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Research Article

Convenient Synthesis of benzo[f][1,3,4]thiadiazocin derivatives

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ABSTRACT

Condensation of some alkyl-2-phenylhydrazinecarbodithioates with 2-chloromethylbenzoylchloride in alkaline boiling acetonitrile afford a group of 7-(alkylsulfanyl)-9-phenyl-5*H*-benzo[*f*][1,3,4]thiadiazocin-10(9*H*)-ones.

Keywords: 2-chloromethylbenzoylchloride, alkyl-2-phenylhydrazinecarbodithioates,benzo[*f*][1,3,4]thiadiazocin, cyclocondensation, dithizone analogues.

1. Introduction

Dithizone and N'-phenylbenzothiohydrazide are common precursors for the preparation of various fused [1,3,4]thiadiazines [1] . In the recent years we have utilized alkyl-2-phenylhydrazinecarbodithioates as affordable alternatives for the previous expensive precursors in the synthesis of such heterocyclic rings [2-7]. In these studies, it was well evidenced that hard-soft kinetic rule determined the structure of the final product.

In the present study, we exhibit the application of alkyl-2-phenylhydrazinecarbodithioates on the synthesis of benzo[*f*][1,3,4]thiadiazocin derivatives, which there was only one example for their preparation on the literature [8].

2. Experimental

2-Chloromethylbenzoylchloride **1** was prepared according to an earlier procedure [9,10]

IR spectra were obtained on a 4300 Shimadzu spectrometer in KBr pellets. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra of products were carried out on Bruker Avance spectrometer in Chloroform-d ($CDCl_3$) with tetramethylsilane (TMS) as an internal standard. Electron ionization mass spectra were obtained on a Varian Mat CH-7 instrument at 70 eV. Elemental analysis was obtained on a Thermo Finnigan Flash EA microanalyzer. Melting points were determined on an Electrothermal 9100 apparatus.

General procedure for the preparation of (7*Z*)-7-(alkylsulfanyl)-9-phenyl-5*H*-benzo[*f*][1,3,4]thiadiazocin-10(9*H*)-ones 3a-e:

A mixture of 2-chloromethylbenzoylchloride 1 (2.5 mmoles, 0.47 gr), alkyl-2-phenylhydrazinecarbo- dithioates 2 (2.5 mmole) in acetonitril (25 ml) was stirred and triethyamine (1ml) was added drop wise. The mixture was boiled under inert atmosphere for 5 hours. After the reaction was completed, the mixture was cooled to room temperature, the solvent was evaporated and the residue was purified by column chromatography over silica gel eluted with chloroform: hexane (1: 1).

7-Methylsulfanyl-9-phenyl-5*H*-benzo[*f*][1,3,4] thiadiazocin-10(9*H*)-one 3a:

This compound was obtained as a yellow powder in 45% yield, mp 185-187^{o}C (dec), IR (KBr disk):ν, 1620 cm^{-1}, 2900 cm^{-1}, 2940 cm^{-1}; ^{1}HNMR: ($CDCl_3$) δ , 2.61 (s, 3H, S-CH_3), 4.45 (s, 2H, S-CH_2) 7.2-7.9 (multiplet, 9H); m/z, 316, 314. *Anal.* Calcd. For $C_{16}H_{14}N_2OS_2$: C, 61.12; H, 4.49; N, 8.91; S, 20.40; Found : C, 60.85; H, 4.58; N, 8.67; S, 20.15

7-Ethylsulfanyl-9-phenyl-5*H*-benzo[*f*][1,3,4] thiadiazocin-10(9*H*)-one 3b:

This compound was obtained as a yellow powder in 52% yield, mp 172-173^{o}C (dec), IR (KBr disk):ν, 1620 cm^{-1}, 2910 cm^{-1}, 2950 cm^{-1} ; ^{1}HNMR:($CDCl_3$) δ, 1.35 (t, 3H, *J*=21Hz,

CH_3), 3.1(q, 2H, *J*=21Hz, S-CH_2), 4.47 (s, 2H, S-CH_2), 7.2-7.9 (multiplet, 9H); m/z, 330, 328. *Anal.* Calcd. For $C_{17}H_{16}N_2OS_2$: C, 62.16; H, 4.91; N, 8.53; S, 19.52; Found: C, 61.88; H, 4.97; N, 8.39; S, 19.31.

