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Studies on Furan Derivatives. IX.[1] Nucleophilic Substitution of 5-Nitro-2-furancarbaldehyde: Preparation of 5-Phenoxy-2-furancarbaldehydes

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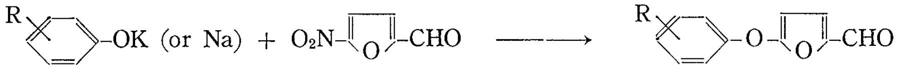
5-(2-, 3-, 4-Substituted phenoxy)-2-furancarbaldehydes were prepared by the reaction of various phenoxides with 5-nitro-2-furancarbaldehyde *via* replacement of the nitro group.

Keywords——aromatic nucleophilic substitution; replacement of nitro group; 5-phenoxy-2-furancarbaldehydes; phenyl 2-furyl ethers, 5-nitro-2-furancarbaldehyde

A few examples of nucleophilic substitution of the nitro group of nitrofurans exist in the literature. For example, 5-nitro-2-furancarbaldehyde reacts with sodium methoxide,[3] hydrogenhalides,[4] sodium azide, sodium arylmercaptides, and sodium benzenesulfinate[5] to afford the corresponding 5-substituted 2-furancarbaldehydes. Other nitrofurans found to undergo similar displacement include 2,5-dinitrofuran,[6] 5-nitro-2-furfurylidenemalonitrile,[7] and 5-nitro-2-furfurylnitrate.[8] However, there is no report on the reaction of nitrofurans with phenoxides.

In this paper, we wish to report a simple preparation of a series of 5-(2-, 3-, 4-substituted phenoxy)-2-furancarbaldehydes from 5-nitro-2-furancarbaldehyde, which is now synthesized industrially.



1a—**r**

Chart 1

5-Nitro-2-furancarbaldehyde is added to a solution of potassium phenoxides (method A) or phenols and sodium hydride (method B) in dimethyl sulfoxide with vigorous stirring. All the reactions were exothermic and were completed within 2 hr at ambient temperature. Simple work-up of the reaction mixture gave practically pure products (**1a**—**r**) in moderate yields, as shown in Table I. The structures of **1a**—**r** were assigned on the basis of elemental analyses and spectral data (Tables I and II).

This substitution is successful irrespective of the electronic character of the substituent attached to the benzene ring in the phenols. The major advantage of this reaction lies in the formation of the various 5-phenoxy-2-furancarbaldehydes[9] from readily available starting materials.

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[2] Location: *Keyakidai 1-1, Sakado-shi, Saitama 350-02, Japan.*

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[8] F. Povazanec, J. Kovak, and D. Hesek, *Collect. Czech. Chem. Commun.*, **44**, 3301 (1979).

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Thus, it was found that the nitro group of 5-nitro-2-furancarbaldehyde underwent nucleophilic substitution with a series of phenoxides. In addition, we recently reported a new nucleophilic alkylation at the 4-position on the 5-nitrofuran ring with N-pyridinium ylides.10) Further work on the synthesis of new types of furans from nitrofurans is planned.

TABLE I. 5-(2-, 3-, or 4-Substituted Phenoxy)-2-furancarbaldehydes

Compd. No.	R	Yield (%)	bp (°C)/torr or mp (°C)	Recryst. solvent	Formula	Analysis (%) Calcd (Found) C	H	N
1a	2-NO_2	33	81—83	Petroleum benzin	$C_{11}H_7NO_5$	56.66 (56.60	3.03 2.95	6.01 6.08)
1b	3-NO_2	41	85—86[a]	Petroleum benzin	$C_{11}H_7NO_5$	56.66 (56.73	3.03 2.91	6.01 6.05)
1c	4-NO_2	13	92—93[b]	Petroleum benzin	$C_{11}H_7NO_5$	56.66 (56.48	3.03 3.21	6.01 5.89)
1d	2-$COOCH_3$	23	180—182/3	—	$C_{13}H_{10}O_5$	63.41 (63.55	4.09 4.02)	
1e	3-$COOCH_3$	52	78.5—79.5	Petroleum benzin	$C_{13}H_{10}O_5$	63.41 (63.18	4.09 4.00)	
1f	4-$COOCH_3$	43	134.5—135.5	Petroleum benzin	$C_{13}H_{10}O_5$	63.41 (63.56	4.09 3.95)	
1g	2-Cl	39	170—175/9	—	$C_{11}H_7ClO_3$	59.35 (59.20	3.17 2.97)	
1h	3-Cl	31	162—163/4	—	$C_{11}H_7ClO_3$	59.35 (59.35	3.17 3.00)	
1i	4-Cl	25	173/6[c]	Petroleum benzin	$C_{11}H_7ClO_3$	59.35 (59.23	3.17 3.17)	
1j	H	32	145/5[d]	—	$C_{11}H_8O_3$	70.21 (70.07	4.29 4.31)	
1k	3-$NHCOCH_3$	45	125—126[e]	Benzene	$C_{13}H_{11}NO_4$	63.67 (63.56	4.52 4.38	5.71 5.62)
1l	4-$NHCOCH_3$	60	133—134	MeOH	$C_{13}H_{11}NO_4$	63.67 (63.80	4.52 4.49	5.71 5.85)
1m	2-C_2H_5	29	153—154/4	—	$C_{13}H_{12}O_3$	72.21 (72.42	5.59 5.57)	
1n	3-C_2H_5	20	159—161/5	—	$C_{13}H_{12}O_3$	72.21 (72.21	5.59 5.57)	
1o	4-C_2H_5	36	150—152/3	—	$C_{13}H_{12}O_3$	72.21 (72.29	5.59 5.52)	
1p	2-OCH_3	35	172—176/5	—	$C_{12}H_{10}O_4$	66.05 (65.94	4.62 4.49)	
1q	3-OCH_3	36	170—173/4	—	$C_{12}H_{10}O_4$	66.05 (66.03	4.62 4.46)	
1r	4-OCH_3	69	81—82[f]	Petroleum benzin	$C_{12}H_{10}O_4$	66.05 (65.88	4.62 4.60)	

