

Kinetic Resolution of Racemic Ketones with *K* Glucoside

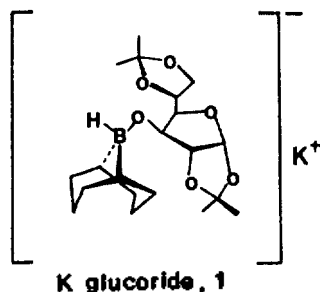
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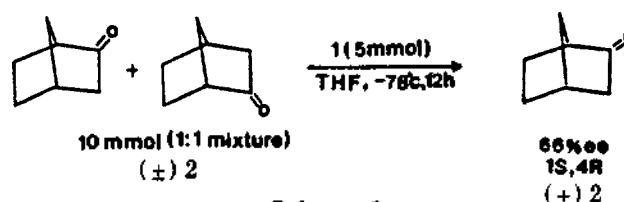
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Recently we have reported that *K* glucoside¹ **1** provides highly effective asymmetric induction for a variety of prochiral ketones.² During the course of study on reducing characteristics of this reagent, we discovered that the reagent could resolve racemic ketones kinetically. To our knowledge, this is the first example for kinetic resolution of racemic ketones with chiral reducing agents.



In a typical experiment, the THF solution (0.5M, 10 ml) of **1** (5 mmol) precooled to -78°C was added to the solution (1 M, 100 ml) of racemic 2-norbornanone **2** (10 mmol) at -78°C via a double ended needle. The reaction mixture was stirred for 12 h at -78°C . Then unreacted hydride was quenched by injecting anhydrous HCl in Et_2O precooled to -78°C , followed by hydrolysis with dilute HCl.³ GC analysis of the mixture revealed that nearly 50% of reduction had been completed. After solvent was pumped off under reduced pressure, the unreacted ketone was isolated by bulb-to-bulb distillation. It was further purified by preparative GC (20% carbowax 20M, 6 ft column) and the rotation was measured: $[\alpha]_D^{22}$ 19.16 (c 1.1, CHCl_3), 66% *ee* based on $[\alpha]_D^{25}$ 29.1 (c 1.5, CHCl_3). (Scheme 1). The result indicated that the partial reduction of racemic ketone **2** with 0.5 equiv of chiral reducing agent **1** provided optically active **2**. This means that **1** has the reducing capability to distinguish between the enantio-



meric forms of **2** with a kinetic resolution manner.⁵ Similar experiments for the other racemic ketones were carried out and the results were summarized in Table 1.

As shown in Table 1, **1** reacted smoothly with racemic ketones such as 2-methylcyclohexanone, 2-propylcyclohexanone and 1-methyl-2-norbornanone at -78°C in contrast to the sluggish reaction for both 2-*tert*-butylcyclohexanone and camphor. For racemic bicyclic ketones, 2-norbornanone and 1-methyl-2-norbornanone, this procedure afforded the corresponding optically active ketones with 66% *ee*, and 55% *ee*, respectively. However, the kinetic resolutions for racemic cyclic ketones such as 2-methylcyclohexanone, 2-propylcyclohexanone and 2-*tert*-butylcyclohexanone were less favorable (3–15.6% *ee*). The reason is unclear. On the other hand, the optically active ketones obtained were enriched with the R enantiomers for the cyclic ketones examined, the [1S, 4R] enantiomer for 2-norbornanone and the [1R, 4S] enantiomers for both 1-methyl-2-norbornanone and camphor. The inversion of absolute configuration in the bicyclic ketones might be attributed to different stereoselectivity by **1**. In fact, **1** produced *endo* alcohol for 2-norbornanone, but the reduction for both 1-methyl-2-norbornanone and camphor gave *exo* alcohols as major products.^{2a}

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Table 1. Kinetic Resolution of Representative Racemic Ketones with *K* Glucoside in THF

Racemic ketones	Reaction conditions	Optically active ketones	<i>ee</i>	abs.
		$[\alpha]_D^{23}$ obsd. deg.	%	config.
2-methylcyclohexanone	-78°C , 6 h	-0.45 (c 0.2, methanol)	3.2 ^a	R ^b
2-propylcyclohexanone	-78°C , 6 h	-2.11 (c 3.0, methanol)	7.5 ^b	R ^b
2- <i>tert</i> -butylcyclohexanone ^c	0°C , 6 h	5.51 (c 1.0, methanol)	15.6 ^d	R ^b
2-norbornanone	-78°C , 12 h	19.16 (c 1.1, chloroform)	66 ^e	1S, 4R ^e
1-methyl-2-norbornanone	-78°C , 12 h	-26.92 (c 1.97, chloroform)	58 ^f	1R, 4S ^f
camphor ^c	0°C , 12 h	11.43 (c 9.5, ethanol)	26 ^g	1R, 4S ^f

