IODINATION OF 6-ARYL-2-PYRONES

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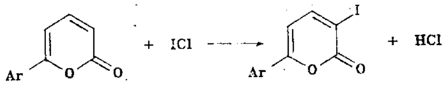
The iodination of 6-aryl-2-pyrones with iodine chloride in glacial acetic acid leads to the corresponding 3-iodo derivatives. 3-Cyano-6-phenyl-2-pyrone and 3-phenylethynyl-6-phenyl-2-pyrone were obtained by replacement of the iodo group by cyano and phenylethynyl groups.

3-Iodo-6-aryl-2-pyrones are of interest for the preparation of the corresponding 3,3'-bis(2-pyrones) via the Ullmann reaction [1]. In addition, they open up the possibility of the synthesis of 2-pyrone derivatives by replacement of the iodine atom by various groupings via reactions similar to those for aryl iodides [2].

However, up until now there has been no convenient method for the synthesis of 3-iodo-2-pyrones. It was shown in [1] that the iodination of 6-aryl-2-pyrones by the action of iodine in the presence of concentrated nitric acid [3] leads to mixtures of 3-iodo- and 3-nitro-2-pyrones. We have studied the iodination of 6-phenyl-2-pyrone by the action of iodine in the presence of hydrogen peroxide, periodic acid, $Na_2S_2O_8$, and yellow mercuric oxide. The results of iodination are presented in Table 1.

The highest yield of 3-iodo-6-phenyl-2-pyrone was obtained in the iodination with iodine in the presence of H_2O_2 in glacial acetic acid. The action of iodine in the presence of periodic acid is accompanied by oxidation of 6-phenyl-2-pyrone to benzoic acid.

We found that iodination with iodine chloride is a convenient method for the preparation of 3-iodo-6-substituted 2-pyrones.

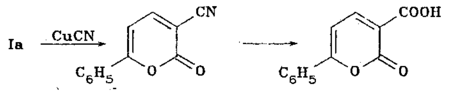


Ia-h

a Ar=C_6H_5; b Ar=p-$CH_3C_6H_4$; c Ar=p-$CH_3OC_6H_4$; d Ar=(2,5CH_3O)C_6H_3; e Ar=2-naphthyl;
f Ar=1-naphthyl; g Ar=p-$NO_2C_6H_4$-; h Ar=m-$NO_2C_6H_4$

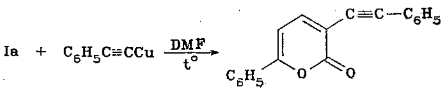
The reaction proceeds smoothly at room temperature in solution in acetic acid or carbon tetrachloride.

Iodination in the pyrone ring rather than in the benzene ring is conformed by the PMR spectra of 3-iodo-6-phenyl- and 3-iodo-6-(p-tolyl)-2-pyrone. The incorporation of iodine in the 3 position rather than in the 5 position of the pyrone ring is confirmed by conversion of 3-iodo-6-phenyl-2-pyrone to the known 6-phenyl-2-pyrone-3-carboxylic acid (III) via the scheme



II III

We demonstrated the possibility of the use of 3-iodo-2-pyrones for the synthesis of other derivatives in the case of reactions to prepare 3-cyano-6-phenyl-2-pyrone (Ia → II) and 3-phenylethynyl-6-phenyl-2-pyrone (Ia → IV).



IV

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TABLE 1. Iodination of 6-Phenyl-2-pyrone

6-Phenyl-pyrone : I_2 ratio	Oxidizing agent	Solvent	Reaction temp., °C	Time, h	Yield, %
1 : 1	HgO	C_6H_6	80	20	36
1 : 0,5	H_2O_2	CH_3COOH	117	8	50
1 : 0,5	H_2O_2	C_2H_5OH	75	30	0
1 : 1	HIO_3	C_2H_5OH	80	22	0
1 : 1	HNO_3 (*d* 1,49)	CH_3COOH CCl_4	90	6	33

TABLE 2. 3-Iodo-6-aryl-2-pyrones

Compound	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	I		C	H	I	
Ia	160—161				$C_{11}H_7O_2I$				70
Ib	185—186	46,4	2,9	40,9	$C_{12}H_9O_2I$	46,2	2,9	40,7	75
Ic	160—161	44,2	2,6	38,4	$C_{12}H_9O_3I$	43,9	2,7	38,7	43
Id	145—146	45,4	2,8	37,2	$C_{13}H_{11}O_4I$	45,6	3,0	37,2	40
Ie	199—200	51,6	2,3	37,0	$C_{15}H_9O_2I$	51,7	2,6	36,6	45
If	202—204	51,5	2,4	37,1	$C_{15}H_9O_2I$	51,7	2,6	36,6	55
Ig	198—199	38,1	2,1	37,0	$C_{11}H_6O_4NI$	38,5	1,8	37,4	50
Ih	187—189	38,2	2,1	37,2	$C_{11}H_6O_4NI$	38,5	1,8	37,4	55

Both of these reactions lead to derivatives of 2-pyrones that were previously difficult to obtain. The structures of the compounds obtained were confirmed by the results of elementary analysis and the IR spectra.

EXPERIMENTAL

The IR spectra were recorded with a UR-10 spectrometer. The PMR spectra were obtained with a WP-200SI spectrometer. The purity of the compounds obtained was confirmed by thin-layer chromatography (TLC) on Silufol UV-254 plates.

