

Note

Degradation of pentafluorobenzyl bromide in the extractive alkylation procedure

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Extractive alkylation with pentafluorobenzyl bromide has been used for the derivatization of organic acids prior to analysis by gas chromatography with electron-capture detection¹⁻⁴. The principle of this one-step extraction and derivatization procedure is the partition of the acid anion as an ion pair with a quaternary ammonium ion to an organic phase containing the alkylating reagent.

In this study, the degradation of pentafluorobenzyl bromide has been studied with methylene chloride as the organic phase and aqueous phases with different pH values, buffer systems and quaternary ammonium ions.

EXPERIMENTAL

Apparatus

A Varian 1400 gas chromatograph with a flame-ionization detector was used. The glass column (150 × 0.2 cm I.D.) was filled with 5% Carbowax terephthalic acid on Chromosorb W (80-100 mesh) or 15% OV-225 on Gas-Chrom Q (100-120 mesh).

Reagents and chemicals

Pentafluorobenzyl bromide was obtained from Pierce (Rockford, Ill., U.S.A.) or P.C.R. (Gainesville, Fla., U.S.A.) and pentafluorobenzyl alcohol from Fluka (Buchs, Switzerland). Tetrabutylammonium hydrogen sulphate was purchased from Labkemi (Gothenburg, Sweden). Tetrapropyl- and tetrapentylammonium iodide were purchased from Eastman (Rochester, N.Y., U.S.A.) and converted into the corresponding hydroxides by shaking with silver oxide⁵.

Quaternary ammonium ion solutions (0.1 M) were prepared by neutralization of the corresponding hydroxide or hydrogen sulphate solution with sulphuric acid or sodium hydroxide.

Methods

The degradation of pentafluorobenzyl bromide was studied in a system containing equal volumes of a methylene chloride solution of pentafluorobenzyl bromide and an internal standard (mesitylene) and a 0.1 M solution of quaternary ammonium ion in sodium hydroxide or buffer. The mixtures were shaken for the appropriate

time at 25°. A suitable volume of the organic phase was withdrawn and shaken with 0.1 M sulphuric acid before analysis.

Quantitation was effected with the aid of the internal standard and reference solutions of pentafluorobenzyl bromide and alcohol.

RESULTS AND DISCUSSION

Degradation products of pentafluorobenzyl bromide

Pentafluorobenzyl bromide is degraded to pentafluorobenzyl alcohol and chloride and bispentafluorobenzyl ether. Pentafluorobenzyl chloride is formed from pentafluorobenzyl bromide and chloride ions, liberated by the degradation of methylene chloride under alkaline conditions⁶.

The time course of the degradation of pentafluorobenzyl bromide and the formation of degradation products is demonstrated in Fig. 1. The change in the concentration of pentafluorobenzyl alcohol and the ether is small after 8 h, when little pentafluorobenzyl bromide remains.

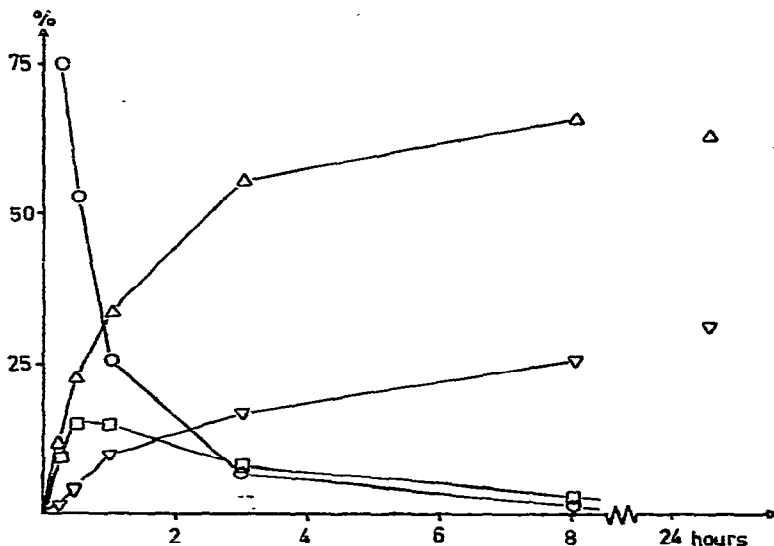


Fig. 1. Degradation of pentafluorobenzyl bromide. Organic phase: methylene chloride with 0.066 M pentafluorobenzyl bromide. Aqueous phase: tetrapentylammonium (0.1 M) in 0.25 M carbonate buffer (pH 10). Equal phase volumes. O, Pentafluorobenzyl bromide; □, pentafluorobenzyl chloride; △, pentafluorobenzyl alcohol; ▽, bispentafluorobenzyl ether.

