Synthesis, Biocidal and Analytical Applications of Some Novel 1- Acyl / benzoyl -1-anilido-4-methyl-aryl-butadiene Derivatives

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Abstract
The present investigation was aimed to synthesis a series of new 1-acyl/ benzoyl -1-anilido-4-methyl - aryl-1, 3-butadiene derivatives (II-IV) for their uses as biocidal and analytical reagents. The compounds were prepared by warming 4-aminoplastyprine, 2-amino-5-chloropyridine, 2-amino-5-nitropyridine, 2-aminobenzthiazole, sulfanilamide and/or sulfadiazine with pre heated ethyl acetacetate and/or ethyl benzyolacetate in dry conditions followed by condensation with crotonaldehyde and/or 4-dimethylaminocinnamaldehyde in boiling ethanol-piperidine. The compounds were fully characterized via their elemental analysis and spectroscopic measurements (UV VIs., IR, NMR). The biocidal effects of the prepared compounds (IIId, e, f, IV d, e, f) as antimicrobial agents and photochemical probe agents was investigated. The voltammetric behavior of the two compounds Ila and IVa in N,N-dimethylformamide was investigated. The compound IVa was successfully tested for the removal and/or separation of bismuth (III) employing polyurethane foam solid sorbent.

Keywords: Synthesis; 1-Acyl/ benzoyl -1-anilido-4-methyl - aryl-1, 3-butadiene; Biocidal voltammetry; Wastewater

Introduction
Recent years have seen an upsurge of interest on the synthesis and spectroscopic characterization of β- diketones as potential ligands [1,2]. Complex formation in this class of compounds is conceived by replacement of the enolic proton by chelation with metal ions in a bidentate fashion [3,4]. The β- diketone 3- salicylidene-2, 4-pentanediones and related compounds have been used successfully as proper chelating agents with a series of many metal ions [5,6,7]. Knoevenagel condensate of substituted benzyldienes with active methylene compounds were performed efficiently employing ultra stable Zeolite as heterogeneous catalyst [8-11] have reported a series of benzoyl -acetaldies and their physico organic properties. The starting material was used by Abdel-Rahman [11] for building a series of novel bio-active pyrazoline derivatives. In addition, the thermodynamic characteristics and spectroscopic characterization of a series of compounds namely hydrazono – 1, 3- bi carbonyl derivatives and their lanthanide complexes have been investigated [9,10].

The chelation behavior of a series of dicarboxyl towards some metal ions has been reported [12-14]. Moreover, metal chelates of β- diones have interesting properties in particular in industrial applications [15-17]. The dimerized species of 2- diazo-3- methyl-1-phenyl-5-pyrazoline produced the compound 4- (5-hydoxy-4-pyrazolxlimino-2-pyrazolin-5- one. Such investigations have indicated that, no work is known on the Knoevenagel condensate β- ketoanilide and its metal chelates. Therefore, in continuation to our previous work [18-23], the present study is focused on the synthesis and characterization of a series of some -diketone derivatives bearing anilido moieties and their unsaturated -diketone derivatives. In view of the voltammetric behavior, one of the prepared compounds was successfully tested as a trapping agent for the pre-concentration of bismuth (III) from aqueous as a highly toxic metal ions the industrial waste water.

Experimental
Reagents and materials
Low density polyethylene (LDPE) bottles, Nalgene were carefully cleaned first with hot detergent, soaked in 50% HCl (Analar), HNO3 (2.0 mol L⁻¹), subsequently washed with dilute HCl (0.5 mol L⁻¹) and finally rinsed with distilled water. N,N-Dimethylformamide (DMF) and the supporting electrolyte tetraethyl ammonium chloride (TMA⁺Cl⁻) were purchased from BDH chemicals.. The sample solution was stored in LDPE bottles and stored at -20°C. Britton – Robinson (B – R) buffers of pH 2-11 were prepared from the acid mixture of phosphoric acid, boric acid, acetic acid (0.04 mol L⁻¹) and adjusting the pH to the required value with sodium hydroxide (0.20 mol L⁻¹). A stock BDH stock solution of bismuth (1 mg/mL) in dilute nitric acid was used. A series of standard diluted bismuth (III) solutions were then prepared in doubly distilled water by dilution. Stock solutions (1×10⁻² mol L⁻¹) of the compounds -acyl-1-anilido-4- methyl-1,3- butadiene, Ila and 1-benzoyl-1-anilido-4- methyl-1,3- butadiene, IVa in DMF were prepared. The supporting electrolyte tetra methylammonium chloride (TMA⁺Cl⁻) was used in the voltammetric experiments as received without further purifications.

