TABLE 1. 7-Aryl-6,7-dihydro-8H-indeno[1',2':2.3]pyrano[3,5-c]benzo[c]pyran-6,8-diones IIIa-c and Their Thio Analogs IVa,b

Compound	mp, °C	IR spectrum, cm^{-1}		Found, %			Empirical formula	Calculated, %			Yield, %
		C—O	C=C	C	H	S[N](Br)		C	H	S[N](Br)	
IIIa	283—284	1025—1358	1660	76,4	3,9	—	$C_{26}H_{16}O_5$	76,4	3,9	—	46
IIIb	293—294	1048—1350	1660	70,8	3,0	[3,2]	$C_{25}H_{13}NO_6$	70,9	3,1	[3,3]	94
IIIc	296	1040—1355	1662	65,6	2,6	(17,4)	$C_{25}H_{13}BrO_4$	65,6	2,8	(17,5)	77
IVa	268—269	1018—1338	1661	73,5	3,7	7,4	$C_{26}H_{16}O_4S$	73,6	3,8	7,5	42
IVb	270—271	1060—1343	1660	68,3	2,9	7,2 [3,1]	$C_{25}H_{13}NO_5S$	68,3	3,0	7,3 [3,2]	89

heated on a boiling-water bath. At the end of the reaction (monitoring by TLC), the contents of the flask were cooled, and the solid phase was removed by filtration and washed successively with acetic anhydride and methanol. All of the IIIa-c and IVa,b obtained were yellow and dissolved when they were heated in benzene, chloroform, and acetone.

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SYNTHESIS, HALOGENATION, AND NITRATION OF 6-METHYL-3-PHENYL-2-PYRONE DERIVATIVES

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Simple methods for the synthesis of 3-aryl-6-methyl-2-pyrones and 3-aryl-5-carbalkoxy-6-methyl-2-pyrones by the reaction of ethyl α-formylarylacetates with acetone and acetoacetic acid esters, respectively, are proposed. Some electrophilic substitution reactions of 6-methyl-3-phenyl-2-pyrone and 5-carbethoxy-6-methyl-3-phenyl-2-pyrone were studied.

2-Pyrones are quasi-aromatic compounds with a complex set of chemical properties. The relative activities of pyrone and phenyl rings in electrophilic substitution reactions of derivatives of 4-phenyl-2-pyrone, 5-phenyl-2-pyrone, and 6-phenyl-2-pyrone have been previously studied [1-4]. It was established that, depending on the nature of the electrophilic agent, the structure of the pyrone, and the reaction conditions, substitution may occur in the 3 and 5 positions of the pyrone ring or in the para and meta positions of the phenyl ring.

Electrophilic substitution in 3-phenyl-2-pyrone derivatives has not been studied; this is apparently due to the difficulty in obtaining these compounds. Only the four-step synthesis of 3-phenyl-6-methyl-2-pyrone from phenylacetonitrile and methyl vinyl ketone in ~10% overall yield is known [5]. In this connection, we have developed two rather simple methods for the synthesis of 3-aryl-6-methyl-2-pyrones and 3-aryl-5-carbalkoxy-6-methyl-2-pyrones and studied their behavior in electrophilic substitution reactions.

The corresponding 3-aryl-6-methyl-2-pyrones IIa-c were synthesized in 20-23% overall yields by condensation of ethyl α-formylarylacetates Ia-c with acetone in the presence of

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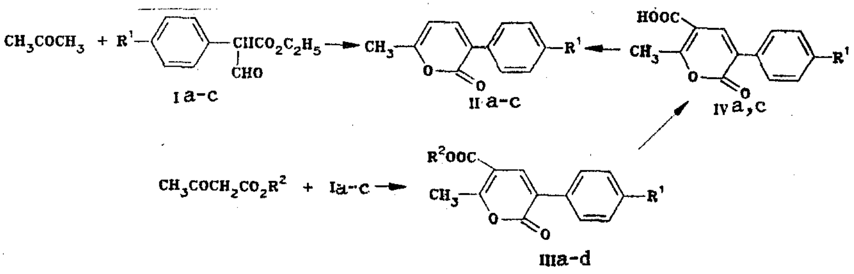
potassium tert-butoxide with subsequent treatment with acetyl chloride. Only the starting reagents were isolated when an attempt was made to subject homologs of acetone, viz., 2-butanone, 2-hexanone, and 2-octanone, to this reaction.