[a] Lit.9) mp 72—75°. [b] Lit.9) mp 82—84°. [c] Lit.9) mp 50—51°. [d] Lit.9) bp 140—144°/2 torr.
[e] Lit.9) mp 121—122°. [f] Lit.9) mp 77—78°. [g] A. F. Oleinik, K. Yu. Novitskii, L. V. Brattseva, T. A. Gus'kova; G. N. Pershin, A. I. Kravchenko, and V. A. Chernov, *Khim.-Farm. Zh.*, **10**, 65 (1976).

Experimental

All melting points and boiling points are uncorrected. The following instruments were used to obtain physical data. NMR spectra (with TMS as an internal standard): JEOL 60HL and PS-100 spectrophotometers. IR spectra: Jasco IRA-1 spectrophotometer. Mass spectra (direct inlet): Shimadzu LKB-9000 machine. Fifty percent sodium hydride was used, purchased from Wako Chemical Industries, Ltd.

5-(2-, 3-, or 4-Substituted Phenoxy)-2-furancarbaldehydes (1a—r) Method A)——5-Nitro-2-furancarbaldehyde (14.1 g, 0.1 mol) was added to a solution of a phenoxide (0.12 mol) in dimethyl sulfoxide (150 ml)

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10) A. Tanaka and T. Usui, *J. Heterocycl. Chem.*, **16**, 1409 (1979); *idem, Chem. Pharm. Bull.*, **27**, 3078 (1979).

with stirring. Stirring was continued for 2 hr at room temperature, then the mixture was poured into ice water. With **1a—c,r**, the resulting precipitate was filtered off and recrystallized from petroleum benzin to give the pure product. With **1g,i—k,n**, the resulting oil was extracted with benzene. The benzene extract was washed with 5% KOH solution and water, dried over $CaCl_2$, and evaporated down. The residual oil was distilled under a vacuum to give the pure product.

Method B)——A solution of a phenol (0.12 mol) in dimethyl sulfoxide (150 ml) was treated with 5.8 g (0.24 mol) of 50% NaH under stirring, and the mixture was cooled to room temperature. Next, 14.1 g (0.1 mol) of 5-nitro-2-furancarbaldehyde was added and stirring was continued for 2 hr at room temperature.

