Bull. Chem. Soc. Jpn., **62**, *519—523 (1989)*

Cr(III) or Ce(IV) Impregnated Perfluorinated Resin-Sulfonic Acid Catalyst for the Oxidation of Alcohols

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(Received July 26, 1988)

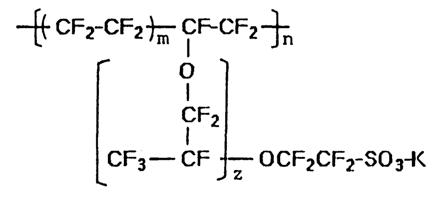
Several polymer supported catalysts are prepared by treatment of Nafion®551 (abbreviated NAFK below) with metal salts. Cr/NAFK and Ce/NAFK are found to be effective catalysts for the dehydrogenative oxidation of alcohols to the corresponding ketones by means of *t*-butyl hydroperoxide. Selective oxidation of secondary alcohols in the presence of primary ones was performed using a Ce/NAFK-$NaBrO_3$ system.

Polymer supported reagents are receiving considerable attention. The advantages of the use of polymeric reagents in organic synthesis have been described in a number of papers which are summarized in a monograph.1) Major advantages of this approach are (1) the ease of purification of the final product and (2) the effective recycling use.

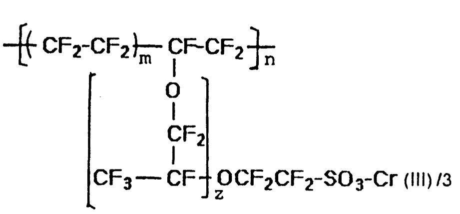
Two kinds of polymer reagents for the oxidation of alcohols to the corresponding aldehydes and ketones are described in literature. One is a reagent generated from poly(*p*-methylthiostyrene) and chlorine,2) and the other is a polymeric analogue of pyridinium chlorochromate3) or pyridinium dichromate.4—6) The oxidation reactions using such stoichiometric reagents is easy to perform, but suffers from a couple of disadvantages including the requirement of a large amount of the reagent and a large volume of the solvent, because the exchange capacity of the polymer oxidant is usually low. Furthermore recycling of the reagents requires troublesome step of workup which prohibits the practical use. It is anticipated that the use of a catalytic amount of a polymer reagent in the presence of suitable co-oxidant such as *t*-BuOOH and $NaBrO_3$ could solve these disadvantages.7) Here we wish to report convenient oxidation of alcohols with *t*-butyl hydroperoxide using a new type of polymer supported catalysts, i.e. Cr(III) and Ce(IV) impregnated perfluorinated resin-sulfonic acids.8)

The structure of NAFK9) is shown in Fig. 1. The perfluorinated resin has high stabilities thermally, chemically, and physically. NAFH (Nafion-H) has been widely used as a solid-state superacid reagent in several reactions.10) Exchange of the counter metal on the polymer sulfonate was easily performed by treatment of the polymer potassium salt (NAFK) with the desired metal salts in deionized water. For instance, stirring of a mixture of NAFK and chromium(III) acetate for 36 h at 25 °C provided chromium impregnated catalyst (Cr/NAFK). Titrations of the generated catalyst indicated a capacity of 0.68 mmol of Cr(III) per gram which corresponds to 75% of the theoretical capacity of a fully loaded resin. Several kinds of metal impregnated perfluorinated resin-sulfonic acid catalysts were prepared and examined in the oxidation of 1-phenylethanol to acetophenone with anhydrous *t*-butyl hydroperoxide.11) Among them, chromium(III) and cerium(IV) salts proved to efficiently catalyze the oxidation of alcohols. In contrast, polymer-supported catalysts carrying metals such as Cu(II), Ni(II), and Mn(II) were found less effective. The alcohols were only partly (at most 30%) converted into ketones with latter catalysts under the same reaction conditions.

