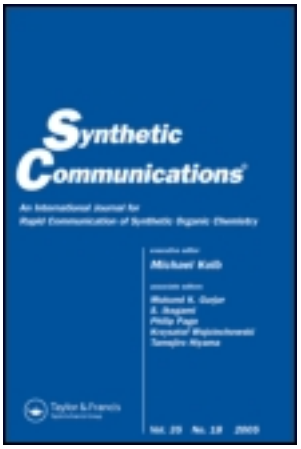

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Mild, Selective Oxidation of Aromatic Alcohols Using β-Cyclodextrin-Functionalized Glass Microparticles: Characterization, Stability, and Application

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MILD, SELECTIVE OXIDATION OF AROMATIC ALCOHOLS USING β-CYCLODEXTRIN-FUNCTIONALIZED GLASS MICROPARTICLES: CHARACTERIZATION, STABILITY, AND APPLICATION

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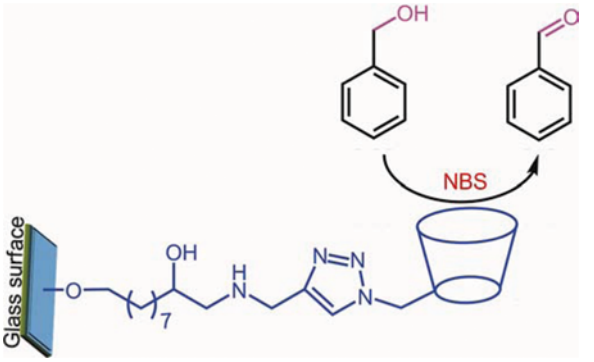
GRAPHICAL ABSTRACT



Abstract *The surface of glass microparticle (GMP) was functionalized with β-cyclodextrin (→ GMP-β-CD) and was characterized by x-ray photoelectron spectroscopy (XPS). GMP-β-CD was used to catalyze oxidation of alcohols into aldehydes and katones with excellent yield (86–92%). The modified surface of GMP-β-CD showed no change or degradation after repeated use as confirmed from XPS analysis after 10 cycles.*

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[Supplementary materials are available for this article. Go to the publisher's online edition of Synthetic Communications® *for the following free supplemental resource(s): Full experimental and spectral details.]*

Keywords Aromatic alcohols; N-bromosuccinimide; catalysis; β-cyclodextrin; glass functionalization; oxidation

INTRODUCTION

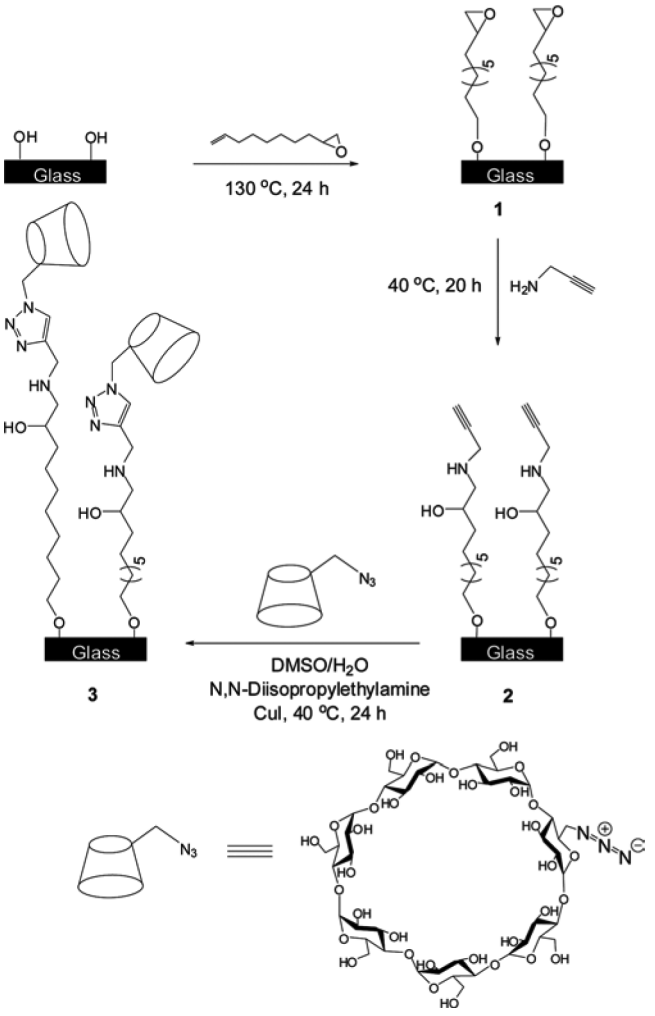
Selective oxidation is a fundamental and pivotal class of chemical transformations and is extensively used for organic synthesis and industrial manufacturing.[1–4] Catalysts, mostly based on transition metals (e.g., Cu, Pd, Ru, Mn, Ti, and Pt), are used for this purpose, which apparently cause serious heavy-metal pollution.[5–9] Therefore, such metal catalysts are often considered unsuitable for the synthesis of intermediates used in pharmaceutical products.[10] Moreover, oxidation by such metal-based catalysts is considered a costly method.[11] Although new oxidation methods have been developed over recent decades,[12] more clean and environmentally friendly methods for such chemical reactions are still needed.

