***Di-p-tolylphosphorohydrazide* (*Ib*).** Over a 2-h period, 0.1 mol of di-*p*-tolylphosphorochloride in 25 mL of benzene was added with stirring to a suspension of (0.25 mol) 95% hydrazine in 100 mL of benzene. The mixture then was refluxed for 3 h, cooled, and filtered. The colorless solid was washed with water and then crystallized from ethanol: mp 125 °C.

In the preparation of the hydrazones (IV and VI), the hydrazides (0.01 mol) were boiled under reflux with the appropriate carbonyl compound (0.01 mol) in ethanol (50 mL) for 2 h. The hydrazones generally separated from the cool, concentrated solution and were recrystallized from ethanol. Analysis and IR spectral data supported the structures Ib, IV, and VI.

***Preparation of the Pyrazolin-5-ones* (*V*).** Acetylacetone hydrazones (IVc,f,k) (1 g) were heated at their melting points for 1 h and then allowed to cool. The viscous oil was triturated with petroleum ether and left for 12 h, whereby a crystalline precipitate was formed. It was removed by filtration and crystallized from ethanol. The pyrazolin-5-one of compound IVk did not crystallize out, and all of the trials to isolate it in analytically pure form failed (melting points (°C): Va, 114–115; Vb, 123–124).

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Reactions with (Arylmethylene)cycloalkanones. 5.[†] Synthesis of 2-Acetyl-5-aryl-5,6,7,8,9,10-hexahydrocyclohepta[*d*]thiazolo[3,2-*a*]pyrimidin-3(2*H*)-ones of Probable Biological Activity

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Cyclohepta[*d*]pyrimidine-2-thiones (III) were prepared by heating 2-(arylmethylene)cycloheptanones with thiourea in ethanolic potassium hydroxide. Compounds III reacted with chloroacetic acid in acetic anhydride to yield the title compounds (IV). Compounds IV condensed with the aromatic aldehydes to yield the 2-(arylmethylene) derivatives V. Also, the 2-(arylhydrazono) derivatives VI were prepared.

In continuation of our previous work on cyclooctanone (*4*), we now report on the synthesis of an analogous series involving the 2-(arylmethylene)cycloheptanone (*1*, *2*). (See Scheme I.) The structures of III–VI are substantiated by IR, UV, MS, and NMR.

Experimental Section

***2-(Arylmethylene)cycloheptanone* (*II*).** The 2-(arylmethylene) derivatives (IIa) are known in the literature (*2*). In this work the arylmethylene derivatives are prepared in ~80% yield as follows.

To a mixture of 11 g (0.1 mol) of cycloheptanone and 10.6 g (0.066 mol) of the appropriate aldehyde was added aqueous potassium hydroxide (4 g of KOH in 70 mL of H_2O). The mixture was refluxed for 12 h, allowed to cool, and then acidified with dilute HCl. The 2-(arylmethylene) derivatives were extracted with methylene chloride. The extract was dried over anhydrous sodium sulfate, and the solvent was evaporated. The crude pale yellow oil (~80%) was used as such.

***4-Aryl-9H-1,2,3,4,5,6,7,8-octahydrocyclohepta[d]pyrimidine-2-thiones* (*III*).** A mixture of 0.02 mol of the crude 2-(arylmethylene)cycloheptanone (II), 1.5 g of thiourea, and 2 g of potassium hydroxide in 100 mL of ethanol and refluxed for 3 h. The mixture was allowed to cool, and then 50 mL of water was added, whereupon a white precipitate appeared. The product was filtered, washed with water, and crystallized from the proper solvent (see Table I).

Table I. 4-Aryl-9*H*-1,2,3,4,5,6,7,8-octahydrohepta[*d*]pyrimidine-2-thiones (III)[a]

compd	mp, °C	solvent[b]	yield, %
IIIa	190	M	70
b	191	M	68
c	188	M	72
d	200	M	75
e	190	P	70

[a] Elemental analyses in agreement with theoretical values were obtained. [b] Solvent key: A = acetic acid, E = ethanol, M = methanol, P = petroleum ether 60/80, NH = normal hexane.