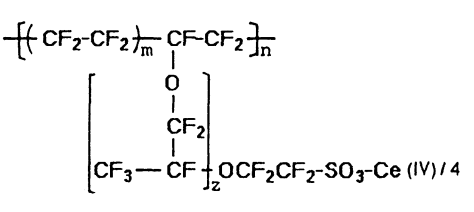
Oxidation of secondary alcohols into ketones was studied using Cr/NAFK-*t*-BuOOH system in a



Nafion®511 (NAFK)



Cr / NAFK



Ce / NAFK

Fig. 1.

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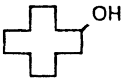
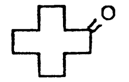
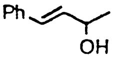
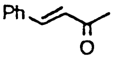
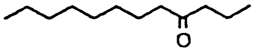
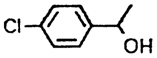
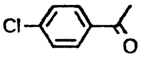
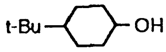
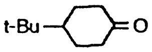
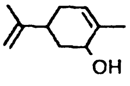
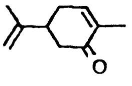
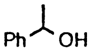
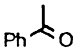
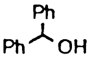
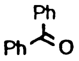
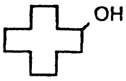
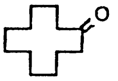
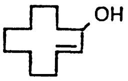
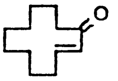
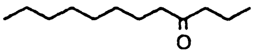
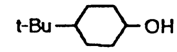
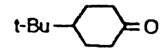
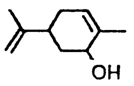
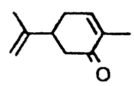
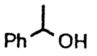
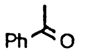
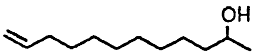
Table 1. Oxidation of Alcohols with Cr/NAFK-*t*-BuOOH System[a,b]

Run	Substrate	Product	Yield /%
1			86
2			81
3			81
4			93
5			81
6			82
7			95
8			98

a) *t*-BuOOH (4.0 mmol) and Cr/NAFK (50 mg, 0.034 mmol) were employed per one mmol of alcohol. b) Yields represent isolated, purified products.

Table 2. Oxidation of Alcohols with Ce/NAFK-*t*-BuOOH System[a,b]

Run	Substrate	Product	Yield /%
1			82
2			82
3			71
4			79
5			98
6			98
7			93
8			80

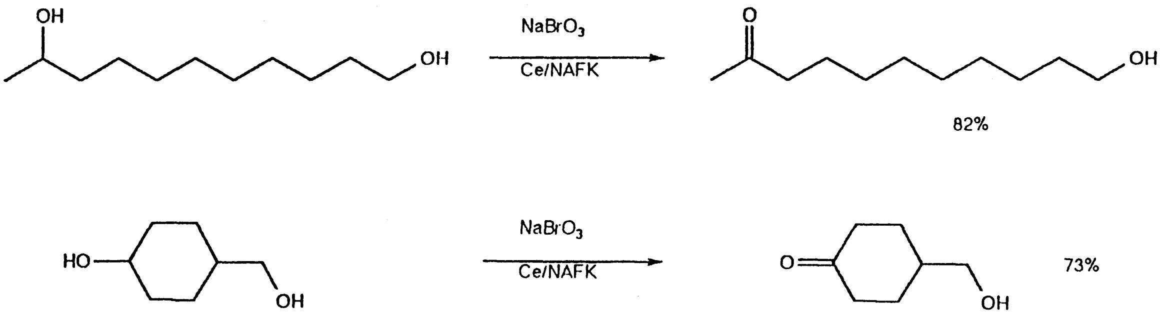
a) The hydroxy compounds (1.0 mmol), *t*-BuOOH (1.5 ml, 4.0 mmol), and Ce/NAFK (50 mg, 0.027 mmol) were combined in benzene and the mixture was stirred for 6 h at 80°C. b) Isolated and purified yields.

