

# CHEMISTRY & BIOLOGY INTERFACE

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## Magnesium Oxide Nanoparticles Facilitates One Pot Wittig Reaction for the Synthesis of Ethyl (2E)-3-(2-chloroquinolin-3-yl)prop-2-enoate Derivatives

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**Abstract:** Synthesized variously substituted ethyl (2E)-3-(2-chloroquinolin-3-yl)prop-2-enoate (3a-e) from 2-chloroquinolin-3-carbaldehyde using magnesium oxide nanoparticles (MgO-NPs) by Wittig reaction. Recovery, reuse and smaller quantity of the catalyst facilitates the reaction good yield about (90-95%) with E-stereoselectivity. This milder and traditional reaction conditions are suitable in getting desired product even labile groups present in the reagents. This methodology can be used for large scale with minimal product purification. Recovery and recyclability of the catalyst is easy, without a significant decrease in activity.

**Keywords:** Wittig reaction, magnesium oxide nanoparticles and quinolines.

### Introduction:

Method development for the stereoselective carbon-carbon double bond formation represents challenges in organic synthesis [1]. The synthesized compounds may be used as intermediates for the synthesis of biologically active entities [2-5]. The Wittig reaction is one of the most important method for carbon-carbon double bond formation using carbonyl compounds [6]. In general, the Wittig reaction is performed in three steps viz. phosphonium salt formation, followed by base treatment to give

an ylide, and subsequent reaction with carbonyl compounds to give olefin products [7]. Such reactions are time consuming and expensive due to work up and product isolation from each step.

Attention fetched by 2-chloroquinolin-3-carbaldehydes and its derivatives due to biological activities [8, 9] viz. antimicrobial, anti-inflammatory, antimalarial and antiviral.

In the recent, the use of nanoparticles for the synthesis of organic compounds are getting

increased. Kanade et.al [10] have synthesized MgO-NPs and used for Wittig reaction by providing single example bezaldehyde. Also Choudary et.al. [11] have used NAP-magnesium oxide for one pot Wittig reaction on aldehydes. Similarly Wittig reaction on 2-chloroquinolin-3-carbaldehyde was reported in two steps using organic bases [12, 13]. Unmet needs are multiple examples, one pot reaction conditions, good yielding and reusable catalyst. In continuation of our research work for greener, simpler approaches [14] and on 2-chloroquinolin-3-carbaldehydes [15, 16] herein we report the one-pot synthesis of substituted ethyl (2*E*)-3-(2-chloroquinolin-3-yl)prop-2-enoate (**3a-e**) in good yields by the reaction of 2-chloroquinolin-3-carbaldehyde with ethyl  $\alpha$ -bromoacetate in presence of triphenylphosphine (TPP) and MgO-NPs.

### Experimental:

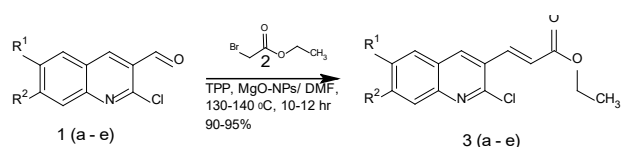
<sup>1</sup>HNMR spectra were recorded on BRUKER spectrometers at 500MHz. Melting points were determined in open capillary tubes and are uncorrected. Thin layer chromatography (TLC) was carried on Merck silica gel plates. All chemicals and solvents used were of laboratory grade. Purity and progress of reaction were monitored on TLC. Products were purified by recrystallization and column chromatography wherever necessary. MgO-NPs are synthesized as per the procedure given in the literature [10].

### Typical experimental procedure:

To a pre-stirred (1hr) solution of TPP (0.19gm, 0.726mmol) and ethyl  $\alpha$ -bromoacetate (0.10ml, 0.968mmol) in DMF (5ml), MgO-NPs (0.04gm) was added at room temperature and stirred for 20 minutes. Then, 2-chloro-6-methylquinolin-3-carbaldehyde (0.1gm, 0.487mmol) was added and heated the reaction mixture at 130 °C- 140 °C for 10 hr. After completion of the reaction (TLC check, ethyl acetate: hexane 0.5:9.5,

V/V), the reaction mixture was allowed to cool. Water was added and extraction was done with ethyl acetate (3 X 5ml). The combined organic layer was washed with brine solution (10ml) and dried over anhydrous sodium sulphate (1g). Filtered and solvent was removed under vacuum on rotary evaporator. Obtained pale yellow crude product was purified by column chromatography eluting ethyl acetate (0-2%) in hexane to afford yellowish solid of ethyl (2*E*)-3-(2-chloro-6-methylquinolin-3-yl)prop-2-enoate (0.127g, 95%).

