Utility of Triphenylphosphine Dihalides in Organic Reactions: Esterification Using Triphenylphosphine Dibromide as the Dehydrating Agent

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ABSTRAK

Satu kaedah baru pengesteran telah dikaji menggunakan trifenilfosfina dibromida sebagai agen pendehidratan. Kajian ini telah menunjukkan bahawa kaedah ini adalah berguna bagi asid aromatik atau arilalilik. Kajian ini juga telah menunjukkan bahawa alkohol primer dan sekunder mengesterkan asid dengan memuaskan, sedangkan alkohol tertier tidak bertindakbalas.
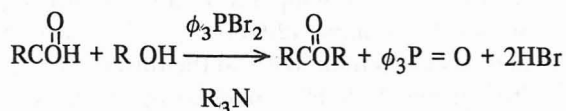
ABSTRACT

A new esterification method was investigated using triphenylphosphine dibromide as a dehydrating agent. This investigation has established that the method is useful when the acid is aromatic or arylallylic. That primary and secondary alcohols esterify acid satisfactorily whereas tertiary alcohols fail to react was also established in this experiment.

INTRODUCTION

The methodology of ester synthesis has always attracted the attention of organic chemists due to the versatility of this functional group (see for examples, Arieta *et al.*, 1983; Kurita *et al.*, 1982; Sekine *et al.*, 1981; Nakao *et al.*, 1981; Kitazume *et al.*, 1980). Aside from its uses as the final product such as flavorant and polymer materials, the functionality has been widely utilized as reaction intermediates and protecting groups in organic synthesis (Hegedus and Wade, 1977; Haslam, 1979; Wade, 1981). Even though several methods of the ester synthesis based on the dehydration reaction have been reported (for examples, Keshavamurthy *et al.*, 1982; Corey *et al.*, 1976; Corey *et al.*, Corey *et al.*, 1975; Kurihara *et al.*, 1976; Hendrickson *et al.*, 1975, Cekovic *et al.*, 1980), the use of triphenylphosphine dibromide in such a reaction has never been mentioned. Since this reagent can be easily prepared from the reaction of triphenylphosphine and bromine, its utilization in this reaction procedure can be attractive alternative to the conventional esterification methods. In this paper we wish to report our finding on the utility of the triphenylphosphine reagent in the synthesis of esters.

$$\underset{\substack{R_3N}}{\overset{\substack{O \\ \| \\ RCOH + R\,OH}}{\xrightarrow{\phi_3PBr_2}}} \overset{O}{\underset{\|}{RCOR}} + \phi_3P = O + 2HBr$$

MATERIALS AND METHODS

All reagents except benzoic acid and ethanol were purified either by distillation or

recrystallization (wherever appropriate) prior to their use. All solvents were dried over sodium metal and distilled before use. Silica gel for chromatography, Lot 35945 (M & B) and silica gel, Type 60F 254 (Merck) were used for column and TLC analysis respectively. The proton nuclear magnetic resonance spectra were recorded either on Bruker WP-80 or Varian EM-60 spectrometers. The chemical shifts were recorded in 5 p.p.m. using tetramethylsilane (0.00 p.p.m.) as the internal standard. Infrared spectra were recorded on a Beckman Acculab T.M. 3 spectrophotometer using 1601 cm^{-1} band of polystyrene for calibrating each spectra.

A general reaction procedure in the preparation of esters using triphenylphosphine dibromide as a dehydrating agent is represented in the preparation of ethyl benzoate from benzoic acid and ethanol below. The same amount of triphenylphosphine dibromide as in this preparation was used for all reactions.

