Tetrahedron. Vol. 24, pp 2839 to 2850 Pergamon Press 1968. Printed in Great Britain

BICYCLIC PYRIMIDINE DERIVATIVES WITH A BRIDGEHEAD NITROGEN ATOM—III[1]

ABSORPTION SPECTRA OF s-TRIAZOLOPYRIMIDINES

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(*Received in the UK* 3 *August* 1967; *accepted for publication* 23 *August* 1967)

Abstract– C-Alkyl-s-triazolo[4.3-a]pyrimidines are distinguished from the s-triazolo[1.5-a]pyrimidines by their UV absorption at longer wavelength. The UV spectra (at pH2 and pH10) also differentiate the isomeric s-triazolopyrimidones (hydroxy-s-triazolopyrimidines); this differentiation may be confirmed by the IR stretching frequency of the CO group. The isomeric N-alkyl-s-triazolopyrimidones are more readily distinguished by their IR spectra.

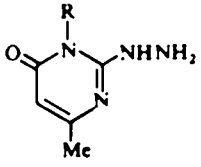
THE syntheses of s-triazolopyrimidines are ambiguous, often giving mixtures of isomers of uncertain structures, so that structure determination is a major problem in this field. The application of physical methods has been used to assign certain structures[2, 3] but we found these methods unreliable; however, modifications have now led to more general application in this field.

s-Triazolo[4.3-a]pyrimidines of known structure may be obtained from symmetrical 2-hydrazinopyrimidines under neutral conditions.[4, 5] Paudler *et al.*[6] have stated that two isomeric trimethyl-s-triazolopyrimidines are obtained by cyclization of 4,6-dimethyl-2-hydrazinopyrimidine with ethyl orthoacetate. However, the main product from their reaction mixture, which also contained aqueous sodium carbonate solution, was the acetyl derivative of the 2-hydrazinopyrimidine. Thus the presence of the s-triazolo[1.5-a]pyrimidine isomer in their reaction mixture could arise from either base catalysed isomerization of the s-triazolo[4.3-a]pyrimidine or as a result of cyclization of the acetyl 2-hydrazinopyrimidine.[7] However, we prepared s-triazolo[4.3-a]pyrimidine and the 5,7-dimethyl and 3,5,7-trimethyl derivatives according to the method of Williams[5] without any indication of the presence of the s-triazolo[1.5-a]pyrimidines.

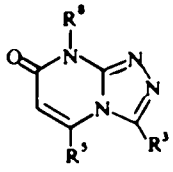
s-Triazolo[4.3-a]pyrimidones are obtained from 2-hydrazinopyrimidones in which one of the ring N atoms is substituted,[7] e.g. cyclization of 1,4-dimethyl-2-hydrazinopyrimid-6-one (I; R = Me) with triethyl orthoformate gave[8] 5,8-dimethyl-s-triazolo[4.3-a]pyrimid-7-one (II; R^3 = H, R^5 = R^8 = Me). If the pyrimidine N atoms are unsubstituted, cyclization can occur in both directions e.g. cyclization of 2-hydrazino-4-hydroxy-6-methylpyrimidine (I; R = H) with triethyl orthoformate gave[2] two isomeric products. Methylation of one of these products gave[8] 5,8-dimethyl-s-triazolo[4.3-a]pyrimid-7-one (II, R^3 = H, R^5 = R^8 = Me) proving the structure

to be 5-methyl-s-triazolo[4.3-a]pyrimid-7-one (II; $R^3 = R^8 = H$, $R^5 = Me$) (i.e. 7-hydroxy-5-methyl-s-triazolo[4.3-a]pyrimidine) and thus the structure of the isomeric product to be 7-methyl-s-triazolo[4.3-a]pyrimid-5-one (III; $R^3 = R^8 = H$, $R^7 = Me$). Isomerization of the last compound gave[2] 5-methyl-s-triazolo[1.5-a] pyrimid-7-one (V; $R^2 = R^4 = R^6 = H$, $R^5 = Me$) which was also obtained by condensation of ethyl acetoacetate with 3-amino-1,2,4-triazole. The fourth possible isomer in this series, 7-methyl-s-triazolo[1.5-a]pyrimid-5-one (IV: $R^2 = R^4 = R^6 = H$, $R^7 = Me$) has been prepared by Williams.[9]

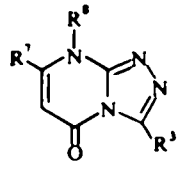
Using these four isomeric s-triazolopyrimidones of accepted structure, together with other model compounds described in the experimental section, we have assigned structures to a large number of s-triazolopyrimidines we had prepared for biological investigation.[1,7] We now report the correlation of physical properties with the structures of these s-triazolopyrimidines.



