Polypyrrole-Supported Graphite Felt for Acetylene Coupling Reaction in Solid Phase

Yoshitomo Kashiwagi,* Shinya Chiba, Hiroshi Ikezoe, Jun-ichi Anzai
Graduate School of Pharmaceutical Sciences, Tohoku University, Aramaki, Aoba-ku, Sendai 980-8578, Japan
Fax +81(22)2176840; E-mail: kashi@mail.pharm.tohoku.ac.jp

Received 10 August 2004

Abstract: Substrate immobilization on graphite felt for solid-phase acetylene coupling reaction was achieved by electrochemical polymerization of the substrate precursor containing a pyrrole side chain, where the amount of substrate on the electrode surface was easily controlled by the number of repeated cyclic voltammetric scannings. Couplings between terminal acetylenes and the iodobenzene-modified graphite felt electrode or aromatic iodides and the terminal acetylene-modified graphite felt electrode in the presence of palladium catalyst proceeded smoothly in satisfactory yields.

Key words: Sonogashira reaction, solid-phase synthesis, polypyrrole, electrochemical polymerization, modified electrode

Solid-phase synthesis has attracted much interest in organic synthesis[1] because it can improve the reaction yield by using an excessive reagent and the used reagent can easily be removed by washing. The solid supports used for solid-phase synthesis are usually polymer resins such as polystyrene. Electrochemistry is at the interface of solution and solid-phase chemistry, as reactions occur in the diffusion layer formed at an electrode surface.[2] The possibility of using electrochemistry in solid-phase synthesis has recently been reported.[3,4] Pilard et al. demonstrated solid-phase chemistry with a modified electrode prepared by electrochemical polymerization of substrate precursors containing a thiophene side chain.[3] Pickett and co-workers developed polypyrrole-supported solid-phase chemistry on an electrode surface.[4] More recently, Kwon and Mrksich reported a study that used as a model reaction the cycloaddition of cyclopentadiene with a self-assembled monolayer (SAM) on an electrode surface by hydroquinone-terminated alkanethiol.[5] However, they used a platinum (Pt) or a gold (Au) electrode as a solid support. Here we report the first efficient, solid-phase chemistry with a graphite felt (GF) electrode as a solid support.

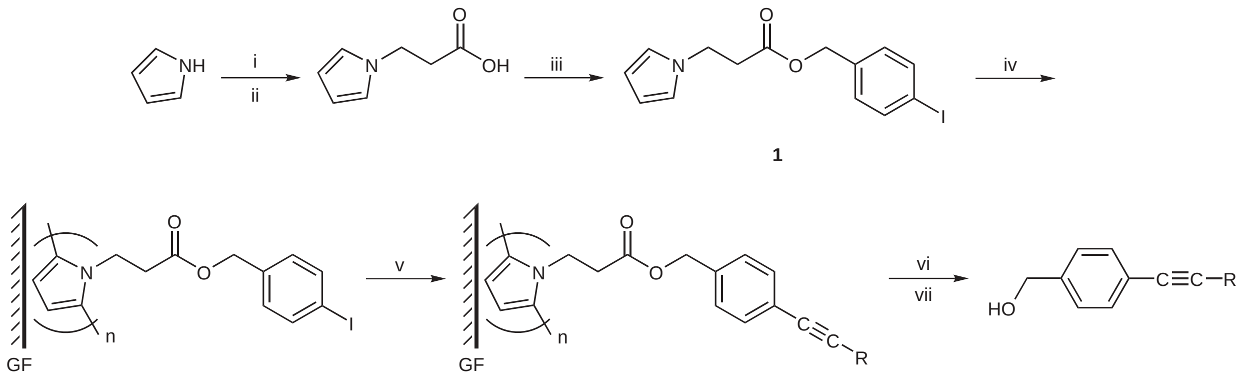
The Sonogashira reaction[6] is a very useful process for preparing disubstituted acetylenes that commonly exist in organic compounds. The reaction involves palladium-catalyzed carbon-carbon bond formation between an aryl halide and a terminal acetylene. The Sonogashira reaction is generally very mild, and does not require strict anhydrous or inert atmosphere conditions, which makes it easily amenable to automation. Intrigued by the potential use of Sonogashira reaction in combinational chemistry, we investigated the Sonogashira reaction on a GF electrode as a solid support.

