

The Identification of Organic Compounds

I. The Preparation of *p*-Bromophenacyl Esters of Carboxylic Acids

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The melting points of twenty *p*-bromophenacyl esters are given. The melting points taken from the literature of the *p*-bromophenacyl esters of formic acid (92° C, 99—100 °C, 134.5° C, 135.2° C and 140° C), oxalic acid (242° C) and fumaric acid (197° C) are discussed and revised by the author to 101° C, 244—245° C and 256—257° C, respectively. Further, the melting point of the oxalate and the fumarate determined on Koflers Heizbank are found to 256° C and 266° C, respectively. An improved method for the preparation of the *p*-bromophenacyl formate and the *p*-bromophenacyl oxalate is given.

It is known to be convenient to identify carboxylic acids as their esters of *p*-halogenophenacyl alcohol and in this paper and in a subsequent paper some new esters will be reported. Judefind and Reid¹ have prepared the *p*-bromophenacyl esters of many acids but they found that some acids did not give derivatives, such as oxalic acid and formic acid. However, Moses and Reid² later prepared the *p*-bromophenacyl formate with m. p. 135.2° C. Hurd and Christ³ reported the m. p. as 140° C, which was confirmed by Summerbell and Bauer⁴.

In 1950 Kubota and Matsuura⁵ pointed out that the compound widely used as a derivative for the identification of formic acid was the *p*-bromophenacyl alcohol and not the ester, and in addition they found that the *p*-iodophenacyl and the *p*-chlorophenacyl formate reported by Moses and Reid² were also the corresponding alcohols. They reported the m. p. of the *p*-bromophenacyl formate as 99—100° C, but they recommended the use of another derivative for the identification of formic acid.

Similary Grove and Suter⁶ in 1950 found the m. p. to be 99° C for the formate, but they could only obtain the pure derivative after chromatography of a benzene solution on activated alumina. In 1952 Neish and Lemieux⁷ stated that the *p*-bromophenacyl formate had a m. p. of 92° C. The ester was

prepared by refluxing equivalent amounts of the reactants in ethanol for 30 minutes giving a yield of 80 %. By refluxing longer the ester was hydrolysed and the derivative was the alcohol with m. p. varying from 137° C to 142° C depending on the rate of heating.

In order to explain some of these discrepancies we have prepared the *p*-halogenphenacyl formates and the m. p. were 87° C, 101° C and 124° C for the *p*-chloro-, *p*-bromo- and *p*-iodophenacyl ester, respectively; these values are in accordance with those given by Kubota and Matsuura⁵. The special procedure used is described in the experimental part; the *p*-bromo phenacyl formate is recommended as an excellent derivative of formic acid.

We found that the derivative, prepared according to the method of Neish and Lemieux⁷ had a m. p. of 92° C, but this was increased to 101° C by repeated recrystallisation from ethanol. The derivative is extremely difficult to purify because of the presence of *p*-bromophenacyl alcohol and unconverted *p*-bromophenacyl bromide.

In 1951 Erickson, Dechary and Kesling⁸ described a new method for the preparation of the *p*-bromophenacyl esters; the acid being converted by *p*-bromo- α -diazoacetophenone in dioxan solution. Apparently this procedure also gives the *p*-bromophenacyl alcohol, as they reported the m. p. of the formic ester as 134.5° C.

Hydrolysis of the p-bromophenacyl esters. Neish and Lemieux⁷ state that the hydrolysis of the formic ester appears to be catalysed by salts of carboxylic acids and that in general it is to be recommended for the preparation of *p*-substituted phenacyl esters that equivalent amounts of reactants should be used and that the reaction time should be kept to a minimum. Procedures in many textbooks for the preparation of the derivatives, prescribe the use of about equal amounts (weight/weight) of the acid and the *p*-bromophenacyl bromide and consequently there will usually be an excess of the salt and this might cause hydrolysis of the ester formed.

However, we have found that by using an excess of the salt — two or three times the equivalent amount — a pure derivative was always obtained after recrystallisation. Furthermore, the refluxing period has been varied and again a pure derivative was isolated after recrystallisation even if the reaction mixture was refluxed for four hours. Certainly a hydrolysis occurs but the crude product can be purified. This hydrolysis can be observed for those derivatives which melt below the melting point of the *p*-bromophenacyl alcohol (143° C) as a derivative contaminated with the *p*-bromophenacyl alcohol only melts partially near the expected m. p. and on further heating it melts completely in the proximity of 143° C. The conclusion must be that in general it is advisable to keep the refluxing period below four hours.

