Chemistry of Seven-Membered Heterocycles. 4. Synthesis and Reactions of 8-Aryl-6,7,10,11-tetrahydro-5*H*,8*H*-benzo[3.4]cyclohepteno[2,1-*d*]-thiazolo[3,2-*a*]pyrimidin-10-ones

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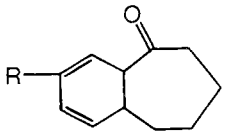
The arylmethylene derivatives of benzocyclohepten-5-one and 6-nitrobenzocyclohepten-5-one reacted with thiourea to form pyrimidine-2-thione derivatives, which reacted with chloroacetic acid to give the title compounds. The title compounds condensed with aromatic aldehydes and coupled with arenediazonium salts.

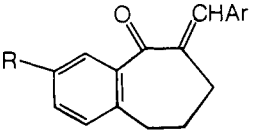
Previous papers in this series (*1–3*) dealt with some reactions of benzothiepins and benzoxepins, in which a seven-membered heterocycle is fused to a benzene ring. However, the literature revealed that the compound in which a homocyclic seven-membered ring is fused to benzene has not been thoroughly studied (*4, 6–9, 11, 12, 14–17*).

This investigation deals with derivatives of benzocyclohepten-5-ones (benzosuberone).

6,7,8,9-Tetrahydrobenzocyclohepten-5-ones (Ia, b) condensed with aromatic aldehydes in the presence of a basic catalyst, such as aqueous sodium hydroxide, sodium ethoxide, or piperidine, to give the corresponding 6-arylmethylene-6,7,8,9-tetrahydrobenzocyclohepten-5-ones (IIa–k).

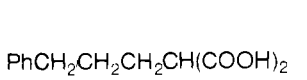


Ia, R = H
b, R = NO_2

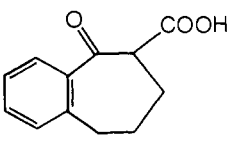


IIa, R = H; Ar = C_6H_5
b, R = H; Ar = $C_6H_5CH{=}CH$
c, R = H; Ar = $C_6H_4OCH_3$-*p*
d, R = H; Ar = $C_6H_4N(Me_2)$-*p*
e, R = H; Ar = $C_6H_3O_2CH_2$-3,4
f, R = H; Ar = $C_6H_4NO_2$-*p*
g, R = NO_2; Ar = C_6H_5
h, R = NO_2; Ar = $C_6H_4OCH_3$-*p*
i, R = NO_2; Ar = C_6H_4Cl-*p*
j, R = NO_2; Ar = $C_6H_4NMe_2$-*p*
k, R = NO_2; Ar = $C_6H_3O_2CH_2$-3,4

6,7,8,9-Tetrahydrocyclohepten-5-one was prepared by cyclization (*6, 11*) of 5-phenylpentanoic acid obtained by reduction and decarboxylation of cinnamylidenemalonic acid (*5*). In one experiment, 3-phenylpropylmalonic acid (A) was unknowingly subjected to cyclization (without being decarboxylated) by phosphoric acid–phosphorus pentoxide. When the reaction product was condensed with anisaldehyde in the presence of ethanolic sodium hydroxide, effervescence was observed and the *p*-methoxybenzylidene derivative (IIc) was formed.



A

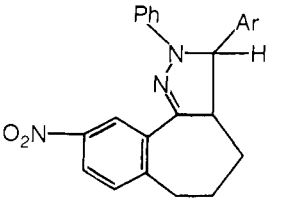


B

This shows that the decarboxylation step of acid A can be dispensed with and makes the route to the arylidene derivatives (II) shorter.

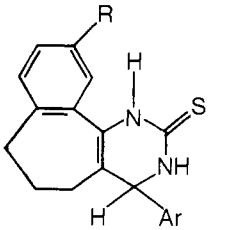
The intermediate acid, benzocyclohepten-5-one 6-carboxylic acid (B), and its decarboxylation are under further investigation.

The arylmethylene derivatives, IIg–i, reacted with phenylhydrazine in refluxing ethanol to yield 3-aryl-9-nitro-2-phenyl-2,3,3a,4,5,6-hexahydrobenzo[3.4]cyclohepteno[2,1-*c*]pyrazoles (IIIa–c).