TABLE II. 5-(2-, 3-, or 4-Substituted Phenoxy)-2-furancarbaldehydes

Compd. No.	MS (M^+)	IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: C=O	NMR[a] δ (in $CDCl_3$)
1a	—	1665	5.78 (1H, d, $J=3.9$ Hz, F-4H), 7.20—8.25 (5H, m, F-3H and phenyl H), 9.40 (1H, s, -CHO)
1b	233	1665	5.85 (1H, d, $J=3.9$ Hz, F-4H), 7.20—8.30 (5H, m, F-3H and phenyl H), 9.37 (1H, s, -CHO)
1c	233	1675	5.93 (1H, d, $J=3.9$ Hz, F-4H), 7.28 (1H, d, $J=3.9$ Hz, F-3H), 7.32 (2H, d, $J=9$ Hz, phenyl H), 8.31 (2H, d, $J=9$ Hz,phenyl H), 9.50 (1H, s, -CHO)
1d	246	1725, 1670	3.80 (3H, s, CH_3), 5.44 (1H, d, $J=3.9$ Hz, F-4H), 7.10—8.10 (5H, m, F-3H and phenyl H), 9.33 (1H, s, -CHO)
1e	246	1720, 1665	3.94 (3H, s, CH_3), 5.67 (1H, d, $J=3.9$ Hz, F-4H), 7.28 (1H, d, $J=3.9$ Hz, F-3H), 7.20—8.10 (4H, m, phenyl H), 9.42 (1H, s, -CHO)
1f	246	1735, 1665	3.94 (3H, s, CH_3), 5.78 (1H, d, $J=3.9$ Hz, F-4H), 7.29 (1H, d, $J=3.9$ Hz, F-3H), 7.21 (2H, d, $J=9$ Hz, phenyl H), 8.12 (2H, d, $J=9$ Hz, phenyl H), 9.46 (1H, s, -CHO)
1g	222	1665	5.53 (1H, d, $J=3.9$ Hz, F-4H), 7.00—7.60 (5H, m, F-3H and phenyl H), 9.38(1H, s, -CHO)
1h	222	1670	5.70 (1H, d, $J=3.9$ Hz, F-4H), 6.90—7.53 (5H, m, F-3H and phenyl H), 9.40 (1H, s, -CHO)
1i	222	1665	5.62 (1H, d, $J=3.9$ Hz, F-4H), 7.00—7.50 (5H, m, F-3H and phenyl H), 9.43 (1H, s, -CHO)
1j	188	1670	5.60 (1H, d, $J=3.9$ Hz, F-4H), 7.07—7.67 (5H, m, F-3H and phenyl H), 9.43 (1H, s, -CHO)
1k	245	1660	2.17 (3H, s, CH_3), 5.63 (1H, d, $J=3.9$ Hz, F-4H), 6.70—7.77 (5H, m, F-3H and phenyl H), 8.87 (1H, broad s, NH), 9.33 (1H, s, -CHO)
1l	245	1660	2.18 (3H, s, CH_3), 5.55 (1H, d, $J=3.9$ Hz, F-4H),7.23 (1H, d, $J=3.9$ Hz, F-3H), 7.13 (2H, d, $J=9$ Hz, phenyl H), 7.61 (2H, d ,$J=9$ Hz, phenyl H), 8.40 (1H, broad s, NH), 9.34 (1H, s, -CHO)
1m	216	1670	1.19 (3H, t, $J=7$ Hz, CH_3), 2.67 (2H, q, $J=7$ Hz, CH_2), 5.21 (1H, d, $J=3.9$ Hz, F-4H), 6.95—7.50 (5H, m, F-3H and phenyl H), 9.40 (1H, s, -CHO)
1n	216	1670	1.22 (3H, t, $J=7$ Hz, CH_3), 2.67 (2H, q, $J=7$ Hz, CH_2), 5.55 (1H, d, $J=3.9$ Hz, F-4H), 7.22 (1H, d, $J=3.9$ Hz, F-3H), 6.80—7.50 (4H, m, phenyl H), 9.35 (1H, s, -CHO)
1o	216	1670	1.23 (3H, t, $J=7$ Hz, CH_3), 2.67 (2H, q, $J=7$ Hz, CH_2), 5.51 (1H, d, $J=3.9$ Hz, F-4H), 6.95—7.45 (5H, m, F-3H and phenyl H), 9.32 (1H, s, -CHO)
1p	218	1670	3.80 (3H, s, CH_3), 5.39 (1H, d, $J=3.9$ Hz, F-4H), 6.75—7.50 (5H, m, F-3H and phenyl H), 9.37 (1H, s, -CHO)
1q	218	1670	3.79 (3H, s, CH_3), 5.62 (1H, d, $J=3.9$ Hz, F-4H), 7.28 (1H, d, $J=3.9$ Hz, F-3H), 6.60—7.50 (4H, m, phenyl H), 9.38 (1H, s, -CHO)
1r	218	1660	3.81 (3H, s, CH_3), 5.33 (1H, d, $J=3.9$ Hz, F-4H), 7.20 (1H, d,$J=3.9$ Hz, F-3H), 6.93 (2H, d, $J=9$ Hz, phenyl H), 7.12 (2H, d, $J=9$ Hz, phenyl H), 9.40 (1H, s, -CHO)

a) s: singlet, d: doublet, m: multiplet, q: quartet, t: triple, F: furan ring.

The mixture was then poured into ice-water. With **1e,f,k,l**, the resulting precipitate was filtered off and recrystallized from a suitable solvent to give the pure product. With **1d,h,n,o,q**, the resulting oil was extracted with benzene. The benzene extract was washed with 5% KOH solution and water, dried over $CaCl_2$, and evaporated down. The residual oil was washed with a little petroleum benzin and distilled under a vacuum to give the pure product.

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