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8. Use of 1 equivalent of sodium hydride and 1 equivalent of LDA instead of 2 equivalents of LDA resulted in extensive decompositon.
9. The product derived from substitutions at both primary and allyic position of **4** was formed in a few % yield.
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15. This compound was identical with **10** from sodium-amalgam reduction of **8**.
16. All new compounds showed satisfactory spectral data.

A Convenient Method for Benzylation of Arenes over Perfluorinated Resinsulfonic Acid (Nafion-H)

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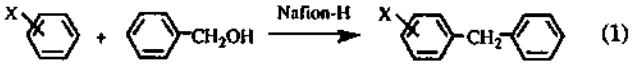
Received May 24, 1991

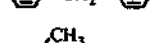
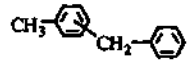
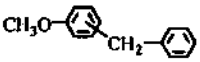
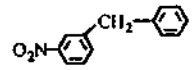
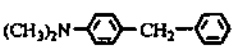
Alkylations of arenes with alcohols generally require molar amount of Lewis acid catalysts or concentrated sulfuric acid, which react with the alcohols to generate the corresponding carbocation intermediates.[1,2] Although the reactions proceed under milder condition when benzyl alcohol is used, the catalysts are usually non-recoverable and should be removed in the work-up.[3-5] We describe now the convenient and efficient method of Nafion-H (a solid perfluorinated resinsulfonic acid having sulfonic acid group in the amount of 0.01 to 5 mequiv/gram resin)[6,7] catalyzed benzylation of arenes with



(1)

benzyl alcohol. The reaction was carried out by refluxing a mixture of benzyl alcohol (1.0 g), substituted benzene (5.0 m*l*), and Nafion-H (0.2 g) for 8 hours. Water was removed with small amount of silica gel in a soxhlet thimble suspended just below refluxing condenser. The product were simply isolated by filtering the hot reaction mixture and distilling off the exess arene. The product yield and the *o/m/p* ratio were determined with gas chromatography on a 25 m capillary column of 5% phenylsilicon when necessary. The results are summarized in Table 1. The reactions are very clean and produce the desired benzylated products in high yields. Benzene and mesitylene afforded single products, whereas toluene and anisole produced mixtures of *o*-, *m*-, and *p*-disubstituted products as predicted by the directing effects of the substituents. For reaction of nitrobenzene, excess amount of benzyl alcohol had to be used because of the lower reactivity. These reactions apparently proceed by the reaction between substituted benzenes and benzyl cation generated on the catalyst surface. If the benzyl cation had long enough life time to migrate into the solution under the reaction condition, benzylation of aniline derivatives may be realized without protecting the amino group. However, N,N-dimethylaniline did not react with benzyl alcohol under the same condition. It appeare that both protonation and benzylation occur on the catalyst surface and the former proceeds at much faster rate.

Table 1. Yields of Benzylation of Arenes (XAr) with Benzyl Alcohol Using Nafion-H

X	Product[a]	Yield (%)[b]
H		73.6 (88.9)[d]
1,3,5-$(CH_3)_3$		73.3
CH_3		68.1 (*o/m/p* = 41/9/15)[f]
CH_3O		85.1 (*o/m/p* = 43/11/46)[f]
NO_2[g]		76.1
$N(CH_3)_3$		*trace*

[a] Products were identified by physical constants and NMR spectra, [b] Isolated yields unless otherwise noted, [c] bp. 88-90℃/1.5 mmHg (lit.[8] bp. 125.5℃/10 mmHg), [d] GC yield, [e] bp. 117-128℃/1.4 mmHg (lit.[9] bp. 120-130℃/1.0 mmHg), [f] Determined by GC (see text), [g] Excess amount (5.0 m*l*) of benzyl alcohol and smaller amount of nitrobenzene (1.0 g) were used.

The present procedure provides an efficient method for benzylation of benzene and substituted benzenes, except for aniline derivatives. In this procedure, only a catalytic amount of the acidic resin is needed, and the heterogeneous catalyst provides for a very simple work-up. Application of Nafion-H on other acid catalyzed reactions are in progress in our laboratory.

Acknowledgement. This investigation was supported by grants from the Basic Science Institute Program, Korea Ministry of Education (1990).