9-Phenyl-7-propylsulfanyl-5*H*-benzo[*f*][1,3,4] thiadiazocin-10(9*H*)-one 3c:

This compound was obtained as a yellow powder in 60% yield, mp 164-166^{o}C (dec), IR (KBr disk):ν, 1620 cm^{-1}, 2910 cm^{-1}, 2950 cm^{-1} ; ^{1}HNMR:($CDCl_3$) δ, 1.09 (t, 3H, *J*=21Hz, CH_3), 1.7 (sextet, 2H, J_1= J_2=21Hz, CH_2), 3.06 (t, 2H, *J*=21Hz, S-CH_2), 4.47 (s, 2H, S-CH_2), 7.2-7.9 (multiplet, 9H); m/z, 344, 342. *Anal.* Calcd. For $C_{18}H_{18}N_2OS_2$: C, 63.13; H, 5.30; N, 8.18; S, 18.73; Found : C, 63.32; H, 5.07; N, 7.97; S, 18.51.

7-Butylsulfanyl-9-phenyl-5*H*-benzo[*f*][1,3,4] thiadiazocin-10(9*H*)-one 3d:

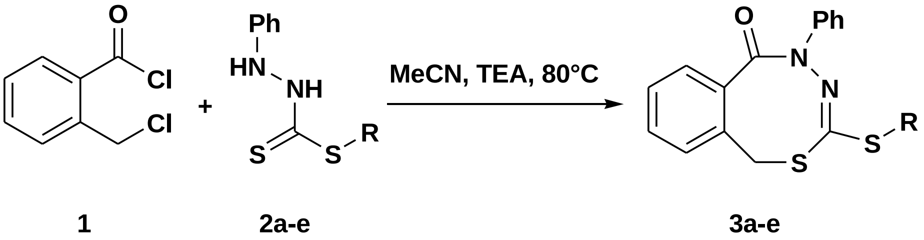
This compound was obtained as a yellow powder in 47% yield, mp 157-159^{o}C (dec), IR (KBr disk):ν, 1610 cm^{-1}, 2920 cm^{-1}, 2950 cm^{-1} ; ^{1}HNMR:($CDCl_3$) δ, 0.95 (t, 3H, *J*=21Hz, CH_3), 1.3-1.8(multiplet, 4H, 2CH_2), 3.1(t, 2H, *J*=21Hz S-CH_2), 4.45 (s, 2H, S-CH_2), 7.2-7.9 (multiplet, 9H);); m/z, 358, 356; *Anal.* Calcd. For $C_{19}H_{20}N_2OS_2$: C, 64.01; H, 5.65; N, 7.86; S, 17.99; Found : C, 63.79; H, 5.76; N, 7.91; S, 17.78.

7-Benzylsulfanyl-9-phenyl-5*H*-benzo[*f*][1,3,4] thiadiazocin-10(9*H*)-one 3e:

This compound was obtained as a yellow powder in 65% yield, mp 194-196^{o}C (dec), IR (KBr disk):ν, 1620 cm^{-1}, 2910 cm^{-1}, 2940 cm^{-1} ; ^{1}HNMR:($CDCl_3$) δ, 4.28 (s, 2H, S-CH_2Ph), 4.45 (s, 2H, S-CH_2), 7-7.9 (multiplet, 14H);); m/z, 392, 390; *Anal.* Calcd. For $C_{22}H_{18}N_2OS_2$: C, 67.66; H, 4.65; N, 7.17; S, 16.42; Found : C, 67.43; H, 4.78; N, 7.25; S, 16.20.

