

SYNTHESIS AND REACTIONS OF 5-SUBSTITUTED 2-FURANCARBOHYDROXIMOYL CHLORIDES*

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Synthesis of 5-X-substituted 2-furancarbohydroximoyl chlorides (X = NO₂, 4-, 3-, 2-NO₂-phenyl) and their reactions with thiols, morpholine and sodium *p*-toluenesulphinate are described.

Carbohydroximoyl chlorides are the best starting compounds for the preparation of the generally very unstable nitrile oxides which readily react with wide variety of nucleophilic reagents by 1,3-additions¹⁻³. Within the framework of investigations of phenylfuran and furan derivatives we synthesized new 5-substituted 2-furancarbohydroximoyl chlorides *I-III* by the reaction of nitro substituted 5-phenyl-2-furaldehyde oximes^{4,5} with nitrosyl chloride and studied their reactions, as well as reactions of 5-nitro-2-furancarbohydroximoyl chloride⁶, with benzenethiol, phenylmethanethiol, 2-furylmethanethiol, morpholine and sodium *p*-toluenesulphinate.

The most convenient method for the preparation of 5-nitrophenyl-2-furancarbohydroximoyl chlorides was the chlorination of the corresponding oximes with nitrosyl chloride in ether at -20°C⁷. Direct chlorination of the oximes with chlorine in chloroform, tetrachloromethane or 8M-HCl did not afford homogeneous products and the yields of carbohydroximoyl chlorides were very low. We transformed the mentioned carbohydroximoyl chlorides by the action of triethylamine in ether at low temperature into nitrile oxides and these were converted by a 1,3-addition with thiols into substituted furancarbohydroximethioates in 70-80% yields, following the procedure of Benn⁸. Similarly we prepared from carbohydroximoyl chlorides and morpholine (in 100% excess) the corresponding substituted furancarbohydroximethioates in 80-93% yields. S, S-Dioxo-S-tolyl-5-substituted furancarbohydroximethioates were prepared in 60-80% yield by boiling carbohydroximoyl chlorides with sodium *p*-toluenesulphinate in acetone. This reaction proceeds most probably as a direct nucleophilic substitution of the chlorine atom. We have obtained no direct evidence about the intermediate nitrile oxide.

The prepared compounds, together with their analytical and spectral data, are

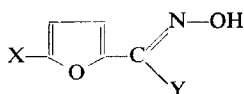
* Part LXXXV in the series Furan Derivatives; Part LXXXIV: This Journal 41, 2577 (1976).

listed in Tables I and II. The purity and homogeneity of the compounds was checked using elemental analysis, IR and $^1\text{H-NMR}$ spectroscopy and thin-layer chromatography.

EXPERIMENTAL

The starting oximes were prepared according to ref.^{4,5,9}. The IR spectra ($800\text{--}3650\text{ cm}^{-1}$) were taken on a double-beam UR-20 spectrophotometer. The UV absorption spectra were measured on a recording spectrophotometer Specord UV VIS (Zeiss, Jena) in the region 200 to 480 nm. The measurements were carried out at room temperature in 1 cm cells, concentration $5 \cdot 10^{-5}\text{ M}$ in ethanol (spectral grade). 5-Nitro-2-furancarbohydroximoyl chloride was prepared according to ref.⁶.

TABLE I
Synthesized Compounds of the Formula



Compound (yield, %)	X Y	Formula (mol. w.)	Calculated/Found		M.p., °C (solvent)
			% N	% S	
<i>I</i> ^a (78)	4-NO ₂ -C ₆ H ₄ Cl	C ₁₁ H ₇ ClN ₂ O ₄ (266.6)	10.50 10.69	—	170—175 —
<i>II</i> ^a (80.4)	3-NO ₂ -C ₆ H ₄ Cl	C ₁₁ H ₇ ClN ₂ O ₄ (266.6)	10.50 10.49	—	170—173 —
<i>III</i> ^a (85.6)	2-NO ₂ -C ₆ H ₄ Cl	C ₁₁ H ₇ ClN ₂ O ₄ (266.6)	10.50 10.56	—	161—162 —
<i>IV</i> (75)	NO ₂ C ₆ H ₅ S	C ₁₁ H ₈ N ₂ O ₄ S (264.2)	10.60 10.65	12.13 11.94	148—150 (benzene)
<i>V</i> (74)	NO ₂ C ₆ H ₅ CH ₂ S	C ₁₂ H ₁₀ N ₂ O ₄ S (278.2)	10.06 10.04	11.52 11.53	83—84 (tetrachloromethane)
<i>VI</i> (72)	NO ₂ C ₄ H ₃ OCH ₂ S	C ₁₀ H ₇ N ₂ O ₅ S (268.2)	10.51 10.73	11.93 11.89	91—92 (benzene)
<i>VII</i> (82.3)	4-NO ₂ -C ₆ H ₄ C ₆ H ₅ S	C ₁₇ H ₁₂ N ₂ O ₄ S (340.3)	8.23 8.25	9.35 9.35	157—158 (ethanol)
<i>VIII</i> (84.3)	4-NO ₂ -C ₆ H ₄ C ₆ H ₅ CH ₂ S	C ₁₈ H ₁₄ N ₂ O ₄ S (354.3)	7.91 7.99	9.04 9.08	195—197 (ethanol)
<i>IX</i> (67)	4-NO ₂ -C ₆ H ₄ C ₄ H ₃ OCH ₂ S	C ₁₆ H ₁₂ N ₂ O ₅ S (344.4)	8.12 8.23	9.30 9.27	191—192 (ethanol)

