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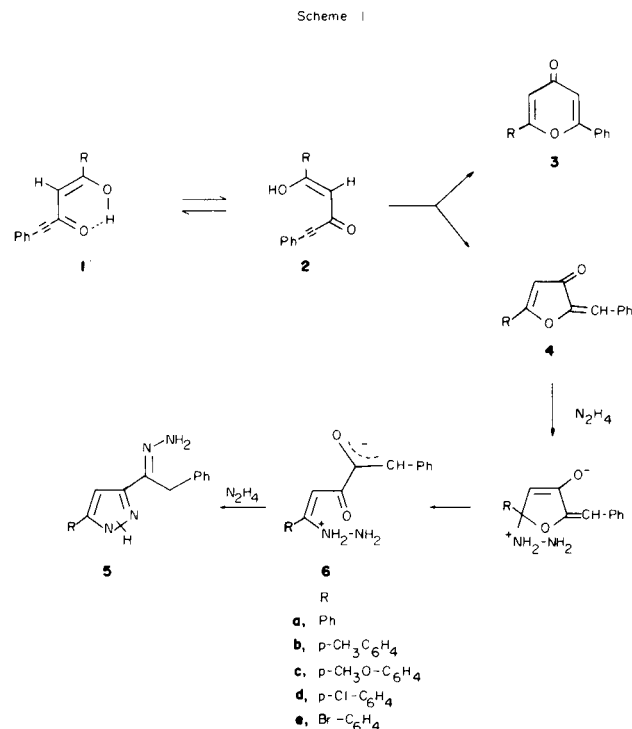
Thermal cyclization of 1,5-diarylpent-1-yne-3,5-diones led to the formation of 2-benzyliden-5-aryl-3(2*H*)-furanones as well as 2,6-diaryl-4*H*-pyran-4-ones as minor products. The structure of the furanones was established from their ir,  $^1\text{H}$  nmr and mass spectral data. Their reaction with hydrazine hydrate gave pyrazole derivatives.

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The 3(2*H*)-furanone ring system is a central structural element of several naturally occurring products such as jatrophone (2), eremantholides (3) and geiparvarin (4) which are known to possess significant anti-tumor properties. Moreover, 3(2*H*)-furanones have been used as building blocks for the synthesis of muscarins (5). However, the chemistry of this increasingly important heterocycle has been little explored. Several methods are reported for the synthesis of 3(2*H*)-furanones. Notable among these are the acid-catalyzed cyclization-dehydration of an appropriately substituted  $\alpha$ -hydroxy-1,3-diketones (6), thermal elimination of dimethyl sulfide from acylated sulfonium ylides (7) and acylation of  $\beta$ -keto-esters with halogenated acid chlorides (8). 2-Arylidene derivatives are prepared by reaction of the 3(2*H*)-furanone with the appropriate carbonyl compound (9) or Schiff base (10).

In the present study, a new route to 3(2*H*)-furanones is described. A series of 2-benzyliden-5-aryl-3(2*H*)-furanones **4a-e** were prepared from 1,5-diarylpent-1-yne-3,5-diones **1a-e** by boiling their solutions in ethanol or benzene. The 4*H*-pyran-4-ones **3a-e** were also formed as minor products in the above reaction (Scheme I). The key intermediate in this synthesis, the acetylenic  $\beta$ -diketones, were prepared by the base-catalyzed condensation of acetylenic esters with suitable ketones according to the method we recently reported (11). Moreover, reinvestigation of the structure of the products obtained alongside the 4*H*-pyran-4-ones **3b,c** from the reaction of ethyl phenylpropiolate with *p*-methyl- and *p*-methoxyacetophenones, respectively, indicated that they are the 3(2*H*)-furanones **4b,c** and not the acetylenic  $\beta$ -diketones **1b,c** as previously described (12).

