

4-ARYL-3-SUBSTITUTED FURANS

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4-Aryl-3-substituted furans *IIIa* – *IIIc* were prepared by Diels–Alder reaction of 4-phenyloxazole (*I*) with compounds *IIa* – *IIc*, containing an activated triple bond, and subsequent thermal decomposition of the cycloadduct.

One of the most important synthetic methods leading to 3,4-disubstituted furans is the Diels–Alder reaction of a suitable diene with a dienophile followed by the retrodiene reaction.

In the original method¹, the diene component is the less accessible furan and the cycloadduct has to be catalytically hydrogenated prior to the thermal decomposition. Because of this preparative complication there has been interest in alternative syntheses based on 1,4-cycloadditions. One of them makes use of substituted 1,3-oxazoles such as 4-methyloxazole², and particularly 4-phenyloxazole³, as dienes which on reaction with various alkynes and subsequent thermolysis afford furan derivatives. The cycloadduct is decomposed at high temperature (about 200 °C) and, in the case of 4-phenyloxazole (in contrast to its 4-methyl analogue), the decomposition takes place at atmospheric pressure. 4-Phenyloxazole became a suitable precursor in syntheses of other β -substituted furans that are otherwise accessible only with difficulty^{4–8}.

3-Benzoyl-4-(4-nitrophenyl)furan (*IIIa*), 3-benzoyl-4-(5-nitrofuryl)furan (*IIIb*), 3-(2-furoyl)-4-phenylfuran (*IIIc*) and ethyl 4-(4-nitrophenyl)-3-furancarboxylate (*IIId*) were obtained by Diels–Alder reaction of 4-phenyloxazole (*I*) with activated acetylenes *IIa* – *IIc* and subsequent decomposition of the cycloadduct at high temperature (Scheme 1).

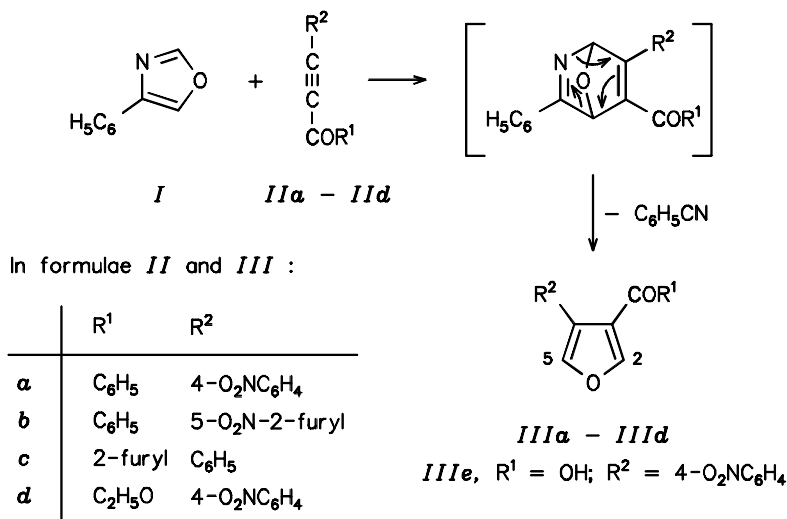
The reaction was carried out by heating equimolar amounts of the reaction components at 180 – 190 °C for 9 h in the atmosphere of an inert gas, in the presence of small amounts of hydroquinone to prevent polymerization. The high boiling point of compound *I* makes it possible to perform the cycloaddition as well as the subsequent decomposition of the cycloadduct (not isolated) at atmospheric pressure. This represents

an advantage because in syntheses involving 4-methyloxazole² or other substituted oxazolones⁹ the decomposition of the cycloadduct has to be made only at an elevated pressure. After isolation, the reaction affords the 3,4-disubstituted furan and benzonitrile as the side product. Saponification of ethyl ester *IIId* with potassium hydroxide in aqueous alcohol gave the corresponding acid *IIIe*.

The structure of the 4-aryl-3-substituted furans *IIIa* – *IIIe* was confirmed by their spectra and elemental analyses (Tables I – IV). The IR spectra of derivatives *IIIa*, *IIIb*, *IIId* and *IIIe* exhibit, in addition to the characteristic bands (Table II), also bands at $1\ 515 - 1\ 545\ \text{cm}^{-1}$ and $1\ 335 - 1\ 345\ \text{cm}^{-1}$ due to the $\nu(\text{NO}_2)_{\text{as}}$ and $\nu(\text{NO}_2)_{\text{s}}$ vibrations, respectively.

