Exhaustive Methylation by Trimethylaluminium

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Summary Trimethylaluminium exhaustively methylates tertiary alcohols to alkanes, ketones to gem-dimethyl compounds, and carboxylic acids to t-butyl compounds.

Alkylation of a carbonyl or carboxyl compound by a reactive organometallic compound normally yields an alcohol. Thus, Grignard reagents convert esters or ketones into tertiary alcohols. Under exceptional circumstances, alkylation stops at the ketone stage, as for example in the reaction of acyl chlorides with organocadmium or organoaluminium halides.

Exhaustive alkylation, *i.e.* complete deoxygenation of the functional group and quaternization of its carbon atom, is even more exceptional. It appears to have been hitherto accomplished only by the action of Grignard reagents upon either 2,2-disubstituted 1,3-benzodioxoles (the pyrocatechol derivatives of ketones)[1] or compounds (*e.g.* methyl 3,5-di-t-butyl-4-hydroxybenzoate,[2] *p*-dimethylaminobenzaldehyde,[3] and methyl *N*-phenylanthranilate[4]) having electron-releasing functional groups which labilise the C–O bond of the intermediate alcoholate. The known reactions[5] of alkylaluminium compounds with carbonyl and carboxyl compounds do not include exhaustive alkylation.

We have found that tertiary alcohols, ketones, and carboxylic acids are exhaustively methylated by excess of trimethylaluminium at temperatures in the range 80—200°. The Table shows some of the results obtained. All of the products have been fully characterized spectroscopically, and the yields have been determined by isolation.

We recommend a temperature of *ca.* 120° for carboxylic acids and a temperature of 150—160° in the presence of added catalyst (see below) for ketones and alcohols (conditions cited in the Table are not optimal). Reaction times of *ca.* 20 h are suggested. Solvent, although not necessary, is desirable, since trimethylaluminium is pyrophoric and reacts with the organic substrates exothermally, often evolving methane. Alkanes, alkylbenzenes, and chlorobenzenes, being inert to the trimethylaluminium, are satisfactory solvents. Some alkylations have been carried out in an unsealed vessel, but mostly we have used a sealed glass tube inside a simple steel bomb. After reaction, the tube is opened (cautiously, because of methane pressure), and its contents are hydrolysed, for example by pipetting into a mixture of ether and aqueous acid.

The following features of the reaction are noteworthy. Firstly, alkylation of alcohols and ketones proceeds autocatalytically. The temperature and time required may be lowered significantly by the addition of a few mol % of water or a carboxylic acid. Apparently the active catalyst is an oxy- or hydroxy-aluminium compound.

Secondly, the reaction displays carbonium ion character, and may usefully be regarded as involving a heterolysis of the C–O bond. Rearrangement may occur. For example, both 1-phenylpropan-2-ol and 2-phenylpropan-1-ol give isobutylbenzene on treatment with trimethylaluminium in benzene at *ca.* 200°.

Side-products are explicable in carbonium ion terms. The most common is the olefin from deprotonation of the ion. Thus, adamantane-1-carboxylic acid gives a mixture of 1-t-butyladamantane and 1-isopropenyladamantane, and pivalic acid gives a mixture of 2,2,3,3-tetramethylbutane and 2,3,3-trimethylbut-1-ene. Benzoic acid gives dominantly t-butylbenzene, accompanied by a little α-methylstyrene and more 1,1,3-trimethyl-3-phenylindane (from $PhCMe_2^+$ and α-methylstyrene). In some cases Friedel–Crafts alkylation of benzene solvent occurs to a minor extent.

Exhaustive methylation reactions and their main products

Reactant	Conditions[a]	Product	Yield (%)
Adamantan-1-ol	64 h at 200° in benzene	1-Methyladamantane	83
1,1-Diphenylethanol	20 h at 85° in benzene	2,2-Diphenylpropane	62
Triphenylmethanol	19 h at 80° in toluene	1,1,1-Triphenylethane	86
Dicyclopropyl ketone	4 h at 150° in *p*-$C_6H_4Cl_2$	2,2-Dicyclopropylpropane	43
2′,5′-Dichloroacetophenone	82 h at 180° in benzene	2,5-Dichloro-t-butylbenzene	60
Di-*p*-tolyl ketone	2·5 h at 170° in dodecane	2,2-Di-*p*-tolylpropane	63
1-Indanone	17 h at 180° in PhCl	1,1-Dimethylindane	50
1-Naphthoic acid	18 h at 165° in benzene	1-t-Butylnaphthalene	75
o-Bromobenzoic acid	16 h at 142—150° in benzene	*o*-Bromo-t-butylbenzene	41
m-Chlorobenzoic acid	3·5 h at 140—150°, neat	*m*-Chloro-t-butylbenzene	62
Palmitic acid	4 h at 127° in benzene	2,2-Dimethylheptadecane	52
Undecylenic acid	16 h at 140—155°, neat	11,11-Dimethyldodec-1-ene	56

[a] Excess of trimethylaluminium is used—commonly 2 mol per mol of alcohol or ketone or 4 mol per mol of acid

Thirdly, α-aryl groups facilitate the C–O bond cleavage. Triphenylmethanol is especially reactive, and aryl alcohols and their precursors, the aryl ketones and arylcarboxylic acids, are more reactive than their purely aliphatic analogues. The reaction may be applied to secondary and primary alcohols when these are aryl substituted. Thus benzyl alcohol and benzaldehyde give ethylbenzene and isopropylbenzene, respectively, at 120° in benzene.

Fourthly, methylation proceeds much more readily when excess of trimethylaluminium is present. However, in atypical cases good results are obtained using only one trimethylaluminium molecule per alcohol molecule. Thus dimethylaluminium triphenylmethanolate and dimethylaluminium 1-adamantoxide can be pyrolysed to give excellent yields of 1,1,1-triphenylethane and 1-methyladamantane, respectively.

Fifthly, the higher trialkylaluminiums are far less suitable for exhaustive alkylation, because reduction competes with alkylation.

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