Apparatus and measurements
A Perkin Elmer (Lambda EZ-210) double beam spectrophotometer (190-1100 nm) with 1cm (path width) was used for recording the electronic spectra of the prepared solutions. Digital pH-meter (model MP220, Metter Toledo) was used for pH measurements. A Perkins Elmer model RXI-FT-IR system 55529 was used for recording the IR spectra of the prepared compounds. A Brucker advance DFX 400 MHz model using TMS as an internal standard was used for recording the 1HNMR spectra of the compounds on deuterated DMSO. A GC-MS-QP 1000-Ex model was used for recording the mass spectra of the compounds. Melting points were determined with an electro thermal Bibby Stuart Scientific Melting Point SMP1 (US). Molecular weights

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of the compounds were preformed on Micro analytical center, Cairo University, Egypt. Microanalysis (Nitrogen %) was performed by microanalytical center Ain-Shams University-Cairo-Egypt. A Metrohm 797 VA trace analyzer and 797 VA stand were used for recording the cyclic voltammetric (CV) experiments. In the CV experiments, a three-compartment (Metrohm) voltammetric cell (10 mL) incorporating Pt wire as working, double-junction Ag/AgCl(3M KCl), as reference and Pt wire (BAS model MW-1032) as counter electrodes, respectively. The surface area of the counter electrode was 100 times larger than the area of the working electrode.

Methodology

Preparation of acyl/benzoyl acetanilide Derivatives (I and III): To preheated ethyl acetocetate and/or ethylbenzylacetate (0.01mol) a selective hetero primary amines and/or sulfa drugs (0.01mol) were added in dry system then warmed for 10-15 min at 100-110°C, cooled and finally washed with diethyl ether. The resultant solid was dried and crystallized to give I and III respectively (Table 1).

Preparation of reagent IVa immobilized polyurethane foam packed column: Polyurethane foam (PUFs) cubes immobilized with the reagent IVa were prepared by mixing the dried foam cubes with the required weight of the reagent (0.05% w/v) in ethanol with efficient stirring for 10 min. The reagent immobilized PUF cubes were then dried to remove the excess reagent with filter papers as reported earlier [19-21]. The reagent immobilized PUFs were packed separately in the glass columns by applying the vacuum method of foams packing.

Pre concentration and/or separation of bismuth (III) by reagent IVa treated PUFs: An accurate weight (0.1 ± 0.01 g) of the reagent IVa treated foam cubes was equilibrated with 50 mL of an aqueous solution containing bismuth (III) ions at concentration of 10 µg mL$^{-1}$. The solutions were then adjusted to the required pH with B-R buffer (pH 2-11). The test solutions were then shaken for 2 h on a mechanical shaker. The aqueous phase was then separated out by decantation and the amount of bismuth (III) remained in the aqueous phase was determined with atomic absorption spectrometry at the optimum wavelength. The amount of bismuth (III) retained on the PUFs cubes was determined from the difference between the concentration of bismuth (III) solution before (Co) and after (Ca) shaking with the foam cubes.

Results and Discussion

Spectroscopic characterization

Synthesis of 1, 3-dicarbonyl anilido and their unsaturated derivatives is very simple and of general applicability. It gives pure compounds with improved yields. Thus, warming some hetero primary amines such as 4-aminoantipyrine, 2-amino-5-chloropyridine, 2-amino-5-nitropyridine, 2-amibenzenothiazole and some sulfa drugs as sulfanilamide and sulfadiazine with preheated ethyl acetocetate and/or ethyl/benzoyl acetate at 100-110°C for 10-15 min in dry condition led to the formation of acyl/benzoyl acetanilide derivatives I and III (Scheme I, II). Knoevenagel condensation of compounds I and III with unsaturated aldehydes as crotonaldehyde and/or 4-dimethylaminocinnamaldehyde in boiling ethanol with few drops of piperidine as catalyst afforded 1-acyl/benzoyl -1-anilido-4-aryl-1,3 butadiene (II) and 1-acyl/benzoyl-1-anilido-4-(4`-dimethylaminophenyl)-1,3-butadiene (IV) respectively (Scheme I-III). Both carbonyl compounds I-IV having a second carbonyl at -position, are termed as -diketones. In general hydrogen bonding is possible only in syn form and not in anti form, where the orientation of enolization is towards the aryl or phenyl groups [5] indicating the high enolic content of 4-aryl-1, 3-diketones and not in 4-methyl-1, 3-diketones. UV – Visible spectra of compounds II and IV have two strong bands around 360 and 260 nm which characteristics bands of carbonyl chromophore and the conjugated C=C of butadiene (n-* and *transition) while that of compounds I and III recorded a low bands at 330 and 240 nm due to a bathochromic shift, indicating the involvement of the two carbonyl groups [5] indicating the high enolic content of 4-aryl-1, 3-diketones respectively [5]. Both carbonyl compounds I-IV having a second carbonyl at -position, are termed as -diketones. In general hydrogen bonding is possible only in syn form and not in anti form, where the orientation of enolization is towards the aryl or phenyl groups [5] indicating the high enolic content of 4-aryl-1, 3-diketones and not in 4-methyl-1, 3-diketones. UV – Visible spectra of compounds II and IV have two strong bands around 360 and 260 nm which characteristics bands of carbonyl chromophore and the conjugated C=C of butadiene (n-* and *transition) while that of compounds I and III recorded a low bands at 330 and 240 nm due to a bathochromic shift, indicating the involvement of the two carbonyl groups isolated by methylene group, assigned to the intramolecular charge transfer interaction involving the whole molecule [6]. IR spectra of compounds

