Regioselective Ring Openings of 2,3-Epoxy Alcohols with Ammonium Halides and Sodium Benzenethiolate Supported on Zeolite CaY

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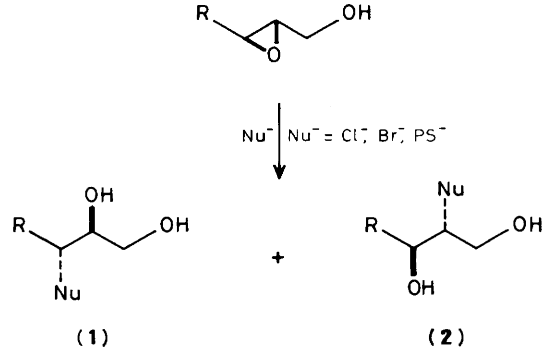
Highly regioselective ring openings of 2,3-epoxy alcohols have been performed by use of zeolite-supported ammonium halides or sodium benzenethiolate; the reactivities of these reagents are highly dependent on the conditions of their preparation.

Since optically pure 2,3-epoxy alcohols are available by Sharpless asymmetric epoxidation,[1] regioselective ring openings of epoxy alcohols with nucleophiles have been frequently utilized in the course of asymmetric syntheses of natural products.[2]

We have demonstrated that sodium azide supported on calcium ion-exchanged Y-type zeolite (CaY) reacts with 2,3-epoxy alcohols to give 3-azido 1,2-diols exclusively.[3] In order further to explore the utility of zeolite-supported reagents, we have now investigated selective ring openings of *trans*-2,3-epoxy alcohols with halide and thiolate ions; these reactions have not been accomplished with high regioselectivity hitherto.

Halide or thiolate ions (Cl^-, Br^-, or PhS^-) were attached to zeolite CaY as follows. In a round-bottomed flask (30 ml) zeolite CaY (cation contents Ca^{2+} 67%, Na^+ 33%; prepared from NaY by ion exchange[4]) (0.8 g) was immersed in a solution of NH_4Cl (3 mmol),† NH_4Br (3 mmol),† or PhSNa (2 mmol) in an impregnation solvent (3—30 ml).‡ The solvent was slowly evaporated off at 20—40 °C and 20 Torr. The amount of residual impregnation solvent contained in the supported reagent was estimated by weight increase.§



(1) (2)

A suspended mixture of the supported reagent (abbreviated NH_4X/CaY or PhSNa/CaY) and a *trans*-2,3-epoxy 1-ol (1 mmol) in an appropriate solvent (5 ml) was stirred under the conditions listed in Table 1. Methanol (6 ml) was added¶ and the mixture was stirred for 0.5 h at room temperature. Solid material was then filtered off and the filtrate was evaporated. The ring opening products were purified on silica gel as a mixture of regioisomers. The regioisomeric ratio was determined by capillary g.l.c. (PEG-HT or OV-1; 25 m) after

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† As the loading of NH_4X on CaY decreases, the reactivity of the supported reagent increases. A loading of *ca.* 4 mmol of NH_4X per g of CaY is sufficient for practical use.

‡ The amount of solvent depends on the solubility of NH_4X and PhSNa.

§ The amount of residual impregnation solvent in the supported reagent can be controlled by adjusting the evaporation temperature and time.

¶ The addition of methanol is necessary for products to be desorbed from zeolite. When water is used instead of methanol, it is often difficult to extract products from an aqueous layer completely.

Table 1. Ring openings of 2,3-epoxy alcohols with NH_4X and PhSNa.

Run	R	Nucleophile	Impreg. solvent[a] (Content)[b]	Reaction solvent[c]	Temp. (°C)	Time (h)	Yield (%)	(**1**):(**2**)
1	Pr^n	NH_4Cl/CaY	H_2O (14)	A	Reflux	8	24	60:40
2	Pr^n	NH_4Cl/CaY	H_2O (24)	A	Reflux	8	77	94: 6
3	Pr^n	NH_4Cl/CaY	H_2O (30)	A	Reflux	8	64	91: 9
4	Pr^n	$NH_4Cl–Ti(OPr^i)_4$[d]		B	Room	0.5	67	70:30
5	cyclo-C_6H_{11}	NH_4Cl/CaY	H_2O (25)	C	Reflux	20	76	90:10
6	cyclo-C_6H_{11}	$NH_4Cl/Ti(OPr^i)_4$[d]		B	40	8	95	44:56
7	Pr^n	NH_4Br/CaY	H_2O (28)	D	Reflux	15	42	84:16
8	Pr^n	NH_4Br/CaY	EtOH (28)	D	Reflux	15	51	89:11
9	Pr^n	NH_4Br/CaY	Me_2CO–EtOH [1:1] (28)	D	Reflux	15	68	91: 9
10	Pr^n	$NH_4Br–Ti(OPr^i)_4$[e]		E	Room	40	70	75:25
11	Pr^n	PhSNa/CaY	MeOH (21)	F	Room	1.5	88	93: 7
12	Pr^n	PhSNa/CaY	MeOH–H_2O [10:1] (22)	F	Room	22	95	94: 6
13	Pr^n	PhSNa–PhSH–$Ti(OPr^i)_4$[f]		A	Room	0.1	68	90:10
14	cyclo-C_6H_{11}	PhSNa/CaY	MeOH (21)	F	Room	16	86	83:17
15	cyclo-C_6H_{11}	PhSNa/CaY	MeOH–H_2O [6:1] (22)	F	Room	43	91	89:11
16	cyclo-C_6H_{11}	PhSNa–PhSH–$Ti(OPr^i)_4$[g]		A	Room	1	92	80:20