At room temperature, the more favoured conformation for acetylenic  $\beta$ -diketones is the *s-cis* **1** stabilized by hydrogen bonding. However, at higher temperatures a shift to the *s-trans* conformer **2** is expected which is susceptible to cyclization to the 4*H*-pyran-4-one or the 3(2*H*)-furanone rings. In accordance with Baldwin rules for ring closure (13), both types of cyclizations, 6-*endo*-digonal for the 4*H*-pyran-4-ones **3** and 5-*exo*-digonal for the furanones **4** are favourable. While normal inductive ef-



fects should favour Michael type addition leading to the 4*H*-pyran-4-ones, spacial requirements appear to make the acetylenic carbon  $\alpha$  to the carbonyl group more accessible to the nucleophilic attack by the enolic OH so that anti-Michael formation of the 3(2*H*)-furanones should be favoured. Moreover, in the five-membered ring there may be also a rate advantage of forming an *exo* double bond as compared with internal double bond in the six-membered ring (14).

It is worthy to mention that similar anti-Michael mechanisms were suggested for the formation of thiacyclopentenone (15) and selenocyclopentenone (16) from the reaction of 1,5-diphenylpentadiyn-3-one with thiourea and hydrogen selenide, respectively, and also for pyrrolinones (15) from the amine adducts of pentadiyn-3-ones.

In agreement with the assigned structures, the  $^1\text{H}$  nmr

spectra of the 3(2*H*)-furanones **4** showed two singlets at  $\delta$  6.13-6.32 and 6.73-6.87 for the C-4 ring and benzylidene protons, respectively. The assignment of the high field signal to the ring proton is supported by the reported data for several 4-unsubstituted 3(2*H*)-furanones (7,17). Moreover, the chemical shift of the arylidene proton in several 2-arylidene-3(2*H*)-furanones appeared in the range  $\delta$  6.73-6.82 (9).

Table I

Infrared and <sup>1</sup>H NMR Spectral Data of 3(2*H*)-Furanones

	IR (cm <sup>-1</sup> )		<sup>1</sup> H NMR Chemical Shift ( $\delta$ /ppm) (a)			
	C=C (b)	C=O	H-4 (s)	Benzylid- ene-H (s)	Ar-H (m)	Others (s)
<b>4a</b>	1657	1695	6.30	6.82	7.7	
<b>4b</b>	1652	1692	6.25	6.80	7.6	2.48
<b>4c</b>	1644	1689	6.13	6.73	7.4	(CH <sub>3</sub> ) 3.88
<b>4d</b>	1659	1702	6.32	6.87	7.7	(OCH <sub>3</sub> )
<b>4e</b>	1652	1691	6.23	6.77	7.5	

(a) s: Singlet, m: multiplet. (b) Exocyclic double bond.

Table II

Relative Intensity of The Most Prominent Peaks in The Mass Spectra of The 3(2*H*)-Furanones

	M	i	ii	iii	iv	v	vi
<b>4a</b>	83	100	13	33	92	88	33
<b>4b</b>	90	100	26	13	66	43	15
<b>4c</b>	97	100	7	72	69	51	34
<b>4d</b>	28, 78	46, 100	4, 10	6, 15	97	81	28
<b>4e</b>	43, 43	55, 53	16, 16	10, 10	100	93	29