In the past few years, there have been many reports where native or modified β-cyclodextrin (β-CD) has been applied as a catalyst in different chemical reactions.[9,13–16] β-CD has certain advantages over heavy-metal-based traditional catalysts (e.g., low cost, nontoxic, biocompatible, biodegradable, and water soluble). Although there are some examples where free β-CD was used as a catalyst in the oxidation reactions,[17–20] to our knowledge there is no example in literature where immobilized β-CD (or any other CD) was used for such a purpose. A common problem observed when using free β-CD in chemical reactions is its ability to complex with water-insoluble substrates to make them water soluble (product moves in aqueous phase during extraction), leading to decrease in yield.[21] β-CD immobilized on a solid surface has many advantages over free β-CD, such as easy separation after completion of reaction and the possibility of applying such modified surfaces in a continuous process. Repeated use of β-CD can make the process economical but its recovery from the reaction mixture after completion of a reaction is time-consuming and laborious work. However, all these problems can be solved by using β-CD immobilized on solid support, such as glass microparticles (GMP). Other materials including silicon, quartz, and organic polymers have also been used to manufacture functional surfaces, but glass is more attractive because it is readily available at low cost and has high mechanical stability, and easy surface-modification techniques are known for this material.[22–24] Because of these advantages, GMP (30–50 μm) was functionalized with β-CD ((GMP-β-CD) through a click reaction and applied as a green catalyst for oxidation of the aromatic alcohols.

RESULTS AND DISCUSSION

Modification of Glass Microparticles

The surface modification of GMP was started with the formation of an epoxide-terminated monolayer on the glass surface (Scheme 1). The layer was



Scheme 1. Immobilization of β-CD on glass microparticles.

characterized by X-ray photoelectron spectroscopy (XPS) and elemental analysis. The narrow-scan C_{1s} XPS spectrum (Fig. 1a), formed from the electrons emitted from C atoms in the alkyl chain of the epoxide terminated monolayer, displayed a signal at 285.0 eV corresponding to C-C bonds and a signal at 287.02 eV corresponding to C-O bonds in the monolayer.[25] The experimental ratio of C-O/C-C bonds calculated from XPS spectrum (Fig. 1a) is 0.41, which is in good agreement with the theoretical value of 0.42. These results indicate that high-quality epoxide monolayers on glass surface were obtained. The change in elemental composition (Table 1) confirms the XPS data. The thickness of the formed epoxide layer, calculated using Eq. (1), was 1.12 nm and is slightly greater than the length of the 1,2-epoxy-9-decene molecule (1.11 nm, as calculated with Chem3D), confirming the monolayer character.