Table II. 2-Acetyl-5-aryl-5,6,7,8,9,10-hexahydrohepta[*d*]-thiazolo[3,2-*a*]pyrimidin-3(2*H*)-ones (IV)[a]

compd	mp, °C	solvent	yield, %
IVa	200	M	78
b	130	M	70
c	240	M	65
d	175	M	65
e	160	M	70

[a] See footnotes of Table I.

The infrared spectra of compounds III show bands assignable to NH (3250 cm^{-1}) and N—C=S (1640 cm^{-1}). The mass spectrum of compound IIIa showed the molecular ion peak (M^+) at *m/e* 258 (10%) and the base peak at *m/e* 181. The ^{1}H NMR spectrum of compound IIIa (in $CDCl_3$) showed the protons of the cycloheptene ring (10 H) as a multiplet in the δ 0.75–2.45 region, and the methine proton (a) as a singlet at δ

[†] For part 4, see ref *4*.

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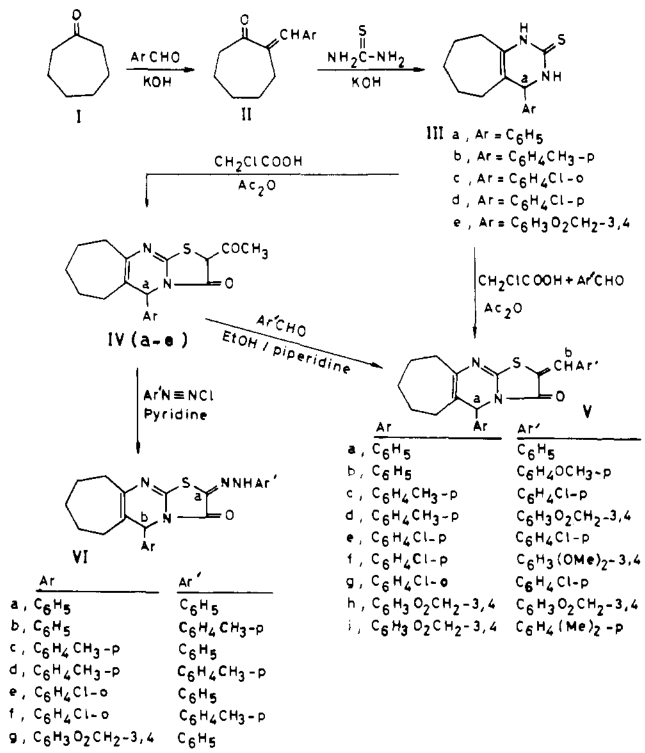
Scheme I



4.90; the NH protons gave two broad singlets at δ 7.5 (1 H) and 6.95 (1 H), and the aromatic protons gave a multiplet (5 H) centered at δ 7.45.

2-Acetyl-5-aryl-5,6,7,8,9,10-hexahydrocyclohepta[d]thiazolo[3,2-a]pyrimidin-3(2H)-ones (IV). A mixture of 1.5 g of compound III, 1 g of chloroacetic acid, and 4 g of anhydrous sodium acetate in 10 mL of acetic acid and 5 mL of acetic anhydride was refluxed for 3 h and left to cool. The reaction mixture was poured into water. The solid obtained was filtered off and crystallized from the proper solvent (see Table II).

The infrared spectra of compounds IV show CO at 1680 cm^{-1} and OH at ca. 3400 cm^{-1} (they give a positive $FeCl_3$ test). The UV spectrum of compound IVa shows three maxima at λ 240 (ε 5000), 280 (ε 6400), and 370 nm (ε 10 800). The mass spectrum of IVa showed a prominant molecular ion peak at *m/e* 340 (41%) and a base peak at *m/e* 263 followed by loss of $COCH_3$ to give a peak at *m/e* 220 (80%). The ^1H NMR spectrum of compound IVa in $CDCl_3$ showed the protons of the cycloheptene ring (10 H) as a multiplet in the δ 0.75–2.30 region, the acetyl CH_3 protons as a singlet at δ 2.48 (3 H), and the methine protons as a singlet at δ 5.65 (1 H), and the aromatic protons gave a multiplet (5 H) centered at δ 7.45.