Preparation of Ethyl Benzaote from Benzoic Acid and Ethanol

In a 100 ml three-necked round bottom flask, 2.88 g (11.0 mmol) of triphenylphospine was dissolved in 50 ml petroleum ether (b.p. 40°C – 60°C). To it, was added 0.6 ml bromine dropwise while stirring. A yellow precipitate of triphenylphosphine dibromide was formed and the stirring was continued for five minutes. The flask was cooled to 0°C and 3.2 ml triethylamine was added. After stirring for another 5 minutes, a solution of 0.7 g (5.7 mmol) of benzoic acid in the minimum amount of petroleum ether was added, followed by the addition of 2.5 ml (42.8 mmol) ethanol. The reaction was allowed to warm up to room temperature and the stirring continued overnight (20 hours). The reaction mixture was then filtered and the filtrate washed with aqueous 10% HCl followed by an aqueous 10% NaHCO$_3$ solution. The organic layer was concentrated and distilled. The liquid collected between 40°C – 50°C at 1.5 mm Hg on kugelrohr distillation was identified as ethyl benzoate. NMR (CCl$_4$, ppm); 1.3 (3H, t, J = 7Hz), 4.3 (2H, q, J = 6Hz); 7.3 (3H, br–m); 8.0 (2H, d–d, J = 2Hz, 8Hz); IR (NaCl, neat, cm^{-1}) 3010, 2980, 1720, 1605, 1450, 1280, 1030, 700.

Preparation of Methyl Benzoate

In a similar manner, 0.7 g (5.7 mmol) of benzoic acid was esterified using methanol 1.0 ml (24.73 mmol) in the presence of triphenylphosphine dibromide. Kugelrohr distillation gave 0.57 (4.16 mmol) of the ester.

NMR (CDCl$_3$, ppm); 4.3 (3H, s), 7.4 (3H, m);
IR (NaCl, neat; cm^{-1}) 3010, 2990, 1720, 1610, 1445, 1280, 1025, 710.

Preparation of Isopropyl Benzoate

In a similar procedure 0.7 g (5, 7 mmol) of benzoic acid was reacted with triphenylphosphine dibromide followed by the addition of 1.0 ml (13.6 mmol) isopropyl alcohol. After kugelrohr distillation, 0.65 g (3.99 mmol) of isopropyl benzoate was isolated.

NMR (CDCl$_3$, ppm); 1.3 (6H, d, J = 7Hz), 5.15 (1H, m, J = 7Hz); 7.35 (3H, d – d, J = 6H, 2Hz); 7.95 (2H, m, J = 6Hz, 2Hz);
IR (NaCl, neat; cm^{-1}): 3100, 3010, 2985, 1730, 1610, 1450, 1280, 1030, 980, 775.

Preparation of Ethyl Cinnamate

The general procedure was followed in this reaction using 1.18 g (8.0 mmol) of cinnamic acid and ethanol 1.15 ml (25.70 mmol) in the presence of triphenylphosphine dibromide. Upon work up and distillation, 1.01 g (5.76 mmol) of methyl cinnamate was isolated.

NMR (CDCl$_3$, ppm) 1.2 (3H, t, J = 7Hz), 4.2 4.2 (2H, t, J = 7Hz), 6.3 (1H, d, J = 14Hz), 7.3 (5H, br-m), 7.5 (1H, d, J = 14Hz).
IR (NaCl, neat, cm^{-1}); 3100, 3010, 1730, 1610.

Preparation of Isopropyl Cinnamate

Similarly, 1.18 g (8.0 mmol) of cinnamic acid was esterified using 1.5 ml (19.60 mmol) of isopropyl alcohol. Upon work up followed by distillation, 1.02 g (5.36 mmol) of isopropyl cinnamate was collected.

NMR (CDCl$_3$, ppm); 1.3 (6H, d, J = 7Hz), 5.15 (1H, m, J = 7Hz), 6.3 (1H, d, J = 14Hz) 7.3 (5H, br – m), 7.5 (1H, d, J = 14Hz);
IR (NaCl, neat, cm^{-1}) 3100, 3010, 1730, 1650, 1630, 1500, 1450, 1320, 1300, 1260, 1180, 1050, 980, 950, 775, 645.

Preparation of Octyl Acetate

Upon reacting 0.47 ml (8.0 mmol) of acetic acid with 1.26 ml (18.0 mmol) of octanol in the presence of triphenylphosphine dibromide, 0.41 g (2.4 mol) of octyl acetate was isolated after kulgelrohr distillation followed by column choromatography (Silica gel/Chloroform).

