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# THE INTERACTION OF MICHAEL ADDUCTS WITH ETHYLENEDIAMINE AND MALONONITRILE

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**Abstract.** In this work reported some transformation reactions of Michael adducts. By the interaction of Michael adducts obtained on the base of dibenzoylmethane with ethylenediamine the compound (**5**) phenyl(5,7,8a-triphenyl-1,2,3,7,8,8a-hexahydroimidazo[1,2-a]pyridin-6-yl)methanone have been synthesized. 2-Acetyl-5-oxo-N,3,5-triphenylpentanamide, that is Michael adduct interacts with malononitrile at the presence of piperidine and forms compound with bicyclic structure, 3-amino-2,6,8-triphenyl-7,8-dihydroisoquinolin-1(2H)-one (**10**). The one-pot synthesis routes and plausible reaction mechanisms were suggested. Structures of all synthesized compounds confirmed by NMR spectroscopy.

***Keywords:*** *chalcone, dibenzoylmethane, etilendiamine, imidazopyridine, acetoacetanilide, dihydroisoquinolin , NMR.*

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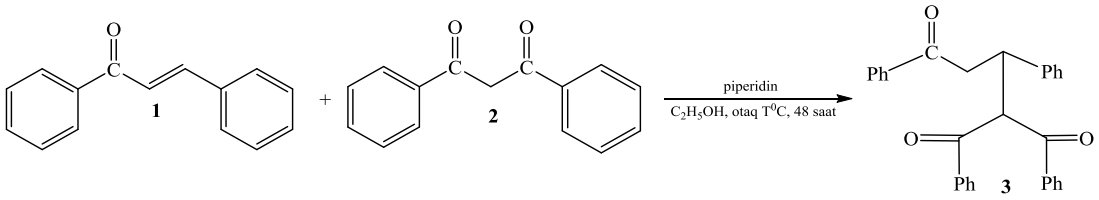
## 1. Introduction

Chalcones containing polarized double bond form various Michael adducts with methylene active compounds. In our previous researches, we reported the synthesis of thiazole and pyridine derivatives (Naghiyev *et al.*, 2020) of esters of functionallized heptane acid (Naghiyev *et al.*, 2016) by Michael addition of benzoylacetone to various chalcones. In other our researches, the obtaining of various hetero or carbocycles with the formation of new C-C, C-N, C=O bonds by the Michael addition and condensation was demonstrated (Naghiyev *et al.*, 2018a; 2018b; Naghiyev *et al.*, 2019a; 2019b; Magerramov *et al.*, 2018; Mamedov *et al.*, 2019). In some reports, there is information about synthesis and biologically activity of imidazo[1,2-*a*]pyridines that are effective anticoccidial agent (Scribner *et al.*, 2008; Kaplancikli *et al.*, 2008). Authors described imidazopyridines as a potent inhibitor of PKG-activity of parasites (Liang *et al.*, 2007). In another study, the synthesis, antitumor activity and other biological properties of substituted tetrahydroisoquinolines have been discussed (Capilla *et al.*, 2008). Tetrahydroisoquinolines was obtained as inhibitors of phosphodiesterase type 4 (PDE4) (Li *et al.*, 2008). Antileishmanial activity of phosphor-substituted new tetrahydroquinoline and quinoline derivatives have been investigated (Tejería *et al.*, 2019). By the relevance of the above, the presented work is dedicated to this topic.