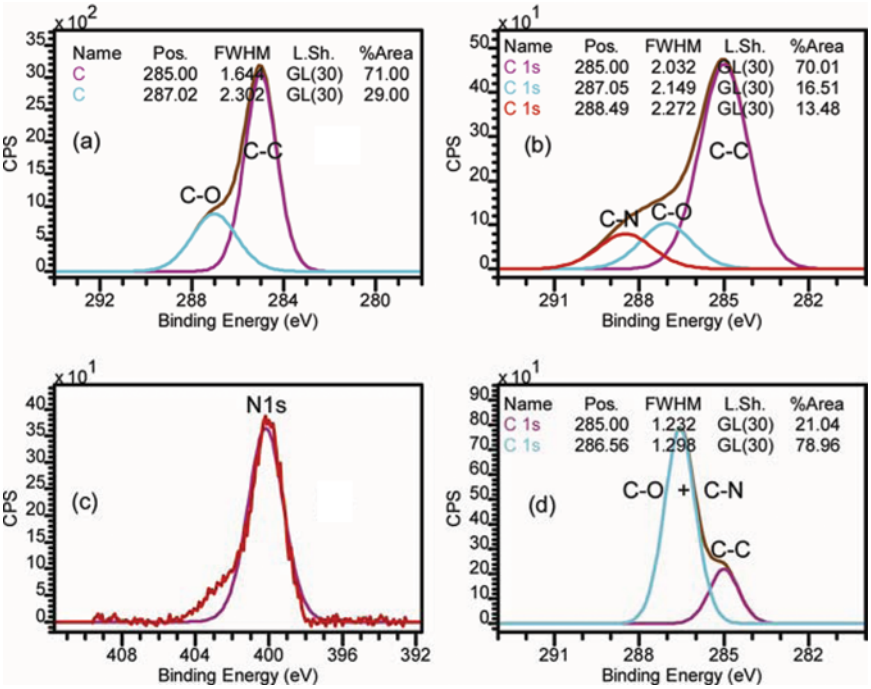


Figure 1. Narrow-scan C_{1s} XPS spectra of epoxide terminated monolayer (a, **1**), propargyl terminated monolayer (b, **2**), narrow-scan N_{1s} XPS spectrum of propargyl terminated layer (c, **2**), and C_{1s} XPS spectrum after immobilization of β-CD on glass micro-particles (d, **3**). (Figure is provided in color online.)

$$I_{si} = I_{si}^{\infty} \exp\left(\frac{-d}{\lambda_{si,c} \cos\theta}\right) \tag{1}$$

The variables I_{si} (absolute silicon peak intensity), I_{si}^{∞} (absolute silicon peak intensity of the unmodified glass), d (thickness of the adsorbed layer), $\lambda_{si,\,c}$ (attenuation length

Table 1. Elemental composition of glass microparticles: without and after functionalization with epoxide, and alkynyl-terminated monolayers, and after click reaction of β-CD-N_3 and relative proportion of different types of linkages

	Elemental comp. atomic (%)				C-C bond		C-X[a] bond	
Substrate	Si	O	C	N	Ther.	Expt.	Ther.	Expt.
Blank glass (before modification)	32.96	67.04	0.00	0.00				
With epoxide-terminated monolayer (**1**)	22.43	36.84	40.74	0.00	7	7.1	3	2.9
With propargyl-terminated monolayer (**2**)	23.11	32.32	41.78	2.79	9	9.1	4	3.9
With β-CD immobilized on glass surface (**3**), – fresh	13.87	29.73	50.52	5.88	7	11.14	48	41.86
After 5 cycles of repeated use (**3**)	14.23	29.97	49.99	5.81	7	11.65	48	41.35
After 10 cycles of repeated use (**3**)	14.26	30.05	49.92	5.77	7	11.71	48	41.29

Note. All XPS spectra are available in the Supplementary Material.
[a]C-X=C-O + C-N bond linkages.

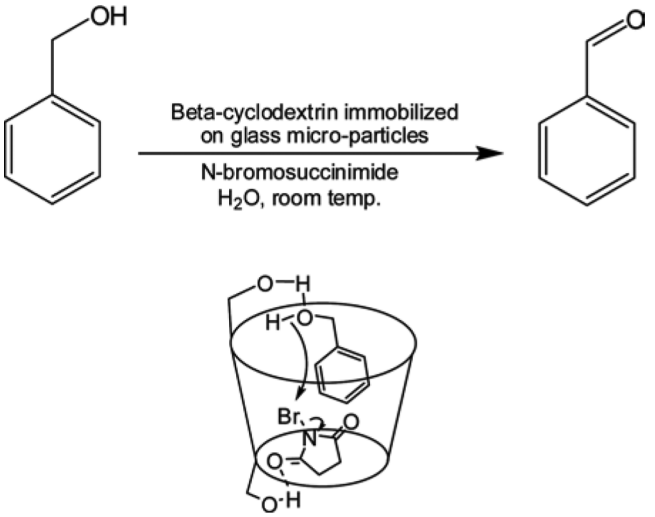
of Si_{2p} electrons in the hydrocarbon layer), and θ (electron takeoff angle) were calculated from the XPS data as described in Ref. 26.

