

Aldol Reaction in Water Catalyzed with Polymer-Supported Proline

Category

Polymer-Supported Synthesis

Key words

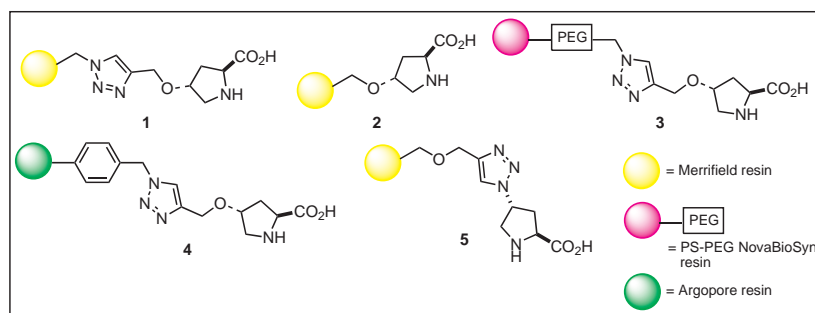
aldol reaction

prolines

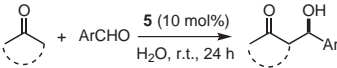
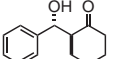
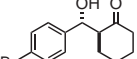
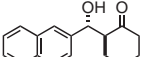
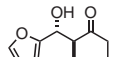
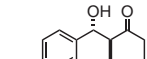
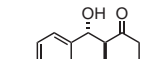
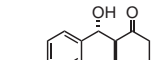
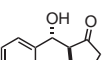
polymer support

1,2,3-triazole linker

SYNFACT
of the month



	t (h)	yield (%)	anti/syn	ee (%)
1 (1% DVB)	84	67	95:5	95
1 (1% DVB)	60	58	94:6	92
2 (2% DVB)	60	70	93:7	40
3	60	10	n.d.	91
4	84	traces	n.d.	70
5	24	74	96:4	98

			
	74% yield <i>anti</i> / <i>syn</i> = 96:4 98% ee		90% yield <i>anti</i> / <i>syn</i> = 97:3 96% ee
	82% yield <i>anti</i> / <i>syn</i> = 97:3 >99% ee		60% yield <i>anti</i> / <i>syn</i> = 84:16 94% ee
	80% yield <i>anti</i> / <i>syn</i> = 95:5 96% ee		98% yield <i>anti</i> / <i>syn</i> = 97:3 96% ee
	16% yield <i>anti</i> / <i>syn</i> = 92:8 96% ee		99% yield <i>anti</i> / <i>syn</i> = 84:16 94% ee

Significance: Polystyrene-support prolines (**1–5**) were prepared by the cycloaddition of the corresponding azides and alkynes. Prolines **1–5** catalyzed the aldol reaction of cyclohexanone with benzaldehyde in water to give the aldol product **6** in traces to 74% yield with 40–98% ee. When proline **5** was used for the reaction, a gel-like single phase was formed in water. Water-swollen proline **5** showed higher catalytic activity for the aldol reaction of cyclohexanone and 4-nitrobenzaldehyde (99% yield and 96% ee) than anhydrous **5** (80% yield and 89% ee). The aldol reaction of cyclic ketones with various aldehydes was also catalyzed by **5** in water at room temperature to afford the corresponding products in 16–99% yield and 94–99% ee.

SYNFACTS Contributors: Yasuhiro Uozumi, Takao Osako
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Comment: In the reaction of cyclohexanone and benzaldehyde, the water-swollen **5** was superior in reaction rate and stereoselectivity to the other polymeric prolines **1–4**. TGA analysis of the water-swollen **5** showed up to 24% water content in weight. Theoretical calculation suggested that water molecules formed a hydrogen-bonding network between the triazole and the amino acid group in **5**. High yields, enantioselectivities, and diastereoselectivities were achieved in the reaction of cyclic ketones and aromatic aldehydes with **5** in water except for the reaction of 4-methoxybenzaldehyde. The catalyst was recycled and re-used at least five times without loss of catalytic activity.