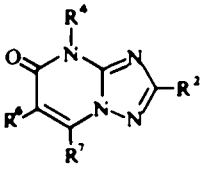
I



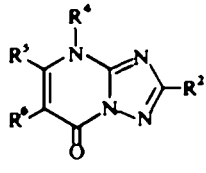
II



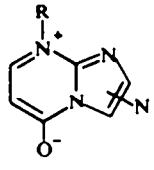
III



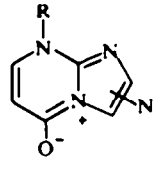
IV



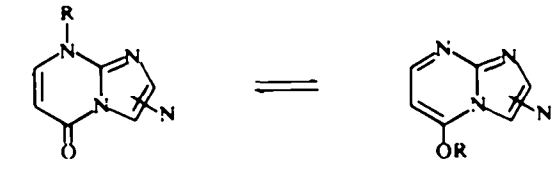
V



Va



Vb



VIa VIb

VIIa VIIb

Infrared spectra

Allen *et al.*[2] showed that hydroxy-s-triazolopyrimidines exist as the s-triazolopyrimidones (i.e. VIa and VIIa. R = H) in the solid state KBr disc). Allen *et al.*[2] and Williams[9] further showed that the CO group in compounds of type VI (R = H) absorbs at higher frequency ($\nu > 1675\,cm^{-1}$) than that in compounds of type VII (R = H) ($\nu = 1675\,cm^{-1}$) in the solid state. We found that solid state spectra (nujol) of the various isomers were sometimes anomalous and obtained better correlation from spectra in acetonitrile solution (Tables 1 and 2. R = H). Compounds of type

TABLE 1. IR SPECTRA OF S-TRIAZOLO[1.5-a]PYRIMIDONES*

Compounds	No. of example	ν_{co} (cm^{-1}) N—R Group R = H†	R = Alkyl‡
X	4		1620–1630
	3	1685–1690	
IV	3		1678–1681
XI	10		1688–1695§
	4	1700–1705	
V	4		1705–1717

* A summary of spectra of compounds reported in this and earlier papers.[1,7]

† in MeCN

‡ in $CHCl_3$

§ in one example an α-Me group caused a shift to 1673 cm^{-1}.

VII absorb at lower frequency (1685–1695 cm^{-1}) than compounds of type VI (1700–1705 cm^{-1}); however these compounds were more readily distinguished by their UV spectra (*vide infra*).

The frequency of the CO group in the N-alkyl-s-triazolo[1.5-a]pyrimidones falls steadily from 1705–1717 cm^{-1} (V) down to 1620–1630 cm^{-1} (X); (Table I). In

chloroform the 3-alkyl-s-triazolo[1.5-a]pyrimid-5-ones (X) have a main peak ca. 1630 cm^{-1} and a smaller peak at ca. 1650 cm^{-1}; the former band was shown to be due to CO absorption by the use of solvents of different polarity.[10] Thus in dioxan (less polar solvent) this band shifts to ca. 1640 cm^{-1} whereas in bromoform (more polar) a shift to lower frequency occurs.

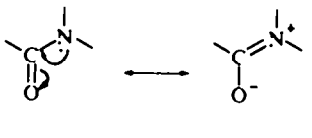
TABLE 2. IR SPECTRA OF S-TRIAZOLO[4.3-a]PYRIMIDONES*

Compounds	No. of examples	ν_{CO} (cm^{-1}) N—R Group H†	Alkyl‡
II	4	1685–1695	
	7		1681 1688
III	4	1700–1705	

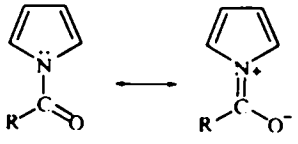
* A summary of spectra of compounds reported in this and earlier papers.[1,7]
† in MeCN
‡ in $CHCl_3$

The CO frequency of the 8-alkyl-s-triazolo[4.3-a]pyrimid-7-ones (II) is similar to the frequency of the 4-alkyl-s-triazolo[1.5-a]pyrimid-5-ones (IV).

The presence of a 6-ethoxycarbonyl group in these compounds causes the CO absorption to shift to higher frequency with a reduction in intensity.

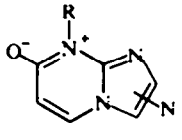


VIII

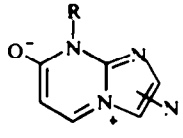


IX

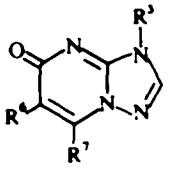
The frequency of the amide CO is lower than the normal CO frequency because of the electromeric effect of the N atom giving the resonance form VIII in which the CO group has some single bond character. In general the electromeric effect far exceeds the opposing inductive effect of the N atom. However, in compounds in which the N lone pair is delocalized and not available for this type of resonance, the inductive effect then becomes important and the CO frequency becomes higher than for normal amides (e.g. IX).[11] Thus the CO stretching frequency of the s-triazolo-pyrimidones depends both on the number of resonance forms contributing to the resonance hybrid (lowering the frequency) and on the inductive effect of neighbouring groups (increasing the frequency).