The epoxide-functionalized glass surface (**1**) was subsequently converted into an alkynyl terminated surface (**2**) via a reaction with propargylamine as described in the experimental section. In the XPS spectrum (Fig. 1b), three signals corresponding to C-C (285.0 eV), C-O (287.05 eV), and C-N (288.49 eV) bonds appeared. Excellent agreement between measured (0.43) and theoretical (0.44) values for the ratio of C-X/C-C (where C-X=C-O + C-N bond linkages) corresponds to 98% conversion of epoxide to propargyl-terminated surface. In addition, appearance of a signal of organic nitrogen at 400.0 eV (Fig. 1c) from the resultant monolayer also indicates the successful reaction between propargylamine and the epoxide-terminated layer (**1**).

In the last step of this reaction, β-CD was converted into its monofunctionlal-zidazide (β-CD-N_3) following the procedure from literature[27,28] and immobilized on a glass surface as described in the experimental section. In the XPS spectrum (Fig. 1d) only two signals corresponding to C-C (285 eV) and C-X (C-O + C-N, 286.56 eV) appeared due to overlapping of C-O and C-N signals. Ratio of C-X/C-C (theoretical 6.85, experimental 3.75) indicates that 55% of the alkynyl groups (**2**) were clicked with β-CD-N_3. Degree of conversion was probably restricted by steric hindrance for the bulky cyclodextrin derivative. Increase of the C content from 41.78 to 50.52% and of N from 2.79 to 5.88% along with decrease in Si content from 23.11 to 13.87% after the click reaction of the alkynyl-terminated layer (**2**) to β-CD-N_3 (Table 1) also indicate the successful immobilization of β-CD on the glass surface.

Oxidation of Alcohols Aatalyzed by GMP-β-CD (3)

In the general procedure, aromatic alcohols were oxidized selectively to aldehydes and ketones with *N*-bromosuccinimide (NBS) in water at room temperature



Scheme 2. Oxidation of aromatic alcohols using β-cyclodextrin immobilized on glass microparticles (GMP-β-CD, **3**) and proposed mechanism for host–guest complex formation of β-CD with alcohol with the help of *N*-bromosuccinimide.

Table 2. Oxidation of alcohols into ketones using *N*-bromosuccinimide in water and catalyzed by β-cyclodextrin immobilized on glass microparticles (GMP-β-CD, **3**)

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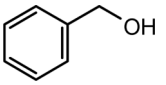
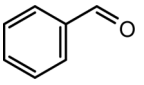
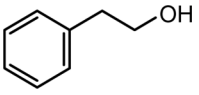
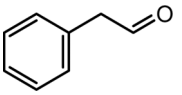
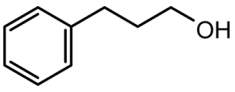
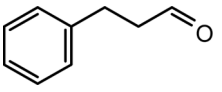
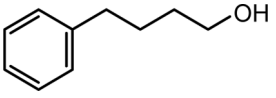
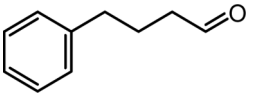
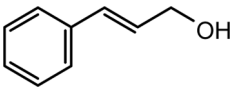
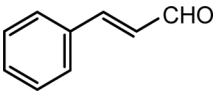
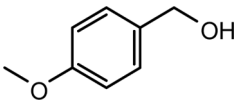
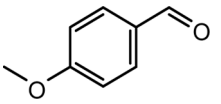
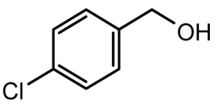
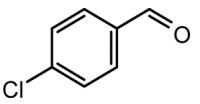
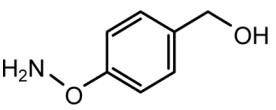
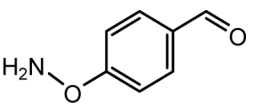
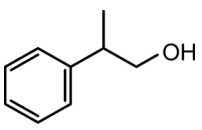
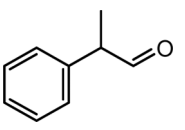
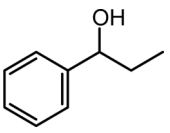
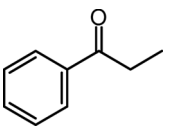
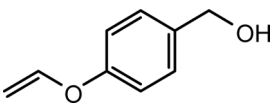
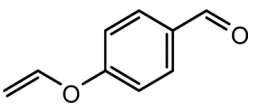
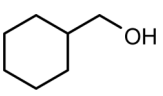
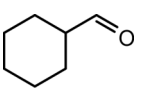
1			4	92
2			4	91
3			5	92
4			5	88
5			4.5	90
6			4	92
7			4	94
8			4.5	91
9			4	87
10			4	86
11			5	88
12			5.5	91

