

Stability of polymer-supports to microwave heating

Microwave-assisted solid phase synthesis

Microwave irradiation is increasingly being used to accelerate the rate of reactions between soluble and polymer-bound reactants [1 - 27]. It is particularly useful for high throughput synthesis, where large numbers of small scale reactions need to be driven to completion as quickly and efficiently as possible.

One of the major concerns when using microwave heating in solid phase synthesis is the stability of polymer-bound linkers and reagents to these conditions. Therefore, we have subjected some of the most frequently used solid phase resins and polymer-supported reagents to prolonged microwave irradiation at high temperatures in NMP and DCE to test their compatibility with this technique.

Stability tests

Resin samples were treated according to the procedure given in Method 1. The results are presented in Table 1.

Method 1

250 mg of each resin were suspended in either NMP or DCE (4.75 ml) and irradiated using a Personal Chemistry Smith Synthesizer. After the reaction, the resins were washed with DMF, DCM, DMF, iPrOH and MeOH, dried under vacuum, and then their loading was tested using standard in-house protocols.

Visual inspection of the resin samples after microwave irradiation revealed no changes in the resin morphology. Resin-bound aldehyde, alcohol and anhydride functionalities appear to be unaffected by the treatment, whereas amine, hydrazine and isocyanate-functionalized supports are degraded under these extreme conditions (Table 1). However, these results do not preclude the use

of these resins, as conversion of the reactive resin-functionalities to microwave stable groups proceeds much faster than any degradation. Indeed, amine-functionalized resins have been used successfully with microwave heating [9].

Table 1: Results of stability tests conducted on various resins.

Abbreviations: DFPE: 2-(3,5-Dimethoxy-4-formylphenoxy)ethyl; FMPB: 4-(Formyl-3-methoxy-phenoxy)butyryl.

Resin	Initial loading (mmole/g)	Final loading after 300s at 200°C in NMP	Final loading after 300s at 160°C in DCM
Aminomethylated polystyrene	1.5	1.3	0.9
Aminomethyl NovaGel	0.8	0.6	0.41
NovaSyn TG amino resin HL	0.44	0.26	0.21
Rink amide resin, no Fmoc group	0.43	0.29	0.12
DFPE resin	0.94	0.90	0.94
FMPB AM resin	1.0	1.0	1.0
Methylisocyanate polystyrene HL	2.4	0.82	1.4
MP anhydride resin	7.6	7.6	7.6
Wang resin	0.46	0.43	0.50

Ordering Information

01-64-0071	Aminomethylated polystyrene VHL (200 - 400 mesh)	5 g 25 g 100 g 1 g 5 g 25 g 1 g 5 g 25 g 1 g 5 g 25 g 100 g 1 g 5 g 25 g 1 g 5 g 25 g 100 g 5 g 25 g 100 g 5 g 25 g 100 g
01-64-0283	Aminomethyl NovaGel™	
01-64-0144	NovaSyn® TG amino resin HL	
01-64-0013	Rink amide resin (100 - 200 mesh)	1 g 5 g 25 g 1 g 5 g 25 g 1 g 5 g 25 g 100 g 1 g 5 g 25 g 1 g 5 g 25 g 100 g 5 g 25 g 100 g 5 g 25 g 100 g
01-64-0014	Wang resin (100 - 200 mesh)	1 g 5 g 25 g 1 g 5 g 25 g 1 g 5 g 25 g 100 g 1 g 5 g 25 g 1 g 5 g 25 g 100 g 5 g 25 g 100 g 5 g 25 g 100 g
01-64-0360	2-(3,5-Dimethoxy-4-formylphenoxy) ethyl polystyrene [DFPE]	
01-64-0209	4-(Formyl-3-methoxy-phenoxy) butyryl AM resin [FMPB]	
01-64-0169	Methylisocyanate polystyrene HL	
01-64-0422	MP anhydride resin	

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