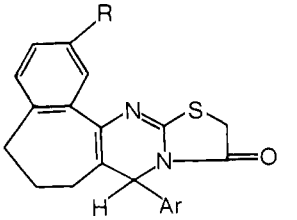
IIIa, Ar = C_6H_5
b, Ar = $C_6H_5OCH_3$-*p*
c, Ar = C_6H_4Cl-*p*

The arylmethylene derivatives, II, reacted with thiourea, either by fusion or by heating in ethanol in the presence of potassium hydroxide, to give 8-aryl-6,7,8,9,10,11-hexahydro-5*H*-benzo[3.4]cycloheptene[2,1-*d*]pyrimidine-10-thiones (IV). (For pertinent literature see ref 2.)



IVa, R = H; Ar = C_6H_5
b, R = H; Ar = $C_6H_4OCH_3$-*p*
c, R = H; Ar = $C_6H_3O_2CH_2$-3,4
d, R = NO_2; Ar = C_6H_5

Compounds IV reacted with chloroacetic acid in the presence of sodium acetate and acetic anhydride to yield tetracyclic compounds formulated as 8-aryl-6,7,10,11-tetrahydro-5*H*,8*H*-benzo[3.4]cyclohepteno[2,1-*d*]thiazolo[3,2-*a*]pyrimidin-10-ones (V), in analogy with previous derivatives (*2, 3*).



Va, R = H; Ar = C_6H_5
b, R = H; Ar = $C_6H_4OCH_3$-*p*
c, R = H; Ar = $C_6H_3O_2CH_2$-3,4
d, R = NO_2; Ar = C_6H_5

The methylene group at position 11 in compounds V proved to be active. They condensed with aromatic aldehydes to give

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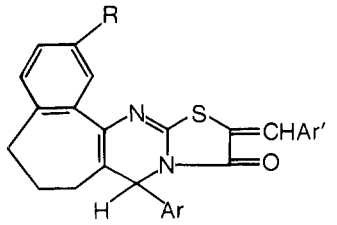
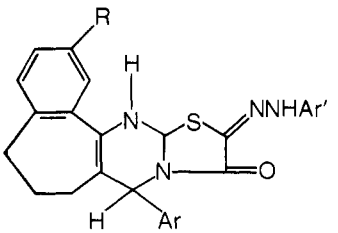
the 11-arylmethylene derivatives, VI, which could be prepared directly from IV. Also, on coupling with arenediazonium salts, compounds V afforded the arylhydrazones VII.



VIa, R = H; Ar = C_6H_5; Ar′ = C_6H_5
b, R = H; Ar = C_6H_5; Ar′ = $C_6H_4OCH_3$-*p*
c, R = H; Ar = C_6H_5; Ar′ = $C_6H_4NMe_2$-*p*
d, R = H; Ar = C_6H_5; Ar′ = $C_6H_3O_2CH_2$-3,4
e, R = H; Ar = $C_6H_4OCH_3$-*p*; Ar′ = $C_6H_3O_2CH_2$-3,4
f, R = H; Ar = $C_6H_3O_2CH_2$-3,4; Ar′ = C_6H_5
g, R = H; Ar = $C_6H_3O_2CH_2$-3,4; Ar′ = $C_6H_4OCH_3$-*p*
h, R = H; Ar = $C_6H_3O_2CH_2$-3,4; Ar′ = $C_6H_4NMe_2$-*p*
i, R = H; Ar = $C_6H_3O_2CH_2$-3,4; Ar′ = $C_6H_3O_2CH_2$-3,4
j, R = H; Ar = $C_6H_3O_2CH_2$-3,4; Ar′ = C_6H_4Cl-*p*
k, R = NO_2; Ar = C_6H_5; Ar′ = $C_6H_4NMe_2$-*p*
l, R = NO_2; Ar = C_6H_5; Ar′ = $C_6H_3O_2CH_2$-3,4



VIIIa, R = H; Ar = C_6H_5; Ar′ = C_6H_5
b, R = H; Ar = C_6H_5; Ar′ = $C_6H_4CH_3$-*p*
c, R = H; Ar = $C_6H_4OCH_3$-*p*; Ar′ = $C_6H_4CH_3$-*p*
d, R = H; Ar = $C_6H_3O_2CH_2$-3,4; Ar′ = C_6H_5
e, R = H; Ar = $C_6H_3O_2CH_2$-3,4; Ar′ = $C_6H_4CH_3$-*p*
f, R = NO_2; Ar = C_6H_5; Ar′ = $C_6H_4CH_3$-*p*

Experimental Section

6-Arylmethylene-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-ones (II). Several methods were used to prepare these arylmethylene derivatives; the first and second methods afforded the best yields. The comparison was made using piperonal.