In the ¹H NMR spectra (Table III) the protons of 3,4-disubstituted furan appear as doublets with $J(2,5) = 1.5 - 1.7\ \text{Hz}$. Signals of the H-2 protons in the region $\delta\ 7.88 - 8.45$ are shifted downfield compared with those of the H-5 protons ($\delta\ 7.56 - 8.16$) as the result of the presence of carbonyl in position 3.

The mass spectra of derivatives *IIIa* – *IIIe* (Table IV) display intense molecular ion peaks which for *IIIc*, *IIId* and *IIIe* represent the base peaks. The presence of the benzoyl group in compounds *IIIa* and *IIIb* is manifested by intense fragment ions $m/z\ 105$, $m/z\ 77$ and $m/z\ 51$. In the case of compound *IIIc*, the presence of a relatively intense peak of $(\text{M} - \dot{\text{O}}\text{H})^+$, $m/z\ 221$ (28%), is interesting. The furoyl group appears in the spectrum as a fragment $m/z\ 95$ (37%) and its presence in the molecule gives rise to three



SCHEME 1

TABLE I
Physico-chemical data of 4-aryl-3-substituted furans *IIIa* – *IIIe*

Compound	M.p., °C Yield, %	Formula (M.w.)	Calculated/Found		
			% C	% H	% N
<i>IIIa</i>	103 – 106	C ₁₇ H ₁₁ NO ₄	69.62	3.78	4.78
	27	(293.3)	69.43	3.66	4.77
<i>IIIb</i>	127 – 128	C ₁₅ H ₉ NO ₅	63.61	3.20	4.95
	28	(283.2)	63.83	3.17	4.97
<i>IIIc</i>	79 – 80	C ₁₅ H ₁₀ O ₃	75.62	4.23	–
	24	(238.2)	75.11	4.06	–
<i>III d</i>	90 – 92	C ₁₃ H ₁₁ NO ₅	59.77	4.25	5.36
	31	(261.2)	59.61	4.26	5.38
<i>IIIe</i>	220 – 221	C ₁₁ H ₇ NO ₅	56.66	3.03	6.01
	76	(233.2)	56.14	2.89	5.84

TABLE II
IR (in KBr) and UV (in methanol, c 1 · 10⁻⁴ mol l⁻¹) spectra of compounds *IIIa* – *IIIe*

Compound	IR spectrum, cm ⁻¹		UV spectrum	
	$\nu(\text{C=O})$	$\nu(\text{C-O-C})_s$	λ_{max} , nm	log ϵ
<i>IIIa</i>	1 650	1 035	251	3.19
			295	3.04
<i>IIIb</i>	1 650	1 025	249	3.19
			352	3.11
<i>IIIc</i>	1 640	1 030	283	3.16
<i>III d</i>	1 730	1 020	299	3.00
<i>IIIe</i>	1 710	1 020	302	3.11

TABLE III

¹H NMR spectral data (δ , ppm; J , Hz) of 4-aryl-3-substituted furans *IIIa* – *IIIe*

Compound ^a	H-2	H-5	$J(2,5)$	Other signals
<i>IIIa</i>	7.88	7.71	1.5	8.00 – 7.80 m and 7.70 – 7.37 m, 2 H and 3 H (benzoyl); 8.19 d and 7.57 d, 2 H and 2 H, $J = 8.2$ (4-nitrophenyl)
<i>IIIb</i>	8.13	7.85	1.7	7.97 – 7.80 m and 7.70 – 7.40 m, 2 H and 3 H (benzoyl); 7.36 and 7.28, AB system $J = 3.7$ (H-4 and H-3 of 5-nitro-2-furyl)
<i>IIIc</i>	8.25	7.56	1.6	7.62 – 7.27 m, 5 H (phenyl); 7.61 dd, 1 H, $J(5,4) = 1.7$, $J(5,3) = 0.7$ (H-5 of 2-furoyl); 7.21 dd, 1 H, $J(3,4) = 3.5$, $J(3,5) = 0.7$ (H-3 of 2-furoyl); 6.54 dd, 1 H, $J(4,3) = 3.5$, $J(4,5) = 1.7$ (H-4 of 2-furoyl)
<i>III d</i>	8.13	7.58	1.7	8.24 d and 7.65 d, 2 H and 2 H, $J = 8.9$ (4-nitrophenyl); 4.25 q, 2 H, $J = 7.1$ (OCH ₂ CH ₃); 1.25 t, 3 H, $J = 7.1$ (OCH ₂ CH ₃)
<i>IIIe</i>	8.45	8.16	1.7	8.25 d and 7.78 d, 2 H and 2 H, $J = 8.8$ (4-nitrophenyl)

^a Compounds *IIIa* – *III d* in CDCl₃, compound *IIIe* in (CD₃)₂SO.