TABLE I
(Continued)

Compound (yield, %)	X Y	Formula (mol.w.)	Calculated/Found		M.p., °C (solvent)
			% N	% S	
<i>X</i> (79.4)	3-NO ₂ -C ₆ H ₄ C ₆ H ₅ S	C ₁₇ H ₁₂ N ₂ O ₄ S (340.3)	8.23 8.31	9.42 9.50	143—145 (ether)
<i>XI</i> (77)	3-NO ₂ -C ₆ H ₄ C ₆ H ₅ CH ₂ S	C ₁₈ H ₁₄ N ₂ O ₄ S (354.3)	7.91 7.94	9.04 8.89	161—162 (ethanol)
<i>XII</i> (72.6)	3-NO ₂ -C ₆ H ₄ C ₄ H ₃ OCH ₂ S	C ₁₆ H ₁₂ N ₂ O ₅ S (344.4)	8.12 8.20	9.30 9.34	150—152 (ethanol)
<i>XIII</i> (84.6)	2-NO ₂ -C ₆ H ₄ C ₆ H ₅ S	C ₁₇ H ₁₂ N ₂ O ₄ S (340.3)	8.23 8.27	9.42 9.37	166—167 (ethanol)
<i>XIV</i> (80)	2-NO ₂ -C ₆ H ₄ C ₆ H ₅ CH ₂ S	C ₁₈ H ₁₄ N ₂ O ₄ S (354.3)	7.91 7.84	9.04 8.97	103—104 (benzene)
<i>XV</i> (83)	2-NO ₂ -C ₆ H ₄ C ₄ H ₃ OCH ₂ S	C ₁₆ H ₁₂ N ₂ O ₅ S (344.4)	8.12 8.22	9.30 9.29	110—111 (benzene)
<i>XVI</i> (74.2)	NO ₂ <i>p</i> -CH ₃ C ₆ H ₄ SO ₂	C ₁₂ H ₁₀ N ₂ O ₆ S (310.3)	9.02 9.08	10.33 10.30	165—166 (ethanol)
<i>XVII</i> (61)	4-NO ₂ -C ₆ H ₄ <i>p</i> -CH ₃ C ₆ H ₄ SO ₂	C ₁₈ H ₁₄ N ₂ O ₆ S (386.4)	7.24 7.09	8.29 8.16	199—200 (acetone)
<i>XVIII</i> (78)	3-NO ₂ -C ₆ H ₄ <i>p</i> -CH ₃ C ₆ H ₄ SO ₂	C ₁₈ H ₁₄ N ₂ O ₆ S (386.4)	7.24 7.32	8.29 8.34	186—187 (ethanol)
<i>XIX</i> (67)	2-NO ₂ -C ₆ H ₄ <i>p</i> -CH ₃ C ₆ H ₄ SO ₂	C ₁₈ H ₁₄ N ₂ O ₆ S (386.4)	7.24 7.30	8.29 8.30	166—168 (dil. ethanol)
<i>XX</i> ^b (80)	NO ₂ 4-morpholinyl	C ₉ H ₁₁ N ₃ O ₅ (241.2)	17.42 17.17	—	134—135 (benzene)
<i>XXI</i> ^c (81)	4-NO ₂ -C ₆ H ₄ 4-morpholinyl	C ₁₅ H ₁₅ N ₃ O ₅ (317.3)	13.24 13.25	—	190—192 (ethanol)
<i>XXII</i> ^c (93)	3-NO ₂ -C ₆ H ₄ 4-morpholinyl	C ₁₅ H ₁₅ N ₃ O ₅ (317.3)	13.24 13.29	—	165—167 (ethanol)
<i>XXIII</i> ^c (90)	2-NO ₂ -C ₆ H ₄ 4-morpholinyl	C ₁₅ H ₁₅ N ₃ O ₅ (317.3)	13.24 13.20	—	129—130 (ethanol)

^a % Cl calculated (% Cl found): *I*, 13.29 (13.37); *II*, 13.29 (13.34); *III*, 13.29 (13.30). ^b Calculated (found) % C: 44.81 (45.04), % H: 4.59 (4.70). ^c Calculated (found) *XXI* % C: 56.78 (56.5), % H: 4.76 (4.81); for *XXII* % C: 56.78 (56.63), % H: 4.76 (4.71); *XXIII* % C: 56.78 (56.71), % H: 4.76 (4.79).

