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The Preparation of 3,5-Diacetoxy-1-cyclopentene[1]

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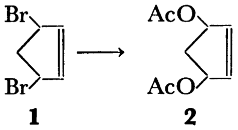
Synopsis. The phase-transfer reaction of 3,5-dibromo-1-cyclopentene with potassium acetate was studied using trialkylamines and a trialkylphosphine as catalysts. Various metal acetates were examined for their effects in this reaction.

We recently reported[2] on the nucleophilic substitution reaction of alkyl bromides with potassium acetate employing a quaternary ammonium ion catalyst in a heterogeneous system. This phase-transfer reaction provided a convenient synthetic method for acetates from the corresponding bromides besides previously developed methods using silver acetate, tetraethylammonium acetate, or potassium acetate in glacial acetic acid and acetic anhydride.[2] Thus, *cis*-3,5-diacetoxy-1-cyclopentene **2** was prepared from *cis*-3,5-dibromo-1-cyclopentene **1**, 4-acetoxy-2-cyclohexen-1-one from 4-bromo-2-cyclohexen-1-one, and octyl acetate from octyl bromide. In the course of the study of the synthesis of prostaglandins, we succeeded

$$\mathrm{RX} \xrightarrow[\text{KOAc}]{\text{phase-transfer catalyst}} \mathrm{ROAc}$$

in converting the diacetate **2** into chiral 4-hydroxy-2-cyclopenten-1-one,[3,4] which is a key intermediate to prostaglandins[5] and their mimics.[6] Furthermore, it was reported that the diacetate **2** was effectively transformed into a useful lactone intermediate for the synthesis of prostaglandins.[7] 4-Cyclopentene-1,3-diol, which is easily accessible from the diacetate **2** is also a useful precursor for the synthesis of prostaglandins[8] and their intermediates.[9] These results led us to study the phase-transfer reaction of 3,5-dibromo-1-cyclopentene **1** indetail and to extend the scope of the reaction using i) various catalysts and ii) various metal acetates.



1 **2**

Quaternary ammonium and phosphonium salts are well known to be good catalysts in phase-transfer reactions.[10] Tertiary amines have also been reported to be effective for the dichlorocarbene generation.[11] More recently, it has been reported that tertiary amines as well as primary and secondary amines catalyzed the nucleophilic conversion of alkyl bromides into alkyl cyanides.[12] Tertiary amines also catalyzed the alkylation of the α-carbon attached to the carbonyl group with alkyl halides.[13] We first carried out the nucleophilic substitution reaction of 3,5-dibromo-1-cyclopentene[14] with potassium acetate in mixtures of water and carbon tetrachloride, using either trioctyl- or tridecylamines. These reactions resulted in the formation of the diacetate **2** in moderate yields (see Table 1).

TABLE 1. PHASE-TRANSFER REACTIONS OF 3,5-DIBROMO-1-CYCLOPENTENE WITH POTASSIUM ACETATE

Catalyst	Yield[a] of 3,5-diacetoxy-1-cyclopentene
Trioctylphoshine	58%
Trioctylamine	49
Tridecylamine	55

a) Isolated yield.

To our knowledge, it has not been reported that trialkylphosphines catalyze the nucleophilic substitution reaction in a heterogeneous system. We were interested to examine the possibility of trialkylphosphines as phase-transfer catalysts, because trialkylphosphines are known[15] to react with alkyl halides, *e.g.*, in refluxing benzene, to form tetraalkylphosphonium salts, which could be catalysts for our reaction. In fact, the phase-transfer reaction of the dibromide **1** with potassium acetate, using trioctylphosphine as a catalyst, proceeded to give the acetate **2** in a 58% yield (Table 1).

In order to examine the effect of metal acetate, phase-transfer reactions were studied using various metal acetates, such as the Group I, II, VII, and VIII metal acetates. Trioctylpropylammonium chloride was used as the catalyst. The results are summarized in Table 2. It is interesting that magnesium acetate and alkali metal acetates were among the most effective acetates. Since magnesium, lithium, and sodium acetates have a higher solubility in water than the other acetates[16] listed in Table 2, our results suggest that the solubility of the metal acetate in the aqueous phase plays an important role this phase-transfer reaction.

Experimental

Using Trioctylphosphine. A mixture of 3,5-dibromo-1-cyclopentene **1** (45.2 g, 0.2 mol), potassium acetate (99 g, 1 mol), and trioctylphosphine (14.8 g, 0.04 mol) in carbon tetrachloride (120 ml) and water (45 ml) was vigorously stirred at 60 °C for 5 h. The reaction mixture was then extracted with carbon tetrachloride (3×30 ml), dried, and evaporated. The residue was distilled to give 3,5-diacetoxy-1-cyclopentene **2** (21.3 g; 58% yield): bp 70.5 °C/0.08 Torr.