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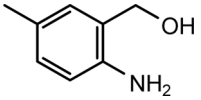
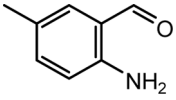
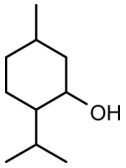
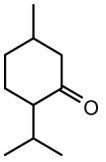
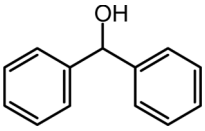
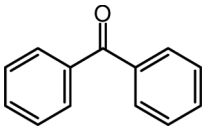
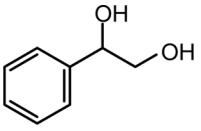
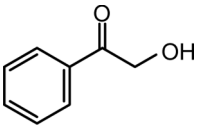
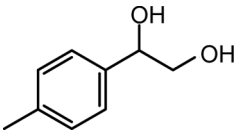
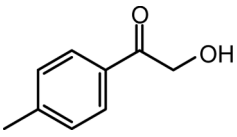
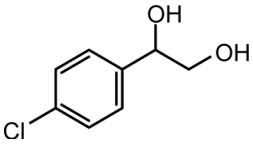
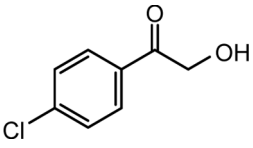
13			5	91
14			6	87
15			6	80
16			5.5	88
17			5.5	89
18			5.5	88

using GMP-β-CD (**3**) as a catalyst (Scheme 2). The course of the reaction was followed by thin-layer chromatography and the product was characterized by NMR spectroscopy. Results from both techniques indicate that the reaction went smoothly, and no side product was detected. As a control, the same reaction under the same conditions but without GMP-β-CD was carried out in parallel, but no product was detected. The same observation was reported by other researchers.[19] Oxidation remained selective and no over oxidation to acids was detected by thin-layer chromatography (TLC) or by NMR spectroscopy. Also it was observed that reaction was selective in the case of vicinal diols, and only secondary alcohol was oxidized selectively (entries 16–18, Table 2). Moreover, no side reaction was observed in the compounds where other functional groups such as methoxy, nitro, halo, amino, hydroxy, and alkene double bonds (see entries 6, 7, 8, 11, 13, and 18 in Table 2) were present.

The mechanism for host–guest complex of β-CD with NBS and aromatic alcohols in such reactions is already reported in the literature.[19] It is suggested that