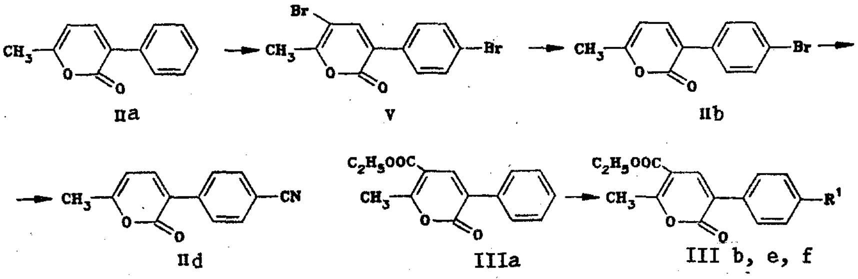


I—IV a R^1=H; I—III b R^1=Br; I—IV c R^1=CH_3O, R^2=C_2H_5; III d R^1=CH_3O, R^2=CH_3

For the synthesis of 3-aryl-6-methyl-2-pyrones we also developed a second method: 3-aryl-5-carbalkoxy-6-methyl-2-pyrones III, the hydrolysis of which in hydrochloric acid gave acids IV in 40-60% yields, were synthesized in 45-75% yields by heating acetoacetic acid esters with I in acetic acid in the presence of catalytic amounts of piperidine. Decarboxylation of IV to give 3-aryl-6-methyl-2-pyrones in 55-90% yields occurs when they are heated in quinoline at 200°C in the presence of copper powder.

Electrophilic substitution in the 3-phenyl-2-pyrone series was studied in the case of 6-methyl-3-phenyl-2-pyrone and 5-carbethoxy-6-methyl-3-phenyl-2-pyrone. It was found that IIa is brominated in the presence of aluminum chloride in trifluoroacetic acid in the 5 position of the pyrone ring and in the para position of the phenyl ring. Compound IIIa is inert with respect to bromine in the presence of iron or aluminum chloride and could be brominated and iodinated only by the Gubo—Birkenbach—Waters method. 3-(p-Bromophenyl)- and 3-(p-iodophenyl)-5-carbethoxy-6-methyl-2-pyrone (IIIb,e) were obtained when the reaction was carried out in 90% sulfuric acid in the presence of silver sulfate.

Substitution also takes place in the para position of the phenyl ring (60% yield) in the nitration of IIIa with a nitrating mixture at 5-10°C.



IIIb R^1=Br, e R^1=I, f R^1=NO_2

We were unable to detect significant amounts of the ortho and meta isomers of IIIb,e,f by thin-layer chromatography (TLC) and gas-liquid chromatography (GLC). The positions of the substituents in the halogenation and nitration of IIa and IIIa were proved by oxidation of IIIb,e,f and V with potassium dichromate in sulfuric acid to the corresponding p-substituted benzoic acids [3] and by means of PMR spectroscopy. Thus the spectrum of V does not contain a signal at 6.1 ppm corresponding to the signal of a proton in the 5 position of the pyrone ring of pyrone IIa, whereas the four protons of the phenyl ring in IIIb,e,f and V give symmetrical spectra that correspond to the four-spin AA^1BB^1 system, which indicates a para orientation of the substituent in the phenyl ring.

Compounds IIa and IIIa do not undergo the Friedel—Crafts reaction with acetyl chloride and aluminum chloride even in the case of refluxing in methylene chloride; this is apparently explained by the electron-acceptor character of the carbonyl group of the pyrone ring. A certain degree of deactivation of the phenyl ring is also observed in the bromination of IIa and IIIa, which does not occur when iron powder or potassium bromate is used and requires the use of stronger catalysts, viz., aluminum chloride and silver sulfate.

