THE SYNTHESIS OF 5-ARYL-2-FURANCARBOXYLIC ACIDS*

A. KRUTOŠÍKOVÁ, J. KOVÁČ and V. SÝKORA

Department of Organic Chemistry,
Slovak Technical University, 880 37 Bratislava

Received September 18th, 1973

In the paper the preparation of substituted 5-phenyl-2-furancarboxylic acids as well as of their methyl esters by Meerwein arylation of pyromucic acid is described.

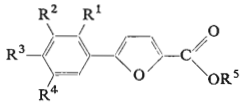
In the preceding paper[1] the preparation of 4-substituted 5-phenyl-2-furancarboxylic acids was described; in this paper the preparation of 3- and 2-substituted or disubstituted 5-phenyl-2-furancarboxylic acids and their methyl esters is investigated. The acids were prepared by modified Meerwein arylation of pyromucic acid. We applied this method successfully to pyromucic acid methyl ester under utilisation of benzenediazonium salts with electron accepting substituent. The methyl esters were also prepared on reaction of the corresponding acid with diazomethane or also by esterification with methanol under catalysis with sulfuric acid.

The yield of arylation of pyromucic acid (Table I) is considerably affected by the substituent on the benzene nucleus, which is in agreement with the literature data[2,3]. When 2- or 3-toluenediazonium salt was used for arylation the attempts at isolation of arylation products were unsuccessful.

5-Aryl-2-furancarboxylic acids were isolated *via* their soluble sodium salts. Together with the product the separated 2-furancarboxylic acid is eliminated by crystallisation which leads, especially in the case of more soluble acids, to considerable losses (Table I). Direct esterification of 5-aryl-2-furancarboxylic acids takes place with good yields (Table II).

The amino derivatives obtained on reduction of methyl esters of 5-(2- or 3-nitrophenyl)-2-furancarboxylic acids were used as starting material for the preparation of corresponding isothiocyanates. An attempt at preparation of methyl 5-(2-isothiocyanatophenyl)-2-furancarboxylate was unsuccessful, probably due to the steric inaccessibility of the amino group.

* Part LIII in the series Furan Derivatives; Part LII: This Journal *39*, 1711 (1974).



	R^1	R^2	R^3	R^4	R^5		R^1	R^2	R^3	R^4	R^5
I,	H	CH_3O	H	H	H	*XVI*,	H	F	H	H	CH_3
II,	H	F	H	H	H	*XVII*,	H	Cl	H	H	CH_3
III,	H	Cl	H	H	H	*XVIII*,	H	Br	H	H	CH_3
IV,	H	Br	H	H	H	*XIX*,	H	CF_3	H	H	CH_3
V,	H	CF_3	H	H	H	*XX*,	H	NCS	H	H	CH_3
VI,	H	NO_2	H	H	H	*XXI*,	H	NO_2	H	H	CH_3
VII,	H	Cl	H	Cl	H	*XXII*,	H	Cl	H	Cl	CH_3
VIII,	H	Cl	Cl	H	H	*XXIII*,	H	Cl	Cl	H	CH_3
IX,	H	CF_3	Cl	H	H	*XXIV*,	H	CF_3	Cl	H	CH_3
X,	H	NO_2	Cl	H	H	*XXV*,	H	NO_2	Cl	H	CH_3
XI,	OCH_3	H	H	H	H	*XXVI*,	NH_2	H	H	H	CH_3
XII,	Cl	H	H	H	H	*XXVII*,	CH_3O	H	H	H	CH_3
XIII,	Br	H	H	H	H	*XXVIII*,	Cl	H	H	H	CH_3
XIV,	NO_2	H	H	H	H	*XXIX*,	Br	H	H	H	CH_3
XV,	H	NH_2	H	H	CH_3	*XXX*,	NO_2	H	H	H	CH_3