^aBased on $[\alpha]_D$ 14.0 (c 0.23, methanol)⁶. ^bBased on $[\alpha]_D^{25}$ 28.2 (c 3.78, methanol)⁷. ^cAt -78°C , the reaction did not give any reduction products even after 24 h. ^dBased on $[\alpha]_D^{24.5}$ 36.0 (c 1.0, methanol)⁸. ^eBase on $[\alpha]_D^{25}$ 29.1 (c 1.5, chloroform)⁴. ^fBased on $[\alpha]_D^{20}$ calculated (max) -46.3 (c 1.7, chloroform)⁹. ^gBased on $[\alpha]_D^{20}$ 43.8 (c 7.5, ethanol); Merck Index 10th ed. p. 1707. ^hK. L. Cheo, T. H. Elliott, and R. C. C. Tao, *J. Chem. Soc. (C)*, 1988 (1966). ⁱDictionary of Organic Compound 5th ed. Chapman and Hall, 1982, p. 970.

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Coupling Reaction of 1-Chloro-2-Iodoperfluorocycloalkenes with 2-Chlorohexafluorocyclopentenylcopper Reagent

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Since the coupling of perfluorovinyl iodides with copper bronze was initially reported by Tatlow,¹ the use of copper powder in coupling reaction of 1-chloro-2-iodo- and 1,2-diiodo-perfluorocycloalkenes has been reported by park *et al.*² to be able to produce coupled product by reductive coupling. In a previous report, the reaction of equal molar quantities of different 1-chloro-2-iodoperfluorocycloalkenes with copper powder was described to give the mixture of a cross-coupled product and self-coupled products.³

A facile synthesis of 2-chlorohexafluorocyclopentenylcopper reagent (**1**)⁴ has prompted our investigation into these coupling reaction. We wish to report a facile synthesis of cross-coupled product by reaction of 1-chloro-2-iodoperfluorocyclopropene (**2**), -cyclobutene (**3**), -cyclohexane (**5**) with the solution of **1** and a high yield of self-coupled product by reaction of 1-chloro-2-iodohexafluorocyclopentene (**4**) with the solution of **1**.

Hitherto inaccessible compound, 2-chloro-1-[1'-(2'-chloro-3',3'-difluorocyclopropenyl)]-hexafluorocyclopentene (**6**), was synthesized by cross-coupling reaction of **2** with the solution of **1** at -30°C in 52% yield. Though the reaction of a few nucleophiles with fluorohalogenocyclopropenes has been investigated,⁵⁻⁷ there has been no report so far on the coupling reaction of fluorohalogenocyclopropenes.

While the reaction of equal molar mixture of **3** and **4** with copper powder gave the mixture of a cross-coupled product and self-coupled products, we could synthesize only a cross-coupled product, 2-chloro-1-[1'-(2'-chlorotetrafluorocyclobutenyl)]-hexafluorocyclopentene (**7**), in 71% yield through treatment of the solution **1** with **3** at -30°C. The only

Table 1. Reaction of 1-chloro-2-iodoperfluorocycloalkenes with **1**^a

Reactant	Product	Yield ^b %	bp °C (mmHg)
2	6	52	56-58 (80) ⁸
3	7	71	69.5-71 (30)
4	8	90	83-84 (50)
5	9	92	60.5-61 (30)

^aDMF was used as solvent, ^bIsolated yield.

by-product obtained from this reaction in ¹⁹F-NMR spectrum was found to be the reduced product, 1H-2-chlorohexafluorocyclopentene.

When **4** is mixed with the solution of **1** at -30°C, the self-coupled product, 2,2'-dichlorododecafluoro-(bi-1-cyclopenten-1-yl) (**8**), is afforded in 90% yield. The treatment of the solution of **1** with **5** gave the cross-coupled product, 2-chloro-1-[1'-(2'-chlorooctafluorocyclohexenyl)]-hexafluorocyclopentene (**9**), in 92% yield. These results represent considerably higher yield than the one obtainable by the