number of solvents under heating. Among them, chlorobenzene gave the best result. Reaction in benzene required a longer reaction time which caused contamination by undesired products. Toluene, which has similar boiling point to chlorobenzene, was not suitable for the oxidation of alcohols, because it was oxidized into benzaldehyde under the reaction conditions. The reaction proceeded upon heating a mixture of a substrate, an oxidant, and the resin catalyst suspended in chlorobenzene at 85 °C for several hours. The resin catalyst was filtered off and washed with ethyl acetate. Workup and purification of crude product gave the desired ketone effectively. Typical examples with Cr/NAFK-*t*-BuOOH chlorobenzene are summarized in Table 1. Secondary alcohols were converted into the corresponding ketones in good yields. Meanwhile, oxidation of primary alcohols generally gave complex mixtures of the unchanged substrates, the desired aldehydes, and the overoxidized carboxylic acids under the same reaction conditions. Ratios of these products were dependent on the reaction conditions (time, temperature). Prolonged reaction time or higher temperature naturally increased the formation of the carboxylic acids.

Recycling of the catalyst could be accomplished by simple filtration, washing with ethyl acetate, and drying. Titration of the recovered catalyst showed that more than 95% of chromium remained on the resin. Thus, 1-phenylethanol was oxidized to acetophenone in 92% (the second run) and 90% (the third run) yields by utilizing the recovered catalyst.

The resin cerium salt (Ce/NAFK) also has proved to be an efficient catalyst for the oxidation of alcohol by means of *t*-butyl hydroperoxide or sodium bromate. The catalyst, Ce/NAFK was prepared by stirring of a mixture of NAFK and $(NH_4)_2Ce(NO_3)_6$ for 36 h at 25 °C. In this catalytic system, the reaction proceeded at lower temperatures than Cr/NAFK-*t*-BuOOH system, so that benzene was found to be the preferred solvent. Table 2 shows the results of the oxidation of secondary alcohols. In contrast to the previously reported $(NH_4)_2Ce(NO_3)_6$-$NaBrO_3$ system,[12] the present system was not interfered with olefinic moiety in the substrates. Thus, 2-cyclododecen-1-ol and 11-dodecen-2-ol as well as carveol gave the corresponding olefinic ketones in good yields upon treatment with Ce/NAFK-*t*-BuOOH. Noteworthy is the fact that the cerium catalytic system does not oxidize primary alcohols into aldehydes. For example, 1-dodecanol was recovered practically unchanged under the general reaction conditions.

Reagents which are sufficiently selective to distinguish between functional groups of the same class are exceedingly valuable in syntheses. Recently several methods have been reported that permit the oxidation of secondary alcohols in the presence of primary ones.[13] It was anticipated that the treatment of primary, secondary diols with our new system would provide another method for selective formation of hydroxy ketones. This was indeed the case and selective oxidation of secondary hydroxyls in the presence of primary ones has been achieved as shown in Scheme



Scheme 1.

1, where choice of solvent and oxidant was critical. Oxidation in benzene with Ce/NAFK-*t*-BuOOH proceeded sluggishly and the desired products were contaminated by some unidentified by-products. For instance, oxidation of 1,10-undecanediol gave only 30% yield of 11-hydroxy-2-undecanone. The optimum yield of 82% was obtained with $NaBrO_3$ as a co-oxidant in AcOH at 55 °C. In similar fashion, 4-hydroxymethyl-1-cyclohexanol was converted into 4-hydroxymethyl-1-cyclohexanone in 73% yield with Ce/NAFK-$NaBrO_3$.

The Cr(III) and Ce(IV) catalysts prepared from Nafion-H (NAFH) also were effective for the transformation of alcohol into carbonyl compounds, but the products were contaminated by the di-*t*-butyl acetals which were generated by the NAFH catalyzed acetalization of the ketones.14)

Experimental

Infrared spectra of neat liquid film samples were determined on a Hitachi grating infrared spectrometer 215, or JASCO IR 810, mass spectra and exact mass on a Hitachi M-80. NMR spectra were recorded on a Varian EM-390, or Varian XL-200 spectrometer using TMS as an internal standard unless otherwise noted. Multiplicity is designated as s, singlet; d, doublet; t, triplet, q, quartet; m, multiplet. Preparative TLC plates were prepared with Merck Kieselgel PF_{254}. Column chromatography was carried out with silica gel (Wakogel C-200) at atmospheric pressure.