An extensive hydrolysis of a derivative only occurs in carboxylic acids of which the esters are known to be highly sensitive to hydrolytic conditions; for example formic acid. Also in the preparation of the *p*-bromophenacyl oxalate some alcohol appears and has been isolated (see later).

It was also observed that in order to obtain a pure derivative it is essential that the reaction mixture should be adjusted to a pH of approximately 5 or below. At higher pH values the reaction mixture acquires a more intense yellow to red colour. The further addition of 10—15 drops of 0.5 N hydro-

chloric acid after the red colour of the indicator has disappeared is therefore suggested in the general procedure given in the experimental part.

The p-bromophenacyl oxalate. Mowry and Brode⁹ have prepared the oxalate, the m. p. of which was 242° C (decomp.); this was determined by using a thermometer of the Anschütz type. However, it is very difficult to prepare this derivative according to Mowry and Brode and we have worked out a special procedure. Due to a decomposition the m. p. was found to be highly dependent on the time in which the substance is in the silicone bath before melting. By introducing the capillary tube into the bath at *ca.* 235° C, the m. p. is found to be 244—245° C (rate of heating: 1—2° C per minute). Determined on Kofler Heizbank the m. p. was 256° C \pm 2° and no decomposition was observed when it melted; destruction occurred after some seconds.

The p-bromophenacyl fumarate. The melting point of this derivative is given in the textbook by Shriner and Fuson^{10,p.225} as 197° C but is has not been possible to find it in the original literature or in other textbooks on organic analysis; only the phenacyl fumarate is found (m. p. 197° C)^{11,p.80}. We have now prepared the fumarate by the general method, given later in the text, and the m. p. was found to be 256—257° C (decomp.). On Kofler Heizbank no decomposition of the melt was observed, and the m. p. was 266° C \pm 2°.

Melting points and microanalysis of twenty *p*-bromophenacyl esters are given in Table 1.

Table 1. Corrected capillary melting points of *p*-bromophenacyl esters.

Acid	Melting point, °C	Formula	% C		% H	
			calc.	found	calc.	found
Formic	101	C ₈ H ₇ Br O ₃	44.47	44.40	2.90	2.96
Vinylacetic	60.5	C ₁₂ H ₁₁ BrO ₃	50.90	50.87	3.92	3.79
β,β -Dimethylacrylic	101	C ₁₃ H ₁₃ BrO ₃	52.54	52.74	4.41	4.43
Oxalic	244—245 d	C ₁₆ H ₁₅ Br ₂ O ₄	44.66	44.75	2.50	2.72
Fumaric	256—257 d	C ₂₆ H ₁₄ Br ₂ O ₄	47.08	47.20	2.77	2.97
d-Camphoric	142.5	C ₂₆ H ₂₄ Br ₂ O ₄	52.54	52.61	4.41	4.42
Diphenylacetic	112	C ₂₂ H ₁₇ BrO ₃	64.56	64.75	4.19	4.21
3,4-Dichlorobenzoic	123	C ₁₈ H ₉ BrCl ₂ O ₃	46.42	46.20	2.34	2.25
4-Bromophenylacetic	100.5	C ₁₆ H ₁₃ Br ₂ O ₃	46.63	46.48	2.94	3.04
<i>d,l</i> -Mandelic	113	C ₁₆ H ₁₃ BrO ₄	55.03	54.85	3.75	3.72
<i>o</i> -Cresotic	172	C ₁₆ H ₁₃ BrO ₄	55.03	54.85	3.75	3.74
<i>p</i> -Cresotic	142	C ₁₆ H ₁₃ BrO ₄	55.03	54.80	3.75	3.93
4-Ethoxybenzoic	141	C ₁₇ H ₁₅ BrO ₄	56.21	56.20	4.16	4.26
Veratric	124	C ₁₇ H ₁₅ BrO ₅	53.84	53.71	3.99	4.02
Piperonylic	165.5	C ₁₈ H ₁₇ BrO ₅	52.91	52.78	3.05	3.23
2-Chlorophenoxyacetic	95.5	C ₁₆ H ₁₃ BrClO ₄	50.09	50.00	3.15	3.32
4-Chloro-3,5-dinitrobenzoic	153	C ₁₈ H ₉ BrClN ₂ O ₇	40.61	40.65	1.82	1.85
3-Nitrophthalic	166	C ₂₄ H ₁₅ Br ₂ NO ₃	47.63	47.50	2.50	2.67
3,4,5-Trimethoxybenzoic	129	C ₁₈ H ₁₇ BrO ₆	52.83	52.84	4.19	4.23
1-Naphthylacetic	112.5	C ₂₆ H ₁₅ BrO ₃	62.68	62.72	3.95	3.99

