Pentaatomic Heteroaromatic Cations. Note III (1). A Convenient Synthesis of Aldehydes from Carboxylic Acids *via* 2-Substituted 1,3-Benzoxathiolium Perchlorates (2).

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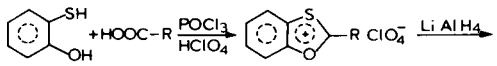
Received July 17, 1974

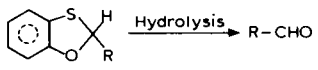
A convenient method for the preparation of aldehydes from the corresponding carboxylic acids is presented. By reaction of the carboxylic acids with *o*-mercaptophenol and perchloric acid in phosphorus oxychloride, the corresponding 2-substituted 1,3-benzoxathiolium perchlorates were obtained. Reduction of the salts with lithium aluminium hydride in dry ether gave 2-substituted 1,3-benzoxathioles, which, when hydrolyzed by mercuric chloride, gave the corresponding aldehydes. Twenty five aldehydes of different structure were obtained in good yields, by a fast and simple procedure.

In the previous note (1) the possibility of converting the benzoic acid into benzaldehyde "*via*" 2-phenyl-1,3-benzoxathiolium perchlorate was shown. This result suggested the possibility of developing a new general method for converting carboxylic acids into the corresponding aldehydes, according to Scheme I.

Scheme I



I



II

For this purpose the possibility of synthesizing a large number of 2-substituted 1,3-benzoxathiolium perchlorates, from a wide variety of acids, was first considered. With suitable changes to the original method, already employed for synthesizing some members in this series (3), twenty five 1,3-benzoxathiolium perchlorates (I) were prepared by cyclization of *o*-mercaptophenol with the carboxylic acids or their chlorides in phosphorus oxychloride followed by treatment with perchloric acid. The salts were always obtained in good yields and with a high degree of purity and could be used directly in the following step. The reduction of the perchlorates (I) with lithium aluminium hydride in dry ether, gave 2-substituted 1,3-benzoxathiole derivatives (II), often in almost quantitative yields, with the only exception being that of the cinnamyl derivative. The hydrolysis of the benzoxathioles (II) was first attempted using hydrochloric acid in aqueous dioxane, but such conditions, already employed for hydrolyzing 2-phenyl-1,3-benzoxathiole (1), could not be generalized owing to the evident existence of equilibria, not always favoring the practical completion of the reactions. Instead, the hydrolysis was easily carried out by mercuric chloride in acetonitrile or, as a better solvent, in dimethyl sulfoxide which allowed very short reaction times. The pure aldehydes were easily isolated in practically quantitative yields; only butyraldehyde, pivalaldehyde and cinnamaldehyde were separated as their 2,4-DNP derivatives. As a particular case, obviously generalizable, the benzaldeyde-α-d was obtained by reduction of 2-phenyl-1,3-benzoxathiolium perchlorate with lithium aluminium deuteride followed by hydrolysis of the thus obtained product. The results show the wide applicability of the method; its effectiveness is also shown by the good overall yields, by the ease and speed of the operating conditions and, above all, by the purity of the isolated aldehydes. Obviously, the importance of the method depends also on the availability of *o*-mercaptophenol; this compound can be easily prepared (4a, b) and may have a good chance of becoming commercially available (5a-c).

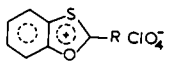
EXPERIMENTAL

General Method for the Preparation of 2-Substituted 1,3-Benzoxathiolium Perchlorates (1-25).

CAUTION. NO DIFFICULTIES WERE ENCOUNTERED, HOWEVER, IT IS WELL TO KEEP IN MIND THAT THE PERCHLORATES ARE POTENTIALLY HAZARDOUS: HENCE

Table I

2-Substituted 1,3-Benzoxathiolium Perchlorates (I)