Preparation of Metal/NAFK Catalyst. Preparation of Cr/NAFK is representative. Anhydrous chromium(III) acetate (0.69 g, 3.0 mmol) was dissolved in deionized water (30 ml). NAFK (1.1 g, 1.0 mmol of sulfonate) was added and the suspension was stirred for 36 h at 25 °C. The polymer catalyst was filtered off and washed with deionized water (10 ml×5) until the washings became practically colorless. The recovered polymer catalyst was dried in vacuo to constant weight, and used.

Capacity of thus prepared resin catalyst was confirmed as follows. Dried resin catalyst (500 mg) was suspended in aqueous hydrochloric acid (6 M; 1 M=1 mol dm^{-3} prepared with deionized water, 3 ml), and stirred for 5 h. The polymer was filtered off and washed with hydrochloric acid (5 ml×2). The recovered polymer catalyst was suspended again in hydrochloric acid (6 M, 3 ml) and the washing processes were repeated twice. Whole washings were collected and chromium(III) dissolved was titrated with ethylenediaminetetraacetic acid according to a described method.15) Titration showed that 0.68 mmol of Cr(III) per gram was supported on the resin catalyst.

Preparation of Ce/NAFK. To a solution of $(NH_4)_2Ce(NO_3)_6$ (1.75 g, 3.0 mmol) in deionized water (30 ml) was added NAFK (1.1 g, 1.0 mmol of sulfonate), and the whole was stirred for 36 h at 25 °C. Titration of the dried resin indicated that 0.54 mmol of Ce(IV) per gram was loaded on the resin catalyst.

Other metal/NAFK catalysts prepared were Cu(II) (from $CuSO_4$ or $Cu(OAc)_2$), Ni(II) ($Ni(OAc)_2$), and Mn(II) ($Mn(OAc)_2$). Titration indicated that each metal/NAFK had capacity of more than 70% of theoretical one of fully loaded resin.

General Procedure for the Oxidation of Secondary Alcohols with *t*-Butyl Hydroperoxide Using Cr/NAFK as Catalyst. A solution of 1-phenylethanol (0.12 g, 1.0 mmol) in chlorobenzene (2.0 ml) was added to a suspension of Cr/NAFK (50 mg. 0.034 mmol as chromium(III) salt) in chlorobenzene (1.0 ml). A solution of *t*-butyl hydroperoxide in benzene (2.64 M, 1.5 ml, 4.0 mmol) was added and the whole was heated at 85 °C for 6 h. The solid catalyst was filtered off and washed with ethyl acetate. The filtrate and washings were combined and washed with aqueous sodium hydrogensulfite and brine successively. Purification of the concentrated crude product by silica gel column chromatography gave acetophenone (0.11 g) in 95% yield.

Oxidation of 1-Dodecanol with *t*-Butyl Hydroperoxide Using Cr/NAFK as Catalyst. To a suspension of Cr/NAFK (50 mg, 0.034 mmol of chromiun(III) salt) in chlorobenzene (2.0 ml) was added 1-dodecanol (0.18 g, 1.0 mmol) and *t*-butyl hydroperoxide in benzene (2.64 M, 1.5 ml. 4.0 mmol). The whole mixture was heated at 80 °C and stirred for 12 h. The resin catalyst was filtered off and the filtrate was treated with aqueous sodium hydrogensulfite. The water layer was acidified with aqueous hydrochloric acid (6 M, 2.0 ml) and extracted with ethyl acetate. Concentration of combined organic layer followed by separation by silica gel column chromatography gave dodecanal (0.07 g. 39%) and dodecanoic acid (0.03 g, 15%). Unchanged 1-dodecanol was also recovered (0.04 g, 24%).

