

# Microwave-assisted immobilization of the REDOX indicator 2,6-dichloroindophenol on PEGylated Merrifield resins

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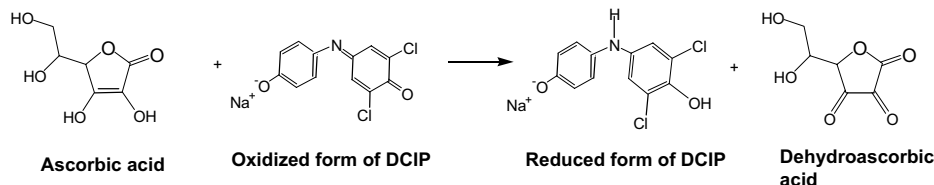
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**Abstract**—The blue organic dye, 2,6-dichloroindophenol (DCIP), was immobilized on PEGylated Merrifield resin after a chlorination step followed by a nucleophilic substitution reaction, using microwave-assisted methodology. The final product was a blue pigmented resin that can be reversibly reduced by ascorbic acid and changes color from blue to light yellow. Structural elucidation of this immobilized indicator was confirmed through FTIR and elemental analyses.

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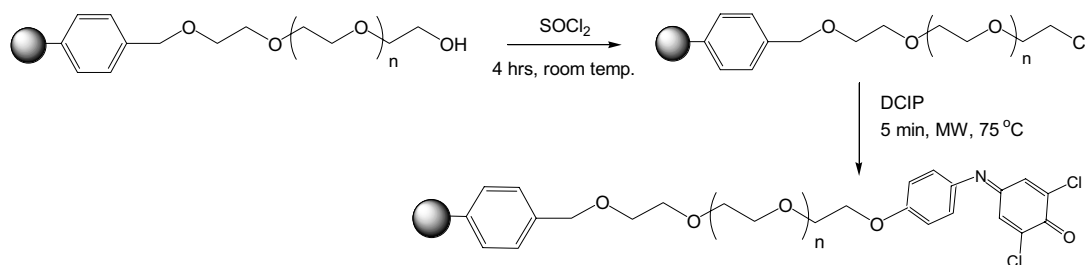
Following the successful introduction of solid-phase based methodologies into the mainstream synthesis strategies, polymer-supported reagents are also gaining increasing popularity mainly due to the ease of handling and convenience of use, especially in combinatorial chemistry applications. Although polymer-supported reagents are similar in their chemical reactivity to their smaller molecule counterparts however, due to their insolubility in most solvents, they can be easily removed by simple filtration and recycled after use.<sup>1</sup> Highly toxic chemicals can be rendered inert and harmless through attachment to a polymer support and their release to the environment can be eliminated. Many colorimetric reagents showing optical interaction with specific analytes, are widely used as visual indicators for pH or redox activity detection. As an approach to the construction of optical sensors, these reagents are often

immobilized by chemical or physical methods onto polymeric materials that are in the form of beads,<sup>2</sup> powders, or films.<sup>3–5</sup> One such reagent is 2,6-dichloroindophenol (DCIP; Tellman's reagent)—a dye that has been used as a pH and redox indicator for various applications.<sup>6</sup> DCIP is blue in alkaline solution and pink in acidic, and can be reduced to a colorless form. One of the most important uses of DCIP is in the chemical analysis<sup>6</sup> of ascorbic acid (vitamin C) using a titrimetric method, in which the dye is reduced by ascorbic acid (Fig. 1) and the end point of the titration is indicated by the appearance of a faint color. Goodlet and Narayanaswamy<sup>2</sup> reported the non-covalent immobilization of DCIP on Amberlite XAD-4 resin and its successful application as an optical sensor for the analysis of vitamin C in orange juice. Here, we report the covalent attachment of DCIP on PEGylated Merrifield resin,<sup>7</sup>



**Figure 1.** Oxidation/reduction reaction of DCIP with ascorbic acid.

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**Figure 2.** Microwave-assisted immobilization of DCIP on PEGylated Merrifield resin. MW = microwave.

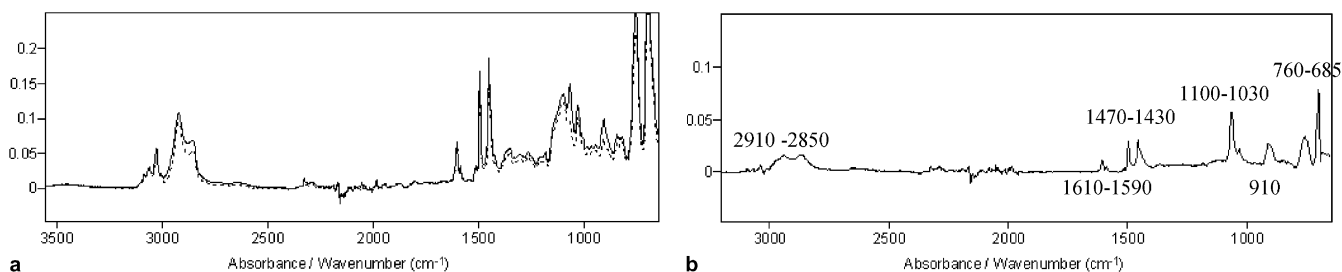
using a microwave-assisted process. PEGylated Merrifield resins<sup>7</sup> have been recently used as scaffolds in solid-phase synthesis for various applications requiring aqueous environment, such as epoxidation<sup>8</sup> and trapping of water pollutants with  $\beta$ -cyclodextrin.<sup>9</sup> The resin was first activated by thionyl chloride followed by the reaction with DCIP as summarized in **Figure 2**.