Iodination of 6-Phenyl-2-pyrone. A) A solution of 0.56 g (2.2 mmole) of iodine in 10 ml of CH_3COOH and 0.12 ml of H_2SO_4 was added to a solution of 0.75 g (4.4 mmole) of 6-phenyl-2-pyrone in 20 ml of CH_3COOH, and the mixture was heated to 90°C. A 1.5-ml sample of 21% hydrogen peroxide was added dropwise with vigorous stirring in the course of 3 h, after which the mixture was refluxed for 8 h. The course of the reaction was monitored by means of TLC. The reaction mixture was poured into water, and the aqueous mixture was extracted repeatedly with ether. The extract was washed with a saturated solution of $Na_2S_2O_3$ and water and dried with $MgSO_4$. The solvent was removed by vacuum distillation, and the residue was recrystallized from ethanol to give 0.6 g (50%) of 3-iodo-6-phenyl-2-pyrone (Ia) with mp 161°C [mp 160-161°C (from alcohol) [3]]. PMR spectrum: 7.92 (1H, d, 4-H); 6.33 (1H, d, 5-H); 7.8, 7.43 ppm (5H, m, C_6H_5).

B) A 0.55-g (2 mmole) sample of iodine and 0.43 g (2 mmole) of HgO were added alternately in the course of 2 h to a solution of 0.34 g (2 mmole) of 6-phenyl-2-pyrone in 20 ml of benzene, and the mixture was refluxed with stirring for 25 h. The precipitated mercuric iodide was removed by filtration and washed repeatedly with benzene. The combined filtrates were shaken with a saturated solution of $Na_2S_2O_3$, washed with water, and dried with $MgSO_4$. The solvent was removed *in vacuo*, and the residue was chromatographed with a column packed with SiO_2 (elution with benzene) to give 0.21 g (36%) of iodopyrone Ia.

C) A solution of 3.08 g of iodine in 15 ml of alcohol was added to 4.3 g (2.5 mmole) of 6-phenyl-2-pyrone in 25 ml of alcohol, the mixture was heated to the boiling point, a solution of 0.88 g of HIO_3 in 15 ml of water was added in the course of 2 h, and the mixture was refluxed for 22 h. It was then poured into water, and the precipitate was removed by filtration to give 2.04 g of the starting compound with mp 67°C (from heptane). The filtrate was extracted with chloroform, and the extracts were combined, washed with water, and dried with $MgSO_4$. The solvent was removed *in vacuo* to give 1 g (37%) of benzoic acid with mp 112°C (from water).

Iodination of 2-Pyrones with Iodine Chloride. A mixture of the 6-aryl-2-pyrone and iodine chloride [5] in a ratio of 1:1 was stirred in glacial acetic acid or in CCl_4 in the dark at room temperature for 2-7 days, during which the reaction was monitored by TLC. The reaction mixture was poured into water, and the liberated oil was extracted with ether or chloroform. The extract was washed with a saturated solution of $Na_2S_2O_3$ and water and dried with $MgSO_4$. The solvent was removed by distillation *in vacuo*, and the residue was recrystallized to give the corresponding 3-iodo-6-aryl-2-pyrone. Data on Ia-h are presented in Table 2.

3-Cyano-6-phenyl-2-pyrone (II). A 0.58-g (2 mmole) sample of Ia and 1.2 g of cuprous cyanide [6] in absolute diglyme was refluxed for 32 h in a stream of argon, after which the hot mixture was filtered, and the precipitate was washed with hot diglyme. The filtrate was poured into water, and the resulting precipitate was separated and chromatographed with a column packed with SiO_2 [elution with benzene—chloroform (3:7)] to give 0.25 g (65%) of yellow crystals of II with mp 184-185°C. IR spectrum: 2220 (CN) and 1730 cm^{-1} (CO). Found: C 73.0; H 3.5; N 6.9%. $C_{12}H_7NO_2$. Calculated: C 73.1; H 3.5; N 7.1%.

3-Cyano-6-(p-tolyl)-2-pyrone. This compound, with mp 198-198.5°C, was obtained by a procedure similar to that used to prepare II. IR spectrum: 2228 (CN) and 1742 cm^{-1} (—CO). Found: C 75.3; H 3.9; N 6.2%. $C_{13}H_9NO_2$. Calculated: C 75.4; H 4.0; N 6.2%.

3-Phenylethynyl-6-phenyl-2-pyrone (IV). A mixture of 0.6 g (3.7 mmole) of copper phenylacetylide [2] and 0.9 g (3 mmole) of Ia in 65 ml of absolute dimethylformamide (DMF) was refluxed with stirring in a stream of argon for 20 h, after which the mixture was poured into water, and the resulting precipitate was removed by filtration, washed with water, dried, and chromatographed on SiO_2 (elution with benzene) to give 0.5 g (62.5%) of yellow crystals with mp 138°C (from hexane). IR spectrum: 2340 ($C{\equiv}C$) and 1720 cm^{-1} (CO). Found: C 83.5; H 4.5%. $C_{19}H_{12}O_2$. Calculated: C 83.8; H 4.4%.

6-Phenyl-2-pyrone-3-carboxylic Acid (III). A 0.1-g (0.6 mmole) sample of 3-cyano-6-phenyl-2-pyrone was refluxed in 10 ml of glacial acetic acid and 2 ml of hydrochloric acid for 8 h, after which the mixture was poured into water, and the aqueous mixture was extracted with chloroform. The extract was washed with water and dried with $MgSO_4$, and the solvent was removed *in vacuo* to give 0.07 g (64.5%) of white crystals with mp 169-170°C (from glacial acetic acid) (mp 169°C [4]).

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