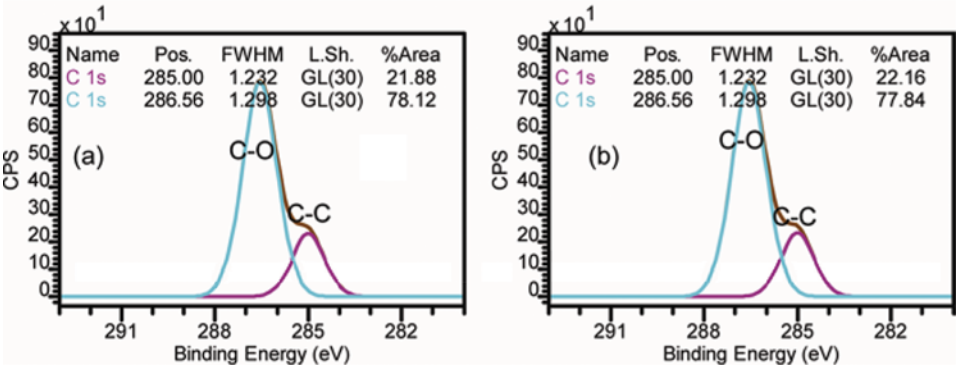


Figure 2. Narrow-scan C_{1s} XPS spectra of β-CD immobilized on glass microparticles after 5 (a) and 10 cycles of repeated use (b) for oxidation of benzyl alcohol (see Scheme 2). (Figure is provided in color online.)

β-CD forms an inclusion complex with alcohol from the secondary side with the attack of NBS from the primary side of the β-CD, enabling the reaction to proceed (Scheme 2).

Repeated Use and Stability of the Functional Glass Surface (GMP-β-CD, 3)

For implementation of such process at an industrial scale, where many cycles of good yield are required, the stability of β-CD immobilized on a glass surface should be high enough to permit its repeated use. To test stability, GMP-β-CD (**3**) was applied as a catalyst for the oxidation of benzyl alcohol for 10 cycles. For this purpose, GMP-β-CD was taken out of the reaction mixture after completion of the reaction, washed with water and acetone, dried under a nitrogen stream, and used again for the next cycle. Stability of β-CD on the glass surface was determined from the change in elemental composition (Table 1) and by recording XPS spectra after 5 and 10 cycles of repeated use (Fig. 2). During repeated use, no change in the yield of the product or reaction rate for the oxidation of benzyl alcohol was observed. Comparison of the XPS spectra recorded for freshly prepared GMP-β-CD (Fig. 1d) and that of after 5 and 10 cycles (Fig. 2) indicate that there was almost no change in the relative proportion of different bond linkages or in elemental composition (Table 1). These results indicate that the modified glass surface remained stable and can be used for several cycles without losing efficiency. Moreover, it also confirms that no side reaction (e.g., oxidation of immobilized β-CD) occurred on modified surface.

EXPERIMENTAL

Materials and methods

β-cyclodextrin (≥97%), *N*-bromosuccinimide (99%), acetone (99.9%), hydrochlo-hydrochloric acid (37%), dimethyl sulfoxide (99.9%), propagylamine (98%),

N,N-diisopropylethylamine (99.5%), and copper(I) iodide (99.5%) were purchased from Sigma-Aldrich. 1,2-Epoxy-9-decene (96%) was from Tokyo Chemical Industry, Japan. Methanol (99.9%), n-hexane (99.9%), isopropanol (99.9%), ethyl alcohol (99.9%), acetonitrile (99.9%), diethyl ether (99.9%), ethyl acetate (99.9%) and sodium hydroxide were from Duksan. Sodium azide was from Junsei Chemical Co., Ltd., Korea; glass microparticles (GMP, 30–50 μm) were purchased from Polysciences Inc., USA; and dimethyl sulfoxide (DMSO-d_6) was from Cambridge Isotope Laboratories, Inc., USA.

Water was purified using Direct-Q Millipore water purification system from SAM WOO S&T Co., Ltd., Korea. β-CD was dried under vacuum until constant weight, 1,2-epoxy-9-decene was further purified by column chromatography ($EtOAc/Et_2O$ 3:1), solvents used for column chromatography were distilled while other chemicals were used without further purification.

