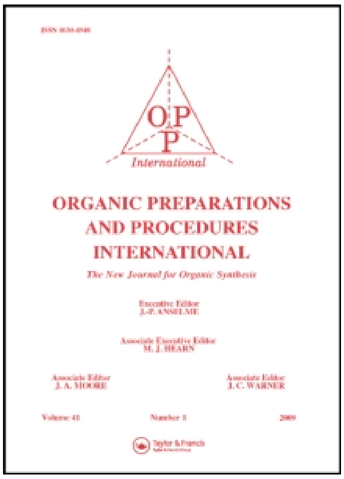

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AN IMPROVED PROCEDURE FOR THE *META*-BROMINATION OF AROMATIC CARBONYL COMPOUNDS

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AN IMPROVED PROCEDURE FOR THE META-BROMINATION OF AROMATIC CARBONYL COMPOUNDS

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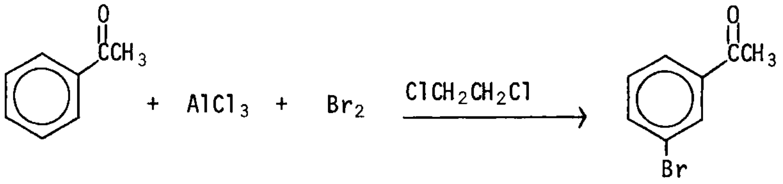
The procedure of Pearson and co-workers, using a large excess of aluminum chloride without solvent at relatively high temperatures, is the method of choice for introduction of bromine in the meta position of a carbonyl-substituted aromatic ring.[1-4] However, there can be some handling and work-up difficulties. We have developed an improved procedure utilizing a solvent[5,6] which gives the same to slightly better yields of the desired m-brominated product with subsequently milder conditions.



Two solvents of choice are methylene chloride and 1,2-dichloroethane.[7] 1,2-Dichloroethane produces 5-8% higher yields with easier handling characteristics. The optimal aluminum chloride to carbonyl compound ratio is 1.7 to 1.0 molar equivalents. Higher ratios of aluminum chloride do not give better yields of m-bromination and lower ratios cause increasing amounts of acyl bromination.[8] Optimal temperatures are in the 35-45° range.

This reaction procedure has been scaled up to kilogram quantities with good reproducibility and has shown generality as shown in the following table using 1,2-dichloroethane as solvent. The physical constants of the compounds reported in the table were consistent with those reported in the literature.[1-4]

Table 1. m-Bromination of Aromatic Aldehydes and Ketones

Reagent	Product	Yield	Lit. Yield[1-4]
Acetophenone	3-Bromoacetophenone	74%	70%
Benzaldehyde	3-Bromobenzaldehyde	75%	59%
Propriophenone	3-Bromopropriophenone	71%	60%
4-Tolualdehyde	3-Bromo-4-tolualdehyde	63%	44%
4-Methyl-acetophenone	3-Bromo-4-methyl-acetophenone	63%	56%

EXPERIMENTAL

3-Bromoacetophenone.-The general procedure is illustrated by the bromination of acetophenone. Into a one liter three-necked flask, equipped with a condenser, dropping funnel and a mechanical stirrer, was added, under nitrogen, 233 g (1.75 mole) of anhydrous aluminum chloride and 300 ml of 1,2-dichloroethane, some of the aluminum chloride does not dissolve. To this reaction mixture was then added 120 g (1.0 mole) of acetophenone at a rate such that the temperature remained between 30-50°. The reaction mixture was stirred for 30 min. at 40°. Bromine (176 g, 1.1 mole) was then added dropwise over a 60 min. period; the reaction temperature should be kept between 30-40° by heating, if necessary, since the addition of the bromine is slightly endothermic. The rate of addition of bromine is dependent upon the efficiency of a scrubber system to neutralize the hydrogen bromide that is liberated during the reaction.[9]

The reaction mixture was allowed to stir for an additional 30 min. after completion of the bromine addition and then cautiously poured over ice (approximately 400 g) with agitation. After all the excess aluminum chloride had been hydrolyzed, the organic layer was separated and the aqueous solution extracted with a 100 ml portion of 1,2-dichloroethane.

The combined organic solutions were concentrated in vacuo and fractionated to yield 139-147 g (70-74%), bp 114-117° (4 mm); n_D^{25} 1.5738-1.5742, mp 7-8°.

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