EXPERIMENTAL

5-Aryl-2-furancarboxylic Acids

25 ml of a 30% sodium nitrite solution were added to a solution of 0·1 mol of arylamine in 60 ml of 15% hydrochloric acid at 0—5°C and the mixture was stirred for 10 minutes. 2-Furancarboxylic acid (11·5 g; 0·1 mol) in 65 ml of acetone and 3 g of $CuCl_2 . 2 H_2O$ in 20 ml of water was added and the mixture stirred for another 6 hours and then allowed to stand at room temperature for 16 hours. The separated precipitate was filtered off under suction, washed with water and dissolved in 10% $NaHCO_3$ solution. After filtration 5-aryl-2-furancarboxylic acid is set free by acidification with hydrochloric acid, and the product is purified by crystallisation. If an oily product is obtained instead of a precipitate, the former is extracted with chloroform and the extract concentrated in a vacuum, the residue being purified *via* the sodium salt as mentioned above.

5-Aryl-2-furancarboxylic Acid Methyl Esters

A. Ten ml of conc. sulfuric acid were added to a solution of 0·1 mol of 5-aryl-2-furancarboxylic acid in 400 ml of methanol and the mixture refluxed for 6 hours. Excess methanol was distilled off and the residue diluted with water and extracted with ether. The extract was washed with 5% sodium carbonate, dried over Na_2SO_4 and evaporated. The residue was crystallised.

B. Etheral diazomethane solution was added to a solution of 0·01 mol of 5-aryl-2-furancarboxylic acid in ether (50—200 ml) until the yellow colour persisted. The mixture was allowed to stand at room temperature for 4 hours, ether was evaporated and the methyl ester crystallised.

TABLE I

Substituted 5-Phenyl-2-furancarboxylic Acids

Compound	Formula (m.w.)	Calculated/Found			M.p., °C (yield %)	Solvent
		% C	% H	% Hal		
I	$C_{12}H_{10}O_4$ (218·2)	66·05 66·15	4·62 4·56	— —	171—173 (19)	40% ethanol
II	$C_{11}H_7FO_3$ (206·1)	64·20 64·24	3·39 3·44	— —	142—146 (16)	50% acetic acid
III	$C_{11}H_7ClO_3$ (222·6)	59·35 59·32	3·17 3·16	15·92 16·09	173—176 (17)	50% acetic acid
IV	$C_{11}H_7BrO_3$ (267·1)	49·47 49·38	2·64 2·66	29·92 29·89	189—192 (17)	50% acetic acid
V	$C_{12}H_7F_3O_3$ (256·2)	56·26 56·28	2·75 2·84	— —	203—208 (28)	50% ethanol
VI	$C_{11}H_7NO_5$ [a] (233·2)	56·66 56·57	3·03 3·06	— —	265—268 (31)	ethyl acetate
VII	$C_{11}H_6Cl_2O_3$ (257·1)	51·39 51·32	2·33 2·31	27·71 27·58	137—139 (13)	45% ethanol
VIII	$C_{11}H_6Cl_2O_3$ (257·1)	51·39 51·39	2·33 2·29	27·71 27·73	232—235 (14)	50% ethanol
IX	$C_{12}H_6F_3ClO_3$ (290·6)	49·59 49·36	2·08 2·07	12·19 12·10	213—215 (56)	50% ethanol
X	$C_{11}H_6ClNO_5$ [b] (267·6)	49·40 49·34	2·24 2·22	13·3 13·35	244—247 (68)	50% ethanol
XI	$C_{12}H_{10}O_4$ (218·2)	66·05 66·07	4·62 4·56	— —	207—209 (14)	50% ethanol
XII	$C_{11}H_7ClO_3$ (222·6)	59·35 59·32	3·14 3·14	15·92 16·04	219—223 (18)	ethanol
XIII	$C_{11}H_7BrO_3$ (267·1)	49·47 49·48	2·64 2·62	29·92 30·00	208—211 (18)	45% ethanol
XIV	$C_{11}H_7NO_5$ [c] (233·2)	56·66 56·65	3·03 3·12	— —	213-215 (33)	50% acetic acid

[a] Calculated 6·01% N, found 5·88% N; m.p. in agreement with the literature[4]; [b] calculated 5·24% N, found 5·22% N; [c] calculated 6·01% N, found 5·96% N.