A GF electrode has a much lager surface area (0.7 m^2/g) in comparison with polystylene resin, the Pt and Au electrodes are commercially available at low price. We were intrigued by the possibility of using electrochemistry to generate a polymer film support on a GF electrode surface with the substrate site attached to the polymer chain. Thus, we prepared a substrate-modified GF electrode by electrochemical polymerization of substrate precursors containing a pyrrole side chain and used for palladium (Pd) catalyst reactions, which are widely researched using polystyrene resin.[7]

The preparation of substrate-modified GF electrodes for Sonogashira reaction as one of the Pd catalyst reactions is shown in Scheme 1. The substrate precursors containing a pyrrole side chain were synthesized from 3-(pyrrol-1-yl)propionic acid[8] and 4-iodobenzyl alcohol. This pyrrole-based monomer **1** was modified on a GF electrode by electrochemical polymerization[9] at repeated cyclic voltammetric scans between 0 and +1.5 V vs Ag/AgCl.[10] The amount of substrate on the GF electrode surface was determined by the amount of recovered 4-iodobenzyl alcohol that was yielded by the treatment of iodobenzene-modified GF electrode with $NaOCH_3$. The relationship between the amount of substrate and the number of repeated cyclic voltammetric scannings is shown Figure 1. The amount of substrate on the GF electrode surface increased with the increasing number of repeated cyclic voltammetric scannings. The loading of substrate on the GF electrode of 20-times scanning was ca. 80 μmol/g. The surface of this modified electrode was stable even if it leaves it for several months.

Preparative Sonogashira reaction was performed on the iodobenzene-modified GF electrode ($3.0 \times 1.0 \times 0.5$ cm) in DMF (10 mL) containing Et_3N (10 mmol), terminal acetylene (5 mmol), $Pd(PPh_3)_4$ (0.25 mmol) and CuI (0.5 mmol, Scheme 1).[11] The result using 1-octyne as terminal acetylene is shown in Figure 2. The coupling product yield was 90% when the substrate-modified GF electrode of 5-times scanning (loading 15 $\mu molg^{-1}$) was used. In addition, the homogeneous Sonogashira reaction using **1** and 1-octyne was carried out with lower yield (30%) than the solid-phase system using the substrate-modified GF electrode. We also tried under standard polymerization and reaction conditions on a Pt plate electrode instead of a GF electrode, however, the generated polymer film was not

SYNLETT 2004, No. 14, pp 2513–2516
Advanced online publication: 20.10.2004
DOI: 10.1055/s-2004-834835; Art ID: U22504ST



Scheme 1 *Reagents and conditions*: i, Acrylonitrile (1.0 equiv), *n*-Bu_4NOH (0.1 equiv), –78 °C: ii, KOH, H_2O, Δ; iii, 4-iodobenzyl alcohol (1.0 equiv), 4-dimethylaminopyridine (5 mol%), DCC (1.5 equiv), CH_2Cl_2, 0 °C; iv, electrochemical polymerization; v, terminal acetylene (5 mmol), Et_3N (10 mmol), $Pd(PPh_3)_4$ (0.1 mmol), CuI (0.2 mmol), DMF; vi, THF, $NaOCH_3$; vii, HCl.

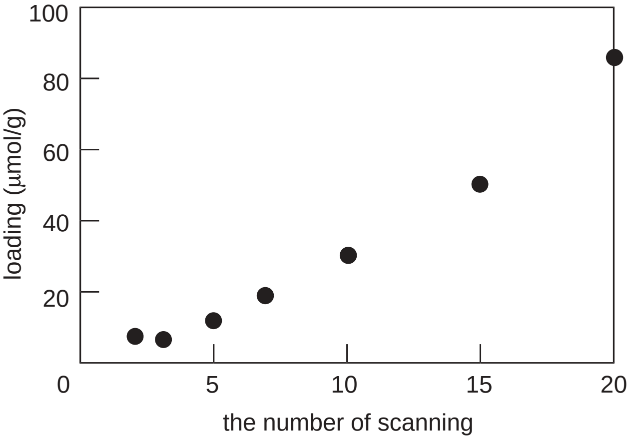


Figure 1

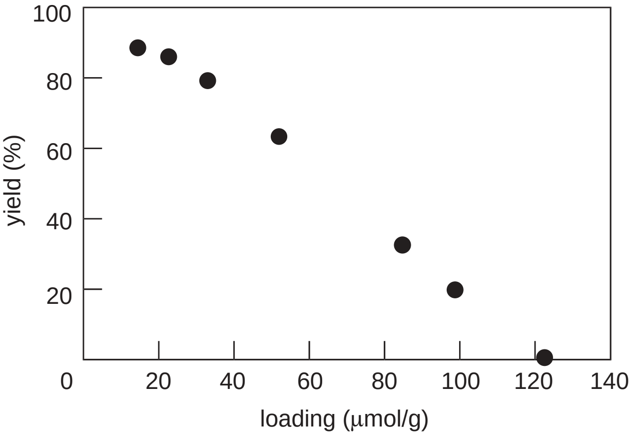


Figure 2

strongly attached to the Pt electrode surface and solid-phase synthesis could not be used. The coupling product yield decreased with the increasing immobilized substrate on the GF electrode surface. This observation suggests that a thick polymer film was formed on the GF electrode surface with the increasing repeated cyclic voltammetric scanning and did not infiltrate the terminal acetylene and catalyst into a polymer layer.