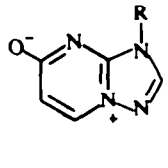
IIa



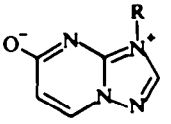
IIb



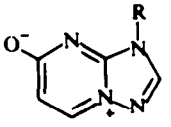
X



Xa

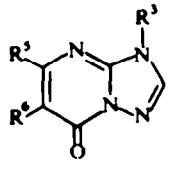


Xb

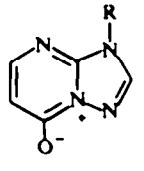


Xc

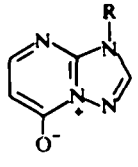
The resonance forms of the 3-alkyl-s-triazolo[1.5-a]pyrimid-5-ones (X) may be represented by Xa-c in which the C—O$^-$ is distant from the triazole ring and therefore the inductive effect is small and the CO frequency low. One of the resonance forms (IIb) of the 4-alkyl-s-triazolo[1.5-a]-pyrimid-5-one (IV) and 8-alkyl-s-triazolo[4.3-a]pyrimid-7-one (II) structures, represented by IIa and b, makes little contribution to the resonance hybrid as this would deplete the π electron sextet of the triazole ring. Also in the other (main) form (IIa) the single bond character of the CO group is reduced by the inductive effect due to the proximity of the charged atoms, thus increasing the frequency. In the resonance forms of the 3-alkyl-s-triazolo[4.3-a]pyrimid-7-ones (XI) represented by XIa-c, the C—O$^-$ attached directly to the triazole ring experiences a strong inductive effect thereby increasing the CO frequency. One of the resonance forms (Vb) of the 4-alkyl-s-triazolo[1.5-a]-pyrimid-7-ones (V), as in the case of the 4-alkyl-s-triazolo[1.5-a]pyrimid-5-ones, makes little contribution and in the other form Va, the C—O$^-$ attached directly to the triazole ring again experiences a strong inductive effect thereby increasing the CO frequency further.



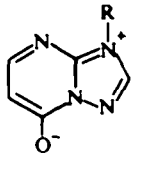
XI



XIa



XIb



XIc

Thus the s-triazolopyrimidones with the N-substituent on the triazole ring have a lower CO frequency than the compounds with the N-substituent on the pyrimidine

ring, and compounds in which the CO group is adjacent to the triazole ring (i.e. type VIa) have a higher CO frequency than the compounds of type VIIa.

Ultraviolet spectra

C-*Alkyl-s-triazolopyrimidines.* The alkyl-s-triazolo[4.3-a]pyrimidines (XII; λ_{max} 290 mμ) are distinguished from the s-triazolo[1.5-a]pyrimidines (XIII; λ_{max} 270 mμ) by the absorption at longer wavelength of the former (Fig. 1, curves 1 and 5).

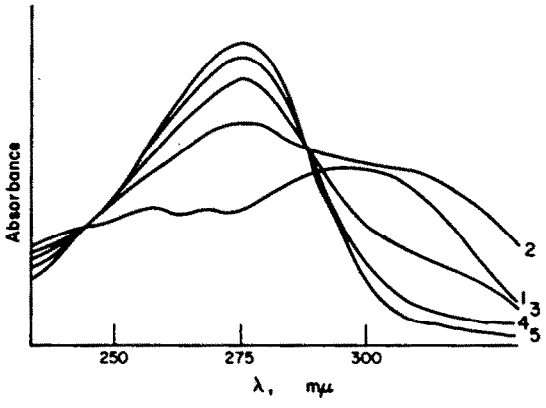
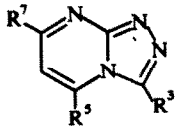


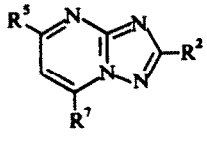
FIG. 1. UV spectra showing the isomerization of s-triazolo[4.3-a]pyrimidine (XII $R^3 = R^5 = R^7 = H$) to s-triazolo[1.5-a]pyrimidine (XIII $R^2 = R^5 = R^6 = R^7 = H$) (1) in water. (2) NaOH added (3) after 2 mins (4) after 6 mins (5) after 10 min.

Paudler[6] has stated that the spectra of the isomeric trimethyl derivatives are identical and therefore that UV spectroscopy cannot be used to differentiate these isomers, but we have found them to be different and cannot account for this discrepancy. The spectra of the s-triazolo[4.3-a]pyrimidines (XII; R^3, R^5, R^7 = H or Me) change to the spectra of the s-triazolo[1.5-a]pyrimidines (XIII; R^2, R^5, R^7 = H or Me) on addition of a small amount of aqueous sodium hydroxide to the solution (Fig. 1). Isomerization is complete in 10 min in the case of the parent heterocycle, whereas the Me derivatives require several hours.

