

Short Note

Diethyl 2,2'-[Biphenyl-4,4'-diyldihydrazin-2-yl-1-ylidene]bis(chloroacetate)

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Received: 26 December 2013 / Accepted: 15 January 2014 / Published: 22 January 2014

Abstract: Diethyl 2,2'-[biphenyl-4,4'-diyldihydrazin-2-yl-1-ylidene]bis(chloroacetate) was synthesized in high yield via Japp–Klingemann reaction. The structure of this compound was fully characterized by IR, ¹H-NMR, ¹³C-NMR, Mass spectra and elemental analysis.

Keywords: Japp–Klingemann reaction; bis-hydrazonoyl chloride; benzidine

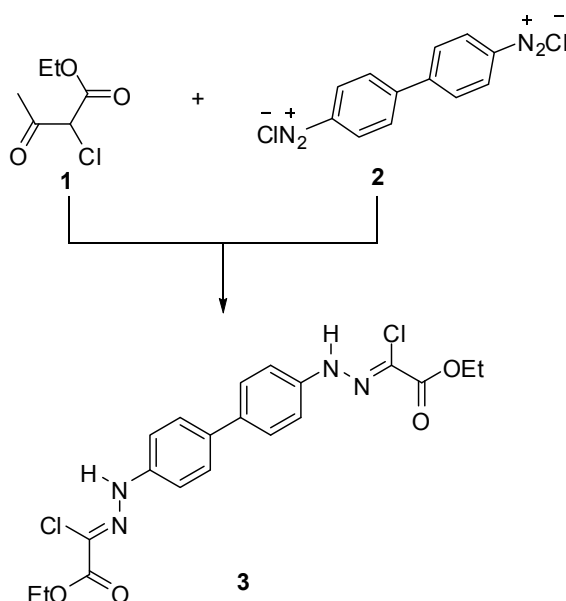
Introduction

Bis-hydrazonoyl chlorides are highly versatile and useful building blocks for the synthesis of a wide variety of *bis*-heterocycles [1–4]. Also, they are reported to be useful insecticides [5]. In continuation of our research work concerned with the synthesis of novel hydrazonoyl halides and their use in the preparation of polysubstituted heterocycles [2], we now report a convenient route to diethyl 2,2'-[biphenyl-4,4'-diyldihydrazin-2-yl-1-ylidene]bis(chloroacetate) (**3**), this compound may prove to be a rather useful synthon for the preparation of a variety heterocycles for biological studies.

Results and Discussion

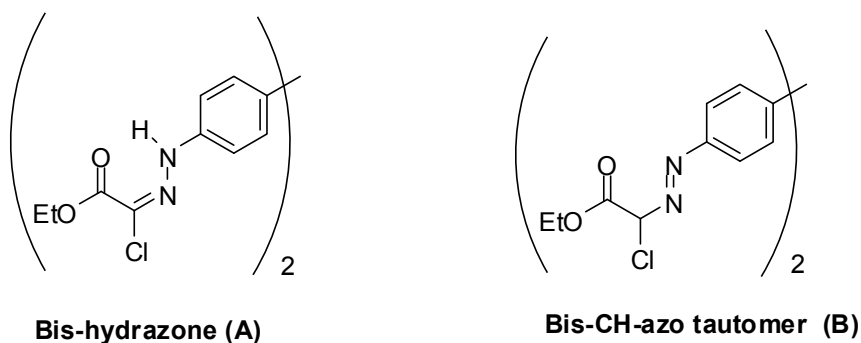
The *bis*-hydrazonoyl chloride **3** was prepared by coupling of benzidine diazonium chloride **2** with 2-chloro-3-oxobutanoate in aqueous-ethanolic sodium acetate (Japp-Klingemann reaction) [6] (Scheme 1). Analytical and spectroscopic data were consistent with the final product **3** (see Experimental).

Scheme 1. Synthesis of diethyl 2,2'-[biphenyl-4,4'-diylidihydrazin-2-yl-1-ylidene]bis(chloroacetate) (**3**).