The results from the Sonogashira reaction of various terminal acetylenes using the iodobenzene-modified GF electrode of 5-times scanning are shown in Table 1. The reaction with acetylenic hydrocarbons was obtained to the corresponding coupling products in high yield (entries 1, 2, and 4). Couplings between acetylenic alcohols and the substrate-modified GF electrode also proceeded smoothly (entries 5 and 6). All terminal acetylenes were converted to the corresponding coupling products in adequate yield (72–94%).

Table 1 Results from the Sonogashira Reaction of Various Terminal Acetyles Using the Iodobenzene-Modified GF Electrode of 5-Times Scanning

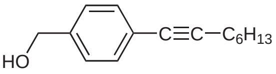
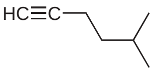
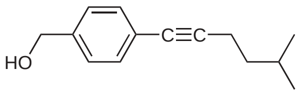
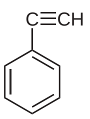
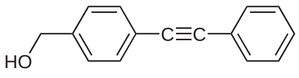
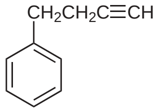
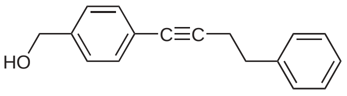
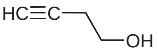
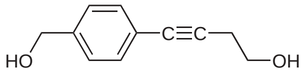
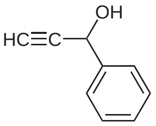
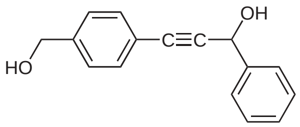
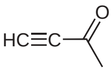
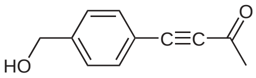
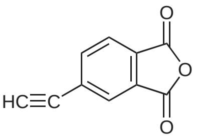
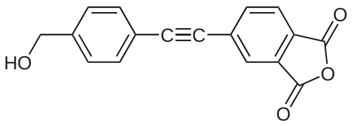
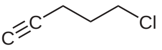
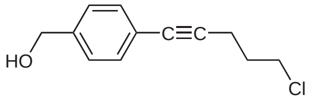
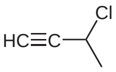
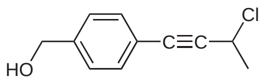
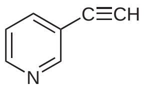
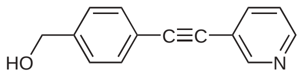
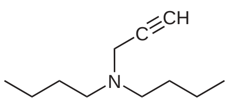
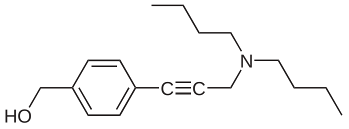
Entry	Substrate	Product	Yield (%)
1	$HC\equiv C-C_6H_{13}$		90
2			86
3			94

Table 1 Results from the Sonogashira Reaction of Various Terminal Acetyles Using the Iodobenzene-Modified GF Electrode of 5-Times Scanning (continued)

Entry	Substrate	Product	Yield (%)
4			88
5			82
6			85
7			80
8			84
9			75
10			72
11			92
12			78

We also attempted the use of a pyrrole-based monomer **2** possessing terminal acetylene instead of iodobenzene. The substrate precursors containing a pyrrole side chain were synthesized from 3-(pyrrol-1-yl)propionic acid and 1-butyne-3-ol. The preparation of the terminal acetylene-modified GF electrode for Sonogashira reaction is shown in Scheme 2. The same tendency is shown as when using the iodobenzene-modified GF electrode for the amount of terminal acetylene on the GF electrode surface by repeated cyclic voltammetric scans. The results from the Sonogashira reaction of various aromatic iodides using the terminal acetylene-modified GF electrode of 5-times scanning are shown in Table 2. All aromatic iodides were converted to the corresponding coupling products in adequate yield (73–95%).

In conclusion, we have reported here the first efficient, immobilization of substrate on a GF electrode by electrochemical polymerization of substrate precursors containing a pyrrole side chain and use for solid-phase synthesis in place of a polystyrene resin. Couplings between terminal acetylenes and the iodobenzene-modified GF electrode or aromatic iodides and the terminal acetylene-modified GF electrode in the presence of a Pd catalyst proceeded smoothly in satisfactory yields. We are now exploring Heck reactions of the iodobenzene-modified GF electrode with olefins.