Table III

Analytical Data of The 3(2*H*)-Furanones

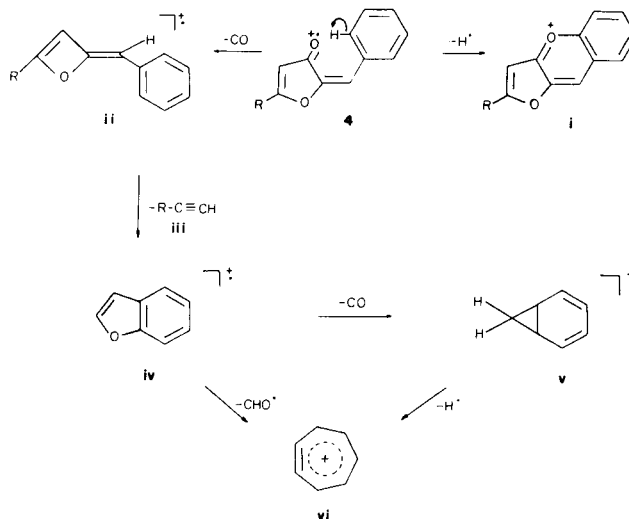
Mp °C	Formula	Calcd. %			Found %		
		C	H	X	C	H	X
<b>4a</b>	138	C <sub>17</sub> H <sub>12</sub> O <sub>2</sub>	82.2	4.9		82.5	4.8
<b>4b</b>	133	C <sub>18</sub> H <sub>14</sub> O <sub>2</sub>	82.4	5.4		82.7	5.2
<b>4c</b>	140	C <sub>18</sub> H <sub>14</sub> O <sub>3</sub>	77.7	5.1		77.3	4.9
<b>4d</b>	167	C <sub>17</sub> H <sub>11</sub> ClO <sub>2</sub>	72.2	4.0	12.5	72.4	4.1
<b>4e</b>	190	C <sub>17</sub> H <sub>11</sub> BrO <sub>2</sub>	62.4	3.4	24.4	62.3	3.6

*E* and *Z* isomerism is possible with benzylidenefuranones. In  $\alpha,\beta$ -unsaturated carbonyl compounds, the anisotropic deshielding of the carbonyl group causes the olefinic proton *cis* to the carbonyl group to resonate at lower field than in the *trans* arrangement so that assignment of configuration can be made on the basis of the chemical shift of the olefinic proton. The observation of a single chemical shift value for the benzylidene proton indicates the exclusive presence of only one form to which the

*Z*-configuration is tentatively assigned. Such conclusion is supported by several observations. The chemical shift value is very close to that reported for a series of 2-benzylidene-4-carboethoxy-5-methyl-3(2*H*)-furanones which were shown to have the *Z* configuration by <sup>1</sup>H nmr spectroscopy using lanthanide shift reagent (18). Also <sup>1</sup>H nmr studies of stereoisomerism of some 3-arylidenebutenolides, 4-arylideneoxazolin- and indazolin-5-ones showed that structures in which the aryl nucleus is more remote from the cyclic carbonyl group are favoured (19). Moreover, the infrared spectra of the furanones **4** exhibited besides the carbonyl absorption in the region 1689-1702 cm<sup>-1</sup>, a strong exocyclic C=C absorption in the range 1644-1659 cm<sup>-1</sup>, similar to that reported for *Z*-2-benzylidenebenzofuran-3(2*H*)-ones (20) and *E*-2-arylideneindanones (21).

The structure of the 2-benzyliden-5-aryl-3(2*H*)-furanones **4** was further confirmed from mass spectral data. The relative intensity of the most prominent peaks are listed in Table II and the possible fragmentation pathways are shown in Scheme II. Pronounced molecular ion peaks were observed for all compounds. Except for **4e**, the base peak in their spectra was the (M-1) species which may be represented as the stable oxonium ion *i* arising by loss of hydrogen from the benzylidene phenyl ring. Examples of such type of reactions in the electron impact mass spectra of 2-benzylidenecoumaran-3-ones (22) and other systems (23) where ring closure is assumed to occur to form stable oxonium ions have been reported. Loss of CO from the molecular ion leads to the moderately intense M-CO peak *ii* which eliminates arylacetylene molecule *iii* giving rise to a very strong peak at m/e 118. The latter can be formulated as the benzofuran odd-electron ion (*iv*), subsequent fragmentation of which affords the odd-electron benzocyclopropene ion (*v*) at m/e 90 and the dehydrotropylum cation (*vi*) at m/e 89 by successive loss of CO and H.

Scheme II



Such fragmentation pattern characterizes the mass spectra of benzofurans (24).

