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# Reaction of 2-propargylphenylcarbamates with diphenyliodonium salts via Meyer-Schuster rearrangement

Hideki Minami [a], Noriko Okamoto [a], Takuya Sueda [a], Takatsugu Sakaguchi [a], Minoru Ishikura [b], Reiko Yanada [a,*]

[a] Faculty of Pharmaceutical Sciences, Hiroshima International University, 5-1-1 Hirokoshingai, Kure, Hiroshima 737-0112, Japan
[b] School of Pharmaceutical Sciences, Health Sciences University of Hokkaido, Ishikari-Tobetsu, Hokkaido 061-0293, Japan

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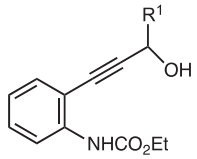
ABSTRACT

The syntheses of 2,3-dihydro-4-quinolones from 2-propargylphenylcarbamates by one-pot tandem process that involves Meyer-Schuster rearrangement or arylative Meyer-Schuster rearrangement/Michael addition of carbamate nitrogen to the resulting vinyl ketones have been developed. Phenylcarbamates tethering tertiary propargyl alcohols underwent arylative Meyer-Schuster rearrangement/Friedel-Crafts alkylation to produce 2,3-dihydroindenones.

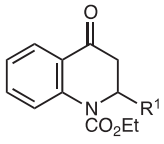


4-Quinolones are known to have various bioactivities including antiviral activities,[1] antitumor activities[2] and HIV-1 integrase inhibitory activities.[3] The fluoroquinolones Norfloxacin and Levofloxacin are used clinically as antibacterial drugs.[4] Attractive pharmacological properties of 2,3-dihydro-4-quinolones have recently been reported (Fig. 1).[5] As part of our continued interest in the syntheses of biologically interesting heterocyclic compounds, we have reported one-pot syntheses of 4-quinolones from 2-alkynylbenzamides[6] and from propargyl alcohol derivatives.[7] Recently, we have also been interested in hypervalent iodine reagents and have reported tandem arylation with diaryliodonium salts/cyclization reaction of 2-alkynylphenyl derivatives.[8] Here we report the novel selective syntheses of 2,3-dihydro-4-quinolones (**2** and **4**) and 2,3-dihydroindenones (**5**) from 2-propargylphenylcarbamates **1** using diphenyliodonium salts under different conditions (Scheme 1).

First, we tried reaction of propargyl alcohol derivatives **1a** with a catalytic amount of $Ph_2IOTf$ (*Route A*). After several trials and errors, we found that the reaction of compound **1a** with 0.1 mol equivalent of $Ph_2IOTf$ in 1,2-dichloroethane (DCE) at 80 °C for 24 h gave the cyclization product 2,3-dihydro-4-quinolone **2a** in 73% yield. Probably, trifluoromethanesulfonic acid was produced from $Ph_2IOTf$ during the reaction and it might have sufficient acidity for tandem Meyer-Schuster rearrangement/ nucleophilic addition of carbamate nitrogen to the resulting vinyl ketone. Substrate **1b** also gave the expected cyclized product **2b** in 75% yield under the same reaction conditions.




**1a**: $R^1$ = H, **1b**: $R^1$ = $^i$Bu




**2a**: $R^1$ = H, **2b**: $R^1$ = $^i$Bu

Copper-catalyzed arylative Meyer-Schuster rearrangement of propargyl alcohols has already been reported by M.J. Gaunt et al.[9] We also focused on arylative Meyer-Schuster rearrangement of 2-propargylphenyl carbamate **1** with $Ph_2IOTf$ (*Route B*). The best result was obtained when $Ph_2IOTf$ (1.2 equiv) was used in combination with 2,6-di-*tert*-butylpyridine (DTBP) (1.2 equiv) and CuCl (0.1 equiv) in DCE at 80 °C (Table 1, entry 1). The yield of **3a** was decreased when CuCl was replaced with CuBr or CuI (entries 2 and 3). The yield of **3a** was not improved by increasing the amounts of $Ph_2IOTf$ and DTBP or by lowering the reaction temperature (entries 4 and 5). Diphenyliodonium salt with $^-$OTf showed

* Corresponding author.
*E-mail address:* ryanada@ps.hirokoku-u.ac.jp (R. Yanada).