EXPERIMENTAL PART *

The capillary melting points are determined in an electrically heated silicone bath with mechanical stirrer. The temperature at which the compound melts completely are registered. The thermometers used were of the Anschütz type calibrated in 0.1 of a degree. The results are corrected melting points to about 0.5° C. Rate of heating *ca.* 1° C/per minute; it is found that generally the melting points are almost independent of the rate of heating. The derivatives have been recrystallised to constant melting points.

Preparation of the *p*-bromophenacyl esters

The procedure used for the preparation of the esters given in Table 1, except the ester of formic acid and oxalic acid, is that given by Judefind and Reid ¹ with some modifications. The detailed description is given below.

Procedure. An amount corresponding to 0.004 equivalents of the acid is dissolved in 5 ml of ethanol (by heating if necessary). The solution is neutralised with 2 N sodium hydroxide to phenolphthalein as indicator. To this solution is added 3 ml of water and 0.5 N hydrochloric acid to remove the red colour and then further 10–15 drops hydrochloric acid. It is important that the solution of the sodium salt is faintly acid in order to prevent the formation of coloured by-products in the subsequent reaction. 1 g of *p*-bromophenacyl bromide, 5 ml of ethanol and some porous plate are added and the solution is heated under reflux for one or two hours according to whether the acid is mono- or dibasic.

If the reaction mixture is not clear on heating to boiling, a little more ethanol is added (10–30 ml). After boiling for 5–10 minutes a precipitate sometimes is formed but the boiling is continued nevertheless.

The solution is immediately cooled under the tap; if an appreciable amount is not precipitated by cooling a little water is added. The ester is removed by suction and washed on the filter with a few ml of ethanol (*ca.* 50 %). Generally the yield of the crude product is 60–80 %, and this is satisfactory as the aim is purity rather than large yields.

The derivative is recrystallised from ethanol or from aqueous ethanol (*ca.* 50 %). Usually one or two recrystallisations are sufficient. If the ester is insoluble in ethanol, glacial acetic acid should be used.

The p-bromophenacyl formate. The procedure above is followed except that the refluxing period is reduced to 30 minutes. The crude product melts at *ca.* 90° C; it should be recrystallised one to three times from ethanol. The *p*-chloro- and the *p*-iodophenacyl formate can be prepared in the same way.

The p-bromophenacyl oxalate. The procedure above could not be used; after refluxing for two hours unreacted sodium oxalate and *p*-bromophenacyl bromide were the main products. Other solvents were tried (dioxan, methyl cellosolve and butyl cellosolve) and by using methyl cellosolve the preparation of the oxalate was successful. The method above is modified so that the oxalic acid is dissolved in 5 ml of methyl cellosolve and the solution is adjusted as above. 1 g of *p*-bromophenacyl bromide, 15 ml of methyl cellosolve and some porous plate are added and the reaction mixture is refluxed for only one hour. After cooling under the tap, the ester is removed by suction and washed on the filter with a little ethanol (50 %). A pure derivative usually is obtained; it can be recrystallised from glacial acetic acid (sparingly soluble).

The *p*-bromophenacyl oxalate is readily hydrolysed to the *p*-bromophenacyl alcohol. By varying the refluxing period it is found that the largest yield of the *p*-bromophenacyl oxalate was obtained by refluxing for about one hour (yield *ca.* 40 %). Also by heating for 30 minutes the oxalate was obtained in good yield but unreacted *p*-bromophenacyl bromide was recovered. By boiling for two hours the yield of the oxalate was about 30 % and the main product was the *p*-bromophenacyl alcohol; this was precipitated by addition of water to the filtrate (yield 50–60 %; m. p. 143° C Kofler Heizbank). When the reaction mixture was boiled for only one hour the filtrate did not give an immediate precipitation upon dilution with water.

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