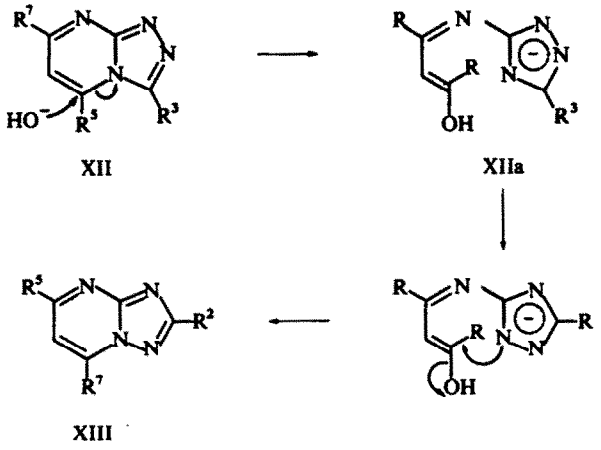
The base catalyzed isomerization of the s-triazolo[4.3-a]pyrimidines (XII) results from nucleophilic attack by hydroxide ion at the 5 position giving the intermediate XIIa. Rotation of the triazole ring, followed by ring closure gives the s-triazolo-[1.5-a]pyrimidines (XIII; see flowsheet).



XII



XIII



XII XIIa XIII

Flow Sheet 1. Base catalyzed isomerization of s-triazolo[4.3-a]pyrimidines.

s-Triazolopyrimidones. Allen *et al.*[2] showed that the spectra of compounds of type VI (R = H) were similar to the spectrum of pyrido[1.2-a]pyrimid-4-one (XIV) and the spectra of compounds of type VII (R = H) were similar to the spectrum of pyrido[1.2-a]pyrimid-2-one (XV). These authors also noted that certain bands could only be observed on the addition of ammonia to the solution; however, N-unsubstituted s-triazolopyrimidones are acids (pK_a 6–7)[9] and therefore the spectra should be measured under acid and alkaline conditions.[12] The spectra of the s-triazolo[1.5-a]pyrimid-7-ones (V; R^4 = H; λ_{max}^{pH2} 240 mμ, 270 mμ) and the s-triazolo-[4.3-a]pyrimid-5-ones (III; R^8 = H; λ_{max}^{pH2} 240 mμ, 285 mμ) i.e. type VI are very

XIV XV

similar, consisting of two bands which shift to longer wavelength with an increase of intensity in alkaline solution (Figs. 2 and 3). The isomers are distinguished by the long wavelength band which is at longer wavelength in the s-triazolo[4.3-a]pyrimidones.[2] The spectra of the s-triazolo[1.5-a]pyrimid-5-ones (IV; R^4 = H; λ_{max}^{pH2} 270 mμ) and the s-triazolo[4.3-a]pyrimid-7-ones (II; R^8 = H; λ_{max}^{pH2} 250 mμ) i.e. type VII consist of one band, which shifts to longer wavelength with a decrease of intensity in alkaline solution (Figs. 4 and 5). The s-triazolo[1.5-a]pyrimid-5-ones absorb at longer wavelength than the s-triazolo[4.3-a]pyrimid-7-ones in acid solution. cf. 9.

The spectra of the N-alkyl-s-triazolopyrimidones, in which the pyrimidine ring bears the N-substituent, resemble the spectra of the parent s-triazolopyrimidones in

acid solution, whereas spectra of the compounds bearing the N-substituent on the triazole ring tend to be similar to the spectra of the parent s-triazolopyrimidones in alkaline solution. The introduction of a ethoxycarbonyl group into these compounds causes a bathochromic shift. The introduction of a Ph group into the s-triazolopyrimidone system causes an increase in intensity of the shorter wavelength peak,

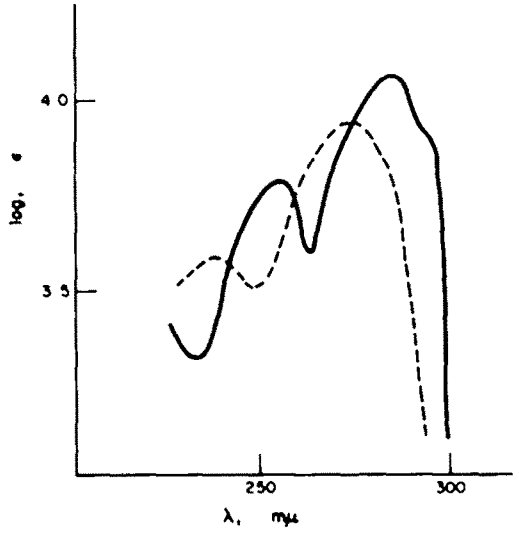


FIG. 2. UV spectra of s-triazolo[1,5-a]pyrimid-7-ones (V, R^4 = H) in aqueous buffer at pH2 - - - - and pH10 — —.

