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Note

On-column organic reactions

Schotten-Baumann benzoylation of phenols on an Extrelut column[*]

AKIRA KUNUGI and KATSUMI TABEI*

Department of Organic Chemistry, Tokyo College of Pharmacy, 1432-1 Horinouchi, Hachioji City, Tokyo 192-03 (Japan)

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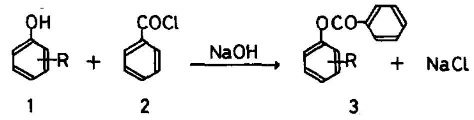
Our attention has been directed to the use of liquid–liquid partition chromatography in organic chemistry. Instead of the separatory funnel method, we have established a mode of column extraction involving the use of Extrelut as the support material[1,2].

In its simplest form, the technique involves the immobilization of an immiscible solvent (stationary phase) on a support material and the passage of another solvent (mobile phase) over it. The two solvents in intimate contact thus allow continuous extraction. Since the solvents comprising an heterogeneous mixture make better contact with each other in a pore volume of the supporting matrix, the column can be used as a vessel for reactions occurring at the surface of the heterogeneous mixture. Thus, a study was made of the reaction of phenols with benzoyl chloride in an aqueous alkaline medium adsorbed on an Extrelut column as a model on-column reaction:



EXPERIMENTAL

Preparation of the column

For the 0.01-mol scale experiment, 15 g of Extrelut (E. Merck) were dry-packed into a glass tube (40 cm × 2 cm) equipped with a stop-cock and a glass-wool bed at the bottom. The supporting matrix thus obtained was 2 cm in diameter and 20 cm in length.

Reaction procedure

The general procedure for the on-column Schotten-Bauman benzoylation of phenols is as follows. A mixture of 0.01 mol of a phenol (1) in 15 ml of 10% sodium

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hydroxide aqueous solution was applied to the column. The resulting stationary phase was allowed to stand for 10 min to stabilize. A solution of 0.01 mol of benzoyl chloride (2) in 5 ml of an appropriate solvent, *e.g.*, dichloromethane was added to the column as a mobile phase and the stop-cock closed after the mobile phase had penetrated the matrix. The two phases were allowed to make intimate contact for 5 min (benzoylation). The product (3) was then eluted with an appropriate solvent; 40 ml of the eluate were collected and the solvent was evaporated without drying. The residual aryl benzoate (3) was recrystallized from an appropriate solvent, *e.g.*, *n*-hexane–benzene, benzene, ethanol or ethanol–water mixture and characterized by melting point determination and infrared spectroscopy.

RESULTS AND DISCUSSION

Benzoyl esters are well known for their use as typical solid derivatives of phenols in mixed melting point determinations in organic analysis; however some of them have rather low melting points[3]. The benzoylation of phenols is generally carried out by shaking a suspension of a phenol and benzoyl chloride in an aqueous alkaline medium at room or lower temperature (0–5°C) in accord with the Schotten-Baumann method[4]. Yeadon *et al.*[5] reported the phase-transfer catalyzed benzoylation of phenols and substituted phenols to the corresponding benzoyl esters in 60–80% yield.

In the present on-column method, a phase-transfer catalyst, an excess amount of benzoyl chloride and shaking of the reaction flask are no longer required. An aqueous solution of a phenol (1) and about 5 mol equiv. of sodium hydroxide are allowed to make contact with a solution of an equivalent molar amount of benzoyl chloride (2) in dichloromethane, chloroform or diethyl ether in an Extrelut column

TABLE I

YIELDS AND MELTING POINTS OF ARYL BENZOATES

Phenol		*Aryl benzoate*			
		No.	*m.p. (°C)**		*Yield (%)***
1a	Phenol	3a	69	[71]	94
1b	*p*-Cresol	3b	71	[72]	93
1c	*m*-Chlorophenol	3c	70	[71]	78
1d	*p*-Chlorophenol	3d	90	[88]	91
1e	*p*-Bromophenol	3e	102	[104]	93
1f	2,4-Dichlorophenol	3f	97	[97]	88
1g	*p*-Methoxyphenol	3g	87	[87]	95
1h	*m*-Nitrophenol	3h	95	[95]	81
1i	2-Naphthol	3i	107	[107]	93
1j	*o*-Nitrophenol	3j	55	[55]	5
1k	*p*-Nitrophenol	3k	114	[114]	7
1l	Resorcinol***	3l	117	[117]	3

* Values taken from ref. 3 are given in square brackets.

** Yield of isolated product.

*** Two mol. equiv. of 2 were used.

at room or lower temperature to afford the corresponding aryl benzoate (3). The product is eluted with the same solvent. When the contact (reaction) period exceeded 5 min, similar results were obtained. This technique has been used to prepare the benzoyl esters of a wide range of phenols and the yields and melting points are listed in Table I.

The yields are fairly good (78–95%) except in the cases of *o*-nitrophenol (1j), *p*-nitrophenol (1k) and resorcinol (1l). The products were virtually free from unreacted benzoyl chloride and starting material and thus could easily be solidified by evaporation of the solvent.

Since the sodium salts of *o*- and *p*-nitrophenol are poorly soluble in 10% sodium hydroxide aqueous solution, they underwent little reaction with benzoyl chloride and consequently the corresponding benzoyl esters (3j,k) were obtained in very low yield. Compound 2 was recovered in 35–40% yield. Resorcinol was oxidized in the stationary phase which became green in colour and the yield of its dibenzoate (3l) was only 3%.

CONCLUSIONS

The advantages of this method may be summarized as follows:

(1) The procedure is simple and easy to carry out, thus minimizing variation in results.

(2) High and reproducible yields can be obtained.

(3) The reaction and work-up are performed on the same column.

(4) The product is directly eluted from the column and the eluate is dried in the clean-up zone during elution.

(5) The time required is minimal.

(6) The Extrelut can easily be refined and reused (washing successively with 5% sodium hydroxide, 5% hydrochloric acid, water and methanol, followed by drying at 130°C for 6 h).

Thus, we recommend this on-column Schotten-Baumann method for the benzoylation of phenols and alcohols.

On-column organic reactions have several limitations: only reactions that proceed in an heterogeneous medium such as a suspension of water and an immiscible solvent can be employed. The reactions can carried out at room or low temperature (cooling in ice). The product must be soluble in an organic solvent immiscible in water. We are now looking for ways to broaden the scope of application of this method.

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