Thus the pyrone ring in 6-methyl-3-phenyl-2-pyrone derivatives decreases the activity of the phenyl ring in the Friedel—Crafts reaction and in bromination but is a p-orienting

TABLE 1. Characteristics of II-V

Comp.	mp, °C	IR spectrum, cm^{-1}	PMR spectrum, ppm	Found, %		Empirical formula	Calc., %		Yield, %
				C	H (N)		C	H (N)	
IIb	87—88	1710, 1630		54,7	3,6	$C_{12}H_9BrO_2$	54,3	3,4	25
IIc	90—92	2920, 1720, 1620		73,2	5,4	$C_{13}H_{12}O_3$	73,6	5,3	20 (A) 55 (B)
IId	166—167	2235, 1712, 1635		72,0	4,1 (6,4)	$C_{13}H_9NO_2$	72,2	4,2 (6,5)	47
IIIa	105—106	2990, 1730, 1705, 1618	8,30, s; 7,90, m; 4,73, q; 3,03, s; 1,70, t	69,4	5,5	$C_{15}H_{14}O_4$	69,8	5,5	73
IIIb	103—104	2990, 1745, 1705, 1620	8,16, s; 7,87, s; 4,70, q; 2,97, s; 1,64, t	53,4	3,7	$C_{16}H_{13}BrO_4$	53,5	3,9	50
IIIc	84—86	2980, 2920, 1745, 1720	8,16, d; 7,80, s; 7,13, d; 4,60, q; 4,10, s; 2,93, s; 1,70, t	67,4	5,3	$C_{16}H_{16}O_5$	67,1	5,6	67
IIId	94—95	2920, 1740, 1720, 1625	7,97, d; 7,70, s; 7,06, d; 4,03, s; 2,86, s	65,4	5,3	$C_{15}H_{14}O_5$	65,7	5,0	50
IIIe	110—112	2940, 1750, 1710, 1630	8,43, s; 7,86; 8,14, q; 4,66, q; 3,06, s; 1,66, t	46,9	3,3	$C_{15}H_{13}IO_4$	46,9	3,4	45
IIIf	148—149	2980, 1755, 1705, 1620	8,53, d; 8,43, s; 8,17, d; 4,73, q; 3,03, s; 1,70, t	60,1	4,2 (4,3)	$C_{15}H_{13}NO_6$	59,9	4,3 (4,6)	60
IVa	220—221	3420, 1730, 1705, 1620		67,6	4,3	$C_{13}H_{10}O_4$	67,8	4,4	55
IVc	187	3410, 2920, 1740, 1710, 1615		64,4	4,7	$C_{14}H_{12}O_5$	64,6	4,6	40
V	151—152	1710, 1615	8,11, s; 8,08, s; 2,35, s	41,3	2,2	$C_{12}H_8Br_2O_2$	41,9	2,3	80

grouping; this is apparently explained by participation of the pyrone ring in stabilization of the transition state in the case of attack by the electrophilic agent at the para position.

The 5-bromo-2-(p-bromophenyl)-6-methyl-2-pyrone (V) that we synthesized is readily reduced to 3-(p-bromophenyl)-6-methyl-2-pyrone (IIb) in 75% yield when it is heated with zinc in acetic acid; IIb was converted to 6-methyl-3-(p-cyanophenyl)-2-pyrone (IId) by the Rosenmund—von Braun reaction in dimethylformamide.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions in $CDCl_3$ were obtained with a Tesla-467 spectrometer (60 MHz) with tetramethylsilane as the internal standard. The physicochemical and spectral characteristics of II-V are presented in Table 1.

6-Methyl-3-phenyl-2-pyrone (IIa). A) A solution of 19 g (0.1 mole) of ethyl α-formylphenylacetate in 20 ml of dry acetone was added gradually to a suspension of 15 g of potassium tert-butoxide in 30 ml of absolute tert-butyl alcohol, after which the mixture was refluxed for 1.5 h. It was then cooled and poured into dilute hydrochloric acid, and the mixture was extracted with benzene. The benzene was removed by distillation, the residue was dissolved in 30 ml of acetyl chloride, and the solution was refluxed for 4 h. The excess acetyl chloride was removed by distillation, and the residue was distilled *in vacuo*. Recrystallization of the distillate from hexane gave 4.3 g (23%) of 6-methyl-3-phenyl-2-pyrone (IIa) with mp 64-65°C (mp 63-64°C) [5]).

3-(p-Bromophenyl)-6-methyl-2-pyrone (IIb) and 3-(p-Methoxyphenyl)-6-methyl-2-pyrone (IIc). These compounds were similarly obtained.

