

REDUCTIVE COUPLING OF CARBONYL COMPOUNDS TO PINACOLS BY USING LOW-VALENT CERIUM

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Summary: Aldehydes and ketones, on treatment with a low-valent cerium reagent, undergo reductive dimerization to produce the corresponding pinacols in high yield.

During the course of our investigation on organocerium compounds,¹⁾ we observed that carbonyl compounds were readily coupled to pinacols in the presence of low-valent cerium. We wish to report herein a first example of the title reaction.

Low-valent cerium was generated by the following methods; 1) reaction of cerium with one equivalent of iodine, 2) reaction of cerium with 1,2-diiodoethane,²⁾ 3) reduction of cerium (III) iodide with potassium, 4) reaction of cerium with iodobenzene, and 5) reaction of cerium with titanium tetrachloride.³⁾ These reactions were carried out in dry tetrahydrofuran (THF) under argon atmosphere.

The reagents thus prepared were allowed to react with acetophenone in order to examine their reducing power. In every case the coupling product, 2,3-dihydroxy-2,3-diphenylbutane, was produced in good to high yield. In the case of Entry 1, better result was obtained when the reaction was carried out in situ; that is, a mixture of acetophenone and cerium was treated with iodine in THF. These results are listed in Table 1.

Satisfactory yields were obtained in the cases of Entries 1-5. While, the use of cerium metal (Entry 6) or cerium (III) iodide (Entry 7) resulted in very poor yield. These facts indicate that low-valent cerium, which is presumably divalent, is active species for the reductive dimerization.

Next, we applied this low-valent cerium-promoted coupling to various aldehydes and ketones. For experimental convenience, Ce-I₂ reagent system was employed in a series of the reactions. The reaction was carried out as follows.

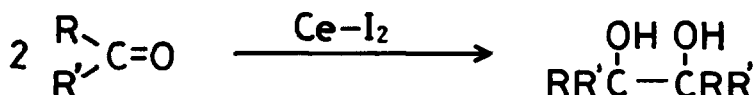


Table 1. Reductive Coupling of Acetophenone to 2,3-Dihydroxy-2,3-diphenylbutane

Entry	Reagent	Conditions ^{a)}	Yield (%)
1 ^{b)}	Ce-I ₂	0°C (2 h), r.t. (12 h)	88
2	Ce-ICH ₂ CH ₂ I ^{c)}	r.t. (15 h)	79
3	CeI ₃ -K ^{d)}	0°C (4 h)	96
4	Ce-C ₆ H ₅ I ^{e)}	0°C (4 h)	95
5 ^{b)}	Ce-TlCl ₄	0°C (5 h)	68
6	Ce	r.t. (15 h)	0
7	CeI ₃ ^{f)}	r.t. (15 h)	trace

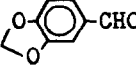
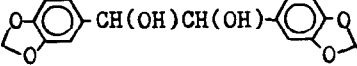
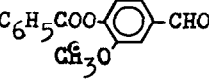
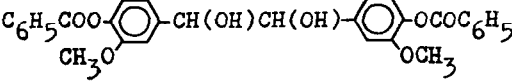
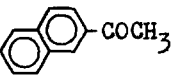
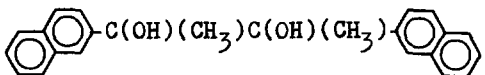
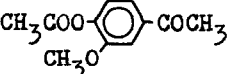
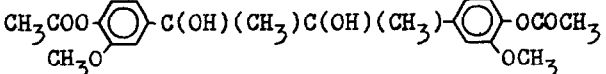

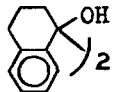
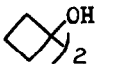
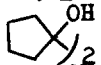
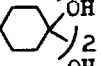
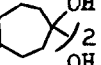
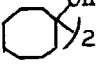
a) Molar ratio of acetophenone : cerium reagent was 1 : 2. b) The reaction was carried out in situ. c) This reagent was prepared by stirring an equimolar mixture of cerium and 1,2-diiodoethane in THF for 15 h at room temperature. d) A slurry of cerium (III) iodide in THF was added with stirring to refluxing THF containing one equivalent potassium pieces, and the mixture was further refluxed for 4 h and cooled. e) An equimolar mixture of cerium and iodobenzene in THF was stirred at room temperature for 3 h. f) A mixture of cerium (2 mmol) and iodine (3 mmol) in THF (6 ml) was stirred at 0°C for 2 h and at room temperature for an additional 12 h.

Iodine (508 mg, 2 mmol) was added to a mixture of freshly cut (ca. 50 mesh) cerium⁴⁾ (280 mg, 2 mmol) and carbonyl compound (1 mmol) in dry THF (6 ml) at 0°C under argon atmosphere. The mixture was stirred at the same temperature for 2 h and at room temperature for an additional 12 h. The reaction mixture was then diluted with water and extracted with ethyl acetate. The combined extracts were dried over Na₂SO₄ and concentrated. The residue was purified by preparative thin layer chromatography on silica gel. The results are summarized in Table 2.