3. Results and Discussions

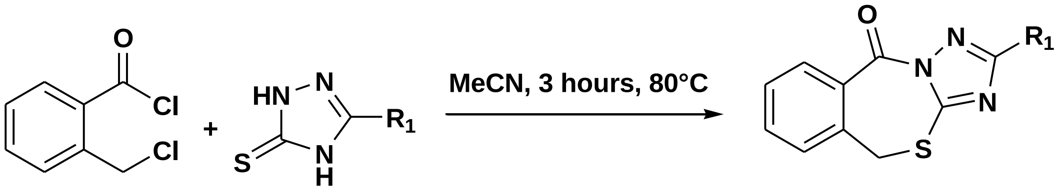
Our strategy for the formation of benzo[*f*][1,3,4]thiadiazocin ring is cyclocondensation of 2-chloromethylbenzoylchloride **1** with alkyl-2-phenylhydrazinecarbodithioates **2a-e** in the alkaline acetonitrile as shown in ***Scheme I***.



R= a: Me; b: Et; c: Pr; d: Bu; e: CH_2Ph

Scheme I. General route of the synthesis of 7-(alkylsulfanyl)-9-phenyl-5*H*-benzo[*f*][1,3,4]thiadiazocin-10(9*H*)-ones

In a previous communication, 2-chloromethylbenzoylchloride **1** was condensed with 1, 2, 4 -triazole-3-thiones for the regioselective preparation of [1, 2, 4]triazolo[3, 2-*b*][2, 4]benzothiazepin-10(5*H*)-ones [9] as shown in Figure 1. Regioselectivity of this reaction was substantiated by X-Ray crystallography of the product.



R_1= H, Me, Ph

Scheme 2. Condensation of chloromethylbenzoylchloride with 1, 2, 4 -triazole-3-thiones.

We found that the yield of the synthesis significantly increase by;

a) Drying of the solvent and base before use, which inhibits the hydrolysis of 2-chloromethylbenzoylchloride **1**. b) Utilization of nitrogen atmosphere for the reaction, which decrease the oxidation of alkyl-2-phenylhydrazinecarbodithioates **2a-e**. c) Optimization of the reaction concentration on 0.1 mol/litr for the reactants, which decrease the polymerization of the reactants to larger rings.

The structures assigned to compounds **3** were substantiated by spectral and microanalytical data. The ^{1}HNMR spectra were devoid of signals at δ 6.0 and 9.0 ppm for NH moieties of precursors **2** and showed a signal at δ 4.45 ppm for the CH_2 moiety of precursors **1** indicating the construction of thiadiazocin ring over the methylene and carbonyl groups of the benzene ring. These results amplified by IR spectra, which lacked N-H stretching frequencies of their precursors **2** and confirm the presence of a carbonyl group of their precursor **1** by a stretching frequency at around 1620 cm^{-1}. Mass spectra showed the expected molecular ion plus a negligible isotopic effect, according to the sulfur atom pattern. Elemental analysis of these compounds showed no significant differences with the calculated amounts from their molecular formula.

For example, condensation of 2-chloromethylbenzoylchloride **1** with methyl-2-phenylhydrazinecarbodithioates **2a** in the alkaline acetonitrile gave a yellow powder in 45% yield. The ^{1}HNMR spectrum showed signals at δ 2.61, 4.45 and 7.2-7.9 ppm assignable to 3, 2 and 9 protons for SCH_3, CH_2 and aromatic hydrogens respectively. IR spectrum showed stretching bands on 1620, 2900 and 2950 cm^{-1} for C=O and CH_3 moieties respectively. Mass spectrum showed the expected molecular ion peaks on m/z = 316 (negligible) and 314. Its elemental values (C, 60.85; H, 4.58; N, 8.67; S, 20.15), has no significant difference to the calculated amounts for $C_{16}H_{14}N_2OS_2$ (C, 61.12; H, 4.49; N, 8.91; S, 20.40). These results strongly confirm the structure 7-(methylsulfanyl)-9-phenyl-5*H*-benzo[*f*][1,3,4]thiadiazocin-10(9*H*)-ones **3a** for this product.

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