Method A. To a hot solution of sodium hydroxide (0.5 g in 1 mL of H_2O) were added 1 g each of the ketone Ia and piperonal. The mixture was heated on a water bath for 0.5 h and stirred occasionally with a glass rod. In the beginning a clear solution was obtained, which became viscous, then solidified in about 15 min. Heating was continued for 15 min more and cooled. Water was added and the product was collected, yield 90%.

Method B. A mixture of 1 g each of Ia and piperonal was treated with a few drops of piperidine, heated at 120 °C for 50 min, and cooled. The reaction mixture was triturated with petroleum ether (bp 40–60) to give pale crystals, yield 95%.

Method C. A solution of 1 g each of Ia and piperonal in 3 mL of absolute ethanol was treated with ethanolic sodium hydroxide (0.2 g in 5 mL). The mixture was heated on a water bath for 2 h and then evaporated. The residue was collected and washed thoroughly with water, yield 88%.

Method D. To a solution of 1 g each of Ia and piperonal in 10 mL of methanol, was added 5 mL of methanolic sodium methoxide (4%). The mixture was heated on a water bath for 2 h and worked up as above, yield 80%.

The 6-arylmethylene derivatives prepared are listed in Table I. Compounds IIf–k were prepared by method B.

3-Aryl-9-nitro-2-phenyl-2,3,3a,4,5,6-hexahydrobenzo[3.4]cyclohepteno[2,1-c]prazoles (III). A suspension of 1 g

Table I. 6-Arylmethylene-6,7,8,9-tetrahydrobenzocyclohepten-5-ones (II) [a]

	Mp, °C (solvent)	Yield, %	Formula (mol wt)	IR, cm^{-1}
IIb	130 (pet.)[b]	90	$C_{20}H_{18}O$ (274.3)	1665
c	113 (MeOH)	70	$C_{19}H_{18}O_2$ (278.3)	1665
d	170 (EtOH)	80	$C_{20}H_{21}NO$ (291.4)	1665
e	120 (pet.)	95	$C_{19}H_{16}O_3$ (292.3)	
f	173 (EtOH)	70	$C_{18}H_{15}NO_3$ (293.3)	1665
g	155 (AcOH)	85	$C_{18}H_{15}NO_3$ (293.3)	1668
h	183 (AcOH)	98	$C_{19}H_{17}NO_4$ (323.3)	1668
i	140 (MeOH)	95	$C_{18}H_{14}ClNO_3$ (327.8)	
j	200 (AcOH)	85	$C_{20}H_{20}N_2O_3$ (336.4)	1668
k	223 (AcOH)	90	$C_{19}H_{15}NO_5$ (337.3)	1668

[a] Satisfactory elemental analyses were found. [b] pet. = petroleum ether, bp 60–80 °C.

Table II. 8-Aryl-9-nitro-2-phenyl-2,3,3a,4,5,6-hexahydrobenzo[3.4]cyclohepteno[2,1-c]pyrazoles (III), 8-Aryl-6,7,8,9,10,11-hexahydro-5H-benzo[3.4]cyclohepteno[2,1-d]pyrimidine-10-thiones (IV), and 8-Aryl-6,7,10,11-tetrahydro-5H,8H-benzo[3.4]cyclohepteno[2,1-d]thiazolo[3,2-a]pyrimidin-10-ones (V) [a]