NMR (CDCl$_3$, ppm); 0.71 − 1.00 (3H, br),
  1.00 − 2.00 (12H, br), 2.00 (3H, S),
  4.10 (2H, t, J = 6Hz).
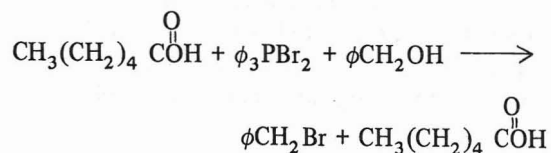IR (NaCl, neat, cm^{-1}); 2950, 2880, 1750, 1450,
  1365, 1225, 1040.

DISCUSSION AND RESULTS

Previous work has shown that triphenylphosphine dihalides react with carboxylic acids to generate unstable acyloxyphosphonium salt intermediates which can later decompose to acid halides (Horner *et al.*, 1959; Regen and Lee, 1975). In this project, one could expect that if another nucleophile is present, its reaction with the acyloxyphoshonium salt should lead to the substitution product *(Scheme I)*.

We examined this reaction using ethanol as the nucleophile. The reaction of triphenylphosphine dibromide with benzoic acid followed by the addition of ethanol in the presence of triethylamine produced ethyl benzoate. The yield was found to be best when the alcohol was present in large excess as compared to the acid. Comparably good results were obtained when methyl and isopropyl alcohol were used as nucleophiles — see Table 1. Esterification of cinnamic acid with ethyl and isopropyl alcohol gave satisfactory yields of the desired products. Extension of this procedure was attempted for the preparation of *tert*-butyl esters. Reaction of benzoic acid with *tert*-butyl alcohol however failed to produce the desired *tert*-butyl benzoate. A similar result was true in the case of cinnamic acid. This observation is not surprising since *tert*-butyl alcohol is too bulky to function as the suitable nucleophile in this reaction.

In order to establish the generality of this reaction, the esterification of saturated aliphatic acids was carried out. The esterification of acetic and hexanoic acids with either primary or secondary alcohol gave only poor yields (Table 1).

Furthermore, the reaction of hexanoic acid and benzyl alcohol gave benzyl chloride as the major product with only a trace amount of benzyl hexanoate (on thin layer chromatography analysis, SiO$_2$/Chloroform).
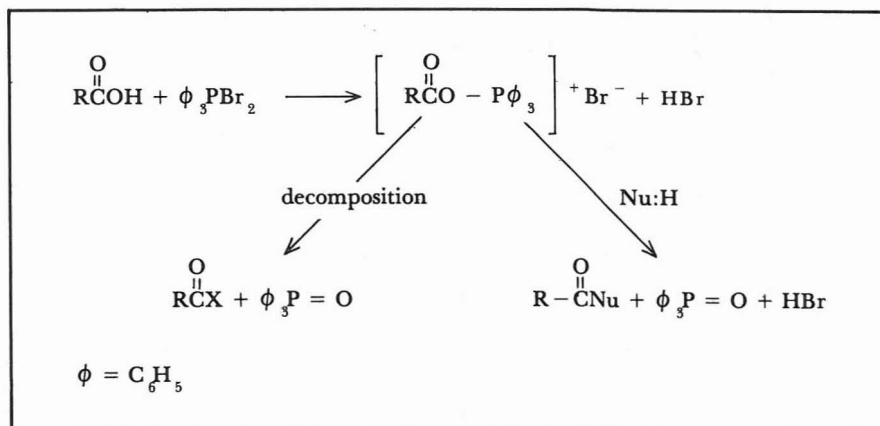
$$CH_3(CH_2)_4 \overset{\overset{O}{\|}}{C}OH + \phi_3PBr_2 + \phi CH_2OH \longrightarrow$$