2-(Arylmethylene)-5-aryl-5,6,7,8,9,10-hexahydrocyclohepta[d]thiazolo[3,2-a]pyrimidin-3(2H)-ones (V). (a) A mixture of 1 g of III, 1.5 g of chloroacetic acid, 0.6 g of the aromatic aldehyde, and 4 g of anhydrous sodium acetate in 15 mL of acetic acid and 10 mL of acetic anhydride was refluxed for 3 h. The reaction mixture was poured into water, and the solid formed was collected and crystallized (see Table III).

(b) To a mixture of 0.5 g of IVa and mL of benzaldehyde in 15 mL of ethanol was added a few drops of piperidine, and the whole mixture was refluxed for 3 h and left overnight. The solid formed was collected and crystallized.

(c) A mixture of 0.5 g of IVa and 0.5 mL of benzaldehyde in 10 mL of ethanol containing 0.1 g of KOH was refluxed for 2 h and left overnight. The solid formed was collected and crystallized. The yields in methods a–c were ~90%. Compound Va prepared by the different methods a–c has the same melting point and mixed melting point.

Table III. 2-(Arylmethylene)-5-aryl-5,6,7,8,9,10-hexahydrocyclohepta[*d*]thiazolo[3,2-*a*]pyrimidin-3(2*H*)-ones (V)[a]

compd	mp, °C	solvent	yield, %
Va	225	A	90
b	193	E	86
c	220	A	84
d	220	A	86
e	150	A	85
f	222	A	90
g	210	A	85
h	205	M	80
i	180	E	83

[a] See footnotes of Table I.

Table IV. 2-Arylhydrazono-5-aryl-5,6,7,8,9,10-hexahydrocyclohepta[*d*]thiazolo[3,2-*a*]pyrimidin-3(2*H*)-ones (VI)[a]

compd	mp, °C	solvent	yield, %
VIa	225	A	70
b	220	A	64
c	185	NH	68
d	205	E	65
e	225	A	70
f	195	A	65
g	170	M	70

[a] See footnotes of Table I.

The infrared spectra of compounds V show CO absorption at ca. 1700 cm^{-1} and C=N at ca. 1613 cm^{-1}. The UV spectrum of compound Va shows two maxima at λ 235 (ε 8666) and 375 nm (ε 15 000). The mass spectrum of Va showed a molecular ion peak at *m/e* 386 (28%) and a base peak at *m/e* 309. The ^1H NMR spectrum of compound Va (in $CDCl_3$) showed the following assignments: a multiplet in the δ 0.65–2.70 region (10 H) for the cycloheptene ring, a singlet at δ 5.50 for the methine proton (a) and singlet at δ 7.65 for the benzylic proton (b); the aromatic protons (10 H) gave a multiplet centered at δ 7.40.

2-(Arylhydrazono)-5-aryl-5,6,7,8,9,10-hexahydrocyclohepta[d]thiazolo[3,2-a]pyrimidin-3(2H)-ones (VI). A cold diazonium salt solution (prepared in the usual way from 0.6 g of the amine) was gradually added with stirring to a cooled solution of 1.5 g of IV in 10 mL of pyridine. The reaction mixture was cooled for 0.5 h and poured into 100 mL of water. The solid formed was collected and crystallized (see Table IV).

The infrared spectra of compounds VI (KBr) showed CO absorption at ca. 1730 cm^{-1} and strong band ($^2/_3$ of CO band) at ca. 1630 cm^{-1} assigned to C=N and NH at 3225 cm^{-1}. The UV spectrum of compound VIa showed two maxima at λ 240 (ε 11 250) and 380 nm (ε 22 500). Monophenylhydrazones exhibit strong absorption at wavelengths higher than 320 nm (*3*, *5*). These spectral data support the arylhydrazone structures of the coupling products VI. The ^1H NMR spectrum of compound VIa (in $CDCl_3$) showed the cycloheptene protons (10 H) as a multiplet in the δ 0.75–2.65 region, a singlet at δ 3.55 for the CH proton (a), and a singlet for the methine proton (b) at δ 5.60, and the aromatic protons (10 H) gave a multiplet centered at δ 7.50. The presence of a peak at δ 3.55 assignable to CH indicates that the coupling products VI exist in solution in the azo form.

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