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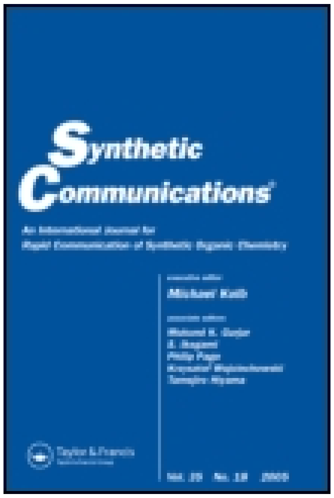

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

# A FACILE SYNTHESIS AND CHARACTERIZATION OF THE NOVEL 2,2-DICHLORO-1-[3-(2,2-DICHLORO-ACETYL)-2-(4-METHOXY-PHENYL)-IMIDAZOLIDIN-1-YL]-ETHANONE

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Published online: 16 Aug 2006.

To cite this article: Canan Ünaleroğlu , Barış Temelli & Tuncer Hökelek (2002) A FACILE SYNTHESIS AND CHARACTERIZATION OF THE NOVEL 2,2-DICHLORO-1-[3-(2,2-DICHLORO-ACETYL)-2-(4-METHOXY-PHENYL)-IMIDAZOLIDIN-1-YL]-ETHANONE, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 32:21, 3255-3261, DOI: 10.1081/SCC-120014029

To link to this article: http://dx.doi.org/10.1081/SCC-120014029

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SYNTHETIC COMMUNICATIONS
Vol. 32, No. 21, pp. 3255–3261, 2002

# A FACILE SYNTHESIS AND CHARACTERIZATION OF THE NOVEL 2,2-DICHLORO-1-[3-(2,2-DICHLORO-ACETYL)-2-(4-METHOXY-PHENYL)-IMIDAZOLIDIN-1-YL]-ETHANONE

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## ABSTRACT

The synthesis of (2,2-dichloro-1-[3-(2,2-dichloro-acetyl)-2-(4-methoxy-phenyl)-imidazolidin-1-yl]-ethanone by a facile one-pot reaction between *N*,*N′*-*bis*(4-methoxy-benzylidene)-ethane-1,2-diamine and dichloroacetyl chloride is described. The structure was confirmed by $^1$H NMR, MS and FTIR techniques and X-ray crystallography.

*Key Words:* Imidazolidin; Imine; Intramolecular cyclization

The reaction of imines with ketenes in the presence of tertiary amines to produce β-lactams (2-azetidiones) is known as the Staudinger reaction, which is very useful in synthetic organic chemistry.[1,2] The cycloaddition

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DOI: 10.1081/SCC-120014029
0039-7911 (Print); 1532-2432 (Online)
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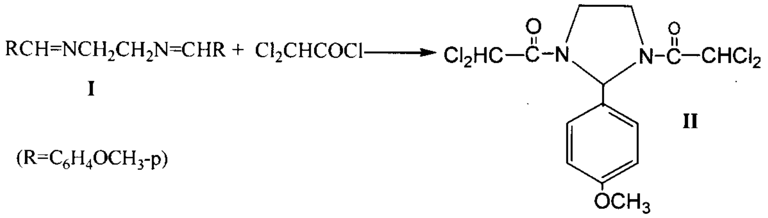
of various types of imines with ketenes derived from acid chlorides yields [2 + 2] cycloaddition products.[3–7] When the imine function is a part of a conjugated system both [2 + 2] and [4 + 2] cycloadducts form.[8,9] Recently, *bis*-β-lactams have been prepared by Bhawal et al. via reaction of bisimines, $R'CH{=}NCH_2CH_2N{=}CHR'$ ($R'{=}C_6H_4OCH_3$, Ph, –CH=CHPh), with ketenes derived from acid chlorides, $ROCH_2COCl$ (R=Ph, Bn, Ac), in the presence of triethylamine in dichloromethane.[10]

In the present work, we have extended the above methodology to the synthesis of a *bis*-β-lactam starting with *N*,*N*′-*bis*(4-methoxy-benzylidene)-ethane-1,2-diamine (**I**), dichloroacetyl chloride and triethylamine in $CH_2Cl_2$. We obtained 2,2-dichloro-1-[3-(2,2-dichloro-acetyl)-2-(4-methoxy-phenyl)-imidazolidin-1-yl]-ethanone (**II**) as a novel product (Eq. 1). Agafonov et al. performed similar reactions between bisimines and benzoyl chloride in the presence of triethylamine and obtained a number of products including mono- and *bis*-acylated imidazolidine derivatives.[11,12]



(1)

We conducted several experiments to show the effect of the addition order of reactants (dropwise adding the acid chloride onto **I** and triethylamine or adding the amine onto the acid chloride and **I**), and solvent effect using a nonpolar solvent (benzene) on the product. **II** was formed as the only product regardless of the order of addition and solvent type. The expected [2 + 2] addition product was not formed. The structure of **II** was confirmed by MS, $^1$H NMR, FTIR techniques and single crystal X-ray analysis for which the ORTEP diagram is given in Fig. 1.