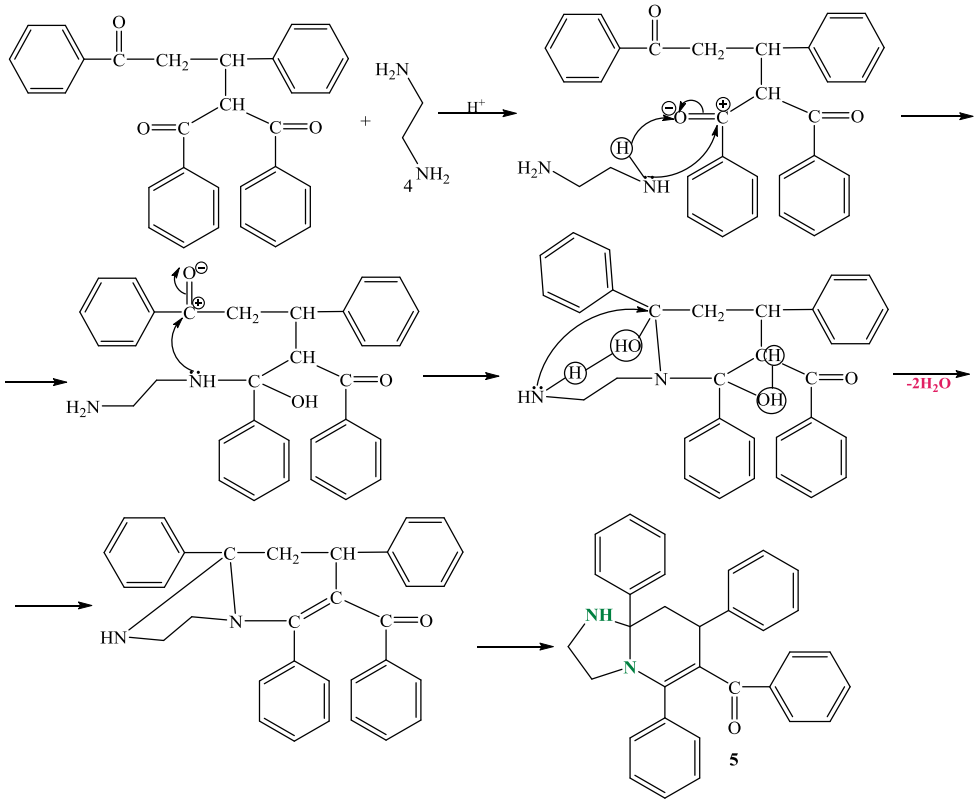
## 2. Results and discussions

Initially, the corresponding Michael adduct was synthesized by the interaction of dibenzoylmethane with chalcones in the presence of piperidine in ethanol media at room temperature.




Michael adduct that obtained in ethanol medium by using HCl at 75-80$^0$C for 4 hours interacts with ethylenediamine and forms phenyl(5,7,8a-triphenyl-1,2,3,7,8,8a-hexahydroimidazo[1,2-*a*]pyridin-6-yl)methanone (**5**).

As a result of research, the probable mechanism of the reaction has been proposed as follows:




It is thought, that at the first stage the nitrogen of one of the amino groups of ethylenediamine containing free electron pair attacks positively charged carbon of carbonyl group that is the electrophilic center of Michael adduct. After was nitrogen forms a hydroxyl group by attacking another carbonyl group by it is next free electron pair. Obtained hydroxyl group combines with hydrogens of the amino group and forms water. In this time, hydroxyl group of other carbon corporates with the hydrogen of neighboring carbon and forms water and double bonds. As a result, compound (**5**) phenyl(5,7,8a-triphenyl-1,2,3,7,8,8a-hexahydroimidazo[1,2-*a*]pyridin-6-yl)methanone was shaped by presented mechanism.