<table>
<thead>
<tr>
<th>Compd No.</th>
<th>M.P. (ºC)</th>
<th>Yield (%)</th>
<th>Solvent</th>
<th>M. Formula</th>
<th>M. Weight</th>
<th>N analysis*</th>
</tr>
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<td>Calcd</td>
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<td>Pet. ether 60-80</td>
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<td>287</td>
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<td>70</td>
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<td>75</td>
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<td>C$_9$H$_9$N$_2$SO$_2$</td>
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<tr>
<td>If</td>
<td>210</td>
<td>85</td>
<td>Pet. ether 60-80</td>
<td>C$_9$H$_9$N$_2$SO$_2$</td>
<td>330</td>
<td>334</td>
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<td>THF</td>
<td>C$<em>{10}$H$</em>{12}$NO$_5$</td>
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<td>Iia</td>
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<td>73</td>
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<td>343</td>
<td>349</td>
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<tr>
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<td>348</td>
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<tr>
<td>IvC</td>
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<td>60</td>
<td>Diethyl ether</td>
<td>C$<em>{12}$H$</em>{14}$NO$_3$</td>
<td>443</td>
<td>453</td>
</tr>
</tbody>
</table>

* All the prepared compounds gave analytical C and H data with ± 0.4-0.7% from the theoretical values.

Table 1: Physical properties of prepared compounds I-IV
**Table 2: The Biocidal and photochemical Effects of Some Compounds.**

<table>
<thead>
<tr>
<th>Compound 50 mg/mL</th>
<th>Bacteria Escherichia coli</th>
<th>Fungi Aspergillus fumigates</th>
<th>Bacteria Escherichia coli</th>
<th>Fungi Aspergillus fumigates</th>
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<tbody>
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<td>18</td>
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<td>22</td>
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<tr>
<td>f</td>
<td>25</td>
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<td></td>
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<tr>
<td>IVd</td>
<td>13</td>
<td>12</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>e</td>
<td>12</td>
<td>10</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>f</td>
<td>14</td>
<td></td>
<td>17</td>
<td>18</td>
</tr>
</tbody>
</table>

* Highly active >20; moderate (15 – 20) and weak < 15.

I and III show no characteristic C=O absorption band (at 1725-1710 cm⁻¹) which is present in the spectrum of acetylacetone (~ 1680 cm⁻¹) while that of II and IV recorded of strong absorption bands at 1650 cm⁻¹ of true C=O group. Also, intramolecular hydrogen bonding are observed in the regions 2700-2500 and 3000-2900 cm⁻¹ respectively. The presence of absorption bands at 1610-1480 cm⁻¹ (C=C) and 960-900 cm⁻¹ confirm the presence of trans –CH=CH-

**Voltammetric study**

The cyclic voltammograms (CVs) of the two compounds 1-acyl-1-anilino-4- methyl-l,3- butadiene, IIa and 1-benzoyl-1-anilino-4-methyl-l,3- butadiene, IVa in DMF - TMA⁺Cl⁻ at Pt working electrode versus Ag/AgCl reference electrode at various scan rate were investigated. The results are shown in Figures 1 and 2. The CV of compound IIa (Figure 1) at 100 mVs⁻¹ revealed two well-defined cathodic peaks at 0.1 and -0.75 V versus Ag/AgCl electrode. One well defined anodic peak at -0.15 V was observed on the reverse scan suggesting the irreversible nature of the observed electrochemical process in the employed potential range (-2.0 - 2.0 V). On raising the scan rate (>100 mV s⁻¹), the potential of the two cathodic peaks were shifted cathodically, while the anodic peak shifted anodically confirming the irreversible nature of the observed electrochemical processes. The observed cathodic peaks are most likely assigned to the reduction of the carbonyl group via 2H⁺/2e in two successive one electron / one proton reduction steps [24]. Continuous scan of the CV significantly decreased the peak current height indicating passivity of the surface of the Pt electrode via formation of polymeric oxidation product or fouling of the Pt electrode by the produced reduction products suggesting prior adsorption on the surface of the electrode in the potential range [24].

