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Short Note

5-(*tert*-Butyldimethylsilyloxy)-1-(2-chloro-5,8-dimethoxyquinolin-3-yl)-3-methylenepentan-1-ol

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Abstract: Novel 5-(*tert*-butyldimethylsilyloxy)-1-(2-chloro-5,8-dimethoxyquinolin-3-yl)-3-methylenepentan-1-ol (**7**) was prepared via allylation of 2-chloro-5,8-dimethoxyquinoline-3-carbaldehyde (**6**) with functionalized allylic iodide as *tert*-butyl-(3-(iodomethyl)but-3-enyloxy)dimethylsilane (**5**), in the presence of metallic indium in anhydrous DMF as solvent at ambient temperature. The structure of the synthesized compound was assigned on the basis of elemental analysis and spectral data.

Keywords: functionalized allylic iodide; allylation; indium; quinoline derivatives

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Introduction

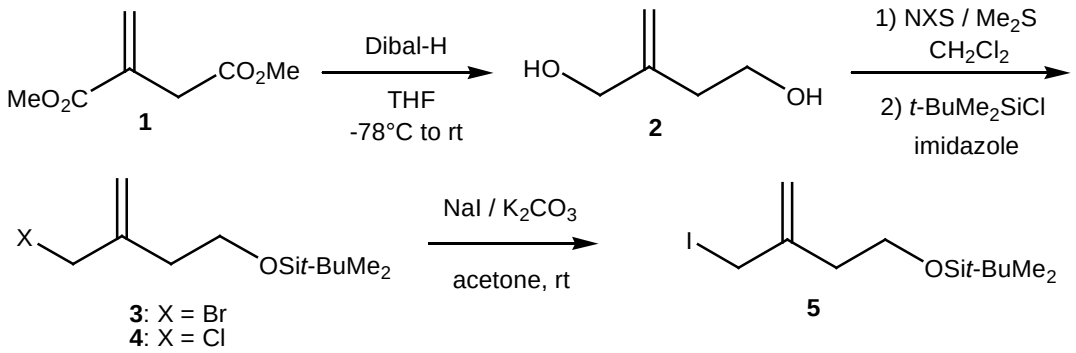
Quinoline and its derivatives form an important class of organic compounds due to their structural chemistry and biological activities as antifungal [1,2], antibacterial [2–7], antiviral [3,8–12], and anticancer [9,13–16] properties. Compounds possessing the quinoline moiety exhibit significant activity against several diseases such as malaria [17], and cardiovascular pathologies [18,19]. In continuation to develop synthesis of compounds possessing biological activities, we report in this paper the synthesis of homoallylic alcohol **7** by allylation [20] of 2-chloro-5,8-dimethoxyquinoline-3-carbaldehyde (**6**) with functionalized allylic iodide **5** using metallic indium. The synthesized homoallylic alcohol **7** is an intermediate for the synthesis of heterocyclic compounds. Tetrahydrofurans and tetrahydropyrans are important moieties of natural biologically active compounds such as antibiotics (Monensine, Lasalocide A) and antimicrobial (Milbemycine,

Avermectines). It was also found that spiroacetals obtained by allylation of cycloalkanones, are contained in many natural compounds produced by insects having pheromonal activity.

Result and Discussion

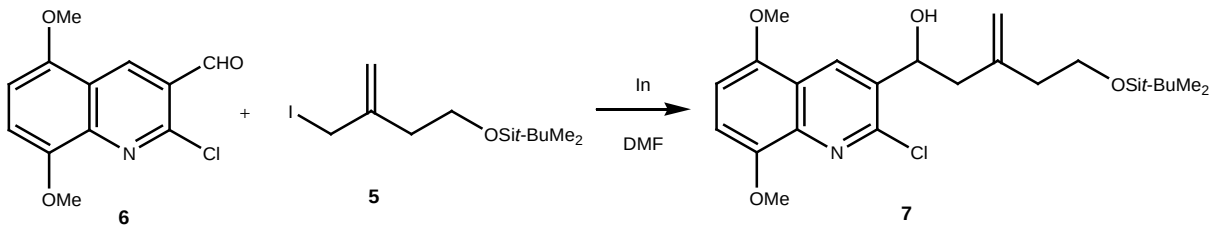
We have synthesized the allylic iodide **5** according to a known method [21] (scheme 1), in three steps starting from dimethyl itaconate (**1**). The iodide was prepared in small quantities because it was unstable and was stored in darkness.

Scheme 1. Synthesis of allylic iodide **5**.