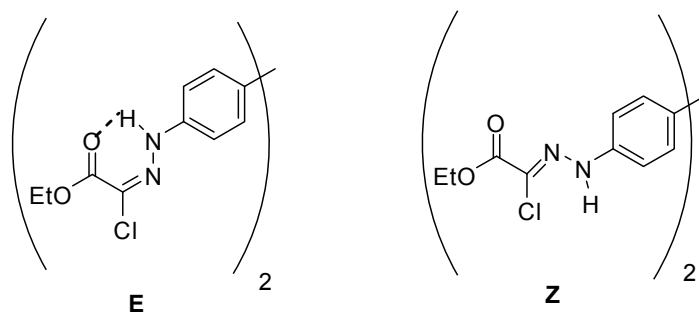
The *bis*-hydrazonoyl chloride **3** can be formulated in different possible tautomeric structures, namely *bis*-hydrazone (**A**), and *bis*-CH-azo tautomer (**B**) (Figure 1). The ^1H -NMR spectrum of the *bis*-hydrazonoyl chloride **3** showed absence of signal at 5.27 ppm [7], which is characteristic for the CH proton of CH-azo form. These spectroscopic analysis rules out the *bis*-CH-azo form (**B**) (Figure 1).

Figure 1. *bis*-hydrazone (**A**), and *bis*-CH-azo tautomer (**B**).



The *bis*-hydrazone tautomer (**A**) can exist in two geometric structures (*E* and *Z* configuration) (Figure 2).

Figure 2. *E* and *Z* geometric structures.



In the IR spectrum, when intramolecular hydrogen bonding occurs in *E* isomer, the N-H stretching vibration was observed at around 3080 cm^{-1} [8]. In the present case, the higher shift in N-H band (observed at around 3255 cm^{-1}) can be attributed to the absence of intramolecular hydrogen bonding. Also, the chemical shift of =NNH proton of *bis*-hydrazonoyl halide **3** is found at δ 10.62. In contrast, the value of δ (NH) in phenylhydrazone that form intramolecular hydrogen bonds to carbonyl oxygen atoms is reported to be in the range of 13–15 ppm [9,10]. Thus on the basis of these evidences, the *bis*-hydrazonoyl halide **3** can be deduced to exist in *Z*-form. Also, it is known that the (*Z*)-isomers are thermodynamically more stable [11].

Experimental

All melting points were measured on a Gallenkamp melting point apparatus (Weiss-Gallenkamp, London, UK). The infrared spectra were recorded in potassium bromide disks on a pye Unicam SP 3300 and Shimadzu FT IR 8101 PC infrared spectrophotometers (Pye Unicam Ltd. Cambridge, England and Shimadzu, Tokyo, Japan, respectively). The NMR spectrum was recorded on a Varian Mercury VX-300 NMR spectrometer (Varian, Palo Alto, CA, USA). ^1H spectrum was run at 300 MHz and ^{13}C spectra were run at 75.46 MHz in deuterated dimethyl sulphoxide ($\text{DMSO}-d_6$). Chemical shifts were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer (Shimadzu) at 70 eV. Elemental analyses were carried out at the Micro-analytical Center of Cairo University, Giza, Egypt.