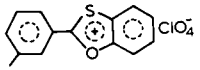
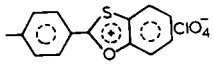
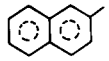
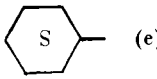
Compound No.	R	Method	Yield %	M.p. °C (a)	Formula	Elemental Analysis Calcd. % C	H	Cl	S	Found % C	H	Cl	S
1	C_6H_5	A (b)	75										
2	o-CH_3-C_6H_4	A	81	202-203	$C_{14}H_{11}ClO_5S$	51.45	3.37	10.87	9.80	51.33	3.38	10.64	9.99
3	m-CH_3-C_6H_4	A (b)	81										
4	p-CH_3-C_6H_4	A (b)	83										
5	o-CH_3O-C_6H_4	A	90	206-207	$C_{14}H_{11}ClO_6S$	49.05	3.21	10.36	9.34	48.95	3.34	10.22	9.50
6	m-CH_3O-C_6H_4	A (b)	69										
7	p-CH_3O-C_6H_4	A (b)	84										
8	o-Cl-C_6H_4	A	68	174-175	$C_{13}H_8Cl_2O_5S$	44.96	2.31	20.46	9.22	44.93	2.40	20.40	9.33
9	m-Cl-C_6H_4	A (b)	58										
10	p-Cl-C_6H_4	A (b)	62										
11	m-NO_2-C_6H_4	B (b)	55										
12	p-NO_2-C_6H_4	B	61	171-172	$C_{13}H_8ClNO_7S$ (c)	43.64	2.24	9.93	8.95	43.46	2.14	9.78	9.03
13	p-CH_3SO_2-C_6H_4	A	59	199 (exp)	$C_{14}H_{11}ClO_7S_2$	43.02	2.82	9.09	16.39	42.91	2.97	9.15	16.47
14	2,4,6-$(CH_3)_3C_6H_2$	A	27 (d)	215-216	$C_{16}H_{15}ClO_5S$	54.16	4.23	10.01	9.03	54.34	4.23	9.86	8.85
15	3,4,5-$(CH_3O)_3C_6H_2$	A	83	192-193	$C_{16}H_{15}ClO_8S$	47.70	3.73	8.82	7.95	47.69	3.87	8.70	8.08
16		C	73	127-128 (exp)	$C_{20}H_{12}Cl_2O_{10}S_2$	43.88	2.19	12.98	11.70	43.75	2.24	12.81	11.67
17		C	73	202 (exp)	$C_{20}H_{12}Cl_2O_{10}S_2$	43.88	2.19	12.98	11.70	43.79	2.16	12.79	11.56
18		A	74	195-196	$C_{17}H_{11}ClO_5S$	56.28	3.03	9.79	8.83	56.43	2.98	9.85	8.83
19		A	80	196-197	$C_{17}H_{11}ClO_5S$	56.28	3.03	9.79	8.83	56.28	3.00	9.67	8.90
20		A	74	213-214	$C_{11}H_7ClO_5S_2$	41.44	2.20	11.15	20.09	41.63	2.24	11.01	19.97
21	n-C_3H_7 (e)	D	80	88-89									
22	t-C_4H_9	D	84	130 (exp)	$C_{11}H_{13}ClO_5S$	45.13	4.44	12.14	10.94	45.20	4.52	12.23	10.78

Table I (continued)

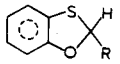
2-Substituted 1,3-Benzoxathiolium Perchlorates (I)

Compound No.	R	Method	Yield %	M.p. °C (a)	Formula	Elemental Analysis Calcd. % C	H	Cl	S	Found % C	H	Cl	S
23	n-$C_{15}H_{31}$	D	72	67-68	$C_{22}H_{35}ClO_5S$	59.13	7.84	7.95	7.17	59.26	7.97	8.04	7.25
24	 (e)	D	79	85-86									
25	$C_6H_5CH{=}CH$	D	72	187-188	$C_{15}H_{11}ClO_5S$	53.18	3.25	10.49	9.45	53.18	3.26	10.37	9.29

(a) The melting points depend on the speed of heating. They always take place with decomposition or explosion (**CAUTION**). (b) This method is an improvement of the original method reported in a previous short communication (3). (c) N%, Calcd. 3.92, Found, 3.90. (d) The yield, taking into account the recovered starting acid was 64%. (e) Not analyzed because decomposed rapidly in the air. However, these salts dissolved in deuteriotrifluoroacetic acid to give stable solutions that exhibited well-defined nmr spectra (7). The two perchlorates were immediately reduced.

