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The Identification of Organic Compounds

V. The Preparation of Some New *p*-Bromophenacyl Esters

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The melting points of forty-eight *p*-bromophenacyl esters are given. A method for preparation of *p*-bromophenacyl esters of acids which do not form esters by the conventional method is proposed. It has been shown that in the preparation of esters of some aromatic hydroxy-acids an alkylation of the phenol group may take place simultaneously with the ester formation. Thus 2,4-dihydroxybenzoic acid forms the expected ester and a compound which is shown to be *p*-bromophenacyl 4-(*p*-bromophenacyloxy)-2-hydroxybenzoate.

As pointed out previously [1] *p*-bromophenacyl esters are excellent derivatives for the identification of acids. Derivatives of some new acids have been prepared and the results are shown in Table 1.

It is known that some acids *e.g.* malonic acid,[2] do not form *p*-bromophenacyl esters when the ordinary procedure is used. By changing two factors, however, we have succeeded in preparing a pure ester of malonic acid. The reaction temperature of the mixture is lowered by using acetone as a solvent. Furthermore, the pH of the solution is adjusted by means of a buffer system consisting of malonic acid/sodium malonate. In this way the formation of coloured by-products is avoided.

Judefind and Reid [3,p.1052] were unable to obtain more than a few milligrams of *p*-bromophenacyl maleate from 0.25 g maleic acid. They obtained two fractions by recrystallisation of the first crop, m.p. 168—170° and 225—230°, respectively. By checking the method we found that the reaction mixture turned dark green after a few minutes of refluxing. By using a buffer system as above a pure ester was obtained. The solvent was changed to methyl cellosolve.

Trichloroacetic acid does not form a *p*-bromophenacyl ester even by using the "buffer method". The resulting compound was identified as pure sodium hydrogen carbonate.

Judefind and Reid [3] found that the *p*-bromophenacyl ester of (±)-tartaric acid and of (+)- or (−)-tartaric acid were unsuitable for identification due

Table 1. Corrected capillary melting points of *p*-bromophenacyl esters. The esters were recrystallised from ethanol (E) or glacial acetic acid (A).