No.	Mp, °C (solvent)	Yield, %	Formula (mol wt)	IR, cm^{-1}
IIIa	185 (EtOH)	95	$C_{24}H_{21}N_3O_2$ (383.4)	
b	165 (EtOH)	80	$C_{25}H_{23}N_3O_3$ (413.5)	
c	175 (EtOH)	90	$C_{24}H_{20}ClN_3O_2$ (417.9)	
IVa	270 (AcOH)	90	$C_{19}H_{18}N_2S$ (306.4)	
d	229 (AcOH)	70	$C_{20}H_{20}N_2OS$ (336.5)	
c	235 (AcOH)	90	$C_{20}H_{18}N_2O_2S$ (350.4)	
d	210 (MeCH)	85	$C_{19}H_{17}N_3O_2S$ (351.4)	
Va	130 (pet.)	60	$C_{21}H_{18}N_2OS$ (346.4)	1745
b	170 (C_6H_6)	70	$C_{22}H_{20}N_2O_2S$ (376.5)	1725
c	190 (MeOH)	80	$C_{22}H_{18}N_2O_3S$ (390.4)	1725
d	140, (cy hex)[b]	70	$C_{21}H_{17}N_3O_3S$ (391.4)	1710

[a] Satisfactory elemental analyses were found. [b] cy hex = cyclohexane.

Table III. 8-Aryl-6,7,10,11-tetrahydro-5H,8H-benzo[3.4]cyclohepteno-[2,1-d]thiazolo[3,2-a]pyrimidin-10-ones (VI) [a]

	Mp, °C (solvent)	Yield, %	Formula (mol wt)	IR, cm^{-1}
VIa	260 (AcOH)	95	$C_{28}H_{22}N_2OS$ (434.5)	1715
b	215 (AcOH)	90	$C_{29}H_{24}N_2O_2S$ (464.6)	1715
c	255 (AcOH)	98	$C_{30}H_{27}N_3OS$ (477.6)	
d	242 (AcOH)	93	$C_{29}H_{22}N_2O_3S$ (478.6)	1715
e	220 (AcOH)	98	$C_{30}H_{24}N_2O_4S$ (508.6)	1700
f	242 (AcOH)	85	$C_{29}H_{22}N_2O_3S$ (478.6)	
g	220 (AcOH)	100	$C_{30}H_{24}N_2O_4S$ (508.6)	
h	260 (AcOH)	98	$C_{31}H_{27}N_3O_3S$ (521.6)	
i	245 (AcOH)	98	$C_{30}H_{22}N_2O_5S$ (522.6)	
j	240 (AcOH)	95	$C_{29}H_{21}ClN_2O_3S$ (513.0)	
k	255 (AcOH)	60	$C_{30}H_{26}N_4O_3S$ (522.6)	
l	200 (AcOH)	75	$C_{29}H_{21}N_3O_5S$ (523.6)	

[a] Satisfactory elemental analyses were obtained.

Table IV. 8-Aryl-6,7,10,11-tetrahydro-5H,8H-benzo[3.4]-cyclohepteno[2,1-d]thiazolo[3,2-a]pyrimidine-10,11-dione 11-Arylhydrazones (VII) [a]

No.	Mp, °C (solvent)	Yield, %	Formula (mol wt)
VIIa	215 (AcOH)	75	$C_{27}H_{22}N_4OS$ (450.6)
b	250 (AcOH)	80	$C_{28}H_{24}N_4OS$ (464.6)
c	160 (EtOH)	85	$C_{29}H_{26}N_4O_2S$ (494.6)
d	222 (AcOH)	70	$C_{28}H_{22}N_4O_3S$ (494.6)
e	238 (AcOH)	78	$C_{29}H_{24}N_4O_3S$ (508.6)
f	150, (cy hex)	70	$C_{28}H_{23}N_5O_3S$ (509.6)

[a] Satisfactory elemental analyses were found.

of IIg–i was treated with 2 mL of phenylhydrazine and heated on the water bath for 2 h and evaporated. The residue was crystallized from the proper solvent. See Table II. Compounds III gave the color reactions characteristic of pyrazolines (*10, 13*).

8-Aryl-6,7,8,9,10,11-hexahydro-5H-benzo-[3.4]cyclohepteneno[2,1-d]pyrimidene-10-thiones (IV). (A) A mixture of 0.01 mol of the arylmethylene derivative (II) and 1 g of thiourea was heated in a metal bath at 170 °C (bath temperature), until the mixture melted. The viscous mass was stirred with a glass rod and the temperature of the bath was allowed to rise to 180 °C during 0.5 h and then to 190 °C. The product was crystallized from the proper solvent.