Low concentrations (< 1%) of pentafluorobenzyl alcohol were observed when the aqueous phase contained 0.1 M sodium hydroxide and tetrapentylammonium was used as the counter ion. The concentration of bispentafluorobenzyl ether increased as long as pentafluorobenzyl bromide was present. This indicates an almost immediate conversion of the alcohol into the ether at the high pH used.

The recoveries of pentafluorobenzyl bromide and its degradation products were in most instances above 90% of the initial concentration. In the presence of phosphate and tris buffers the recovery was only about 50% (24 h).

Influence of the counter ion and hydroxyl ion concentration

The degradation of pentafluorobenzyl bromide using aqueous phases with different quaternary ammonium ions is demonstrated in Table I. The degradation of pentafluorobenzyl bromide increases with increasing lipophilic character of the counter ion. This is probably due to an enhanced extraction of hydroxyl ions into the organic phase⁷, which increase the hydrolysis rate of the reagent. This is supported by the data given in Table II, which shows the degradation of pentafluorobenzyl bromide in the presence of different concentrations of hydroxyl ions with tetrabutylammonium as the counter ion. More than 20% of the initial pentafluorobenzyl bromide concentration has been destroyed after 30 min in 1 M sodium hydroxide solution.

TABLE I

INFLUENCE OF THE COUNTER ION ON THE DEGRADATION OF PENTAFLUOROBENZYL BROMIDE

Organic phase: methylene chloride with 0.066 M pentafluorobenzyl bromide. Aqueous phase: tetraalkylammonium ion (0.1 M) in 0.1 M sodium hydroxide solution. Equal phase volumes.

Counter ion	Pentafluorobenzyl bromide (%) remaining after			
	0.5 h	1 h	3 h	24 h
Tetrapropylammonium	100	96	104	97
Tetrabutylammonium	99	94	90	56
Tetrapentylammonium	32	21	9	2

TABLE II

INFLUENCE OF THE HYDROXYL ION CONCENTRATION ON THE DEGRADATION OF PENTAFLUOROBENZYL BROMIDE

Organic phase: methylene chloride with 0.066 M pentafluorobenzyl bromide. Aqueous phase: tetrabutylammonium (0.1 M) in 0.1 or 1 M sodium hydroxide solution. Equal phase volumes.

Concentration of sodium hydroxide solution (M)	Pentafluorobenzyl bromide (%) remaining after			
	0.5 h	1 h	3 h	24 h
0.1	99	94	90	56
1	78	58	33	6

TABLE III

INFLUENCE OF THE BUFFER SYSTEM ON THE DEGRADATION OF PENTAFLUOROBENZYL BROMIDE

Organic phase: methylene chloride with 0.007 M pentafluorobenzyl bromide. Aqueous phase: tetrapentylammonium (0.1 M) in 0.25 M buffer (pH 10). Equal phase volumes.

Buffer system	Pentafluorobenzyl bromide (%) remaining after					ΔpH
	0.5 h	1 h	2 h	4 h	24 h	
Citrate	64	43	17	0		-0.46
Carbonate	69	43	21	12	0	-0.24
Phosphate	94	91	79	73	24	-0.43
Borate	94	82	81	61	20	-0.36
Tris	95	80	75	70	36	-0.28

Influence of the buffer systems

The stability of pentafluorobenzyl bromide was studied using five different buffer systems. The concentration change with time is given in Table III together with the shift in pH observed after 24 h. The initial concentration of pentafluorobenzyl bromide was 10 times lower in these experiments than under ordinary extractive alkylation conditions. Preliminary studies showed pronounced pH deviations (citrate —2.1, phosphate —1.8) in the buffer systems with the normal pentafluorobenzyl bromide concentration.

From the data given in Table III it can be seen that carbonate and citrate buffers are more detrimental to the stability than are borate, phosphate and tris buffers.

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