Acknowledgment

This work was supported in part by Grants-in-Aid (No. 15590035) from Japan Society for the Promotion of Science. The Sumitomo Foundation and the Takeda Science Foundation are also acknowledged for financial support.

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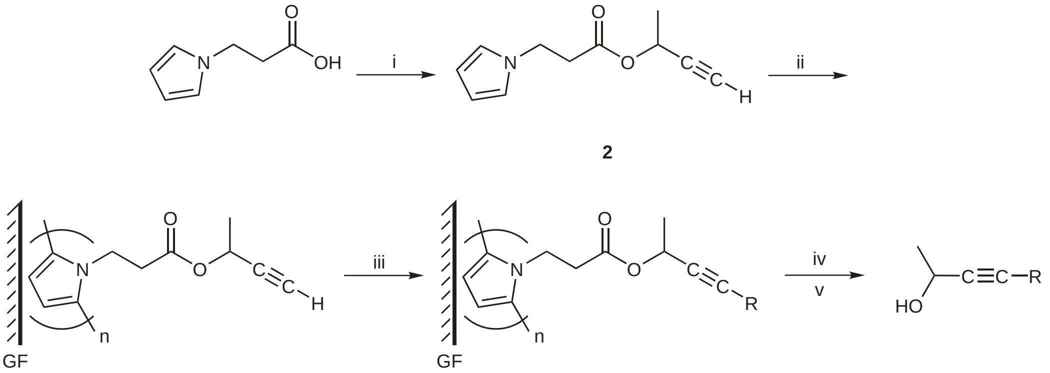
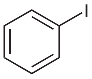
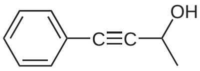
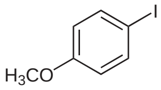
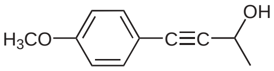
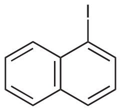
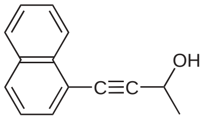
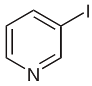
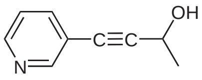
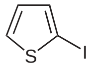
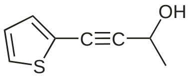


2

Scheme 2 *Reagents and conditions*: i, 1-Butyn-3-ol (1.0 equiv), 4-dimethylaminopyridine (5 mol%), DCC (1.5 equiv), CH_2Cl_2, 0 °C, ii, electrochemical polymerization; iii, iodide compound (5 mmol), Et_3N (10 mmol), $Pd(PPh_3)_4$ (0.1 mmol), CuI (0.2 mmol), DMF; iv, THF, $NaOCH_3$; v, HCl.

Table 2 Results from the Sonogashira Reaction of Various Aromatic Iodides Using the Terminal Acetylene-Modified GF Electrode of 5-Times Scanning

Entry	Substrate	Product	Yield (%)
1			92
2			90
3			73
4			95
5			85

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(10) **General Procedure for Electrochemical Polymerization.** Electrochemical polymerization was performed in a one-compartment cell with graphite felt (3.0 × 1.0 × 0.5 cm) as the working electrode and a platinum wire as the counter electrode, respectively. An Ag/AgCl electrode was used as the reference electrode. All electrochemical polymerization experiments were performed in MeCN solution with 0.01 M monomer concentration and 0.1 M tetraethylammonium perchlorate as the supporting electrolyte. Repeated cyclic voltammetric scans between 0 and +1.5 V at 50 mV/s led to the formation of a conducting polymer film at the GF electrode.

(11) **General Procedure for Sonogashira Reaction on the Iodobenzene-Modified GF Electrode.**
The iodobenzene-modified GF electrode (3.0 × 1.0 × 0.5 cm) was added to the dry DMF solution (10 mL) containing Et_3N (10 mmol), terminal acetylene (5 mmol), $Pd(PPh_3)_4$ (0.25 mmol) and CuI (0.5 mmol). The reaction mixture was stirred for 12 h at r.t. At the end of the reaction, the GF electrode was separated, and washed three times with THF. Then, this GF electrode was added to THF (10 mL) and 28% NaOMe in MeOH (5 mL). The reaction mixture was stirred for 1 h at r.t. At the end of the reaction, this reaction mixture was added to H_2O (10 mL) and 3 N HCl (10 mL), extracted three times with EtOAc (10 mL × 3), and filtered in vacuo. This extracted solution was evaporated, and the product was identified by ^1H NMR spectroscopy.