### Scheme:



### Result and discussion:

Present strategy is for the synthesis of substituted ethyl (2*E*)-3-(2-chloroquinolin-3-yl)prop-2-enoate starting from 2-chloroquinolin-3-carbaldehyde by Wittig reaction. The reusable and suitably aligned MgO-NPs catalyzed Wittig reaction afforded desired products with *E* selectivity. To have easiest alternative approach different solvents like benzene, toluene, tetrahydrofuran (THF) and N, N-Dimethylformamide (DMF) had been used (Table 1). DMF furnished expected results therefore selected as a solvent for all reactions. MgO-NPs was added to the suspension obtained from ethyl  $\alpha$ -bromoacetate and TPP in DMF. Resultant homogeneous mixture obtained after addition of substituted 2-chloroquinolin-3-carbaldehyde to the above was heated at 130 °C- 140 °C. After completion of the reaction (10-12hr), the reaction mixture was worked up. Obtained crude compounds were purified by either recrystallization or column chromatography to afford titled compounds. Catalyst was separated and recovered during compound recrystallization process. Recovered

catalyst was recycled after several water washings and dryings. Similar procedure was followed for the preparation of remaining compounds, catalyst recyclability check and its results are tabulated in (Table 1 & 2).

### Conclusion:

Milder, cost effective and easily accessible approaches have been developed for the syntheses of 6 or 7 substituted ethyl (2*E*)-3-(2-chloroquinolin-3-yl)prop-2-enoate by one pot Wittig reaction using MgO-NPs as a reusable catalyst. Reactions were performed to afford excellent yield of the products having minimum work up and less isolation efforts. The recycling ability of the catalyst also checked and found consistence in results for 3 times.

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**Table 1:** Wittig reaction between 2-chloro-6-methylquinolin-3-carbaldehyde (**1a**) and ethyl  $\alpha$ -bromoacetate/ TPP in various solvents.

Entry	Solvents	Reaction time (hr)	Yield <i>E</i> (%)
I	Benzene	10	45
II	Toluene	10	53
III	THF	10	67
IV	<b>DMF</b>	<b>10</b>	<b>95/ 92<sup>a</sup>/ 90<sup>b</sup></b>

<sup>a, b</sup> Yield obtained by the first and second recycle of the catalyst.

**Table 2:** One pot synthesis of substituted ethyl (2*E*)-3-(2-chloroquinolin-3-yl)prop-2-enoate from substituted 2-chloroquinolin-3-carbaldehyde

Product No.	Substituents		Reaction time (hr)	Melting point (°C)	Yield (%)	<i>E</i> : <i>Z</i>	<sup>1</sup> H NMR (500 MHz, CDCl <sub>3</sub> ) $\delta$ ppm( <i>E</i> )
	R <sub>1</sub>	R <sub>2</sub>					
3a	CH <sub>3</sub>	H	10	120	95	91:09	1.38 (t, 3H, <i>J</i> =7Hz), 2.55 (s, 3H), 4.32 (q, 2H, <i>J</i> =7Hz), 6.55 (d, 1H, <i>J</i> =16Hz), 7.55-7.56 (m, 2H), 7.89 (s, 1H), 8.11 (d, 1H, <i>J</i> =16Hz), 8.28 (s, 1H).
3b	H	CH <sub>3</sub>	10	98	95	93:07	1.37 (t, 3H, <i>J</i> =7Hz), 2.57 (s, 3H), 4.31 (q, 2H, <i>J</i> =7Hz), 6.55 (d, 1H, <i>J</i> =16Hz), 7.41-7.43 (m, 1H), 7.73-7.79 (m, 2H), 8.12 (d, 1H, <i>J</i> =16Hz), 8.33 (s, 1H).
3c	OCH <sub>3</sub>	H	10	122	92	85:15	1.38 (t, 3H, <i>J</i> =7Hz), 3.95 (s, 3H), 4.31 (q, 2H, <i>J</i> =7Hz), 6.55 (d, 1H, <i>J</i> =16Hz), 7.42 (m, 1H), 7.73-7.80 (m, 2H), 8.12 (d, 1H, <i>J</i> =16Hz), 8.33 (s, 1H).
3d	H	H	11	102	93	92:08	1.38 (t, 3H, <i>J</i> =7Hz), 4.31 (q, 2H, <i>J</i> =7Hz), 6.57 (d, 1H, <i>J</i> =16Hz), 7.58-7.61 (m, 1H), 7.75-7.77 (m, 1H), 7.78-7.79 (m, 1H), 8.02-8.03 (m, 1H), 8.13 (d, 1H, <i>J</i> =16Hz), 8.39 (s, 1H).
3e	H	OCH <sub>3</sub>	12	112	94	90:10	NA

NA- Not analyzed

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