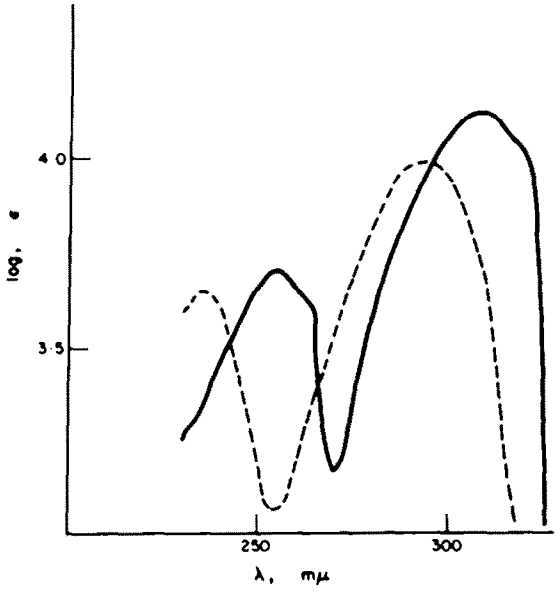


FIG. 3. UV spectra of s-triazolo[4,3-a]pyrimid-5-ones (III, R^8 = H) in aqueous buffer at pH2 - - - - - and pH10 ·····——.

except in the 3-phenyl-5-methyl-s-triazolo[4.3-a]pyrimid-7-ones where the normal band at 250 mμ is reduced to a shoulder at ca. 230 mμ by interaction between the 3-Ph and the 5-Me groups.

NMR spectroscopy was also investigated as an aid to structure determination, but was found to be of no value in the case of the s-triazolopyrimidones.

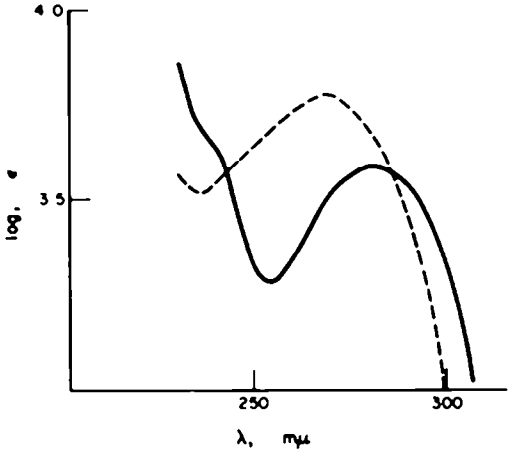


FIG. 4. UV spectra of s-triazolo[1.5-a]pyrimid-5-ones (IV, R^4 = H) in aqueous buffer at pH2 - - - - and pH10 ———.

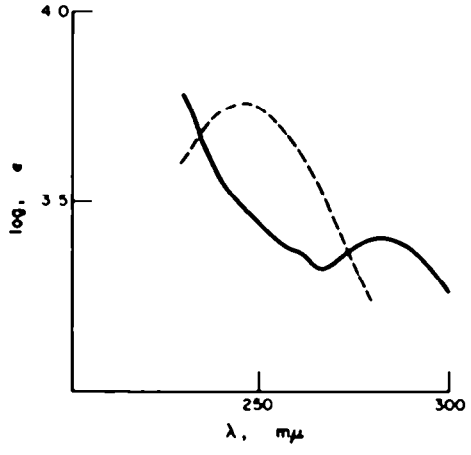


FIG. 5. UV spectra of s-triazolo[4.3-a]pyrimid-7-ones (II, R^9 = H) in aqueous buffer at pH2 - - - - and pH10 — — —.

In the synthetic routes to s-triazolopyrimidines there is no likelihood of 4-alkyl-s-triazolo[1.5-a]pyrimid-5-ones (IV) and 3-alkyl-s-triazolo[1.5-a]pyrimid-7-ones (XI) occurring in the same reaction mixture, consequently, although the differences between the carbonyl frequencies of these particular isomers are small, the application of IR and UV spectroscopy may be used to establish the structures unequivocably.

EXPERIMENTAL

IR spectra were determined using Unicam S.P. 200 and Beckman IR 9 spectrophotometers. UV spectra were determined using Unicam S.P. 800 and Beckman D.K. 2 spectrophotometers. NMR spectra were determined using a Varian A-60 instrument. M.ps are corrected. TLC was carried out on silica gel (H.F. 254) plates and the spots located by viewing under a UV lmap (254 mμ). Petroleum ether refers to the fraction b.p. 60–80°.

The preparation of the compounds, apart from the following has been reported previously.[1,7]

s-Triazolo[4.3-a]*pyrimid-5-one* (III; $R^3 = R^7 = R^8 = H$). 2-Hydrazino-4-hydroxypyrimidine (6·4 g, 0·05 mole) was heated under reflux with ethyl orthoformate (50 ml) in ethylene glycol (100 ml) for 3 hr. The soln was concentrated and allowed to crystallize. The solid was collected and recrystallized from water (charcoal) to give the *product* as needles (2·3 g) m.p. 292–295° (dec), 34% yield. TLC R_f 0·75 (MeOH). (Found: C, 44·60; H, 2·96; N, 41·17, $C_5H_4N_4O$ requires: C, 44·12; H, 2·96; N, 41·17%); λ_{max}^{pH2}: 237 and 284 mμ (log ε 3·64 and 4·00); λ_{max}^{pH10}: 254 and 308 mμ (log ε = 3·71 and 4·13); ν_{co} (MeCN) 1705 cm^{-1}.

