038173), $\nu_{max.}$ 1710 (C=O) and 1630 (C=C) cm^{-1}.

The pyrrolotriazine-7-carboxylic acid (13) (0·2 g) was heated in refluxing methanol containing a little concentrated sulphuric acid for 16 h. Concentration of the solution to 10 cm^3 gave a brown solid which was refluxed with methanol and animal charcoal to give *methyl* 1,2,3,4-*tetrahydro*-2,4-*dioxopyrrolo*[1,2-a][1,3,5]*triazine*-7-*carboxylate* (12) (0·17 g, 79%), plates, m.p. 288° (decomp.) (from methanol) (Found: C, 45·9; H, 3·7; N, 20·1%; M^+, 209. $C_8H_7N_3O_4$ requires C, 45·9; H, 3·4; N, 20·1%; M, 209), $\nu_{max.}$ 3200 and 3100 (N–H), 1740, 1720, and 1700 (C=O), 1630 (C=C) and 1220 (C–O) cm^{-1}, τ [$(CD_3)_2SO$] (dimethyl sulphoxide, 7·38, internal standard) 2·42 (1H, d, J 2 Hz, 6-H), 4·20 (1H, d, J 2 Hz, 8-H), and 6·15 (3H, s, CO_2Me).

To a solution of the ethyl pyrrolotriazine-7-carboxylate (10) (0·5 g) in ethanol (20 cm^3) was added potassium hydroxide (0·2 g) in the minimum of ethanol, and the dipotassium salt which rapidly separated was collected and dried *in vacuo* (0·5 g, 75%). The potassio-derivative was then stirred with methyl iodide (0·5 g) in dimethylformamide (5 cm^3) for 21 h and the mixture poured into water (20 cm^3) to yield *ethyl* 1,2,3,4-*tetrahydro*-1,3-*dimethyl*-2,4-*dioxopyrrolo*[1,2-a][1,3,5]*triazine*-7-*carboxylate* (16) (0·5 g, 83%), needles, m.p. 178—178·5° (from ethanol) (Found: C, 52·6; H, 5·2; N, 16·7%; M^+, 251. $C_{11}H_{13}N_3O_4$ requires C, 52·3; H, 5·2; N, 17·0%; M, 251), $\nu_{max.}$ 1735 and 1700 (C=O), 1620 (C=C) and 1200 (C–O) cm^{-1}, τ ($CDCl_3$) 2·24 (1H, d, J 2 Hz, 6-H), 4·00 (1H, d, J 2 Hz, 8-H), 5·65 (2H, q, J 7 Hz, CO_2CH_2Me), 6·55 (6H, s, 1- and 3-Me), and 8·63 (3H, t, J 7 Hz, CO_2CH_2Me).

Attempted Preparations of 7-*Phenylpyrrolo*[1,2-a][1,3,5]*triazine*-2,4(1H,3H)-*dione*.—(*a*) The 6-methyltriazinedione (2) (1·27 g) and phenacyl bromide (2·0 g) were heated under reflux in methanol (100 cm^3) for 2 weeks. The triazine was recovered unchanged.

(*b*) The methyltriazinedione (2) (1·3 g) and phenacyl bromide (2·0 g) were heated together, in the absence of solvent, for 17 h at 80°. The resulting oil was triturated with acetone to give the triazinedione hydrobromide (1·5 g, 72%) as a pale yellow solid, m.p. 280—283°, $\nu_{max.}$ 1780 and 1725 (C=O) cm^{-1}. None of the required pyrrolotriazine could be gained from the mother liquors.

(*c*) The 6-methyltriazinedione (2) (2·6 g) and phenacyl bromide (2·2 g) were heated under reflux in 2-ethoxyethanol for 45 h. Removal of the solvent under reduced pressure gave a black tar from which only phenacyl bromide could be recovered.