To establish the role of triethylamine, the reaction was repeated in the absence of the amine in $CH_2Cl_2$. Compound **II** was formed again in high yield. Thus, the exclusive formation of imidazolidine (**II**) indicates that [2 + 2] cycloaddition reaction through a ketene pathway is disfavored in this system.

We suggest two possible mechanisms for the formation of imidazolidine (**II**): i. the reaction of **I** with dichloroacetyl chloride gives B via

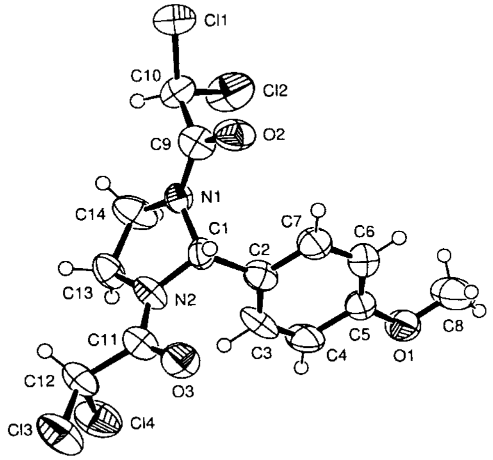
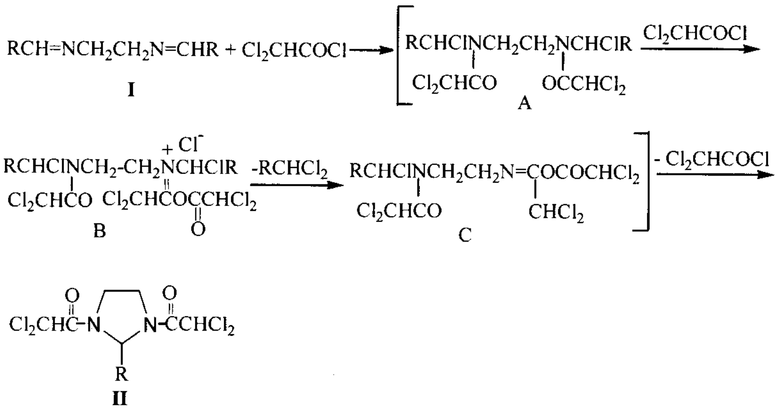
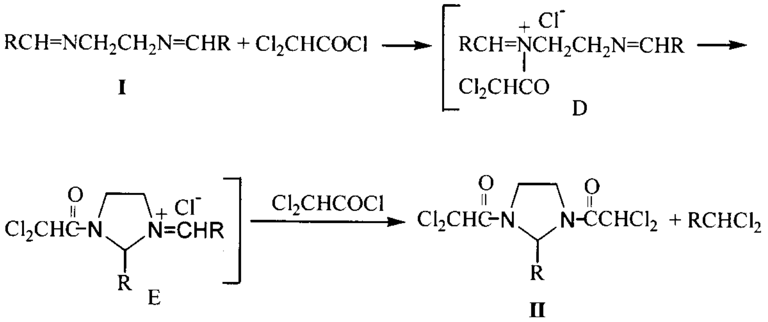


*Figure 1.* An ORTEP[14] diagram of **II** with the atom-numbering scheme. The thermal ellipsoids are drawn at the 50% probability level.



(2)

formation of A. Elimination of $RCHCl_2$ following the intramolecular cyclization through C can furnish the desired product II (Eq. 2), or ii. the reaction of dichloroacetyl chloride with **I** gives D which is followed by the intramolecular cyclization to E. Then the reaction of E with dichloroacetyl chloride yields the product **II** (Eq. 3). These proposed mechanisms agree with the related reports available in the literature.[11–13]



(3)

The method described here provides a facile one-pot route for the high yield synthesis of 2-substituted imidazolidines that can be isolated easily. The formation of a *bis*-acylated product in higher selectivity is another advantage of this system.