Preparation of bis-Hydrazonoyl Chloride **3**

To a cold solution of ethyl 2-chloro-3-oxobutanoate (**1**) (0.164 g, 1 mmol) in EtOH (30 mL), buffered with sodium acetate trihydrate (2 g), was added the diazonium chloride [prepared by diazotizing the benzidine (0.092 g, 0.5 mmol) dissolved in concentrated hydrochloric acid (2 mL) with sodium nitrite solution (0.07 g, 1 mmol) in water (2 mL)]. The addition was carried out portion-wise with stirring at 0–5 °C over a period of 30 min. After complete addition, the reaction mixture was stirred for further 4 h, at room temperature, then kept in an ice chest for 12 h, and finally diluted with water. The precipitated solid was collected by filtration, washed with water, dried and finally recrystallized from DMF to afford the *bis*-hydrazonoyl chloride **3** in 68% yield, yellow crystals, mp. 274–275 °C; IR (KBr) ν_{max} : 3255 (NH), 2982 (aliphatic CH), 1707 (C=O) cm^{-1} ; ^1H -NMR ($\text{DMSO}-d_6$): δ 1.32 (t, 6H, 2CH₃, $J = 7.2\text{ Hz}$), 4.30 (q, 4H, 2CH₂, $J = 7.2\text{ Hz}$), 7.43 (d, 4H, $J = 8.4\text{ Hz}$), 7.63 (d, 4H, $J = 8.4\text{ Hz}$), 10.62 (s, 2H, 2NH); ^{13}C -NMR ($\text{DMSO}-d_6$): 14.06, 62.11, 113.69, 115.03, 126.83, 133.76, 141.68, 159.31; MS m/z (%) 453 (3.18), 452 (8.22), 451 (M^+ , 2.39), 302 (2.2), 225 ($1/2\text{M}^+$, 2.35), 149 (2.04), 73 (3.07). Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{Cl}_2\text{N}_4\text{O}_4$ (451.30): C, 53.23; H, 4.47; N, 12.41. Found: C, 53.34; H, 4.39; N, 12.50%.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Farag, A.M.; Kheder, N.A.; Budesinsky, M. Regioselective synthesis of polysubstituted 3,3'-bi-1*H*-pyrazole derivatives via 1,3-dipolar cycloaddition reactions. *Tetrahedron* **1997**, *53*, 9293–9300.
2. Kheder, N.A.; Riyadh, S.M.; Asiry, A.M. Azoles and bis-azoles: Synthesis and biological evaluation as antimicrobial and anti-cancer agents. *Chem. Pharm. Bull.* **2013**, *61*, 504–510.
3. Sayed, A.R. Synthesis of 1,3,4-thiadiazines, bis-1,3,4-thiadiazoles, [1,2,4]triazino[3,4-*b*][1,3,4]thiadiazine, thiazolines from carbonothioic dihydrazide. *Tetrahedron* **2012**, *68*, 2784–2789.
4. Sayed, A.R. Synthesis of novel thiadiazoles and bis-thiadiazoles from carbonothioic dihydrazide. *Tetrahedron Lett.* **2010**, *51*, 4490–4493.
5. Dow Chemical Co. 2,4-Dichloro-*N*-[chloro-(2,4-dichlorophenyl)methylene]benzenecarbohydrazonoyl chloride. *Jpn. Kokai Tokkyo Koho* 80,98,148, 25 July 1980; [*Chem. Abstr.* **1981**, *94*, 30332t].
6. Phillips, R.R. The Japp-Klingemann reaction. *Org. React.* **1959**, *10*, 143–178.
7. Schantl, J.G.; Hebeisen, P. 1-Phenylazo-1-alkenes. *Tetrahedron* **1990**, *46*, 395–406.
8. Sahay, A. Synthesis and characterization of copper(II) and nickel(II) complexes of ethyl-2,3-dioxobutyrate-2-*o*-aminophenyl-hydrazone and pentane-2,3,4-trioxo-3-*o*-aminophenyl hydrazone. *Asian J. Chem.* **1994**, *6*, 476–480.
9. Prasad, R.M. Studies on the Structure and Properties of Some Arylhydrazones. Ph.D. Thesis, Bihar University, Muzaffarpur, India, 1985.
10. Prasad, D.; Prasad, N.; Prasad, R.M.; Ferrier, R.J.; Milgate, S.M. ¹³C-NMR Examination of ethyl cyano(arylhydrazono)acetates. *J. Chem. Soc. Perkin Trans. I* **1984**, 1397–1399.
11. Rowe, J.E.; Papanelopoulos, D.A. Mechanisms of nucleophilic attack at carbon-nitrogen double bonds. The reaction of benzohydrazonoyl compounds with methoxide ion. *Aust. J. Chem.* **1995**, *48*, 2041–2046.