Using Trioctylamine. A mixture of the dibromide **1** (151 g, 0.67 mol), potassium acetate (300 g, 3 mol), and trioctylamine (10 g, 0.029 mol) in carbon tetrachloride (400 ml) and water (150 ml) was vigorously stirred at 60 °C for 12 h. The mixture was then treated as above to give the diacetate **2** (68.7 g; 55% yield).

Table 2. Phase-transfer reactions of dibromide **1** with various metal acetates in the presence of $(C_8H_{17})_3C_3H_7N^+Cl^-$ a)

Metal acetate,	g (mmol)	Solvent		Reaction conditions		Yield b) of diacetate **2**	Solubility c)
		H_2O	CCl_4				
$LiOAc \cdot 2H_2O$	10.2 (100)	6 ml	15 ml	70°C	5 h	52%	300
$NaOAc \cdot 3H_2O$	4.1 (30)	2	6	60	4	37	76
$Mg(OAc)_2 \cdot 4H_2O$	6.4 (30)	4	8	60	18	35	120
$Ca(OAc)_2$	2.6 (30)	3.5	6	60	6	8	37
$Ba(OAc)_2$	7.6 (15)	4	7	60	6	14	59
$Cu(OAc)_2 \cdot H_2O$	6.0 (30)	6	15	60	3	15	7
$Zn(OAc)_2 \cdot 2H_2O$	6.6 (30)	10	25	60	3	13	31
$Mn(OAc)_2 \cdot 4H_2O$	7.4 (30)	10	25	70	5	17	—
$Co(OAc)_2 \cdot 4H_2O$	7.5 (30)	10	25	70	3	15	—
$Pb(OAc)_2 \cdot 3H_2O$	11.4 (30)	3	7	60	6	9	46

a) All the reactions were carried out using 2.26 g (10 mmol) of 3,5-dibromo-1-cyclopentene **1** and 0.86 g (2 mmol) of trioctylammonium chloride. The reaction conditions and yields are not optimized.

b) Isolated yield. c) Solubility in grams per 100 ml in cold water.16)

Using Tridecylamine. The dibromide **1** (54 g, 0.139 mol), potassium acetate (90 g, 0.9 mol), tridecylamine (5.9 g, 0.014 mol), water (45 ml), and carbon tetrachloride (120 ml) were used. The yield of the acetate **2** was 21.6 g (49%).

Using Various Metal Acetates. The reactions were carried out substantially as has been described above under the conditions summarized in Table 2.

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References

1) Prostaglandin Chemistry X. Part IX: *Chem. Lett.*, **1976**, 1341.

2) T. Toru, S. Kurozumi, T. Tanaka, S. Miura, M. Kobayashi, and S. Ishimoto, *Synthesis*, **1974**, 867, and references cited therein.

3) a) S. Miura, S. Kurozumi, T. Toru, T. Tanaka, M. Kobayashi, S. Ishimoto, and S. Matsubara, *Tetrahedron*, **32**, 1893 (1976); b) T. Tanaka, S. Kurozumi, T. Toru, S. Miura, M. Kobayashi, and S. Ishimoto, *ibid.*, **32**, 1713 (1976).

4) This chiral compound has also been prepared from a chiral precursor. K. Ogura, M. Yamashita, and G. Tsuchihashi, *Tetrahedron Lett.*, **1976**, 759.

5) G. Stork and M. Isobe, *J. Am. Chem. Soc.*, **97**, 4745, 6260 (1975).

6) a) T. Tanaka, S. Kurozumi, T. Toru, M. Kobayashi, S. Miura, and S. Ishimoto, *Tetrahedron Lett.*, **1975**, 1535; b) *Tetrahedron* in press.

7) S. Takano, K. Tanigawa, and K. Ogasawara, *J. Chem. Soc., Chem. Commun.*, **1976**, 189.

8) J. Fried, C. H. Lin, J. C. Sih, P. Dalven, and G. F. Cooper, *J. Am. Chem. Soc.*, **94**, 4342 (1972).

9) K. Kondo, M. Matsumoto, and F. Mori, *Angew. Chem.*, **87**, 109 (1975).

10) For a review, see J. Dockx, *Synthesis*, **1973**, 441.

11) a) K. Isagawa, Y. Kimura, and S. Kwon, *J. Org. Chem.*, **39**, 3171 (1974); b) M. Makosza, A. Kacprowica, and M. Fedorynski, *Tetrahedron Lett.*, **1976**, 2119.

12) W. P. Reeves and M. R. White, *Synth. Commun.*, **6**, 193 (1976).

13) R. Fornasier and F. Montanari, *Tetrahedron Lett.*, **1976**, 1381.

14) L. N. Owen and P. N. Smith, *J. Chem. Soc.*, **1952**, 4035.

15) A. Maercker, "Organic Reactions," Vol. 14, ed by A. C. Cope, J. Wiley & Sons (1965), p. 388.

16) R. C. Weast, "Handbook of Chemistry and Physics," 55th ed, 1974—1975, CRC Press, p. C-75.