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## REACTIONS OF (BENZAMIDOMETHYL)TRIETHYLAMMONIUM CHLORIDE WITH SOME 1,3-DIKETONES IN AQUEOUS MEDIA

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**Abstract:** (Benzamidomethyl)triethylammonium chloride (1) smoothly reacts with several 1,3-diketones, in aqueous media, under alkaline conditions (pH ≥ 9), at ambient temperature. From reaction of 1 with dibenzoylmethane (2a) and benzoylacetone (2b) only mono-C-benzamidomethylation products (3a, 3b) were isolated, respectively. Reaction of 1,3-indandione (2c) with 1, gave di-C-benzamidomethylation product (3c).

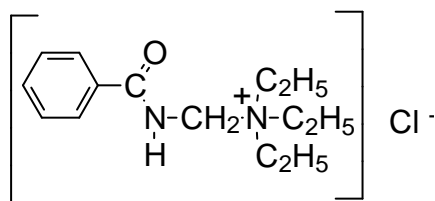
*O*-benzamidomethyl alkylation products have not been detected or isolated. The reactions occurred under mild conditions to give products in moderate yields.

**Keywords:** C–C bond formation, aqueous medium, benzamidomethylation, 1,3-Diketones.

## 1. INTRODUCTION

In the past a large number of benzamidomethyl compounds have been synthesized, compounds which have different properties. Many of them are used as radiolabels [1], functional derivatives of  $\alpha$ -amino acids and peptides [2], antibiotics [3, 4], antiviral drugs [5, 6], emulators [7], as intermediers for synthetic resin [8], etc. Preparation of different benzamidomethyl compounds was an object of interest in our previous research work, which showed that (benzamidomethyl)triethylammonium chloride (1) is an excellent agent for nucleophilic substitution in aqueous media, in reactions with different nucleophiles that occur under mild conditions, with high yields and simple isolation of the products [9-11]. The emphasis of this paper is based on the possibility of quaternary ammonium salt **1** to build C-C bonds in aqueous media, with different 1,3-Diketones. C-C bond formation is the essence of organic synthesis and provides the foundation for generating more complicated organic compounds from the simpler ones. Many C-C bond forming processes involve reaction between a nucleophilic carbon atom and an electrophilic one [12]. Water as a medium can promote various reactions of this type that can be carried out as diverse as those in nonaqueous conditions. Organic synthesis in

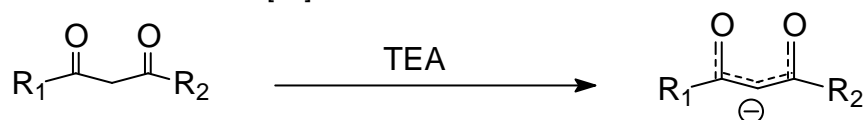
water can significantly shorten the synthetic route, increase product selectivity and reduce volatile organic consumption [13].