This method is applicable not only to aromatic but also to aliphatic carbonyl compounds, but it has limitation in some cases. Benzophenone did not react under the conditions, and cyclododecanone was not converted into the corresponding pinacol but to cyclododecanol in 70 % yield.

The present method, although it can not be widely applicable, has a notable characteristic which was not observed previously.⁵⁾ The methods hitherto reported are scarcely applied to the compounds having other functional groups such as ester, nitrile, and vinylic halide, presumably because complicated side reactions are accompanied. In contrast, our method is efficiently applicable to such compounds, producing the pinacols in satisfactory yield (Entries 3, 7, 8, and 10).

Table 2. The Reaction of Carbonyl Compounds with Ce-I₂^{a)}

Entry	Carbonyl Compound	Product ^{b)}	(Yield, %)
1	C ₆ H ₅ CHO	C ₆ H ₅ CH(OH)CH(OH)C ₆ H ₅	(94)
2			(94)
3			(65)
4	C ₆ H ₅ COCH ₃	C ₆ H ₅ C(OH)(CH ₃)C(OH)(CH ₃)C ₆ H ₅	(88)
5	C ₆ H ₅ GOC ₂ H ₅	C ₆ H ₅ C(OH)(C ₂ H ₅)C(OH)(C ₂ H ₅)C ₆ H ₅	(85)
6	p-CH ₃ OC ₆ H ₄ COCH ₃	p-CH ₃ OC ₆ H ₄ C(OH)(CH ₃)C(OH)(CH ₃)C ₆ H ₄ OCH ₃ -p	(82)
7	p-NCC ₆ H ₄ COCH ₃	p-NCC ₆ H ₄ C(OH)(CH ₃)C(OH)(CH ₃)C ₆ H ₄ CN-p	(91)
8	p-BrC ₆ H ₄ COCH ₃	p-BrC ₆ H ₄ C(OH)(CH ₃)C(OH)(CH ₃)C ₆ H ₄ Br-p	(63) ^{c)} (96) ^{d)}
9			(91)
10			(85)
11			(87)
12	C ₆ H ₅ GOC ₆ H ₅	_____ e)	
13	Cyclobutanone		(80)
14	Cyclopentanone		(84)
15	Cyclohexanone		(95)
16	Cycloheptanone		(86)
17	Cyclooctanone		(64), Cyclooctanol (27)
18	Cyclododecanone	Cyclododecanol	(70)

a) The reaction conditions were not optimized. b) All products displayed satisfactory spectral data (¹H-NMR and IR). c) The reaction temperature was gradually elevated from -78°C to room temperature. d) The reaction was carried out using reagent system, Ce-C₆H₅I. e) No reaction proceeded.

In summary, we have developed a new method for the reductive coupling of aldehydes and ketones to pinacols. The reactions may be useful in organic synthesis.

References and Notes

- 1) T. Imamoto, Y. Hatanaka, Y. Tawarayama, and M. Yokoyama, *Tetrahedron Lett.*, 1981, 4987.
- 2) H. B. Kagan et al. reported that samarium or ytterbium diiodide was easily prepared by the reaction of samarium or ytterbium metal with 1,2-diiodoethane in THF. P. Girard, J. L. Mamy, and H. B. Kagan, *J. Am. Chem. Soc.*, 102, 2693 (1980); H. B. Kagan, J. L. Mamy, and P. Girard, *Tetrahedron, Supplement*, 37, 175 (1981); P. Girard, R. Couffignal, and H. B. Kagan, *Tetrahedron Lett.*, 1981, 3959.
- 3) Reductive coupling of carbonyl compounds with titanium tetrachloride and zinc was reported by T. Mukaiyama et al. T. Mukaiyama, T. Sato, and J. Hanna, *Chem. Lett.*, 1973, 1041.
- 4) Cerium ingot, which was purchased from Rare Metallic Co., Ltd., Tokyo, was very carefully scraped by the use of a rasp. The scraping should be carried out slowly and cautiously, since cerium filings are apt to burn spontaneously.
- 5) Various coupling reagents have been reported; a) TiCl_4 -Zn: reference 3; b) TiCl_3 - LiAlH_4 : J. E. McMurry and M. P. Fleming, *J. Am. Chem. Soc.*, 96, 4708 (1974); c) TiCl_3 -K: J. E. McMurry and M. P. Fleming, *J. Org. Chem.*, 41, 896 (1976); J. E. McMurry, M. P. Fleming, K. L. Kees, and L. R. Krepski, *J. Org. Chem.*, 43, 3255 (1978); d) TiCl_4 -Mg(Hg) and CpTiCl_3 - LiAlH_4 : E. J. Corey, R. L. Danheiser, and S. Chandrasekaran, *J. Org. Chem.*, 41, 260 (1976); e) TiCl_3 -Mg: S. Tyrlík and M. I. Wolochowicz, *Bull. Soc. Chim. Fr.*, 2147 (1973); f) TiCl_2 -pyridine: D. Lenoir, *Synthesis*, 1977, 553; g) $(\text{CH}_3)_3\text{SiCl}$ -Mg: T. H. Chan and E. Vinokur, *Tetrahedron Lett.*, 1972, 75.

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