## EXPERIMENTAL

Ethylenediamine and dichloroacetyl chloride were obtained from Aldrich. All reagents were dried prior to use. NMR spectra were recorded in $CDCl_3$ solution using TMS as internal standard on a DPX-400 instrument (Bruker). FTIR spectra were obtained on a SHIMADZU FTIR-8101 spectrophotometer as KBr discs. MS data were measured with a GC-MS Thermoquest Trace 2000 instrument. Melting point was measured on a Gallenkamp apparatus.

### X-Ray Analysis

Data of **II** were measured on an Enraf-Nonius CAD-4 diffractometer using graphite monochromated Cu-$K_\alpha$ ($\lambda = 1.54184$ Å) radiation. Crystals belongs to orthorhombic space group $P2_1ab$ with $a = 9.883(2)$, $b = 11.527(1)$, $c = 15{,}384(2)$ Å; $V = 1752.6(4)$ Å$^3$; $Z = 4$, $D_x = 1.516\,\mathrm{Mg \cdot m^{-3}}$, $\mu = 6.273\,\mathrm{mm^{-1}}$. Out of 1363 reflections measured, 076 were treated observed with $[I \geq 2.0\,\sigma(I)]$. The structure was solved by direct methods, SHELXS97.[15] Least square refinement of scale factor, positional and anisotropic thermal parameters for non hydrogen atoms converged to $R = 0.0648$, $wR = 0.1528$. The H atoms were positioned geometrically, and a riding model was used during the refinement. Refinements were carried out by using SHELXL97.[16]

***N,N′-bis*(4-Methoxy-benzylidene)-ethane-1,2-diamine:** Anisaldehyde (4.57 g, 33.60 mmol) was dissolved in ethanol (20 mL). Ethylenediamine (0.88 g, 14.66 mmol) was then added and the solution was heated at 60°C. After 1 h, the reaction was completed. The product was filtered and recrystallized in methanol. Yield: 90%, m.p.: 110°–111°C, IR (cm$^{-1}$): 3080 ($\nu_{\text{C-H aromatic}}$); 2840–2900 ($\nu_{\text{C-H aliphatic}}$); 1641 ($\nu_{\text{C=O}}$); 1109 ($\nu_{\text{C-O}}$). The crystal structure of *N,N′-bis*(4-methoxy-benzylidene)-ethane-1,2-diamine (**I**) was described.[17]

**2,2-Dichloro-1-[3-(2,2-dichloro-acetyl)-2-(4-methoxy-phenyl)-imidazolidin-1-yl]-ethanone:** A solution of dichloroacetyl chloride (2.98 g, 20.24 mmol) in dry $CH_2Cl_2$ (15 mL) was slowly added to a solution containing imine **I** (1.5 g, 5.06 mmol) and triethylamine (2.05 g, 20.24 mmol) in $CH_2Cl_2$ (15 mL) at 0°C, under nitrogen. The reaction mixture was then allowed to warm to r.t. and stirred further for 24 h. It was then washed with satd. $NaHCO_3$ ($2 \times 20$ mL), brine and dried ($CaCl_2$). Crude product was separated through addition of EtOAc and recrystallized in EtOAc. Yield: 78%, m.p.: 188°–189°C, MS (EI): $m/z$ 398 ($M^+$) and the isotopic patterns of $M+2$, $M+4$, $M+6$ and $M+8$, $m/z$ 363 [$m/z$ 398–35 (Cl)], $m/z$ 328 [$m/z$ 398–70 (2Cl)], $m/z$ 291 [$m/z$ 398–107 ($C_6H_4OCH_3$)], $m/z$ 287 [$m/z$ 398–111 ($COCHCl_2$)]; $^1$H NMR (DMSO-d$_6$) δ: 3.83 (s, 3H, –$OCH_3$), 4.01 and 4.19 (2s (br), 4H, $NCH_2CH_2N$), 6.58 (s, 1H, NCHN), 6.85–6.93 (m, 4H, 2(–$CHCl_2$) and H$_{\text{aromatic}}$), 7.28–7.35 (m, 2H, H$_{\text{aromatic}}$); IR (cm$^{-1}$): 3025 ($\nu_{\text{C-H aromatic}}$); 2825–2900 ($\nu_{\text{C-H aliphatic}}$); 1680 ($\nu_{\text{CO-N}}$); 1090 ($\nu_{\text{C-O}}$).

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Received in the UK August 15, 2001

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