7-Methyl-s-triazolo[4.3-a]*pyrimid-5-one* (III; $R^3 = R^8 = H$, $R^7 = Me$)[2]. 2-Hydrazino-4-hydroxy-6-methylpyrimidine (7·0 g, 0·05 mole), ethyl orthoformate (50 ml) and ethylene glycol (100 ml) were heated under reflux for 3 hr then allowed to cool. The solid was collected and recrystallized from water to give the *product* as needles (1·9 g) m.p. 284–285°, 24% yield. TLC R_f 0·70 (MeOH) (lit.,[2] m.p. 252–254°) λ_{max}^{pH2} 238 and 291 mμ (log ε = 3·43 and 4·04); λ_{max}^{pH10}: 254 and 300 mμ (log = 3·72 and 4·12); ν_{co} (MeCN) 1700 cm^{-1}. The reaction mixture mother liquors were evaporated under reduced press and allowed to crystallize. The solid was recrystallized from water (charcoal) to give *5-methyl-s-triazolo*[4.3-a]*pyrimid-7-one* as plates (0·6 g) m.p. 303° (dec) 7·5% yield. TLC R_f 0·40 (MeOH) (lit.,[2] m.p. 296–298°); λ_{max}^{pH2} 250 mμ (log ε = 4·05); λ_{max}^{pH10} 250 mμ (shoulder) 280 (log ε 3·37); ν_{co} (MeCN) 1695 cm^{-1}.

s-Triazolo[4.3-a]*pyrimid-7-one* (II; $R^3 = R^5 = R^6 = R^8 = H$). 2-Hydrazino-4-hydroxypyrimidine (2·5 g, 0·02 mole) and CS_2 (2·5 g, 0·03 mole) were heated together in boiling aqueous pyridine (60 ml, 50%) for 4 hr under reflux. The mixture was evaporated and the residue crystallized from water. The yellow solid was recrystallized from water to give *3-mercapto-s-triazolo*[4.3-*a*]*pyrimid-7-one* as yellow needles (0·4 g) m.p. 284–286°. TLC R_f 0·85 (MeOH). (Found: C, 35·79; H, 2·33; N, 33·58. $C_5H_4N_4OS$ requires: C, 35·72; H, 2·40; N, 33·33%). (A small amount of the isomeric 3-mercapto-s-triazolo[4.3-a]pyrimid-5-one was also isolated from the mother liquors, but could not be purified.)

3-Mercapto-s-triazolo[4.3-a]pyrimid-7-one (0·2 g) was added to a soln of conc HNO_3 (5 ml) and $NaNO_2$ (0·05 g) in water (10 ml) and the mixture stirred at room temp for 2 hr. The soln was evaporated and the residue neutralized with dil ammonia then the water removed by azeotropic distillation. The residue was extracted with EtOH and the extract evaporated to give a solid which was dissolved in water and treated with $AgNO_3$. The Ag salt was filtered on to *hyflo* and the filter cake suspended in water while H_2S was passed. The mixture was filtered and the filtrate evaporated. The solid was recrystallized from water (charcoal) to give the *product* as needles (5 mg) m.p. 295–299 (dec). TLC R_f 0·45 (MeOH). (Found: N, 41·28, $C_5H_4N_4O$ requires: N, 41·17%); λ_{max}^{pH2} 247 mμ (log ε = 3·76) λ_{max}^{pH10} 260 mμ (shoulder) 282 mμ (log ε = 3·40).

4-Benzyl-7-methyl-s-triazolo[1.5-a]*pyrimid-5-one* (IV; $R^2 = R^6 = H$, $R^4 = PhCH_2$, $R^7 = Me$). 3-Benzylamino-1,2,4-triazole (2·5 g, 0·015 mole) and ethyl acetoacetate (3 ml) were heated together at 180–190° for 15 min. The solid was collected, washed with light petroleum and recrystallized from EtOH (charcoal) to give the *product* as needles (1·65 g) m.p. 139–141° (lit.[13] m.p. 138–139°); λ_{max}^{EtOH} 249 mμ (log ε = 3·75) 275 mμ (shoulder); ν_{co} ($CHCl_3$) 1681 cm^{-1}.