TABLE II

Methyl Esters of Substituted 5-Phenyl-2-furancarboxylic Acids

Compound	Formula (m.w.)	Calculated/Found % C	% H	% Hal	M.p., °C (yield, %)
XV	$C_{12}H_{11}NO_3$[a]	66·35	5·10	—	87
	(217·3)	66·52	5·13	—	(82)
XVI	$C_{12}H_9FO_3$	65·5	4·1	—	82
	(220·1)	65·59	4·12	—	(95)
XVII	$C_{12}H_9ClO_3$	60·90	3·83	14·98	76
	(236·6)	60·91	3·82	14·97	(92)
XVIII	$C_{12}H_9BrO_3$	51·27	3·23	28·43	54
	(281·1)	51·32	3·19	28·52	(94)
XIX	$C_{13}H_9F_3O_3$	57·79	3·36	—	89
	(270·2)	57·72	3·42	—	(86)
XX	$C_{13}H_9NO_3S$[b]	60·03	3·47	—	94
	(259·2)	60·05	3·43	—	(84)
XXI	$C_{12}H_9NO_5$[c]	58·30	3·67	—	146
	(247·2)	58·11	3·76	—	(96)
XXII	$C_{12}H_8Cl_2O_3$	53·15	2·95	25·78	136
	(271·1)	52·14	2·87	25·84	(90)
XXIII	$C_{12}H_8Cl_2O_3$	53·2	2·95	25·78	113
	(271·1)	53·28	3·01	25·93	(87)
XXIV	$C_{13}H_8F_3ClO_3$	51·25	2·64	11·63	113
	(304·6)	51·26	2·72	11·56	(92)
XXV	$C_{12}H_8ClNO_5$[d]	51·17	2·85	12·58	149
	(281·6)	51·26	2·87	12·58	(94)
XXVI	$C_{12}H_{11}NO_3$[e]	66·35	5·10	—	88
	(217·2)	66·32	5·11	—	(78)
XXVII	$C_{13}H_{12}O_4$	67·23	5·21	—	63
	(232·2)	67·30	5·26	—	(93)
XXVIII	$C_{12}H_9ClO_3$	60·90	3·83	14·98	68
	(236·6)	60·86	3·85	14·93	(91)
XXIX	$C_{12}H_9BrO_3$	51·27	3·23	28·43	62
	(281·1)	51·22	3·26	28·54	(94)
XXX	$C_{12}H_9NO_5$[f]	58·30	3·67	—	62—63
	(247·2)	58·32	3·62	—	(93)

% N calculated/found: [a] 6·48/6·49; [b] 5·41/5·49; [c] 5·67/5·68; [d] 4·97/5·02; [e] 6·48/6·56; [f] 5·67/5·69; compound *XXI* was crystallised from methanol, the rest from hexane.

TABLE III

UV and IR Spectra of Substituted 5-Phenyl-2-furancarboxylic Acids and Their Methyl Esters