B) A mixture of 2.3 g (0.01 mole) of acid IVa, 2 ml of quinoline, and 0.5 g of copper powder was heated at 200-210°C until gas evolution was complete (∿1 h). It was then cooled and treated with 30 ml of benzene, and the benzene solution was washed with dilute hydrochloric acid (three 20-ml portions) and water (three 20-ml portions) until the wash water was neutral. The organic layer was dried over sodium sulfate, the benzene was removed by distillation, and the residue was recrystallized from hexane to give 1.6 g (88%) of IIa with mp 65°C.

3-(p-Methoxyphenyl)-6-methyl-2-pyrone. This compound was similarly obtained.

6-Methyl-3-(p-cyanophenyl)-2-pyrone (IId). A mixture of equimolar (0.01 mole) amounts of IIb and copper cyanide in 15 ml of dimethylformamide (DMF) was refluxed for 3 h, after which the reaction mixture was decomposed with a hydrochloric acid solution of ferric chloride. The resulting precipitate was removed by filtration, washed with water, and recrystallized from alcohol.

3-Aryl-5-carbalkoxy-6-methyl-2-pyrones IIIa-d. A mixture of 0.01 mole of ethyl acetoacetate, 0.01 mole of the corresponding I, 10 ml of acetic acid and 0.3 ml of piperidine was refluxed for 14-16 h. At the end of the reaction, the reaction mixture was poured into ice water, and the precipitate was removed by filtration and recrystallized from alcohol.

3-Aryl-5-carboxy-6-methyl-2-pyrones IVa,c. A mixture of 0.05 mole of III and 70 ml of concentrated hydrochloric acid was refluxed for 4-5 h, after which it was cooled and poured into water. The aqueous mixture was extracted with chloroform, and the organic layer was washed with water and a saturated solution of sodium bicarbonate (three 70-ml portions). The wash waters were acidified with hydrochloric acid, and the resulting precipitate was removed by filtration, washed with water, and recrystallized from 60% aqueous alcohol. Unchanged ester III remained in the chloroform layer.

5-Bromo-3-(p-bromophenyl)-6-methyl-2-pyrone (V). A 1-ml sample of bromine was added gradually at 20-30°C to a mixture of 3.7 g (0.02 mole) of IIa, 4 g (0.03 mole) of aluminum chloride, and 20 ml of trifluoroacetic acid, after which the reaction mixture was maintained at 20-30°C for 1 h and at 50-60°C 1 h. It was then poured into a solution of 2 g of sodium sulfate in 70 ml of water, and the resulting precipitate was removed by filtration, washed with water, and recrystallized from alcohol to give V, with mp 153°C, in 80% yield. 3-(p-Bromophenyl)-6-methyl-2-pyrone (IIb) was formed in 75% yield in the reduction of V with zinc dust in refluxing acetic acid.

Halogenation of 5-Carbethoxy-6-methyl-3-phenyl-2-pyrone. A 0.03-mole sample of bromine or iodine was added at 20°C to a solution of 5 g (0.02 mole) of IIIa and 3 g (0.01 mole) of silver sulfate in 50 ml of 90% sulfuric acid, and the mixture was stirred for 1 h. The precipitated silver halide was removed by filtration, and the filtrate was poured into a solution of 2 g of sodium sulfite in 150 ml of ice water. The precipitate was removed by filtration, washed with water, and recrystallized from alcohol. 3-(p-Bromophenyl)-5-carbethoxy-6-methyl-2-pyrone (IIIb) was obtained in 50% yield, and 3-(p-iodophenyl)-5-carbethoxy-6-methyl-2-pyrone (IIIe) was obtained in 45% yield.

3-(p-Nitrophenyl)-5-carbethoxy-6-methyl-2-pyrone (IIIf). An equimolar amount of nitric acid (d = 1.5) was added gradually dropwise at 0-5°C to a solution of IIIa in 30 ml of concentrated H_2SO_4, and the resulting solution was stirred at 10-15°C for 4 h. It was then poured over ice, and the resulting precipitate was removed by filtration, washed with water, and recrystallized from alcohol to give IIIf in 60% yield.

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