4-Benzyl-5-methyl-s-triazolo[1.5-a]*pyrimid-7-one* (V; $R^2 = R^6 = H$, $R^4 = PhCH_2$, $R^5 = Me$). 3-Benzylamino-1,2,4-triazole (5·2 g, 0·03 mole) and ethyl acetoacetate were heated together in boiling AcOH (20 ml) under reflux for 4 hr. The soln was evaporated and the residue triturated with a little EtOH. Insoluble 3-benzylamino-1,2,4-triazole was removed by filtration and the filtrate allowed to crystallize. The solid was collected, washed with hot water and recrystallized from isopropanol to give the *product* as needles (0·75 g) m.p. 181–182°, 10% yield. (Found: C, 64·68; H, 5·34, $C_{13}H_{12}N_4O$ requires: C, 64·97; H, 5·04%); λ_{max}^{EtOH} 246·5 and 276·5 mμ (log ε = 3·72 and 4·13); ν_{co} ($CHCl_3$) 1709 cm^{-1}.

4-Benzyl-6-ethoxycarbonyl-2-phenyl-s-triazolo[1.5-a]*pyrimid-7-one* V; R^2 = Ph. $R^4 = PhCH_2$, $R^5 = H$, $R^6 = COOEt$). 3-Benzylamino-5-phenyl-1,2,4-triazole (1·5 g, 0·06 mole) and ethyl α-ethoxycarbonylacrylate (2·2 g, 0·1 mole) were heated together in boiling AcOH (25 ml) under reflux for 24 hr. The soln was evaporated and the residue crystallized from isopropanol. The solid was collected, washed with hot EtOH and recrystallized from $CHCl_3$–light petroleum to give the product as needles (0·4 g) m.p. 216–219°; 11% yield. TLC R_f 0·70 (AcOEt). (Found: C, 67·17; H, 4·76; N, 14·92. $C_{21}H_{18}N_4O_3$ requires: C, 67·37; H,

4·85, N, 14·97%); λ_{max}^{EtOH} 249, 278·5, 286 and 297·5 mμ (log ε 4·58, 4·09, 4·08 and 4·09); ν_{co} 1720 cm^{-1}, and 1755 cm^{-1} (ester). The isopropanolic mother liquors were evaporated and the residue crystallized from $CHCl_3$–light petroleum to give *4-benzyl-2-phenyl-s-triazolo*[1.5-a]*pyrimid-7-one* (V; R^2 = Ph, R^4 = $PhCH_2$, R^5 = R^6 = H) as a felt mat (0·2 g) m.p. 180–182°, 5·5% yield. TLC R_f, 0·65 (EtOAc). (Found: C, 71·01; H, 5·07; N, 18·38. $C_{18}H_{16}N_4O$ requires: C, 71·50; H, 4·69; N, 18·54%); λ_{max}^{EtOH} 245·5, 267 and 283·5 mμ (log ε = 4·48, 4·23 and 4·14); ν_{co} ($CHCl_3$) 1705 cm^{-1}. The hot ethanolic washings gave *4-benzyl-6-ethoxycarbonyl-2-phenyl-s-triazolo*[1.5-a]*pyrimid-5-one*[7] as needles (50 mg) m.p. 163–165° TLC R_f, 0·95 (EtOAc); λ_{max}^{EtOH} 268·5, 282 and 316·5 mμ (log ε = 4·02, 3·98 and 4·16); ν_{co} ($CHCl_3$) 1680 cm^{-1} and 1710 cm^{-1} 1745 cm^{-1} (ester).

3-Benzyl-7-methyl-s-triazolo[1.5-*a*]*pyrimid-5-one* (X; R^3 = $PhCH_2$, R^6 = H, R^7 = Me.[13] 3-Amino-4-benzyl-1,2,4-triazole (3·5 g, 0·02 mole) and ethyl acetoacetate (10 ml) were heated together at 160–180° for ½ hr, then allowed to cool. The solid was collected and chromatographed on alumina with benzene–chloroform (5:1) to give 3-benzyl-5-methyl-s-triazolo [1.5-a]pyrimid-7-one[13] as plates (0·85 g) m.p. 206–208° (EtOH) 20% yield. TLC Me_2CO R_f, 0·85 (lit.[13] m.p. 203–205°); λ_{max}^{EtOH} 249 and 284·5 mμ (log ε = 3·70, 4·13 and 288 mμ (shoulder); ν_{co} ($CHCl_3$) 1693 cm^{-1}. Eluting the column with $CHCl_3$ gave the *product* as prisms (1·0 g) m.p. 256–259° (EtOH) 23% yield. TLC R_f, 0·30 (Me_2CO) (lit.[13] m.p. 251–253°). (Found: C. 65·12; H, 5·41; N, 23·47 calc. for $C_{13}H_{12}N_4O$: C, 65·00; H, 5·03; N, 23·32%); λ_{max}^{EtOH} 239 and 272 mμ (log ε = 4·17 and 4·08); ν_{co} ($CHCl_3$) 1628 cm^{-1}.