NMR spectra were recorded on a Bruker AMX spectrometer at 500 MHz. Thin-layer chromatography (TLC) was carried out on Merck Kieselgel 60 F254 plates. X-ray photoelectron spectroscopic (XPS) spectra were recorded by using a Sigma Probe (ThermoVG, UK) photoelectron spectrometer. High-resolution spectra were obtained using monochromatic *Al-Kα* X-ray radiation at 15 kV and 100 W and an analyzer pass energy of 50 eV (1.0 eV step size) for wide scan and 20 eV (0.1 eV step size) for narrow scan. All high-resolution spectra were corrected with a linear background before fitting. Mono-6-(*p*-toluenesulfonyl)-6-deoxy-cyclodextrin (β-CD-OTs) was synthesized from β-CD as described in Ref. 27, which in the next step was converted into mono-6-azido-β-cyclodextrin (β-CD-N_3) according to the procedure described in Ref. 28. ^{1}H NMR data of the products was in accordance with Refs. 27 and 28 (detailed procedure is described in the electronic supplementary material). β-CD-N_3 was immobilized on the glass surface through a click reaction.

Modification of Glass Surface with Epoxide-Terminated Monolayer (1)

Modification was carried out as described in Ref. 25 with some changes. GMP (5 g) was washed with acetone, n-hexane, methanol, and ethanol, followed by sonication for 5 min per solvent and etched for 30 min in a freshly prepared solution of HCl (37%) and ethanol (1:1 v/v). After etching, the samples were rinsed with ultrapure water and methanol for 5 min per solvent and dried under nitrogen stream. Immediately after cleaning and drying, GMP were transferred into a dried glass flask followed by addition of 1,2-epoxy-9-decene (5 g, 32.4 mmol) while keeping under nitrogen atmosphere before closing tightly. To remove the traces of oxygen and moisturethat might enter into the reaction flask, it was dipped into the liquid nitrogen to freeze the coated 1,2-epoxy-9-decene on GMP (while under a nitrogen atmosphere) and allowed to liquefy again at room temperature under vacuum. This freeze–thaw cycle was repeated three times. Finally, the reaction flask was backfilled with nitrogen, dipped into silicon oil bath, and heated at 130°C for 24 h while under slight nitrogen pressure (Scheme 1). GMP coated with epoxide-terminated layer (**1**) was removed from the reaction flask, washed thoroughly with deionized water, n-hexane, and acetone, sonicated for 5 min per solvent, and dried under a nitrogen stream.

Alkynyl Functionalization of Glass Surface (2)

Subsequently, the GMP was transferred to degassed propargylamine. The reaction was carried out at 40°C for 20 h, followed by washing and cleaning steps as described previously.

Immobilization of β-CD on Glass Surface (3)

β-CD-N_3 (675 mg, 0.57 mmol) was dissolved in DMSO/H_2O (8:1, 36 mL) followed by addition of *N,N*-diisopropylethylamine (222 mg, 1.71 mmol, 3 eq./azide group) and CuI (28.5 mg, 0.15 mmol, 0.25 eq./azide group). The GMP functionalized with propargylamine (**2**) was incubated in the reaction mixture and heated at 40°C for 24 h followed by cleaning and drying steps.

General Procedure for Oxidation of Alcohols

Aromatic alcohol (1–2 mmol) was dissolved in methanol (or acetone in some cases, 2–4 mL) at room temperature, followed by addition of the aqueous solution of *N*-bromosuccinimide (1.5 eq./alcohol) with continuous stirring. GMP-β-CD (**3**, 100 mg/mmol of alcohol) were added in the reaction mixture and stirring was continued. Progress of the reaction was monitored by TLC until the reaction was completed (4–6 h). GMP was separated by filtration after completion of the reaction. The reaction mixture was extracted with ethyl acetate (4×5 mL), combined organic layers were dried over Na_2SO_4, and solvent was removed under reduced pressure. The product was further purified by flash column chromatography and analyzed by NMR spectroscopy.

CONCLUSION

The glass microparticle surface was successfully functionalized with β-CD. Modified glass microparticles can be used as a green catalyst (instead of heavy-metal-based catalysts) for the oxidation of a variety of alcohols in water using NBS. The modified surface remained stable and can be used for several cycles without losing efficiency. Thus, this simple and clean methodology can be applied for continuous process at larger scale. This environmentally benign technique may can be applied in surface coating of microreactors for continuous process for the same or other synthetic reactions.

SUPPLEMENTARY MATERIAL

Synthetic procedure for β-CD-N_3 and XPS spectra are available in the Supplementary Material.