In DMF- TMA⁺Cl⁻ the CVs of the compound IVa (Figure 2) at the Pt working electrode showed two reduction peaks at 0.1 -0.15 and -0.65 - -0.8 V coupled with one broad anodic peak in the potential range 0.3-0.4 V at scan rates of 50-1000 mVs⁻¹ versus Ag/AgCl electrode. The cathodic peaks are safely assigned to the reduction of the carbonyl group in two successive H⁺/e redox steps [18]. The peak –peak potential difference (ΔEp=Ep,a-Ep,c) between the cathodic (Ep,c) and anodic peaks (Ep,a) indicated that, the observed redox processes are irreversible. On raising the scan rate both cathodic and anodic peaks are shifted to more negative and positive potential, respectively confirming the irreversible nature of the observed redox process (Bard and Fullkner, 1980). The plot of the the cathodic peak current (iₘ) versus the square root of the scan rate was linear indicating that the electrochemical processes is diffusion controlled processes [24]. The plot of Eₘ versus log scan rate was found linear at Ag/AgCl. Thus, it can be concluded that, the first reduction processes of the compound precede according to the well known electrode- coupled (EC) chemical reaction mechanism [24].

**Retention behavior of bismuth (III) onto reagent IVa immobilized PUFs**

In preliminary experiments the use of the reagent IVa immobilized PUFs for the extraction of bismuth (III) from aqueous solution was 

**Biocidal effect**

Some synthesized compounds were tested in-vitro using the agar diffusion disk method [20,21]. The antimicrobial potenialities of the two compounds were estimated by placing pre sterilized filter paper disks (11 mm diameter) impregnated with 50 mg/disk using DMSO as solvent, which showed no inhibition zone (IZ) of tested compounds (mm) were measured after 24h incubation at 37°C for bacteria and after 5-days incubation at 28°C for fungi (Table 2). Photochemical probe effects of these compounds can be determined using UV – 360 as second test. Compounds IIIe,d,f and IVe,d,f showed a highly biocidal effect and only compound IIIe,d,f characterized by photochemical probe action than other prepared compounds.
examined by batch mode of separation. Reasonable amount of bismuth (III) ions are retained onto the reagent immobilized PUFs from the test aqueous solutions and the amount of bismuth (III) retained on the PUFs depends on the solution pH. Thus, the sorption profile of bismuth (III) at selected concentration (10.0 µg mL⁻¹) from the test aqueous solution (50.0 mL) containing excess of KCl, KBr or KI at different pH (pH 2–8) onto the reagent loaded foams was examined. After shaking the solutions for 2 h, the amount of bismuth (III) remained in the aqueous solution was determined. The amount of bismuth (III) retained, the extraction percentage, %E and the distribution ratio, D was then calculated as reported earlier [19-21]. Maximum retention of bismuth (III) by the immobilized reagent PUFs was achieved from the aqueous media at pH 2-3 containing iodide ions and the sequence of the uptake followed the order: iodide>bromide>chloride. The uptake of bismuth (III) from the aqueous iodide media decreases on increasing the solution pH.

The observed decrease on the bismuth (III) retention at pH>3.5 is most likely attributed to the instability of bismuth–iodide or the ternary complex involving [BiI₄]⁻ or [BiI₃]⁻ due to the hydrolysis of the species formed between [BiI₄]⁻ and the reagent immobilized polyurethane foams. Similar trends were also reported earlier [19-21]. Thus, a “weak base anion exchanger” and a “solvent extraction” mechanism of the [BiI₄]⁻ may be proposed for the uptake onto the protonated ether (–CH₂–HO–CH₂–) or urethane (–NH–COO–) linkages of the immobilized PUFs.

The effect of contact time and shaking time on the retention of bismuth by the treated AMP-PUFs of bismuth (III) from the aqueous solution containing high excess of KI (5-7% w/v) by AMP-loaded foam was carried out at pH 2.0. The bismuth (II) uptake was fast and reached maximum within ~10-15 min contact time. The half-life time (t₁/₂) of the equilibrium sorption of bismuth (III) as calculated from the plot of -log ((Cᵦ – Cₛ)/Cb) versus time onto the reagent immobilized PUFs from the aqueous media to reach 50% saturation of the sorption capacity was in the range 1-1.5 min (Figure 3). The uptake of bismuth (III) ions was fast within the first 10 min and increased up to a constant value in less than 60 min shaking time. Thus, a shaking time of 60 min was adopted in subsequent experiments.

Conclusion

The redox behavior of the tested compounds suggest the possible application of the compounds as chelating agent for the determination of ultra trace concentration of heavy metal ions employing differential pulse – adsorptive stripping voltammetry. Moreover, immobilization of one of the prepared compounds on polyurethane foam solid sorbent as trapping agent for minimization and/or separation of bismuth (III) from industrial wastewater was achieved. Work is still continuing for application of the compound in cathodic stripping voltammetric procedures for trace metal analysis in different matrices.

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