3-Benzyl-7-ethyl-s-triazolo[1.5-a]*pyrimid-5-one* (X; R^3 = $PhCH_2$, R^6 = H, R^7 = Et). 3-Amino-4-benzyl-1,2,4-triazole (2·0 g, 0·011 mole) and ethyl 3-oxopentanoate (5 ml) were heated together at 160–180° for 30 min. The solid was collected, dissolved in $CHCl_3$ and the unreacted triazole removed by filtration. The filtrate was concentrated and chromatographed on alumina with benzene: $CHCl_3$ (5:1) followed by $CHCl_3$. The first fractions gave 3-Benzyl-5-ethyl-s-triazolo[1.5-a]pyrimid-7-one as plates (1·05 g) m.p. 166–170° (EtOH) 38% yield; TLC Me_2CO R_f, 0·9. (Found: C, 66·16; H, 5·45; N, 22·02. $C_{14}H_{14}N_4O$ requires: C, 66·14; H, 5·55; N, 22·04%); λ_{max}^{EtOH} 249 and 284 mμ (log ε = 3·67 and 4·11) 290 mμ (shoulder); ν_{co} ($CHCl_3$) 1689 cm^{-1}. Later fractions from the column gave the *product* as needles (0·35 g) m.p. 193–196° (isopropanol–light petroleum) 12% yield, TLC Me_2CO R_f, 0·2. (Found: C, 65·89; H, 5·35; N, 22·02; $C_{14}H_{14}N_4O$ requires: C, 66·14; H, 5·55; N, 22·04%); λ_{max}^{EtOH} 236·5 243 and 268 mμ (log ε = 3·90, 3·89 and 3·77) 275 mμ (shoulder); ν_{co} ($CHCl_3$) 1629 cm^{-1}.

3-Benzyl-6, 7-dimethyl-s-triazolo[1.5-a]*pyrimid-5-one* (X; R^3 = $PhCH_2$, R^6 = R^7 = Me). 3-Amino-4-benzyl-1,2,4-triazole (2 g, 0·011 mole) and ethyl α-methylacetoacetate (5 ml) were heated together at 160–180° for 30 min. The solid was collected and chromatographed on alumina with benzene:$CHCl_3$ (4:1). The first fractions gave *3-benzyl-5,6-dimethyl-s-triazolo*[1.5-a]*pyrimid-7-one* as needles (0·1 g) m.p. 201–204° (EtOH) 3·5% yield, TLC Me_2CO R_f, 0·8. (Found: C, 66·04; H, 5·60; N, 21·99; $C_{14}H_{14}N_4O$ requires: C, 66·12; H, 5·55; N, 22·04%); λ_{max}^{EtOH} 253 and 292 mμ (log ε = 3·66 and 4·11); ν_{co} ($CHCl_3$) 1673 cm^{-1}. Later fractions gave the *product* as needles (0·75 g) m.p. 250–254° (isopropanol–light petroleum) 27% yield, TLC Me_2CO R_f, 0·25. (Found: C, 66·20; H, 5·46; N, 21·84; $C_{14}HN_4O$ requires: C, 66·12; H, 5·55; N, 22·04%); λ_{max}^{EtOH} 238, 245 and 268·5 mμ (log ε = 3·75, 3·55 and 3·87) 275 mμ (shoulder); ν_{co} ($CHCl_3$) 1620 cm^{-1}.

3-o-Chlorobenzyl-7-methyl-s-triazolo[1.5-a]*pyrimid-5-one* (X; R^3 = *o*-$ClC_6H_4CH_2$, R^6 = H, R^7 = Me). 3-Amino-4-*o*-chlorobenzyl-1,2,4-triazole (2·5 g, 0·012 mole) and ethyl acetoacetate (7·5 ml) were heated together at 180° for 30 min. The solid was collected, washed with EtOH and recrystallized from water (charcoal) to give 3-*o*-chlorobenzyl-5-methyl-s-triazolo[1.5-a]pyrimid-7-one[7] as needles (0·45 g) m.p. 177–9°; TLC Me_2CO R_f, 0·9; λ_{max}^{EtOH} 246 and 280 mμ (log ε = 3·69 and 4·15); ν_{co} ($CHCl_3$) 1693 cm^{-1}. The mother liquors from the crystallization and the reaction mixture were combined and evaporated. The residue was chromatographed on alumina with benzene:$CHCl_3$ (3:1) to give further s-triazolo[1.5-a]pyrimid-7-one (total yield, 0·75 g, 23% yield). Later fractions gave the *product* as needles (0·65 g) m.p. 235–238° (isopropanol) 20% yield; TLC Me_2CO R_f, 0·2. (Found: C, 56·99; H, 4·18; N, 20·50 $C_{13}H_{11}ClNO$ requires: C, 56·84; H, 4·04; N, 20·40%); λ_{max}^{EtOH} 236·5, 243 and 268 mμ (log ε = 3·90, 3·92 and 3·80) 272 mμ (shoulder); ν_{co} ($CHCl_3$) 1630 cm^{-1}.

Acknowledgements—We thank Mr. M. J. Graham for microanalyses and Miss E. V. Eggington and Dr. A. A. Chalmers for determining some of the IR and UV spectra.

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