(*d*) The 6-methyltriazinedione (2) (0·7 g) and phenacyl bromide (0·6 g) were refluxed in dimethylformamide (5 cm^3). After 8 h, removal of the solvent, under reduced pressure, gave a dark brown oil, which on trituration with 2N-hydrochloric acid afforded a dark brown solid. This was washed with ether and treated with animal charcoal in refluxing methanol to give 3(or 1)-phenacyl-7-phenylpyrrolo[1,2-*a*][1,3,5]triazine-2,4(1*H*,3*H*)-dione as a mauve-brown powder, m.p. decomp. slowly above 300°. An analytically pure sample could not be obtained (Found: M^+, 345. Calc. for $C_{20}H_{15}N_3O_3$: M, 345), $\nu_{max.}$ 1750 and 1690 (C=O) and 1620 (C=C) cm^{-1}, τ (CF_3CO_2H) 2·30 (12H, m, CH_2COPh, 7-Ph and 6- and 8-H) and 4·28 (2H, s, CH_2COPh).

Bromination of the Dimethyl Derivative (16).—The pyrrolotriazine (16) (0·26 g) and *N*-bromosuccinimide (0·18 g) were heated under reflux in chloroform (4 cm^3) for 10 min. The cooled mixture was filtered, washed with sodium hydroxide solution (10%) and water, and dried ($MgSO_4$). The resulting solution was concentrated and applied to a 20 cm preparative t.l.c. plate (0·1 cm silica gel with $CaSO_4$ binder) and the chromatogram was developed with benzene–ethyl acetate (9 : 1). Under u.v. light two bands were visible, and these were removed and extracted with chloroform. The faster running fraction was *ethyl* 8-*bromo*-1,2,3,4-*tetrahydro*-1,3-*dimethyl*-2,4-*dioxopyrrolo*[1,2-a][1,3,5]*triazine*-7-*carboxylate* (17) (0·06 g, 17·5%), needles, m.p. 169—170° (from ethanol) (Found: C, 39·8; H, 3·7; N, 12·6%; M^+, 329. $C_{11}H_{12}N_3O_4{}^{79}Br$ requires C, 40·0; H, 3·6; N, 12·7%; M, 329). The second fraction was *ethyl* 6,8-*dibromo*-1,2,3,4-*tetrahydro*-1,3-*dimethyl*-2,4-*dioxopyrrolo*[1,2-a][1,3,5]*triazine*-7-*carboxylate* (18) (0·02 g, 5%), needles, m.p. 115° (from ethanol) (Found: M^+, 406·911491. $C_{11}H_{11}N_3O_4{}^{79}Br_2$ requires M, 406·911729). A similar reaction using 0·36 g of *N*-bromosuccinimide and a refluxing time of 1 h gave approximately equal amounts of the mono- and di-brominated products as shown by the n.m.r. spectrum of the crude mixture, τ ($CDCl_3$) 2·19 [1H, s, 6-H in (17)], 5·60 [2H, q, J 7 Hz, CO_2CH_2Me in (18)], 5·66 [2H, q, J 7 Hz, CO_2CH_2Me in (17)], 6·14 [3H, s, 1-Me in (18)], 6·16 [3H, s, 1-Me in (17)], 6·55 [3H, s, 3-Me in (18)], 6·57 [3H, s, 3-Me in (17)], 8·59 [3H, t, J 7 Hz, CO_2CH_2Me in (18)], and 8·62 [3H, t, J 7 Hz, CO_2CH_2Me in (17)].

3-*Phenacyl*-7-*phenylpyrrolo*[1,2-a][1,3,5]*triazine*-2,4(1H,3H)-*dione* (20).—The 6-methyl-1,3-diphenacyltriazine dione (19) (0·1 g) and acetic acid (5 cm^3) were refluxed for 15 h and then cooled to yield the *pyrrolotriazine* (20) (0·25 g, 26·5%), fawn needles, m.p. 280° (from aqueous dimethylformamide) (Found: C, 67·7; H, 4·9; N, 11·6%; M^+, 345·111598. $C_{20}H_{15}N_3O_3,0{\cdot}5H_2O$ requires C, 68·1; H, 4·6; N, 11·9%; $C_{20}H_{15}N_3O_3$ requires M, 345·111334), $\nu_{max.}$ 1740 and 1685 (C=O) and 1640 (C=C) cm^{-1}.

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