$$\phi CH_2Br + CH_3(CH_2)_4 \overset{\overset{O}{\|}}{C}OH$$

Scheme 1

TABLE 1
Yields of esterification using triphenylphosphine dibromide

| Acid	Alcohol	Ester (Yield %)
⬡— COOH	CH_3OH	⬡— CO_2CH_3 (73)
⬡— COOH	CH_3CH_2OH	⬡— $CO_2CH_2CH_3$ (85)
⬡— COOH	$(CH_3)_2CH$ OH	⬡— $CO_2CH(CH_3)_2$ (70)
⬡— COOH	$(CH_3)_3COH$	not formed
⬡— CH = CH COOH	CH_3CH_2OH	⬡— CH = CH $CO_2CH_2CH_3$ (72)
⬡— H = CH COOH	$(CH_3)_2CH$ OH	⬡— CH = CH CO_2 $CH(CH_3)_2$ (67)
⬡— CH = CH COOH	$(CH_3)_3COH$	not formed
CH_3COOH	$CH_3(CH_2)_7OH$	$CH_3CO_2(CH_2)_7CH_3$ (30)
$CH_3(CH_2)_4COOH$	CH_3CH_2OH	$CH_3(CH_2)_4CO_2CH_2CH_3$ (27)

These observations suggest that the acyloxy-phosphonium salt intermediates undergo reaction with alcohols either by the attack on the carbonyl carbon to form esters or by displacing the acyloxy group from the phosphorus to form an alkoxyphosphonium salt. A similar suggestion has been mentioned previously on the reaction of alcohols and carboxylic acid in the presence of triphenylphosphine and carbon tetrachloride (Apel R., 1975) see *Scheme II*. Whereas in the case of benzoyloxy and cinnamoyloxphospho-

nium salts, the attack on the carbonyl carbon by alcohol is more predominant the acyloxyphosphonium salts of aliphatic acids undergo acyloxy-displacement reaction more predominantly. This is not surprising since the carbonyl carbon of the benzoyl and cinnamoyl group are more susceptible to nucleophilic attack then the aliphatic acyl groups. This isolation of benzyl bromide in the reaction of hexanoic and with benzyl alcohol shows that the phenylmethoxy-phosphonium salt readily decomposes to benzyl bromide as soon as this intermediate is formed.

Scheme 2

$$\phi_3PBr_2 + R\overset{O}{\overset{\|}{C}}OH \longrightarrow \left[\phi_3P - O\overset{O}{\overset{\|}{C}}R \right]^+ Br^- + HBr$$

$$\left[\phi_3P - O\overset{O}{\overset{\|}{C}}R \right] Br^- + \quad \xrightarrow{\text{path a}} RO\overset{O}{\overset{\|}{C}}R + \phi_3PO + HBr$$

$$b \quad a \qquad \xrightarrow{\text{path b}} \left[\phi_3POR' \right]^+ Br^- + R\overset{O}{\overset{\|}{C}}OH$$

$$R'OH \qquad\qquad\qquad\qquad\qquad R'Br + \phi_3PO$$
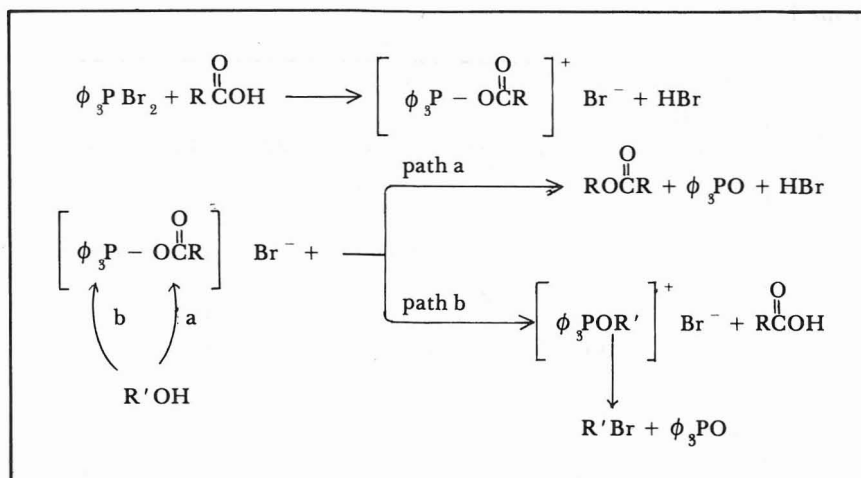
CONCLUSION

The esterification method using triphenyl phosphonium dibromide is useful for aromatic acids, with primary or secondary alcohols. The reaction can be an alternative preparation of esters when the system needs a basic reaction condition.

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