Table (II)

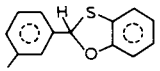
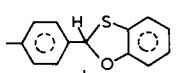
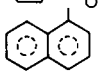
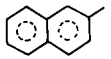
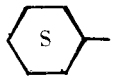
2-Substituted 1,3-Benzoxathioles (II)



Compound No.	R	Yield %	M.p., °C	Recryst. solvent (a)	B.p., °C (mm)	Formula	Elemental Analysis Calcd. % C	H	S	Found % C	H	S
26	C_6H_5 (b)	quant. (3)										
27	o-CH_3-C_6H_4	91	27-28	M		$C_{14}H_{12}OS$	73.68	5.26	14.04	73.60	5.31	14.18
28	m-CH_3-C_6H_4	98			134-135 (0.3)	$C_{14}H_{12}OS$	73.68	5.26	14.04	73.48	5.38	14.01
29	p-CH_3-C_6H_4	99	35-36	M		$C_{14}H_{12}OS$	73.68	5.26	14.04	73.59	5.31	14.15
30	o-CH_3O-C_6H_4	98	45-46	E		$C_{14}H_{12}O_2S$	68.85	4.92	13.11	68.68	4.83	13.25
31	m-CH_3O-C_6H_4	99			149-150 (0.3)	$C_{14}H_{12}O_2S$	68.85	4.92	13.11	68.97	5.09	13.04
32	p-CH_3O-C_6H_4	95 (c)	44-45	E		$C_{14}H_{12}O_2S$	68.85	4.92	13.11	68.70	4.77	13.17
33	o-Cl-C_6H_4	quant.	39-40	E		$C_{13}H_9ClOS$ (d)	62.78	3.62	12.88	62.59	3.58	12.95
34	m-Cl-C_6H_4	97			156-157 (0.7)	$C_{13}H_9ClOS$ (e)	62.78	3.62	12.88	62.60	3.81	13.00
35	p-Cl-C_6H_4	96	31-32	M		$C_{13}H_9ClOS$ (f)	62.78	3.62	12.88	62.85	3.61	12.79
36	m-NO_2-C_6H_4	93 (c, g)	51-52	E		$C_{13}H_9NO_3S$ (h)	60.23	3.47	12.36	60.29	3.44	12.45
37	p-NO_2-C_6H_4	95 (c, g)	78-79	E		$C_{13}H_9NO_3S$ (i)	60.23	3.47	12.36	60.23	3.52	12.48
38	p-CH_3SO_2-C_6H_4	90	125-126	E		$C_{14}H_{12}O_3S_2$	57.53	4.11	21.92	57.65	4.20	22.03
39	2,4,6-$(CH_3)_3C_6H_2$	quant.	103-104	E		$C_{16}H_{16}OS$	75.00	6.25	12.50	74.89	6.31	12.61

Table II (continued)

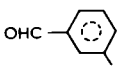
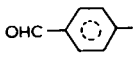
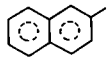
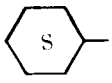
2-Substituted 1,3-Benzoxathioles (II)

Compound No.	R	Yield %	M.p., °C	Recryst. solvent (a)	B.p., °C (mm)	Formula	Elemental Analysis Calcd. % C	H	S	Found % C	H	S
40	3,4,5-$(CH_3O)_3C_6H_2$	99	81-82	E		$C_{16}H_{16}O_4S$	63.16	5.26	10.53	63.10	5.25	10.39
41		90 (c, l)	92-94	E		$C_{20}H_{14}O_2S_2$	68.57	4.00	18.29	68.49	3.97	18.35
42		90 (c, l)	156-158	B-PE		$C_{20}H_{14}O_2S_2$	68.57	4.00	18.29	68.45	3.95	18.24
43		98	128-129	B		$C_{17}H_{12}OS$	77.27	4.55	12.12	77.35	4.70	12.20
44		95	90-91	E		$C_{17}H_{12}OS$	77.27	4.55	12.12	77.10	4.64	12.03
45		97 (c)	36-37	M		$C_{11}H_8OS_2$	60.00	3.64	29.09	59.89	3.72	29.18
46	n-C_3H_7	90			126-127 (11)	$C_{10}H_{12}OS$	66.67	6.67	17.78	66.84	6.74	17.65
47	t-C_4H_9	91			67-68 (0.4)	$C_{11}H_{14}OS$	68.04	7.22	16.49	68.15	7.31	16.35
48	n-$C_{15}H_{31}$	98			190-191 (0.3)	$C_{22}H_{36}OS$	75.86	10.34	9.20	75.89	10.46	9.28
49		quat.			104-105 (0.3)	$C_{13}H_{16}OS$	70.91	7.27	14.54	70.83	7.41	14.47
50	$C_6H_5CH{=}CH$(c,m)											