Acid	M.p.°C	Formula	% C		% H	
			calc.	found	calc.	found
o-Acetamidobenzoic	143 (E)	$C_{17}H_{14}BrNO_4$	54.27	54.52	3.75	3.86
m-Acetamidobenzoic	167 (E)	$C_{17}H_{14}BrNO_4$	54.27	54.34	3.75	3 87
p-Acetamidobenzoic	256 d.[a] (A)	$C_{17}H_{14}BrNO_4$	54.27	54.31	3.75	3.58
4-(*p*-Bromophenacyloxy)-2-hydroxybenzoic	196 (A)	$C_{23}H_{16}Br_2O_6$	50.39	50.59	2.94	2.98[b]
p-Bromophenoxyacetic	153 (E)	$C_{16}H_{12}Br_2O_4$	44.89	44.76	2.83	2.76
5-Bromosalicylic	160 (E)	$C_{15}H_{10}Br_2O_4$	43.51	43.40	2.43	2.42
m-Chlorophenoxyacetic	93 (E)	$C_{16}H_{12}BrClO_4$	50.09	50.22	3.15	3.16
4-Chloro-3-methylphenoxy-acetic	123.5 (E)	$C_{17}H_{14}BrClO_4$	51.35	51.20	3.55	3.57
4-Chloro-3-nitrobenzoic	157.5 (A)	$C_{15}H_9BrClNO_5$	45.20	45.33	2.28	2.37
2-Chloro-4-nitrobenzoic	146.5 (E)	$C_{15}H_9BrClNO_5$	45.20	45.20	2.28	2.36
meso-α,β-Dibromosuccinic	190 (A)	$C_{20}H_{14}Br_4O_6$	35.85	35.71	2.11	2.23
3,5-Dibromosalicylic	190.5 (A)	$C_{15}H_8Br_3O_4$	36.55	36.56	1.84	1.83
2,5-Dichlorobenzoic	93.5 (E)	$C_{15}H_9BrCl_2O_3$	46.42	46.66	2.34	2.30
2,4-Dichlorobenzoic	127.5 (E)	$C_{15}H_9BrCl_2O_3$	46.42	46.38	2.34	2.35
2,4-Dihydroxybenzoic	191 (E)	$C_{15}H_{11}BrO_5$	51.30	51.19	3.16	3.11[c]
3,4-Dimethoxyphenylacetic	72 (E)	$C_{18}H_{17}BrO_5$	54.98	54.72	4.36	4.38
3,5-Dimethylphenoxyacetic	92.5 (E)	$C_{18}H_{17}BrO_4$	57.31	57.42	4.54	4.67
2,4-Dimethylphenoxyacetic	76 (E)	$C_{18}H_{17}BrO_4$	57.31	57.22	4.54	4.64
Diphenic	146.5 (A)	$C_{30}H_{20}Br_2O_6$	56.60	56.59	3.17	3.18
o-Ethoxybenzoic	100 (E)	$C_{17}H_{15}BrO_4$	56.22	56.32	4.16	4.20
Ethylmalonic	118 (E)	$C_{21}H_{18}Br_2O_6$	47.93	48.00	3.45	3.37
m-Ethylphenoxyacetic	99 (E)	$C_{18}H_{17}BrO_4$	57.31	57.44	4.54	4.46
β-(2-Furyl)acrylic	133 (E)	$C_{15}H_{11}BrO_4$	53.75	53.88	3.31	3.27
3-Hydroxy-2-naphthoic	197 (A)	$C_{19}H_{13}BrO_4$	59.24	59.42	3.40	3.43
Iodoacetic	101.5 (E)	$C_{10}H_8BrIO_3$	31.36	31.26	2.11	2.12
p-Isopropylbenzoic	120.5 (E)	$C_{18}H_{17}BrO_3$	59.85	59.67	4.74	4.77
p-Isopropylcinnamic	181 (A)	$C_{20}H_{19}BrO_3$	62.03	62.07	4.95	5.00
Maleic	172 d.[a] (A)	$C_{20}H_{14}Br_2O_6$	47.07	47.01	2.77	2.88
DL-Malic	179 d.[a] (E)	$C_{20}H_{16}Br_2O_7$	45.48	45.23	3.05	3.23
Malonic	188 d.[a] (A)	$C_{19}H_{14}Br_2O_6$	45.81	45.98	2.83	2.95
2-Methoxy-4-allylphenoxy-acetic	100 (E)	$C_{20}H_{19}BrO_5$	57.29	57.39	4.57	4.45
m-Methoxybenzoic	116 (E)	$C_{16}H_{13}BrO_4$	55.03	55.07	3.75	3.84
o-Methoxyphenoxyacetic	113 (E)	$C_{17}H_{15}BrO_5$	53.84	53.80	3.99	4.16
o-Methylphenoxyacetic	87 (E)	$C_{17}H_{15}BrO_4$	56.22	56.46	4.16	4.16
m-Methylphenoxyacetic	103 (E)	$C_{17}H_{15}BrO_4$	56.22	55.97	4.16	4.22
p-Methylphenoxyacetic	155.5 (E)	$C_{17}H_{15}BrO_4$	56.22	56.29	4.16	4.06
2-Naphthoic	144 (E)	$C_{19}H_{13}BrO_3$	61.80	61.65	3.55	3.45
5-Nitroisophthalic	182 (A)	$C_{24}H_{15}Br_2NO_8$	47.63	47.83	2.50	2.34
p-Nitrophenoxyacetic	164.5 (A)	$C_{16}H_{12}BrNO_6$	48.75	48.78	3.07	3.10
o-Nitrophenylacetic	113 (A)	$C_{16}H_{12}BrNO_5$	50.81	51.07	3.20	3.18
o-Nitrophenylpyruvic	116 (E)	$C_{17}H_{12}BrNO_6$	50.27	50.39	2.98	3.03
4-Nitrophthalic	180.5 (A)	$C_{24}H_{15}Br_2NO_8$	47.63	47.60	2.50	2.38
γ-Phenylbutyric	57 (E)	$C_{18}H_{17}BrO_3$	59.85	59.95	4.74	4.78
($\pm$)-α-Phenylbutyric	54.5 (E)	$C_{18}H_{17}BrO_3$	59.85	59.88	4.74	4.88
($\pm$)-Tartaric	218 d. (A) (see text)	$C_{20}H_{16}Br_2O_8$	44.14	44.25	2.96	3.07
(−)-Tartaric	231 d. (A) (see text)	$C_{20}H_{16}Br_2O_8$	44.14	43.95	2.96	2.91
Tetrachlorophthalic	177.5 (A)	$C_{24}H_{12}Br_2Cl_4O_6$	41.30	41.30	1.73	1.69
2,3,5-Triiodobenzoic	176 (A)	$C_{15}H_8BrI_3O_3$	25.85	26.06	1.16	1.30

a) Capillary tube introduced 12—15° below the m.p.; rate of heating 4—5°/min.
b) % Br found 29.32; calc. 29.16.

to a very low yield of the ester and due to decomposition near the melting point. These esters have now been prepared in a yield of about 60 %. Reproducible melting points were obtained when a special technique was used.

