
5 New Paths for the Introduction of Organic Ester Moieties

Both the investigation of new solvents and the adaptation of esterification methodologies used in peptide synthesis have driven the new synthetic paths for carboxylic acid ester formation. The introduction of organic solvents such as DMSO, formamide and DMF, and combinations of these solvents with LiCl for dextran, pullulan and curdlan, and DMAc/LiCl and DMSO/TBAF for cellulose and starch have made the homogeneous esterification into an efficient synthesis path using dehydrating agents, e.g. DCC and CDI. The solvents and the reagents used are discussed with focus on the preparation of cellulose acetate as basic reaction but, in addition, a broad variety of specific esterification reactions is given to illustrate the enormous structural diversity accessible by these new and efficient methods.

5.1 Media for Homogeneous Reactions

Homogeneous reaction conditions are indispensable for the introduction of complex and sensitive ester moieties because they provide mild reaction conditions, selectivity, and a high efficiency. In contrast to heterogeneous processes, they can be exploited for the preparation of highly soluble, partially substituted derivatives because these conditions guarantee excellent control of the DS values. Moreover, they may lead to new patterns of substitution for known derivatives, compared to heterogeneous preparation. In addition to formamide, DMF, DMSO and water, which are good solvents for the majority of polysaccharides (Table 5.1), new solvents have been developed especially for cellulose, with its extended supramolecular structure.

A summary of cellulose solvents used for acetylation is given in Table 5.2. The dissolution process destroys the highly organised hydrogen bond system surrounding the single polysaccharide chains.

Although a wide variety of these solvents have been developed and investigated in recent years [122], only a few have shown a potential for a controlled and homogeneous functionalisation of polysaccharides. Limitations of the application of solvents result from: high toxicity; high reactivity of the solvents, leading to undesired side reactions; and the loss of solubility during reactions, yielding inhomogeneous mixtures by formation of gels and pastes that can hardly be mixed, and even by formation of de-swollen particles of low reactivity, which precipitate from the reaction medium.

Table 5.1. Solubility of polysaccharides in DMSO, DMF and water

Polysaccharide	Solubility in DMF	DMSO	Py	H ₂ O
Cellulose	–	+ (TBAF)	–	–
Chitin	–	–	–	–
Starch	–	+ (80 °C)	–	– ^a
Amylopectin	–	+ (80 °C)	–	+
Curdlan	–	+	–	–
Schizophyllan	+ (80 °C, LiCl)	+	–	–
Scleroglucan	–	–	–	–
Pullulan	+ (80 °C)	+	+ ^b	+
Xylan	+ (LiCl)	+	–	– (NaOH)
Guar	–	–	–	–
Alginate	–	–	–	+
Inulin	+	+	+	+
Dextran	+ (LiCl)	+ (40 °C)	–	+ ^c

^a Amylose is water soluble at 70 °C^b Depending on the source^c The crystalline form is insoluble [121]**Table 5.2.** Solvents and reagents exploited for the homogeneous acetylation of cellulose

Solvent	Acetylating reagent	DS _{max}	Ref.
<i>N</i> -Ethylpyridinium chloride	Acetic anhydride	Up to 3	[123]
1-Allyl-3-methyl-imidazolium chloride	Acetic anhydride	2.7	[124]
<i>N</i> -Methylmorpholine- <i>N</i> -oxide	Vinyl acetate	0.3	[125]
DMAc/LiCl	Acetic anhydride	Up to 3	[126]
	Acetyl chloride	Up to 3	[127]
DMI/LiCl	Acetic anhydride	1.4	[128]
DMSO/TBAF	Vinyl acetate	2.7	[129]
	Acetic anhydride	1.2	[27]

5.1.1 Aqueous Media

Water dissolves or swells most of the polysaccharides described here (see Table 5.1). Thus, water can be used both as solvent for homogeneous reactions and as slurry medium. Manageable solutions are obtained for starch with a high amylopectin content, scleroglucan, pullulan, inulin and dextran by adding small amounts of the