(a) M=methanol; E=ethanol; B=benzene; B-PE=benzene-petroleum ether. (b) The use of lithium aluminium deuteride produced in comparable yield the C-2 deuterated derivative. This showed physical data identical with those of 2-phenylbenzoxathiole (3); nmr (deuteriochloroform): 2.27-2.67 τ and 2.80-3.16 (2m, 5:4). (c) Reaction run at 0°. (d) *Anal.* Calcd. for Cl: 14.29. Found: 14.35. (e) *Anal.* Calcd. for Cl: 14.29. Found: 14.38. (f) *Anal.* Calcd. for Cl: 14.29. Found: 14.17. (g) Molar ratio of perchlorate: lithium aluminium hydride was 1:0.75. (h) *Anal.* Calcd. for N: 5.41. Found: 5.55. (i) *Anal.* Calcd. for N: 5.41. Found: 5.36. (l) Molar ratio of perchlorate: lithium aluminium hydride was 1:2. (m) Not isolated. In this case the reaction gave a very complex mixture and attempts to purify by distillation, crystallization or chromatography, failed.

Table III

R CHO

Compound No.	R	Solvent (a)	Reflux time (minutes)	Yield %	Over-all Yield (b) %
51	C_6H_5 (c)	A	15	quant.	71
		D	5	quant.	71
52	o-CH_3-C_6H_4	A	5	98	72
53	m-CH_3-C_6H_4	A	5	quant.	79
54	p-CH_3-C_6H_4	D (d)	10	96	79
55	o-CH_3O-C_6H_4	A	5	quant.	88
56	m-CH_3O-C_6H_4	A	10	quant.	68
57	p-CH_3O-C_6H_4	A	5	quant.	80
		D	5	98	78
58	o-Cl-C_6H_4	A	150	97	66
		D	15	96	65
59	m-Cl-C_6H_4	A	90	99	56
		D	15	96	54
60	p-Cl-C_6H_4	A	20	97	58
61	m-NO_2-C_6H_4	D	30	88	45
62	p-NO_2-C_6H_4	D	45	88	51
63	p-CH_3SO_2-C_6H_4 (e)	A	840	92	49
		D	60	98	52
64	2,4,6-$(CH_3)_3C_6H_2$	D	5	96	61 (f)
65	3,4,5-$(CH_3O)_3C_6H_2$	A	10	95	78
		D	5	95	78
66		D (g)	10	97	64
67		D (g)	10	97	64
68		A	10	97	70
69		A	10	97	74
70		A	5	95	68
71	n-C_3H_7	D	45	95 (h)	68
72	t-C_4H_9	D	45	95 (i)	73
73	n-$C_{15}H_{31}$	D	75	96	68
74		D	60	quant.	79
75	$C_6H_5CH{=}CH$	D	5	50 (l)	36

(a) A = acetonitrile; D = dimethyl sulfoxide. (b) Over-all yield from the starting acid. (c) The hydrolysis of 2-deutero-2-phenylbenzoxathiole afforded the pure benzaldehyde-α-d. (d) Reaction run at 50°. (e) M.p. 157-158° by ethanol, lit. (8) 156-158°. (f) Calculated taking into account the recovered starting acid. (g) Extraction with benzene. (h) Isolated as 2,4-DNP derivative, m.p. 123° (9). (i) Isolated as 2,4-DNP derivative, m.p. 210° (9). (l) Isolated as 2,4-DNP derivative, m.p. 251° (9).

