

# The use of isoprene as a dienophile in stereo- regioselective synthesis of new isoindolo[2,1-a]quinolin-11(5*H*)-ones via PMA-catalyzed three component Povarov reaction

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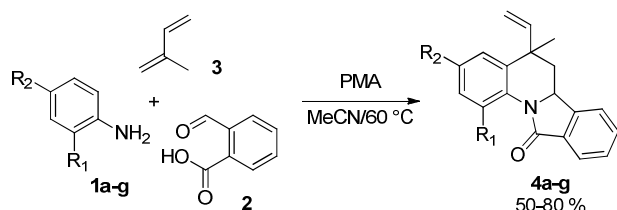
**Keywords:** isoprene, multicomponent Povarov reaction, isoindolo[2,1-a]quinolin-11(5*H*)-ones, PMA catalyst

## INTRODUCTION

The research about of the isoprene system (2-methyl-1,3-butadiene) have effects in some relevant scientific areas as environmental,<sup>1</sup> phytochemical,<sup>2</sup> polymers,<sup>3</sup> etc. However, their more interesting synthetic applications consist in the construction of new molecular models with the isoprenyl moiety, because many natural and synthetic isoprene-based products are widely used in the pharmaceutical, cosmetic, and alimentary industry due to its biochemical features. This molecule represents an important precursor in the Diels-Alder reaction, generally used as an active diene in the synthesis of carbocyclic adducts and some rare heterocyclic compounds.<sup>4</sup> In our research we used this molecule as an electron-rich dienophile<sup>5</sup> in the little explored Povarov reaction, catalyzed by phosphomolybdic acid (PMA) in MeCN to obtain the new 5-methyl-5-vinyl-isoindolo[2,1-a]quinolin-11(5*H*)-ones.

## RESULTS AND DISCUSSION

Initially, we studied the better conditions for the synthesis of aza-polycyclic compounds. Some Lewis acid, BF<sub>3</sub>·OEt<sub>2</sub>, InCl<sub>3</sub>, AlCl<sub>3</sub>, ZnCl<sub>2</sub> and Brønsted acid Ph(COOH)<sub>2</sub>, SiO<sub>2</sub>-SO<sub>3</sub>H (SSA) and PMA, were used in different solvents. The better system was the PMA/MeCN to 60 °C (Scheme 1).



**Scheme 1.** Synthesis of 5-methyl-5-vinyl-isoindolo[2,1-a]quinolin-11(5*H*)-ones

In some cases large catalyst quantities decreased the reaction yield. On the other hand, the BF<sub>3</sub>·OEt<sub>2</sub> showed similar results than PMA, nevertheless the last one is more easy to handle and less hazardous. Therefore, according to the diversity-oriented synthesis we used different anilines (**1a-g**), 2-carboxybenzaldehyde (**2**) and isoprene (**3**) to obtain

a small molecular library of new aza-polycyclic molecules (**4a-g**) (table 1).

**Table 1.** Physicochemical properties of the 5-methyl-5-vinyl-isoindolo[2,1-a]quinolin-11(5*H*)-ones (**4**)

4	R <sub>1</sub>	R <sub>2</sub>	Yield (%)	mp (°C)	Time (h)
a	H	H	64	210-212	7
b	H	Me	73	190-192	5
c	H	MeO	78	200-202	5
d	H	Et	70	215-216	6
e	NO <sub>2</sub>	H	58	214-215	8
f	H	NO <sub>2</sub>	50	203-205	10
g	H	F	76	217-218	6

The synthesis was carried out in mild reaction conditions. After work up, the reaction crude was purified by recrystallization in ethyl acetate to give isoindolo[2,1-a]quinolin-11(5*H*)-one molecules. The characterization and its stereochemistry were done by GC-MS, <sup>1</sup>H, <sup>13</sup>C NMR, and 2D NMR experiments.

## CONCLUSION

We synthesized a new series of isoindolo[2,1-a]quinolin-11(5*H*)-ones by the one-pot process via Povarov reaction and intramolecular cyclization. The isoprene was used like a new dienophile in this methodology. All compounds were elucidated by instrumental technique that indicated only one regio-isomer (**4**) and the stereoselectivity towards *axial-axial* system.

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