Compound	λ_{max}, nm	log ε	λ_{max}, nm	log ε	λ_{max}, nm	log ε	ν(C=O) cm^{-1}
I	317	4·26	298	4·46	206	4·45	1 695
II	314	4·42	301	4·51	210	4·37	1 700
III	316	4·27	301	4·40	205	4·35	1 702
IV	316	4·28	310	4·41	206	4·36	1 706
V	313	4·32	299	4·46	213	4·20	1 720
VI	314	4·31	298	4·44	207	4·30	1 735
VII	318	4·38	301	4·49	207	4·54	1 738
VIII	320	4·46	304	4·58	206	4·49	1 735
IX	321	4·51	306	4·64	203	4·40	1 730
X	316	4·505	304	4·06	214	4·43	1 738
XI	335	4·42	315	4·45	204	4·54	1 698
XII	313	4·08	297	4·23	203	4·20	1 731
XIII	313	4·28	298	4·47	204	4·43	1 735
XIV	294	4·12	284	4·19	204	4·03	1 739
XV	301	4·38	—	—	214	4·29	1 712
XVI	301	4·50	294	4·46	214	4·20	1 721
XVII	301	4·44	223	3·98	208	4·22	1 720
XVIII	301	4·44	229	3·98	208	4·22	1 714
XIX	300	4·49	—	—	216	4·20	1 722
XX	298	4·54	—	—	217	4·55	1 722
XXI	305	4·52	284	4·50	217	4·55	1 727
XXII	301	4·45	316	4·32	211	4·30	1 722
XXIII	305	4·56	320	4·45	209	4·31	1 723
XXIV	306	4·56	320	4·43	221	4·17	1 724
XXV	305	4·44	—	—	217	4·22	1 726
XXVI	298	4·25	347	4·14	213	4·41	1 720
XXVII	321	4·44	294	4·28	208	4·31	1 713
XXVIII	298	4·49	228	4·06	216	4·22	1 719
XXIX	299	4·41	232	4·02	210	4·22	1 721
XXX	283	4·29	—	—	213	4·18	1 724

Methyl 5-(3- or 2-Aminophenyl)-2-furancarboxylate (*XV, XXVI*)

Two ml of acetic acid were added to a suspension of 4 g of iron powder in 500 ml of water heated on a boiling water bath, followed by the slow addition of 6 g of methyl 5-(3- or 2-nitrophenyl)-furancarboxylate. The mixture was heated for another hour. Iron was then precipitated by saturated sodium carbonate solution and the amine extracted with ether. After evaporation of the solvent the crude methyl ester was crystallised.

Methyl 5-(3-Isothiocyanatophenyl)-2-furancarboxylate (*XX*)

A solution of 0·02 mol of methyl 5-(3-aminophenyl)-2-furancarboxylate in 50—100 ml of chloroform was added dropwise to an emulsion of 100 ml of water and 2·5 g (0·022 mol) of thiophosgene dissolved in 100 ml of chloroform under stirring over 30—60 minutes. During the addition the pH value of the mixture was kept neutral by addition of $CaCO_3$. The mixture was stirred for another hour, filtered, the chloroform layer separated, washed with water, dried over calcium chloride, boiled with charcoal, filtered and evaporated. The crude ester was purified by chromatography on silica gel using chloroform as eluent.

Spectral Measurement (see Table III)

The infrared absorption spectra of the synthetized compounds were measured on a two-beam UR-20 spectrophotometer in the 3600—800 cm^{-1} region. Calibration was carried out with a polystyrene foil 25 μm thick. The IR spectra of 5-aryl-2-furancarboxylic acids were measured at 1 . 10^{-2} mol/l concentration and the spectra of their methyl esters at 2 . 10^{-2} mol/l in spectral chloroform, using a 1 mm NaCl cell.

Electron absorption spectra were measured on a registration spectrophotometer Specord UV VIS (Zeiss, Jena) in the 200—480 nm region. The measurements were carried out at room temperature in a 1 cm cell in spectral dioxane at a 3 . 10^{-5} mol/l concentration.

We thank Mrs V. Takáčová for assitance during the spectral measurements.

REFERENCES

1. Krutošíková A., Kováč J., Rentka J., Čakrt M: This Journal *30*, 767 (1974).
2. Rentka J.: *Thesis*. Slovak Technical University, Bratislava 1972.
3. Oda R.: Mem. Fac. Eng. Kyoto Univ. *14*, 195 (1952).
4. Marthur K. B. L., Mehra H. S.: J. Chem. Soc. *1961*, 2567.

Translated by Ž. Procházka.