5-Substituted 2-Furancarbohydroximoyl Chlorides *I—III*

Nitrosyl chloride (2 ml) was added at -20°C to a solution of the oxime (0.01 mol) in ether and the mixture was stirred for 0.5 h at -20°C . After standing overnight the solvent was removed *in vacuo* at a temperature below 20°C and the residue was crystallized from dichloroethane–light petroleum.

TABLE II

IR and UV Data for the Compounds *I—XXIII* (λ in nm, $\nu(\text{NO}_2)$, $\nu(\text{C}=\text{N})$ in cm^{-1})

Compound	λ	$\log \epsilon$	λ	$\log \epsilon$	λ	$\log \epsilon$	$\nu(\text{NO}_2)_{\text{as}}$	$\nu(\text{NO}_2)_{\text{s}}$	$\nu(\text{C}=\text{N})$
<i>I</i>	355	4.33	—	—	—	—	—	1 350	1 615
<i>II</i>	315	4.64	—	—	—	—	—	1 360	1 620
<i>III</i>	303	4.23	—	—	—	—	—	1 359	1 622
<i>IV</i>	333	4.09	208	4.26	—	—	1 532	1 350	1 638
<i>V</i>	352	4.06	209	4.25	—	—	1 535	1 354	1 637
<i>VI</i>	351	4.05	227	4.29	—	—	1 537	1 350	1 630
<i>VII</i>	372	4.38	207	4.19	—	—	1 517	1 337	1 603
<i>VIII</i>	373	4.42	208	4.40	—	—	1 520	1 338	1 606
<i>IX</i>	372	4.38	220	4.34	—	—	1 518	1 338	1 606
<i>X</i>	314	4.20	210	4.30	—	—	1 537	1 347	1 623
<i>XI</i>	320	4.19	211	4.26	—	—	1 527	1 347	1 606
<i>XII</i>	318	4.41	219	4.44	—	—	1 526	1 345	1 604
<i>XIII</i>	305	4.37	209	4.41	—	—	1 530	1 364	1 619
<i>XIV</i>	298	4.23	211	4.42	—	—	1 547	1 372	1 618
<i>XV</i>	299	4.28	221	4.44	—	—	1 534	1 638	1 620
<i>XVI</i> ^a	207	4.25	234	4.32	324	4.15	1 549	1 358	1 603
<i>XVII</i> ^b	206	4.40	231	4.40	364	4.54	1 530	1 360	1 611
<i>XVIII</i> ^c	207	4.26	228	4.27	321	4.37	1 520	1 355	1 605
<i>XIX</i> ^d	208	4.42	229	4.41	310	4.38	1 515	1 360	1 620
<i>XX</i>	222	4.11	250	3.92	317	4.08	1 538	1 365	1 638
<i>XXI</i>	207	4.27	269	4.09	369	4.44	1 527	1 365	1 612
<i>XXII</i>	213	4.30	307	4.40	—	—	1 548	1 358	1 635
<i>XXIII</i>	210	4.24	292	4.26	—	—	1 541	1 362	1 638

^a $\nu(\text{SO}_2)_{\text{as}}$ 1 331 cm^{-1} ; ^b $\nu(\text{SO}_2)_{\text{as}}$ 1 342 cm^{-1} ; ^c $\nu(\text{SO}_2)_{\text{as}}$ 1 332 cm^{-1} ; ^d $\nu(\text{SO}_2)_{\text{as}}$ 1 338 cm^{-1} .

5-Substituted 2-Furancarbohydroximethioates *IV—XV*

Triethylamine (0.02 mol) was added portionwise to a solution of the corresponding chloride (0.01 mol) and thiol (0.01 mol) in ether (approx. 100 ml) at -30° to -35°C . The mixture was stirred for 30 minutes at about -15°C and for 1 h at room temperature. The pH was adjusted to a slightly acid reaction by addition of 0.25M- H_2SO_4 , the ethereal layer was separated and the aqueous layer was extracted several times with ether. The combined ethereal solutions were dried over sodium sulphate, the solvent was evaporated *in vacuo* and the residue was crystallized from an appropriate solvent.

5-Substituted S,S-Dioxo-2-furancarbohydroximethioates *XVI—XIX*

A mixture of the corresponding chloride (0.01 mol) and sodium *p*-toluenesulphinate (0.01 mol) in acetone was refluxed for 3 hours. After cooling, the separated NaCl was filtered off, the solvent was removed *in vacuo* and the solid residue was crystallized from a suitable solvent.

5-Substituted 2-Furancarbo-morpholidoximes *XX—XXIII*

A solution of morpholine (0.02 mol) in ether (5 ml) was added at -30°C to the corresponding chloride (0.01 mol) in ether in the course of 5 minutes and the mixture was stirred for 6 hours at room temperature. After addition of 0.25M- H_2SO_4 (about 30 ml) the ethereal layer was separated and the aqueous layer was extracted several times with ether. The combined ethereal extracts were dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. The residue was crystallized from a suitable solvent.

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