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Stereochemical Control in Baker's Yeast Reduction 1.: Diastereoselective Reduction of Alkyl β-Keto-α-methylpentanoates with Three Different Forms of Baker's Yeasts

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Received May 24, 1991

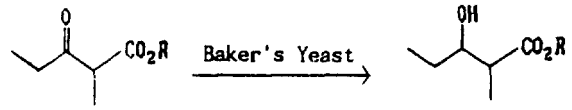
The stereoselective synthesis of α-substituted β-hydroxy ester has been studied in recent years because of its widespread applicability to biologically active substrate synthesis. A variety of chemical methods such as stereoaldol condensation[1] and reduction [$Zn(BH_4)_2$][2] have produced *syn* α-substituted β-hydroxy ester while the α-alkylation[3] of β-hydroxy ester has afforded *anti* ester. However, these methods require an optically active starting material in order to obtain the enantioselective product. Therefore, in order to directly prepare the chiral α-substituted β-hydroxy ester from an achiral starting material, α-substituted β-keto esters were chemically prepared and then reduced by means of certain microbes. Especially, baker's yeast (*Saccharomyces cerevisiae*) which is an inexpensive and facile microbe has frequently been used in the synthesis of valuable chiral building blocks.[4] But the baker's yeast reduction of alkyl β-keto-α-methylpentanoates (**1**) has not much been studied[5] compared with that of alkyl β-keto-α-methylbutanoates.[6] In this paper, we describe the results from the baker's yeasts reduction of **1a-h** using three different forms of baker's yeast, raw baker's yeast (RBY), dry baker's yeast (DBY), and immobilized baker's yeast (IMBY).[7]

In a typical procedure, to the suspension of RBY (30 g) and water (50 m*l*) was added sugar (4 g). The suspension was activated for 30 min, then substrate[8] (1 mmol in EtOH) was added. The reaction mixture was allowed to be stirred (180 rpm) at rt. Sugar (4 g) was added every 12 hrs. After 48 hrs, the mixture was stirred vigorously with Celite and EtOAc, then filtered. Filtrate and the Celite layer were extracted with EtOAc(×3). Combined organic layer was washed with water, sat. $NaHCO_3$ sol'n, and brine, dried (anhyd. $MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed with silica gel (cyclohexane : ether = 4 : 1) to yield β-hydroxy-α-methylpentanoates (**2**). The stereochemistry of **2a-h** were deduced by comparisons of their ^{13}C-NMR[9] and ^1H-NMR[10] data with those of racemic alkyl β-hydroxy-α-methylpentanoates (**3**) obtained by reduction with $NaBH_4$.[11] The stereochemical composition (*syn/anti* ratio) of the compound **2** were determined by GLC (HP-1, capillary column).[12]

Table 1. Reduction of Alkyl β-Keto-α-Methylpentanoates by Baker's Yeast

Substrate	Yeast	*syn/anti*[a]	Reduction ratio[d]
1a	RBY	2/97	24
	DBY[b]	7/93	12
	IMBY[c]	8/92	9
1b	RBY	5/95	32
	DBY	7/93	27
	IMBY	9/91	44
1c	RBY	3/97	50
	DBY	6/94	58
	IMBY	6/94	72
1d	RBY	2/98	444
	DBY	3/97	68
	IMBY	6/94	536
1e	RBY	4/96	220
	DBY	5/95	30
	IMBY	8/92	13
1f	RBY	9/91	32
	DBY	7/93	20
	IMBY	–	–
1g	RBY	11/89	22
	DBY	9/91	12
	IMBY	–	–
1h	RBY	12/88	17
	DBY	10/90	8
	IMBY	–	–

[a] Determined by GLC (HP-1, capillary column), the structures of *syn* and *anti* isomer were identified with ^{13}C-NMR[8] and ^1H-NMR (270 MHz).[9] [b] Substrate 1 mmol; DBY 15 g; H_2O 50 m*l*; sucrose 4 g per 12 hrs. [c] Substrate 1 mmol; IMBY made up of RBY 30 g, 1.5% sodium alginate sol'n (500 m*l*), 2% $CaCl_2$ sol'n. [d] Reduction ratio = $\frac{(\text{product} \times 100)}{\text{unreduced substrate}}$



1 *anti*-**2**

1a R = Methyl **1e** R = n-Pentyl
1b R = Ethyl **1f** R = n-Hexyl
1c R = n-Propyl **1g** R = n-Heptyl
1d R = n-Butyl **1h** R = n-Octyl