Alkylation of aromatic hydroxy-acids

During the preparation of esters of aromatic hydroxy-acids it was observed that two products could often be isolated from the reaction mixture. It has now been proved that besides the ester formation an alkylation of the phenol group may take place. This occurs with vanillic acid, *o*-coumaric acid, *m*- and *p*-hydroxybenzoic acid, and syringic acid.

From 2,4-dihydroxybenzoic acid the *p*-bromophenacyl ester was isolated as well as an alkylated ester. The data from an elemental analysis indicated unambigously that the alkylated ester was a mono-anisol. We were unable to distinguish the *ortho*-anisol from the *para*-anisol by means of the IR-spectra. It was found, however, that *p*-hydroxybenzoic acid formed an anisol by refluxing with *p*-bromophenacyl bromide whereas salicylic acid did not give an anisol. It is therefore concluded that the monoalkylated ester is the *p*-bromophenacyl ester of 4-(*p*-bromophenacyloxy)-2-hydroxybenzoic acid. Procedures for the preparation of a pure ester and of a pure anisol-ester are given below. Further work on the anisol formation is in progress.

EXPERIMENTAL

The melting points were determined and corrected as described in a previous paper.[1] The derivatives have been recrystallised to constant melting points.

The procedure used for the preparation of the esters from most of the acids mentioned in Table 1 was that previously given.[1,p. 641] Generally the yield of the crude product was 60–80 %.

p-*Bromophenacyl malonate.* Malonic acid (0.2 g) is dissolved in 5 ml of acetone and 1 ml of water. The solution is neutralised with 2 N sodium hydroxide (phenolphthalein). 0.2 g of malonic acid, 1 g of *p*-bromophenacyl bromide, 10 ml of acetone and some porous plate are added and the reaction mixture is refluxed for only 30 min. After cooling under the watertap, the precipitated ester is immediately removed by suction and washed on the filter with a little ethanol (50 %). A pure derivative usually is obtained. The yield is only about 32 % but the aim was purity rather than a large yield.

p-*Bromophenacyl maleate.* Maleic acid (0.25 g) is dissolved in 5 ml of methyl cellosolve. The solution is neutralised as above. 0.25 g of maleic acid, 1 g of the reagent, 10 ml of methyl cellosolve and some porous plate are added and the solution is refluxed for 30 min. The solution is cooled and the procedure above is followed. The yield is about 25 %. The ester can be recrystallised from acetic acid. If the reaction mixture is refluxed for 1 h or more the yield of ester is diminished and a large amount of *p*-bromophenacyl alcohol can be isolated from the mother liquid.

An extensive hydrolysis of a *p*-bromophenacyl ester has previously been reported for the esters of formic acid and of oxalic acid.[1]

p-*Bromophenacyl 2,4-dihydroxybenzoate.* The general procedure [1,p. 641] was followed. The alkylation of the phenol groups was avoided by the addition of extra 0.2 g of 2,4-dihydroxybenzoic acid prior to refluxing.

p-*Bromophenacyl 4-(*p-*bromophenacyloxy)-2-hydroxybenzoate.* 2,4-Dihydroxybenzoic acid (0.35 g) is dissolved in 15 ml of ethanol. 2 ml of 2 N sodium hydroxide, 1 g of *p*-bromophenacyl bromide and some porous plate are added and the solution is refluxed for one hour. Yield about 30 %.

M.p. of p-*bromophenacyl (±)-tartrate.* The ester can be prepared by following the general procedure.[1] Yield about 60 %. Judefind and Reid [3] have given the m.p. as 204–

206° (decomp.). It has now been found that the observed m.p. is highly dependent on the temperature at which the capillary tube is introduced. A reproducible value of 218° (decomp., corr.) is obtained if the capillary tube is introduced when the temperature of the bath is 12—15 degrees lower than the expected melting point. Rate of heating: 4—5°/min. It sinters at 213° and melts completely at 218°.

M.p. of p-*bromophenacyl(—)-tartrate.* The m.p. has been reported [3] as 210—215° (decomp.). A reproducible value of 231° (decomp., corr.) is obtained when the same conditions as above are followed. It sinters at 225° and melts completely at 231°.

Stability of p-*bromophenacyl iodoacetate.* The ester cannot be stored for more than a few months. It gradually turns dark and is eventually completely decomposed.

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