The 3(2H)-furanone ring is susceptible to ring opening and subsequent recyclization by nucleophilic reagents leading to new cyclic compounds. Thus, the reaction with hydrazines leads to pyrazole derivatives (25) and with primary amines, pyrrolinones are formed (26). In the present study, the reaction of 2-benzyliden-5-aryl-3(2H)-furanones **4a-e** with hydrazine hydrate in ethanol afforded 5(3)-aryl-3(5)-[ $\alpha$ -hydrazonophenylethyl]pyrazoles **5a-e** in good yield. The mechanism of this reaction involves a Michael addition of the hydrazine at C-5 of the furanone, ring opening to the resonance-stabilized enolate **6** which subsequently cyclizes to the pyrazole **5** (27) (Scheme I). Evidently, the above reaction is, so far, the best route to the pyrazoles **5** since in the alternative methods for their synthesis from acetylenic  $\beta$ -diketones (11) or diacetylenic ketones (28) and hydrazine, relatively poor yields were obtained due to formation of isomeric mixtures.

## EXPERIMENTAL

Microanalyses were performed by the Microanalysis Unit, Cairo University, Cairo. Infrared spectra were measured with a Unicam SP 1025 spectrophotometer for potassium bromide pellets or in Nujol. The  $^1\text{H}$  nmr spectra were recorded on a Varian EM-390 90 MHz spectrometer for solutions in deuteriochloroform with TMS as internal standard. Mass spectra were recorded on an AEI MS 30 spectrometer.

### 1,5-Diarylpent-1-yne-3,5-diones.

They were prepared from the respective copper salts as described earlier (11).

#### 1-Phenyl-5-*p*-chlorophenylpent-1-yne-3,5-dione (**1d**).

This compound was obtained as needles (methanol), mp 135°; ir:  $\nu$  max ( $\text{cm}^{-1}$ ) 1597 (C=O), 2212 (C $\equiv$ C);  $^1\text{H}$  nmr: ( $\delta$ /ppm) 6.35 (s, ethylenic H-4), 7.8 (m, Ar-H).

Anal. Calcd. for  $\text{C}_{17}\text{H}_{11}\text{ClO}_2$ : C, 72.2; H, 3.9; Cl, 12.5. Found: C, 72.1; H, 3.7; Cl, 12.2.

#### 1-Phenyl-5-*p*-bromophenylpent-1-yne-3,5-dione (**1e**).

This compound was obtained as needles (ether), mp 105°; ir:  $\nu$  max ( $\text{cm}^{-1}$ ) 1590 (C=O), 2217 (C $\equiv$ C);  $^1\text{H}$  nmr: ( $\delta$ /ppm) 6.54 (s, ethylenic H-4), 7.7 (m, Ar-H).

Anal. Calcd. for  $\text{C}_{17}\text{H}_{11}\text{BrO}_2$ : C, 62.4; H, 3.4; Br, 24.4. Found: C, 62.2; H, 3.6; Br, 23.9.

### 2-Benzyliden-5-aryl-3(2H)-furanones (Tables I, II, III).

A solution of the acetylenic  $\beta$ -diketone (0.002 mole) in 95% ethanol (10 ml) or benzene (10 ml) was refluxed for 1-2 hours. After removal of most of the solvent under reduced pressure, the separated solid was subjected to fractional crystallization from ethanol or methanol. The furanones (50-60% yield) separated first, and from the mother liquors, 2-phenyl-6-aryl-4H-pyran-4-ones were obtained (20-30% yield).

#### 5(3)-Aryl-3(5)-[ $\alpha$ -hydrazonophenylethyl]pyrazoles.

A solution of the 3(2H)-furanone (0.002 mole) in 95% ethanol (10 ml) was refluxed with 99% hydrazine hydrate (1 ml, 0.02 mole) for 2-3 hours. After removal of most of the solvent and dilution with water, the separated pyrazoles (70-90% yield) were crystallized from benzene-petroleum ether (bp 60-80°). These pyrazoles were found to be completely identical

(mp, mixed mp, ir and  $^1\text{H}$  nmr spectra) with authentic samples prepared from acetylenic  $\beta$ -diketones and hydrazine hydrate (11).

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