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REFERENCES

1. Guo, H.; Liu, W.-D.; Yin, G. *Appl. Organomet. Chem.* **2011**, *25*, 836–842.
2. Smith III, A. B.; Carroll, P. J.; Kashman, Y.; Green, D. *Tetrahedron Lett.* **1989**, *30*, 3363–3364.
3. Crombie, L.; Mistry, J. *Tetrahedron Lett.* **1990**, *31*, 2647–2648.
4. De Munari, S.; Frigerio, M.; Santagostino, M. *J. Org. Chem.* **1996**, *61*, 9272–9279.
5. Stevens, R. V.; Chapman, K. T.; Weller, H. N. *J. Org. Chem.* **1980**, *45*, 2030–2032.
6. Holum, J. R. *J. Org. Chem.* **1961**, *26*, 4814–4816.
7. Lee, D. G.; Spitzer, U. A. *J. Org. Chem.* **1970**, *35*, 3589–3590.
8. Menger, F. M.; Lee, C. *Tetrahedron Lett.* **1981**, *22*, 1655–1656.
9. Fujita, K.; Shinoda, A.; Imoto, T. *Tetrahedron Lett.* **1980**, *21*, 1541–1544.
10. Cheng, X. Y.; Li, K. F.; Wang, Q. J.; Wang, C. Y.; Ying, T. K. *Chin. Chem. Lett.* **2012**, *23*, 801–804.
11. Tanaka, A.; Hashimoto, K.; Kominami, H. *J. Am. Chem. Soc.* **2012**, *134*, 14526–14533.
12. Hudlicky, M. *Oxidation in Organic Chemistry*; ACS: Washington, DC, 1990.
13. Palmer, D. R. J.; Buncel, E.; Thatcher, G. R. J. *J. Org. Chem.* **1994**, *59*, 5286–5291.
14. Fragoso, A.; Cao, R.; Baños, M. *Tetrahedron Lett.* **2004**, *45*, 4069–4071.
15. Zhou, Y.-H.; Zhao, M.; Mao, Z.-W.; Ji, L.-N. *Chem. Eur. J.* **2008**, *14*, 7193–7201.
16. Marinescu, L.; Bols, M. *Curr. Org. Chem.* **2010**, *14*, 1380–1398.
17. Marinescu, L. G.; Doyagüez, E. G.; Petrillo, M.; Fernández-Mayoralas, A.; Bols, M. *Eur. J. Org. Chem.* **2010**, *2010*, 157–167.
18. Surendra, K.; Krishnaveni, N. S.; Rao, R. *Can. J. Chem.* **2004**, *82*, 1230–1233.
19. Krishnaveni, N. S.; Surendra, K.; Rama Rao, K. *Adv. Synth. Catal.* **2004**, *346*, 346–350.
20. Surendra, K.; Krishnaveni, N. S.; Reddy, M. A.; Nageswar, Y. V. D.; Rao, K. R. *J. Org. Chem.* **2003**, *68*, 2058–2059.
21. Shin, J.-A.; Lim, Y.-G.; Lee, K.-H. *J. Org. Chem.* **2012**, *77*, 4117–4122.
22. Manz, A.; Becker, H. *Microsystem Technology in Chemistry and Life Science*; Springer: Heidelberg, 1998.
23. Henry, C. S. *Methods in Molecular Biology*; Humana Press: Totowa, 2006.
24. Kuzmin, A.; Poloukhtine, A.; Wolfert, M. A.; Popik, V. V. *Bioconjugate Chem.* **2010**, *21*, 2076–2085.
25. Nguyen, A. T.; Baggerman, J.; Paulusse, J. M. J.; van Rijn, C. J. M.; Zuilhof, H. *Langmuir* **2011**, *27*, 2587–2594.
26. ter Maat, J.; Regeling, R.; Yang, M.; Mullings, M. N.; Bent, S. F.; Zuilhof, H. *Langmuir* **2009**, *25*, 11592–11597.
27. Wang, Y.; Chen, H.; Xiao, Y.; Ng, C. H.; Oh, T. S.; Tan, T. T. Y.; Ng, S. C. *Nat. Protoc.* **2011**, *6*, 935–942.
28. Lovrinovic, M.; Niemeyer, C. M. *Chem Bio Chem.* **2007**, *8*, 61–67.