**1**

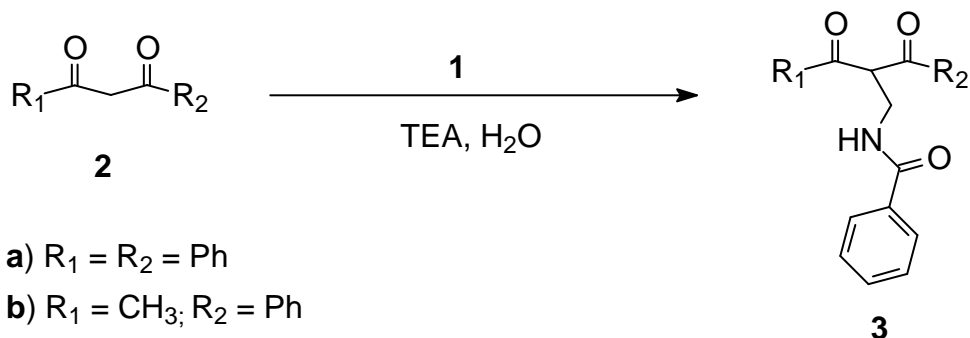
## 2. RESULTS AND DISCUSSION

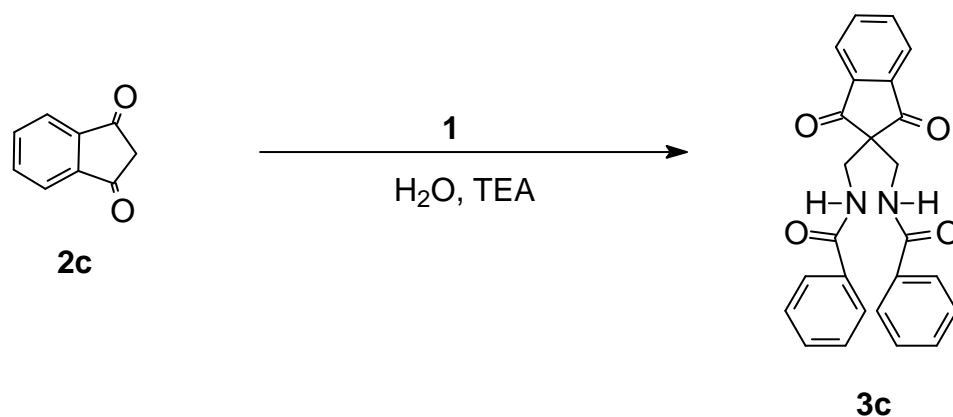
Reactions of **1** with the enolate-anions (derived from 1,3-diketones) were performed in stirred aqueous conditions, in the presence of small quantities of triethylamine (TEA) pH  $\geq 9$ , at ambient temperature. A very general means of generating C-nucleophiles involves removal of a proton from a carbon atom (between two C=O groups, in the molecule of the diketone), by a Bronstead base [12]. The C=O group bonded directly to the anionic carbon can delocalize the negative charge by resonance (Scheme I). Actually the presence of two electron-withdrawing substituents favours formation of the enolate-anion [12].



Scheme I

We were interested in the alkylation reactions of different enolate-anions (Scheme II).





Scheme II

The reaction of the symmetrical **2a** and unsymmetrical **2b** diketone with **1** gave mono-C-alkylation products, **3a** and **3b**, respectively, while the reaction of the symmetrical **2c** with **1** gave di-C-alkylation product **3c**. The reasons for these different reaction products are due to the differences in acidity of the enolate-anions, which means that the protons from the carbon atom situated between two-withdrawing groups (C=O) in **2c** are more acidic than the ones in **2a** and **2b**. Because of the acidity of the previously named protons in the molecule of **2c**, the kinetics of the reaction of **2c** with **1** is significantly higher than the one with **2a** and **2b**, which resulted in attachment of two benzamidomethyl groups to the molecule of the **2c** enolate-anion, instead of one in the **2a** and the **2b** enolate-anions. In these reactions the process of alkylation of enolat-anions occurs at the carbon atom (instead of the oxygen atom), which is affected by using water as a solvent (process of solvation at the oxygen atom, which directs the process of nucleophilic addition to take place primarily on the C atom [14]). In the case of **3a** and **3b**, the mass spectra indicate that in the reactions between **1** and **2a-b** a mono alkylation process occurs. The IR spectra gave peaks from Amide I and Amide II groups in both cases. In the IR spectrum of **3a** one peak from the carbonyl group (split in two from C-COPh) at  $1696\text{ cm}^{-1}$  can be observed, while in the spectrum of **3b**, there are two peaks from two carbonyl groups (C-COPh and C-COCH<sub>3</sub>) at  $1723\text{ cm}^{-1}$  and  $1661\text{ cm}^{-1}$  present. <sup>1</sup>H-NMR spectra are the final evidence for the molecule structures. In <sup>1</sup>H-NMR spectra of **3a**, a triplet from protons of CH<sub>2</sub> (NHCH<sub>2</sub>-CH) group can be noticed, while in the spectra of **3b** two quadruplets from the protons of the same group can be noticed. These differences are due to the attachment of CH<sub>2</sub> group to a chiral center in the molecule of **3b**, which makes the two protons unequal in their properties. In the case of **3c**, the mass spectrum indicates that in the reaction between **1** and **2c** a dialkylation process occurs. The IR spectrum similarly as above gave peaks from Amide I and Amide II groups and one peak from both carbonyl groups (C-CO). <sup>1</sup>H-NMR gives a dublet from the protons of the CH<sub>2</sub> (NHCH<sub>2</sub>) group which confirms the absence of a proton at the C atom between the two carbonyl groups.

### 3. CONCLUSIONS

This paper is evidence that C-C bond forming processes can occur in aqueous media in reaction between quaternary ammonium salt **1** and different 1,3-diketones. The reactions gave mono and di-C-alkylation products respectively, under mild reaction conditions with moderate yield. The products are easily isolated from the reaction mixture by simple filtration.