In a typical experiment, PEGylated MR<sub>200</sub> ( $0.54 \pm 0.02$  g) was suspended in fivefold excess of thionyl chloride ( $\text{SOCl}_2$ ), stirred magnetically at room temperature for 4 h. The product was filtered and washed with dichloromethane and methanol. The chlorinated resin ( $0.38 \text{ g} \pm 0.02 \text{ g}$ ) was then suspended in 10 mL of acetonitrile and 1 mg of sodium salt of DCIP was added. The reaction was carried out under microwave irradiation at atmospheric pressure, the microwave was operated under constant temperature mode such that the power was varied to maintain a value of  $75^\circ\text{C}$  for a total of 5 min using the Synthwave<sup>TM</sup> 402 (Prolabo, France). The product was filtered and washed with methanol and water until the filtrate was colorless.

The resulting immobilized DCIP remained dark blue even after continuous washing with methanol and water. This indicated the covalent attachment of DCIP to the

resin, as the starting resin is off-white to light yellow in color. Upon reaction<sup>10</sup> with vitamin C the resin changed color from dark blue back to light yellow. However, equilibration of this light yellow resin in a carbonate buffer of pH 10, restored back the blue color indicating the reversibility of the active moiety on the resin. The FTIR spectrum<sup>11</sup> of the immobilized DCIP was compared with that of thionyl chloride activated PEGylated MR (see **Fig. 3a**). Due to the overlapping bands, it was difficult to distinguish between the reactant and product without spectral subtraction. **Figure 3b** shows the subtracted spectrum (1:1 ratio). The characteristic features of DCIP can be seen, such as benzene ring breathing bands at  $685\text{--}760\text{ cm}^{-1}$ , aromatic carbon–chlorine stretching bands at  $1030\text{--}1100\text{ cm}^{-1}$ , alkene bands at  $1430\text{--}1470\text{ cm}^{-1}$ , and  $910\text{ cm}^{-1}$  and a weak imine band at  $1590\text{--}1610\text{ cm}^{-1}$ .

Results from the elemental analysis (**Table 1**) indicated that based on the percent weight gain of chlorine in resin bound DCIP, a loading of  $1.4 \times 10^{-2}$  mmol DCIP/g resin could be calculated. It was also observed that the attachment to the resin eliminated the odor of DCIP. Finally, stability studies have indicated that polymer bound DCIP was stable for up to three months in the dry state at  $4^\circ\text{C}$ .



**Figure 3.** (a) FTIR spectra of chlorinated resin (---) and resin with bound DCIP (—). (b) Subtracted spectrum of chlorinated resin from the resin with bound DCIP.

**Table 1.** Yields, elemental analysis,<sup>12</sup> and loading values for various intermediates

	% Cl	% O	Theoretical yield <sup>a</sup> (g)	Calculated yield <sup>b</sup> (g)	Actual yield (g)	Loading (mmol/g resin)
PEG <sub>200</sub> -MR	1.67	6.34	<sup>c</sup>	<sup>c</sup>	<sup>c</sup>	$74.9 \times 10^{-2}$
Cl-PEG <sub>200</sub> -MR	3.46	2.31	0.54	0.53	0.52	$50.5 \times 10^{-2}$
DCIP-PEG <sub>200</sub> -MR	3.51	2.51	0.42	0.38	0.38	$1.4 \times 10^{-2}$

<sup>a</sup> Based on loss or gain of oxygen, carbon, hydrogen, and chlorine atoms from molecular structures using nominal molecular weights.

<sup>b</sup> Estimated yield based on elemental analysis of chlorine.

<sup>c</sup> See Ref. 7 for average values.

## References and notes

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10. Resin bound DCIP (~0.10 g) was packed in a column made from a pasteur pipette. The resin was swelled in DCM. Vitamin C (0.01 mmol) solution was prepared in methanol and water (1:1) and was passed through the column. Any color changes of the resin were recorded.
11. Infrared spectra were recorded on a Bio-Rad Excalibur Series FT-IR spectrometer (Bio-Rad, Cambridge, MA, USA) purged with dry air. The spectra of the resins were acquired on a Golden Gate Single Reflection Diamond ATR. A total of 128 scans at  $4\text{ cm}^{-1}$  resolution were co-added. Processing of the FTIR data was performed using GRAMS/32 AI version 6.01.
12. Elemental analysis was performed by Guelph Chemical Laboratories Ltd. (Guelph ON, Canada). Data reported are the average of duplicate measurements.