(B) A mixture of 0.02 mol of II, 1.5 g of thiourea, and 2 g of potassium hydroxide in 100 mL of absolute ethanol was heated on a water bath for 4 h and left overnight. The product was filtered off and washed with water until free from alkali. See Table II.

8-Aryl-6,7,10,11-tetrahydro-5H,8H-benzo[3.4]cyclohepteno[2,1-d]thiazolo[3,2-a]pyrimidin-10-ones (V). A mixture of 0.02 mol of IV, 3.2 g of chloroacetic acid, and 8 g of fused sodium acetate, in 40 mL of acetic acid and 20 mL of acetic anhydride was refluxed for 4 h, cooled, and poured into water. The solid (V) that separated was collected, washed with water and crystallized from the proper solvent. The products did not dissolve in sodium carbonate nor in sodium hydroxide solutions. See Table II.

8-Aryl-11-arylmethylene-6,7,10,11-tetrahydro-5H,8H-benzo[3.4]cycloheptenо[2,1-d]thiazolo[3,2-a]pyrimidin-10-ones (VI). (A) A mixture of 1 g of V, an equimolecular amount of the aldehyde, and a few drops of piperidine was heated at 150 °C for 0.5 h and cooled, and the product was crystallized.

(B) A mixture of 0.005 mol of IV, 1 g of chloroacetic acid, 2 g of fused sodium acetate, an equimolecular amount of the appropriate aldehyde in 15 mL of acetic acid, and 10 mL of acetic anhydride was refluxed for 4 h. The reaction mixture was cooled and poured onto ice. The precipitate formed was collected and crystallized. See Table III.

8-Aryl-6,7,10,11-tetrahydro-5H,8H-benzo-3,4-cyclohepteno[2,1-d]thiazolo[3,2-a]pyrimidine-10,11-dione 11-Arylhydrazones (VII). A cold diazonium salt solution (prepared in the usual way from 0.002 mol of the amine) was gradually added with stirring to a cooled solution of 0.002 mol of V in 10 mL of pyridine. The reaction mixture was cooled for 0.5 h and poured into 100 mL of water. The precipitate formed was collected and crystallized. See Table IV.

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Exocyclic Olefins: Reactions of Some Semistabilized Phosphonium Ylides with Substituted Fluorenones

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The reactions of some semistabilized phosphonium ylides with 2,7-disubstituted fluorenones have been reported to give exocyclic olefins, 9-arylidene-2,7-disubstituted-fluorenes (compounds 4a–5k). The structural assignments of the products were based on IR and NMR spectral evidence.

The reactions of nonstabilized phosphonium ylides with cyclic ketones have been extensively studied to give cyclic olefins (*7, 9, 10, 12, 19*). However, the stabilized phosphonium ylides with cyclic ketones were found to be successful under forcing conditions (*6, 7, 9, 13, 14*) and in some cases failure was observed (*8*). But, little attention has been paid toward the reactions involving interaction of semistabilized phosphonium ylides with cyclic ketones (*15, 20*). Recently, we have reported the utility of some semistabilized ylides in the syntheses of various acyclic (*16, 17*) and exocyclic (*17, 18*) olefins. In the present work, the reactions of two substituted fluorenones with a series of semistabilized phosphonium ylides have been studied with a view to examine their synthetic potentiality in the carbonyl olefination of substituted fluorenones.

Results and Discussion

The reactions of ylides (compounds **2a–k**) with 2,7-dinitrofluorenone (compound **3a**) and 2,7-dibromofluorenone (compound **3b**) were carried out at reflux temperature for 25–40 h affording exocyclic olefins, i.e., 9-arylidene-2,7-dinitrofluorenes (compounds **4a–k**), 9-arylidene-2,7-dinitrofluorenes (compounds **4a–k**), and 9-arylidene-2,7-dibromofluorenes (compounds **5a–k**), respectively, in 25–65% yields (Scheme I). It is interesting to note that ketone **3b** failed to react with ylides **2a–k** at room temperature but reacted successfully at elevated temperature. Ketone **3a** is more reactive than ketone **3b,** since the ylides **2a–k** reacted more readily with the former and afforded better yields of exocyclic olefins (compounds **4a–k**) in less time, probably due to the electron-withdrawing nature of nitro groups. Our attempts to react the stabilized ylides (com-

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