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EASY AND EFFICIENT ANION ALKYLATIONS IN SOLID-LIQUID PTC CONDITIONS

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<u>Abstract</u>: Alkylation of anionic nucleophiles such as potassium acetate or potassium indole can be achieved in good yields without solvent either in the presence of NBu<sub>4</sub>Br and small amounts of TiO<sub>2</sub> or in the presence of Aliquat 336 (Oct<sub>4</sub>MeN<sup>+</sup>Cl<sup>-</sup>).

We describe here a new method for alkylating organic anions, which requires neither solvent nor solid support, and works in very mild conditions and with a very easy work-up. Two examples are selected which concern anions which either are stable (e.g.  $CH_3COO^-$ ) or must be obtained from their conjugated acid (e.g. the anion from indole).

## ALKYLATIONS OF THE ACETATE ANION

The synthesis of esters by alkylation of carboxylate anions is usually performed using the silver or mercuric salt in a protic or ether solvent or, more recently, the sodium or potassium salt in dipolar aprotic solvents (1). Carboxylate alkylations can also be carried out using phase transfer catalysis (PTC) (2); however, formation of n-octyl acetate from  $CH_{3}COO^{-}$  and n-OctX requires temperatures higher than  $80^{\circ}C$ .

Very recently, alternative methods have been proposed :

- i) use of reagents impregnated on mineral solid supports (3),
- ii) gas-liquid PTC, at a temperature ca 150°C and under reduced pressure (20 Torr) (4),
- iii) use of polyethyleneglycols immobilized on  $Al_2O_3$  or  $SiO_2$  as PTC catalyst (5).

Our new methods are simpler :

<u>Method I</u>: The reaction was carried out by simply mixing finely ground  $CH_3COOK$  with pure n-octyl bromide in the presence of 1 %  $NBu_4Br$  and small amounts of  $TiO_2$  ( $TiO_2$ : acetate = 0.2 w/w) (6). After stirring for 5 minutes, the mixture was heated at 60°C for 2 hours to afford n-octyl acetate in 93 % yield. This easy alkylation must certainly imply both an anionic activation of  $CH_3COO^-$  by  $NBu_4Br$  and an activation of n-OctBr by electrophilic assistance by  $TiO_2$ , resulting in a weakening of the C-Br bond.

<u>Method II</u> : By using Aliquat 336 (essentially  $Oct_3MeN^+Cl^-$ ) as the PTC catalyst, n-octyl acetate was obtained in 98 % yield (20 h - room temperature) even in the absence of TiO<sub>2</sub>. Very good yields (> 93 %) in benzyl, allyl, n-butyl and cetyl acetates were observed in similar conditions.

The reaction products were easily recovered by simple filtration after addition of

ether. They were qualitatively and quantitatively analyzed by VPC (internal standard) and characterized by IR and NMR.

## ALKYLATION OF POTASSIUM INDOLE



The N-alkylation of potassium indole is usually achieved using a dipolar aprotic solvent (DMSO, HMPA) (7) or PTC conditions (8).

To potassium indole prepared by stirring indole with 2.5 mole.eq of ground KOH for 5 minutes in the presence of 1 % NBu<sub>4</sub>Br, was then added the pure alkylating agent (e.g. EtI or Et<sub>2</sub>SO<sub>4</sub>) and the mixture was stirred for 10 minutes at room temperature. After addition of ether and filtration, N-ethyl indole was isolated in 98 % yield. The less reactive n-octyl bromide also reacted smoothly (2 h - 50°C) to give N-octyl indole (yield : 98 %).

Addition of an organic solvent or mineral solid supports did not improve the yield and even proved, in some cases, to be prejudicial to the reaction (9) : for example excess  $TiO_2$  ( $TiO_2$  : acetate = 4),  $Al_2O_3$  or  $SiO_2$  inhibit the alkylation of  $CH_3COOK$  by n-UcBr ;  $Al_2O_3$  prevents N-alkylation of potassium indole by Et-I.

The procedures described here, in particular the one using Aliquat 336, are more efficient, less expensive and milder than those published previously, which require more lengthy procedures (3), higher temperatures (3-5) or low pressure conditions (4). We sincerely thank Dr J. SEYDEN-PENNE for very fruitful discussions.

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