General Procedure for the Oxidation of Secondary Alcohols with *t*-Butyl Hydroperoxide Using Ce/NAFK as Catalyst. Oxidation of carveol to carvone was representative. Carveol (0.15 g, 1.0 mmol) and *t*-butyl hydroperoxide (2.64 M benzene solution, 1.5 ml, 4.0 mmol) were added to a suspension of Ce/NAFK (50 mg, 0.027 mmol of cerium(IV) salt) in benzene (2.0 ml). The mixture was stirred for 2 h at 80 °C.

The resulting mixture was diluted with ethyl acetate, then Ce/NAFK catalyst was filtered off and washed with ethyl acetate on a glass filter. The organic layer was washed with aqueous sodium hydrogensulfite and brine, and dried over anhydrous sodium sulfate. Concentration gave a residual oil which was submitted to silica-gel column chromatography to give carvone (0.15 g) in 98% yield.

11-Hydroxy-2-undecanone: To a suspension of sodium bromate (0.15 g, 1.0 mmol) and Ce/NAFK (0.1 g, 0.054 mmol) in acetic acid (2.0 ml) was added a solution of 1,10-undecanediol (0.19 g, 1.0 mmol) in the same solvent (1.0 ml). The resulting mixture was stirred at 55 °C for 3 h. The resin catalyst was filtered off and washed with ethyl acetate. The filtrate and washings were combined and treated with aqueous sodium hydrogencarbonate, sodium hydrogensulfite, and brine. Concentration and purification by silica-gel column chromatography (hexane : ethyl acetate=2 : 1) gave the title compound (0.16 g) in 82% yield. Mp 42—43 °C; IR (neat) 3424, 1709, 1358, 1042 $\mathrm{cm^{-1}}$; ^{1}H NMR (CCl_4) δ=1.1—1.8 (m, 14H), 2.09 (s, 3H), 2.36 (t, J= 6.6 Hz, 2H), 3.58 (t. J=6.8 Hz, 2H), 3.78 (b, 1H). Found: C, 70.65; H, 11.90%. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90%.

4-Hydroxymethyl-1-cyclohexanone: The product was identical with the authentic sample.[16]

Oxidation of 4-*t*-Butylcyclohexanol with *t*-Butyl Hydroperoxide Using Ce/NAFH as Catalyst. Ce/NAFH catalyst was generated in the same manner as the preparation of Ce/NAFK. Titration indicated the capacity of 0.60 mmol of Ce(IV) per one gram of resin. To a suspension of Ce/NAFH (50 mg, 0.03 mmol of Ce(IV) salt) in benzene (4.0 ml) was added 4-*t*-butylcyclohexanol (0.16 g, 1.0 mmol) and *t*-butyl hydroperoxide (2.64 M in benzene, 1.5 ml, 4.0 mmol) and the resulting mixture was stirred at 80 °C. The starting alcohol was consumed within 1.5 h and the resulting mixture was diluted with ethyl acetate. The resin catalyst was separated and washed with ethyl acetate. The filtrate and washings were treated with aqueous sodium hydrogensulfite and brine, dried over anhydrous sodium sulfate and concentrated. Purification of crude oil by silica-gel column chromatography (hexane : ethyl acetate=10 : 1) gave 4-*t*-butylcyclohexanone (0.05 g, 30%) and 4-*t*-butylcyclohexanone di-*t*-butyl acetal (0.15 g, 50%).

Buffering the reaction mixture by adding sodium hydrogencarbonate improved the yield of 4-*t*-butylcyclohexanone and suppressed the formation of acetal. Treatment of a mixture of Ce/NAFH (50 mg, 0.03 mmol of cerium(IV) salt), 4-*t*-butylcyclohexanol (0.16 g, 1.0 mmol) and sodium hydrogencarbonate (0.04 g, 0.5 mmol) in benzene (4.0 ml) with *t*-butyl hydroperoxide (2.64 M in benzene, 1.5 ml, 4.0 mmol) gave 4-*t*-butylcyclohexanone (0.11 g, 68%) which was contaminated by small amount of acetal (7%). Oxidation proceeded somewhat slower than the reaction without sodium hydrogencarbonate (80 °C, 3 h).

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