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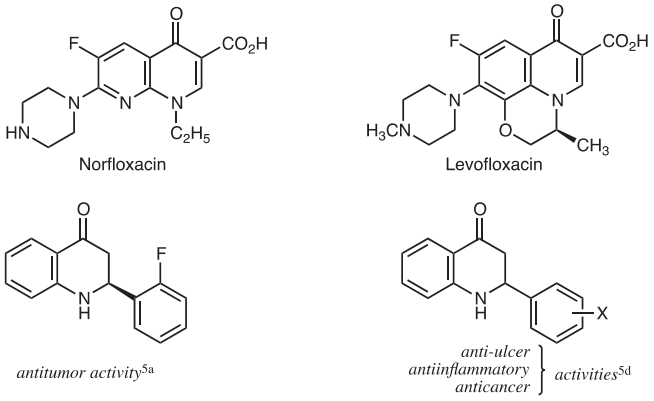
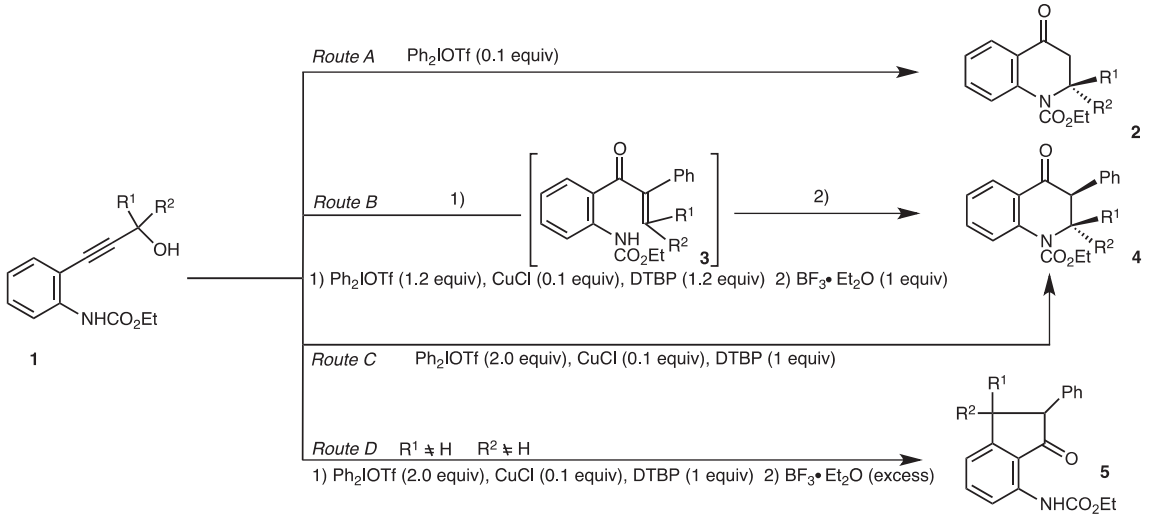



**Fig. 1.** Bioactive 4-quinolones.

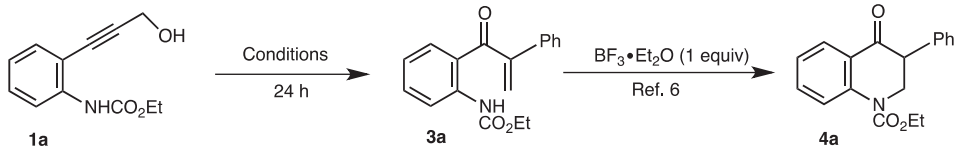
much better activity than that of the other anions $^{-}BF_4$ and $^{-}PF_6$ (entries 1, 6 and 7). The yield was not improved by switching to another solvent such as AcOEt or dioxane (entries 8 and 9). In the absence of DTBP or a copper catalyst, the yields of **3a** were low (entries 10 and 11). These blank tests indicate that DTBP and a copper catalyst are essential for the arylative Meyer-Schuster rearrangement. We previously reported intramolecular aminocyclization of carbamate nitrogen to the α,β-unsaturated ketones by $BF_3{\cdot}Et_2O$.[6] We then tried reaction of compound **3a** with 1 equiv of $BF_3{\cdot}Et_2O$ in DCE at 80 °C for 22 h. As expected, 3-phenyl-3,4-dihydroquinolone **4a** was obtained in 83% yield.

In our continuing efforts toward tandem arylative Meyer-Schuster rearrangement/nucleophilic addition of carbamate nitrogen to the resulting vinyl ketone, we found a method for one-step synthesis of compound **4** (*Route C*). With only the use of $Ph_2IOTf$ (2 equiv), CuCl (0.1 equiv), and DTBP (1 equiv) in DCE at 80 °C for




**Scheme 1.** Selective syntheses of 4-quinolones and indenones.

**Table 1**
Optimization of Cu-catalyzed arylative Meyer-Schuster rearrangement and Michael cyclization.




| Entry | Catalyst (0.1 equiv) | $Ph_2IX$ (equiv) | Solvent | DTBP (equiv) | Temp (°C) | Yield of **3a** (%) |
|---|---|---|---|---|---|---|
| 1 | CuCl | 1.2 (X = OTf) | DCE | 1.2 | 80 | 78 |
| 2 | CuBr | 1.2 (X = OTf) | DCE | 1.2 | 80 | 60 |
| 3 | CuI | 1.2 (X = OTf) | DCE | 1.2 | 80 | 48 |
| 4 | CuCl | 3.6 (X = OTf) | DCE | 3.6 | 80 | 65 |
| 5 | CuCl | 1.2 (X = OTf) | DCE | 1.2 | 50 | 63 |
| 6 | CuCl | 1.2 (X = $BF_4$) | DCE | 1.2 | 80 | 48 |
| 7 | CuCl | 1.2 (X = $PF_6$) | DCE | 1.2 | 80 | 31 |
| 8 | CuCl | 1.2 (X = OTf) | AcOEt | 1.2 | 80 | 25 |
| 9 | CuCl | 1.2 (X = OTf) | Dioxane | 1.2 | 80 | 25 |
| 10 | CuCl | 1.2 (X = OTf) | DCE | None | 80 | 41[a] |
| 11 | None | 1.2 (X = OTf) | DCE | 1.2 | 80 | 0[b] |

[a] Compound **2a** was obtained in 23% yield.
[b] Starting material **1a** was recovered in 85% yield.