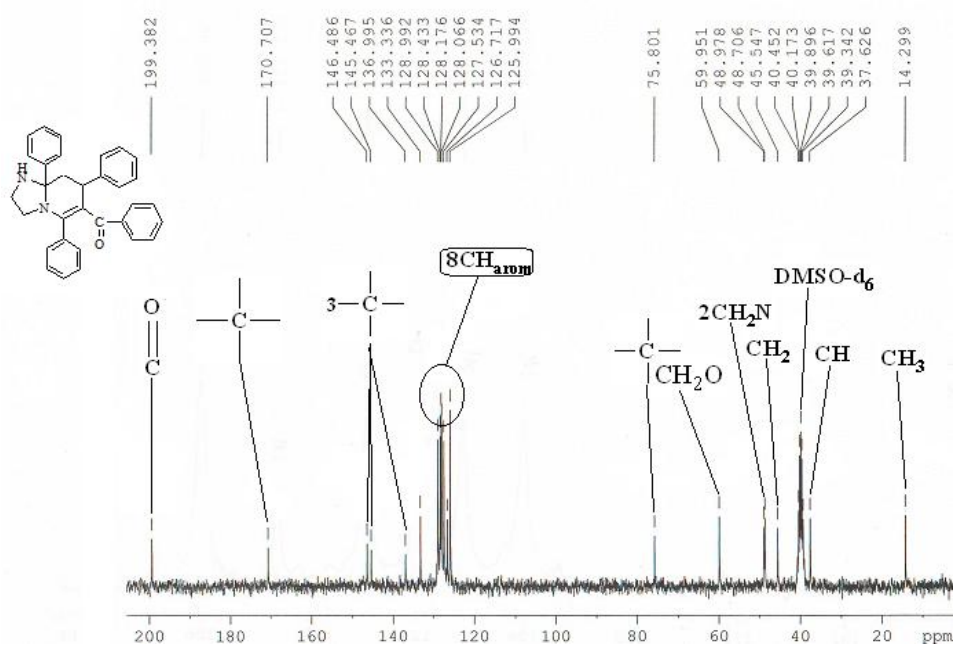
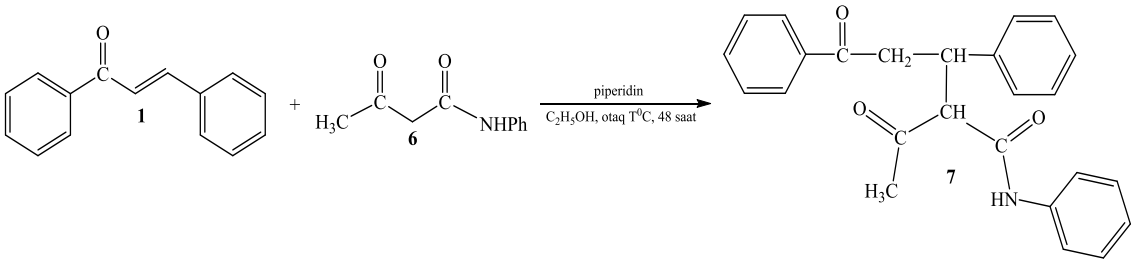
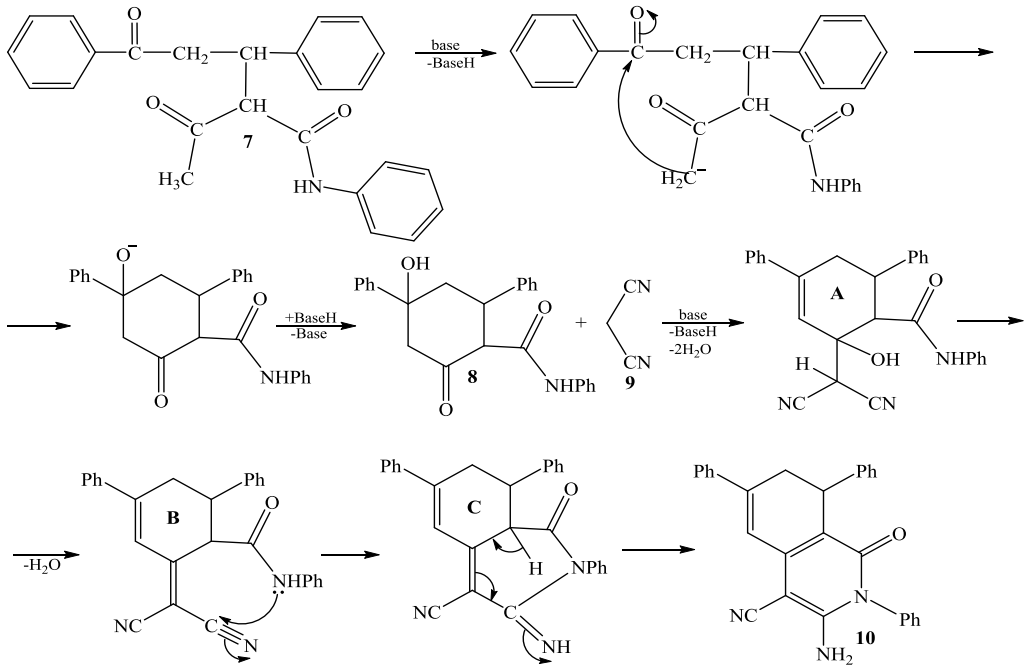



**Figure 1.** $^{13}$C NMR spectrum of phenyl(5,7,8a-triphenyl-1,2,3,7,8,8a-hexahydroimidazo[1,2-*a*]pyridin-6-yl)methanone **(5)**

The formation of 2-acetyl-5-oxo-N,3,5-triphenylpentanamide (**7**) that is corresponding Michaels adduct was established by Michael addition of chalcone to acetoacetanilide in ethanol medium and the presence of piperidine at room temperature for 48 hours.




The probable mechanism of this reaction has been proposed by us as follows. According to this mechanism, the methyl group converted to the corresponding anion in the presence of a base. The resulting anion attacks the carbon of carbonyl group that is active electrophilic center by forming hexanone-anion. This anion combines with hydrogen and gives compound **8**. Then, in base conditions, the simultaneous separation of water and attack of malononitrile anion to the carbon of carbonyl group takes place and **A**-intermediate forms. The **B**-intermediate obtained by water elimination from **A**-intermediate. After all, the nitrogen of amid fragment attacks with its free electron pair to another electrophilic center that is the carbon of nitrile group by forming **C**-intermediate. By migration of hydrogen in **C**-intermediate a 3-amino-2,6,8-triphenyl-7,8-dihydroisoquinolin-1(2H)-one (**10**) has been synthesized.