TABLE IV

The EI mass spectra of 4-aryl-3-substituted furans *IIIa* – *IIIe*

Compound ^a	m/z , %
<i>IIIa</i>	293 M ⁺ • (18), 189 (20), 142 (11), 114 (25), 113 (15), 105 (36), 88 (11), 77 (100), 63 (25), 51 (48)
<i>IIIb</i>	283 M ⁺ • (62), 237 (52), 209 (62), 181 (38), 153 (41), 152 (62), 105 (64), 77 (100), 76 (24), 51 (28)
<i>IIIc</i>	238 M ⁺ • (100), 221 (28), 209 (30), 181 (57), 153 (39), 152 (34), 115 (69), 95 (37), 63 (26), 39 (47)
<i>III d</i>	261 M ⁺ • (100), 233 (37), 216 (63), 170 (58), 142 (28), 114 (42), 113 (32), 77 (32), 63 (39), 51 (26)
<i>IIIe</i>	233 M ⁺ • (100), 203 (33), 169 (13), 157 (15), 131 (33), 113 (26), 103 (30), 77 (33), 63 (30), 51 (15)

^a For each compound 10 most abundant peaks are given.

subsequent eliminations of CO or CO + $\dot{\text{H}}$ from the $\text{M}^{+\bullet}$ ion. The most intense fragment ions in the spectrum of compound *IIId* are $(\text{M} - \dot{\text{O}}\text{C}_2\text{H}_5)^+$, m/z 216 (63%) and the ion m/z 170 (58%) arising by subsequent loss of the $\dot{\text{N}}\text{O}_2$ radical. On the other hand, in the spectrum of compound *IIIe* the fragment $(\text{M} - \dot{\text{O}}\text{H})^+$, m/z 216, is of very low intensity (less than 2%). In this case, the formation of the fragment $(\text{M} - \dot{\text{N}}\text{O})^+$, m/z 203 (33%) is preferred.

EXPERIMENTAL

The melting points were determined on a Kofler block. IR spectra were recorded on an M-80 spectrometer, UV spectra (λ in nm, ϵ in $\text{m}^2 \text{mol}^{-1}$) on a Specord UV-VIS M-40 instrument (both Zeiss, Jena). ^1H NMR spectra in deuteriochloroform were obtained with a Tesla BS 587 spectrometer using tetramethylsilane as internal standard. Mass spectra (EI) were measured on an AEI MS 902 S (Manchester); direct inlet, ionization energy 70 eV, electron current 100 μA , source temperature 150 $^\circ\text{C}$.

The starting compounds were prepared according to the literature: 4-phenyloxazole¹⁰ (*I*), 1-phenyl-3-(4-nitrophenyl)-2-propyn-1-one¹¹⁻¹³ (*IIa*), 1-phenyl-3-(5-nitro-2-furyl)-2-propyn-1-one¹⁴ (*IIb*), 3-phenyl-1-(2-furyl)-2-propyn-1-one¹⁵ (*IIc*), and ethyl 3-(4-nitrophenyl)-2-propynoate¹⁶ (*IIId*).

General Procedure for Preparation of Compounds *IIIa* – *IIId*

A mixture of 4-phenyloxazole (*I*; 2.0 g, 14 mmol), compound *IIa* – *IIId* (14 mmol) and hydroquinone (0.1 g) was heated at 180 – 190 $^\circ\text{C}$ for 9 h under continuous stirring by introduction of nitrogen. After cooling, the crude product was dissolved in a minimum amount of chloroform (*IIIa* and *IIIb*), benzene (*IIIc*) or chloroform–1,2-dichloroethane (2 : 1) (*IIId*) and chromatographed on a column of silica gel in the respective solvent. After removal of the solvent, the product was further purified by crystallization from ether–light petroleum (*IIIa*), ethanol (*IIIb*, *IIId*) or hexane (*IIIc*). For yields, melting points and elemental analyses see Table I.

4-(4-Nitrophenyl)-3-furancarboxylic Acid (*IIIe*)

Ester *IIId* (0.4 g, 1.5 mmol) was refluxed with a solution of potassium hydroxide (0.2 g, 3 mmol) in 50% aqueous ethanol (20 ml) for 4 h. The alcohol was evaporated, the residue diluted with the same amount of water and extracted twice with 1,2-dichloroethane (10 ml). The aqueous solution of the potassium salt was treated with charcoal, filtered, cooled and acidified with dilute (1 : 1) hydrochloric acid. The deposited crude product was crystallized from ethanol. For yields, melting points and elemental analyses of the obtained acid *IIIe* see Table I.

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