#### 4. EXPERIMENTAL

Melting points were determined with Reichert heating plate and were uncorrected. Nitrogen elemental analysis was carried out by the Dumas method.  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectra were recorded on a Bruker 400 MHz and 100 MHz, respectively using  $\text{DMSO-d}_6$  and  $\text{CDCl}_3$  as solvents. Infrared spectra were measured on a Perkin-Elmer System 2000 FT IR, by the method of KBr pellets. All the reagents and solvents were obtained from commercial sources and were used without further purification.

*(Benzamidomethyl)triethylammonium chloride (1)* was obtained in manner described in previous work [9].

*N-(2-benzoyl-3-oxo-3-phenylpropyl)benzamide (3a)*.

A solution of **1** (0.85 g, 3.14 mmol) in water (10 ml) was added to acetone solution of **2a** (0.47 g, 2.10 mmol) and TEA (pH  $\geq$  9). The mixture was stirred for 1 h at ambient temperature and the product **3a** was collected by filtration. Yellow crystals, recrystallized from acetone; Yield 54.6 %; mp = 157-158 °C (lit. 158-160 °C [15]); (Calc. 77.29 C, 5.36 H, 3.92 N, Found 77.11 C, 5.59 H, 3.76 N); IR(KBr)/ $\text{cm}^{-1}$ : 3400 ( $\nu\text{NH}$ ), 1696 (CO), 1685 (CO), 1648 (Amide I), 1529 (Amide II);  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-d}_6$ ): 8.03 (t, 1H, CONH), 7.71-7.40 (m, 15H, Ar), 6.085 (t, 1H, CH), 3.89 (t, 2H,  $\text{NHCH}_2$ );  $^{13}\text{C-NMR}$  (100 MHz,  $\text{DMSO-d}_6$ ): 195.44 (C=O), 166.98 (CONH), 68.39 (CH), 54.76 ( $\text{CH}_2$ ), Aromatics: 135.64, 133.97, 133.89, 131.23, 129.04, 128.39, 128.16, 127.10.

*N-(2-benzoyl-3-oxobutyl)benzamide (3b)*.

A solution of **1** (1.5 g, 0.006 mmol) in water (10 ml) was added to water solution of **2b** (0.45 g, 0.003 mmol) and TEA (pH  $\geq$  9). The mixture was stirred for 1 h at ambient temperature and the product **3b** was collected by filtration. White crystals, recrystallized from acetone; Yield 57.3 %; mp = 105-107 °C (lit. 112-113 °C [15]); (Calc. 73.20 C, 5.80 H, 4.74 N, Found 72.93 C, 6.08 H, 4.55 N); IR(KBr)/ $\text{cm}^{-1}$ : 3323 ( $\nu\text{NH}$ ), 1723 (CO), 1637 (Amide I), 1534 (Amide II);  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 8.13 (t, 1H, CONH), 5.06 (t, 1H, CH), 4.10 (q, 1H,  $\text{NHCH}_2$ ), 3.90 (q, 1H,  $\text{NHCH}_2$ ), 2.25 (d, 3H,  $\text{COCH}_3$ );  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 204.20 (C=O), 196.72 (Ph-CO), 168.53 (CONH), 61.64 (CH), 39.52 ( $\text{CH}_2$ ), 30.51 ( $\text{CH}_3$ ), Aromatics: 136.47, 134.91, 134.52, 132.44, 129.78, 129.60, 129.30, 127.62.

*N-[(1,3-dioxo-2,3-dihydro-1H-inden-2-yl)methyl]benzamide (3c)*.

**3c** was synthesized in a similar manner as **3b**. Purple crystals, recrystallized from acetone; Yield 49.8 %; mp = 200-203 °C; (Calc. 72.8 C, 4.89 H, 6.79 N, Found 72.6 C, 5.09 H, 6.89 N); IR(KBr)/ $\text{cm}^{-1}$ : 3313 ( $\nu\text{NH}$ ), 1698 (CO), 1657 (Amide I), 1541 (Amide II);  $^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-d}_6$ ): 8.62 (t, 2H, CONH), 7.90-7.35 (m, 14H, Ar), 3.73 (d, 4H,  $\text{NHCH}_2$ );  $^{13}\text{C-NMR}$  (100 MHz,  $\text{DMSO-d}_6$ ): 199.26 (C=O), 166.90 (CONH), 58.40 ( $\text{CH}_2$ ), 40.12 (C), Aromatics: 141.51, 135.80, 133.94, 131.25, 128.17, 127.10, 122.90.

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