## 3. Experimental part. General remarks

All commercially available chemicals were obtained from Merck and Fluka (Sigma Aldrich) companies and used without further purification. Melting points were measured on an Stuart SMP30 apparatus without correction. $^{1}H$, $^{13}C$ NMR spectra were recorded on Bruker Avance 300-MHz spectrometer at 300 and 75 MHz, respectively. Thin-layer chromatography (TLC) on commercial aluminum-backed plates of silica gel (60 F254) was used to monitor the progress of reactions.

***Experimental procedures:***

**Phenyl(5,7,8a-triphenyl-1,2,3,7,8,8a-hexahydroimidazo[1,2-a]pyridin-6-yl)methanone (5):** 0.19 g of Ethylenediamine and 5 drops of HCl were added to the solution of 1.3 g (3 mmol) of 2-benzoyl-1,3,5-triphenylpentane-1,5-dione in 35 ml of ethanol in glass-pot equipped with thermometer, counter-cooler and stirrer. The reaction mixed for 15 minutes at room temperature and refluxed for 4 hours and transferred to glass beaker. The progress of the reaction was monitored by TLC (EtOAc/n-hexane, 3:1). Crystals were precipitated after evaporation of solvent, filtered, recrystallized from the ethanol-water mixture and obtained in pure form (yield 1.05 g, 76.64%). $T_{mp.}$ = 192°C.

$^{1}H$ NMR spectrum (300 MHz, DMSO-$d_6$, δ): 2.28 (dd, 2H, $CH_2N$); 2.77 (dd, 2H, $CH_2N$); 3.02 (t, 1H, CH); 3.41-3.63 (dd, 2H, $CH_2$); 6.82-7.78 (m, 20H, 4Ar).

$^{13}C$ NMR spectrum (75 MHz, DMSO-$d_6$, δ): 37.63 (CH), 45.55 ($CH_2$), 48.71 ($N\underline{CH_2}$), 48.98 ($N\underline{CH_2}$), 75.80 ($C_{tert}$), 125.99 ($3CH_{arom.}$), 126.72 ($CH_{arom.}$), 127.53 ($3CH_{arom.}$), 128.06 ($3CH_{arom.}$), 128.18 ($2CH_{arom.}$), 128.43 ($3CH_{arom.}$), 128.54 ($CH_{arom.}$), 128.99 ($3CH_{arom.}$), 133.34 ($CH_{arom.}$), 136.99 ($C_{ar.}$), 145.47 ($2C_{ar.}$), 146.49 ($C_{ar.}$), 170.71 ($2{=}C_{tert}$), 199.38 (C=O).

**3-Amino-1-oxo-2,6,8-triphenyl-1,2,7,8-tetrahydroisoquinoline-4-carbonitrile (10):** To the solution of 1.15 g (3 mmol) 2-acetyl-5-oxo-N,3,5-triphenylpentanamide in 40 ml of acetonitrile, 0.2 g (3.1 mmol) malononitrile was added in pot equipped with thermometer, counter-cooler and stirrer. Then mixed for 5 minutes. 0.19 g (3.1 mmol)

of ethylenediamine is added the reaction mixture and refluxed for 4 hours and transferred to glass-beaker. The progress of the reaction was monitored by the TLC (EtOAc/n-hexane, 3:1). Crystals were precipitated after evaporation of solvent, filtered, recrystallized from the ethanol-water mixture and obtained in pure form (yield 0.85 g, 68.55%). $T_{mp.}$ = 281°C.

$^{1}$H NMR spectrum (300 MHz, DMSO-$d_6$, m.h.): 3.22 (dd-dd, 2H, $CH_2$); 4.25 (dd, 1H, CH-Ar); 6.70 (s, 2H, $NH_2$); 6.84 (s, 1H, CH=); 6.97-7.55 (m, 15H, 15Ar−H).

$^{13}$C NMR spectrum (75 MHz, DMSO-$d_6$, m.h.): 35.17 (CH−Ar), 43.57 ($CH_2$), 109.86 (=CH), 117.67 (=$C_{quat}$), 119.52 (CN), 125.96 (2$CH_{arom}$), 126.72 (2$CH_{arom}$), 126.86 ($CH_{arom}$), 127.39 ($CH_{arom}$), 127.99 (2$CH_{arom}$), 128.66 (2$CH_{arom}$), 128.89 (2$CH_{arom}$), 128.89 (2$CH_{arom}$), 129.21 (=$C_{quat}$), 129.56 ($CH_{arom}$), 129.94 (=$C_{quat}$), 135.27 (N−$C_{ar.}$), 139.07 ($C_{ar.}$), 139.40 ($C_{ar.}$), 144.14 (=$C_{quat}$−N), 160.73 (O=$C_{quat}$-N), 167.96 (=$C_{quat}$−Ar).

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