[a] Impregnation solvent for NH_4X and PhSNa. [b] Wt. % of residual solvent in the supported reagent after evaporation. [c] Reaction solvents: A, benzene; B, dimethyl sulphoxide; C, heptane; D, pentane; E, tetrahydrofuran; F, hexane. [d] NH_4Cl (2 equiv.) and $Ti(OPr^i)_4$ (1.5 equiv.) were used. [e] NH_4Br (1.5 equiv.) and $Ti(OPr^i)_4$ (1.5 equiv.) were used. [f] Results from ref. 6. [g] PhSNa (2.0 equiv.), PhSH (2.0 equiv.), and $Ti(OPr^i)_4$ (1.5 equiv.) were used.

peracetylation with Ac_2O and pyridine. Table 1 summarizes the results.

The ammonium chloride-supported reagent (NH_4Cl/CaY) was prepared from aqueous NH_4Cl. In this case, residual water in the reagent was found to affect both yield and regioselectivity of products (Runs 1—3). The presence of 24—30 wt.% of water is optimal for a highly reactive reagent. It has been pointed out that a certain amount of a polar solvent such as water improves the reactivity of a supported reagent.[5] As a source of a chloride ion, NH_4Cl is the most suitable. NaCl- and CsCl-supported reagents showed little reactivity in openings of epoxides.

In the case of 3-cyclohexyl-2,3-epoxypropan-1-ol, the NH_4Cl/CaY reagent was much superior in regioselectivity to the homogeneous system $NH_4Cl–Ti(OPr^i)_4$[6] (Run 5).[‖]

Ring opening by bromide ion was also investigated. 3-Bromo 1,2-diols are less stable than 3-chloro 1,2-diols, so the ring opening had to be performed at lower temperature. The choice of impregnation solvent for NH_4Br greatly influenced both reactivity of the supported reagent and regioselectivity in the ring opening. Thus a change of impregnation solvent from water to ethanol or to 1:1 ethanol–acetone, improved the yields of (**1**) and (**2**) as well as the regioselectivity for (**1**) with respect to (**2**) (Runs 7—9). NH_4Br is freely soluble in water, moderately soluble in ethanol, and sparingly soluble in acetone. The solubility differences of NH_4Br might affect the size of NH_4Br crystals deposited on the zeolite surface during formation of the supported reagent.

The influence of impregnation solvent on ring opening was also observed in the case of PhSNa/CaY. As compared with pure methanol (a 'good' solvent for PhSNa), aqueous methanol (85—90 vol. %, a 'poor' solvent) is preferable, resulting in an improvement in regioselection (Runs 11, 12, 14, and 15).

For zeolite-induced ring openings of epoxides, calcium ions in the zeolite play two decisive roles: (1) they increase the acid strength of the zeolite, facilitating ring cleavage; and (2) they regulate the ring-opening site. Sugars and polyols are known to form complexes with calcium ions;[8] the present epoxy alcohols probably generate five-membered chelate complexes with calcium ions in the zeolite [in a similar manner to the case of $Ti(OPr^i)_4$[6]], thus regulating the ring opening.

In conclusion, a combination of nucleophile and zeolite CaY can promote specific interactions of zeolite surfaces with substrates to bring about highly regioselective openings of 2,3-epoxy 1-ols. In preparing a reactive supported reagent, particular attention should be paid to the choice of impregnation solvent and the amount of residual impregnation solvent in the reagent.

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[‖] In the case of an internal 2,3-epoxy alcohol (*threo*-1-cyclohexyl-1,2-epoxyheptan-3-ol) high regioselectivity (>100:1) by use of $ClTi(OPr^i)_3$ was reported.[7]