We first studied the addition of allylic bromide **3** with aldehyde **6** in the presence of metallic indium in different solvents. Compared to acetonitrile, methanol and dichloromethane, DMF was found to be a good solvent. Allylic iodide **5** and bromide **3** were equally reactive. However, the reactivity of allylic chloride **4** was markedly diminished.

Scheme 2. Synthesis of 5-(*tert*-butyldimethylsilyloxy)-1-(2-chloro-5,8-dimethoxyquinolin-3-yl)-3-methylenepentan-1-ol (**7**).



Experimental

All reactions were carried out under nitrogen atmosphere. DMF was dried on BaO and distilled under reduced pressure and stored on molecular sieves 4Å. Progress of the reactions and purity of the compounds were monitored by thin layer chromatography (TLC) using ethyl acetate/*n*-hexane as eluting system on silica gel (60–120 mesh), UV apparatus and anisaldehyde solution as visualizing agents.

^{1}H (400 MHz) and ^{13}C (100 MHz) spectra were recorded on a Bruker FT-ARX 400 spectrometer in $CDCl_3$ using TMS as internal standard. The IR spectra were recorded on a Nicolet 205 FT spectrometer as KBr pellets. Elemental analysis was performed by the regional center of analysis of Rennes, CRMPO (Centre régional de mesures physiques de l'Ouest), Rennes, France.

To a suspension of indium powder (345 mg, 3 mmol) in dry DMF (3 mL) was added allylic iodide **5** (977.7 mg, 3 mmol) in DMF (1 mL) and 2-chloro-5,8-dimethoxyquinoline-3-carbaldehyde (**6**) (503.0 mg, 2 mmol) in DMF (1 mL). An exothermic reaction occurred immediately, the mixture was stirred at room temperature for 1 h and the mixture was quenched by addition of diluted hydrochloric acid. The product was extracted with ether and purified by column chromatography on silica gel (petroleum ether/ethyl acetate 50:50) to afford homoallylic alcohol **7** as yellow oil.

Yield: 0.76 g (84%).

IR (KBr, cm^{-1}) ν 3415 (OH), 1647 (C=C).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H, H-C_4), 7.04 (d, 1H, *J* = 8.6 Hz, H-C_7), 6.83 (d, 1H, *J* = 8.6 Hz, H-C_6), 5.27 (ddd, 1H, *J* = 9.9, 2.4, 2.3 Hz, C$\underline{H}$OH), 5.10 (m, 1H, C=C$\underline{H}_2$), 5.08 (broad ddd, 1H, *J* = 1.8, 1.6, 1.2 Hz, C=C$\underline{H}_2$), 4.03 (s, 3H, OC$\underline{H}_3$), 3.98 (s, 3H, OC$\underline{H}_3$), 3.94–3.83 (m, 2H, C$\underline{H}_2$OSi), 3.39 (d, 1H, *J* = 2.4 Hz, O$\underline{H}$), 2.86 (ddd, 1H, *J* = 14.0, 2.4, 1.4 Hz, C$\underline{H}_2$CHOH), 2.44 (pseudo broad tt, 2H, *J* = 6.4, 1.0 Hz, C$\underline{H}_2$CH$_2$OSi), 2.20 (ddd, 1H, *J* = 14.0, 9.9, 0.5 Hz, C$\underline{H}_2$CHOH), 0.92 (s, 9H, *t*-Bu), 0.10 (s, 6H, Si(C$\underline{H}_3$)$_2$).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.81 (C_{quat}, C_8), 148.40 (C_{quat}, C_5), 146.86 (C_{quat}, C_{8a}), 143.59 (C_{quat}, $\underline{C}$=CH$_2$), 142.52 (C_{quat}, C_2), 135.87 (C_{quat}, C_3), 135.65 ($\underline{C}$H, C_4), 130.0 ($\underline{C}$H, C_7), 127.57 (C_{quat}, C_{4a}), 127.06 ($\underline{C}$H, C_6), 115.89 (C=$\underline{C}$H$_2$), 68.71 ($\underline{C}$HOH), 62.44 ($\underline{C}$H$_2$OSi), 56.24 (O$\underline{C}$H$_3$), 55.98 (O$\underline{C}$H$_3$), 45.65 ($\underline{C}$H$_2$CHOH), 38.58 ($\underline{C}$H$_2$CH$_2$OSi), 25.96 (3C, C($\underline{C}$H$_3$)$_3$), 18.42 (C_{quat}, $\underline{C}$(CH$_3$)$_3$), −5.29 (Si-$\underline{C}$H$_3$), −5.33 (Si-$\underline{C}$H$_3$).

Elemental analysis: Calculated for $C_{23}H_{34}ClNO_4Si$: C, 61.13%; H, 7.53%; O, 14.17%; found: C, 61.05%; H, 7.47%; O, 14.08.

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