DUE PRECAUTION SHOULD BE EXERCISED AT ALL TIMES (6), MAINLY PERFORMING ON LARGER THAN 10-20 MMOLES SCALE.

Method A.

A mixture of 10 mmoles (1.26 g.) of *o*-mercaptophenol (4a, b) and 10 mmoles of the appropriate carboxylic acid in 5 ml. of phosphorus oxychloride was refluxed at 110° for 30 minutes in an oil-bath. After cooling, 1 ml. of perchloric acid was cautiously added dropwise and then the salts were precipitated by dry ether.

Method B.

A mixture prepared according to method A, was refluxed for 45 minutes at 110° (oil-bath) and then, after cooling and addition of perchloric acid, left at room temperature for 6 hours. The perchlorates were precipitated in the same way as described above.

Method C.

A mixture of 10 mmoles (1.66 g.) of isophthalic or terephthalic acid and 24 mmoles (5.00 g.) of phosphorus pentachloride in 5 ml. of phosphorus oxychloride, was refluxed at 110° (oil-bath) for 90 minutes. After cooling, 20 mmoles (2.52 g.) of *o*-mercaptophenol and then 2 ml. of perchloric acid were added dropwise and the resulting mixture was left at room temperature for 5 hours, in the case of perchlorate **16**, and 20 hours in the case of perchlorate **17**. The resultant brown precipitates were treated with 10 ml. of acetonitrile, filtered and washed several times with dry ether.

Method D.

To a mixture of 10 mmoles (1.26 g.) of *o*-mercaptophenol and 10 mmoles of the appropriate carboxylic acid in 5 ml. of phosphorus oxychloride, 1 ml. of perchloric acid was added dropwise. This mixture was left at room temperature for 24 hours. The salts were then precipitated by dry ether. All the perchlorates are stable at room temperature, with the exception of **21** and **24**. They were purified by reprecipitation from acetonitrile-ether, with the exception of **16** and **17** which were purified from trifluoroacetic acid-acetic acid. The structures of the perchlorates were confirmed by their nmr spectra (in deuteriotrifluoroacetic acid) (7). For yields, physical and analytical data, see Table I.

General Method for the Preparation of 2-Substituted 1,3-Benzoxathioles (**26-50**).

To a stirred suspension of 10 mmoles of perchlorate, freshly prepared, in about 150 ml. of dry ether (300 ml. for **16** and **17**), 0.5 mmoles of lithium aluminium hydride were added in small portions over a period of 5 minutes. Stirring was continued for an additional 15 minutes, then the reaction mixture was poured into an ice-cold saturated ammonium chloride solution and extracted with ether. The ether layer was washed with 5% sodium hydroxide and then with water. The solvent was dried and evaporated to afford the 2-substituted 1,3-benzoxathiole, sufficiently pure for use in the following step.

The use of lithium aluminium deuteride produced the C-2 deuterated derivative of **26**.

These compounds were stable if kept at a low temperature. Analytical samples were prepared by distillation or recrystallization. The structures of the products were confirmed by nmr spectra (in deuteriochloroform) (7). Yields, physical and analytical data are reported in Table II.

General Method for the Hydrolysis of 2-Substituted 1,3-Benzoxathioles (**25-50**).

To a solution of 5 mmoles of 2-substituted 1,3-benzoxathiole in 18 ml. of dimethyl sulfoxide:water (5:1) or acetonitrile:water (5:1), 15 mmoles (4.07 g.) of mercuric chloride were added. A yellow solution was obtained, that was gently refluxed. The solution was then diluted with water and extracted with ether. The ether layer was washed with 10% potassium iodide, 5% sodium hydroxide and then with water. The solvent was dried and evaporated to afford the pure aldehyde.

The isolated aldehydes were identified by comparison with authentic compounds by ir and nmr spectroscopy and, when possible, by mixed melting points. The aldehydes used for the comparison were commercial products (Fluka) that were purified by crystallization or distillation, with the exception of *p*-(methylsulfonyl)benzaldehyde (**63**) which was prepared as described in literature (8). The reflux times, solvents and yields are reported in Table III.

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