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8-Aryloct-7-en-2,4,6-triones as Useful Precursors for the Regioselective Synthesis of Some New 2-Methyl-5-styryl-7-thioxo-6,7-dihydropyrazolo[1,5-c] pyrimidines

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ABSTRACT Dehydroacetic acid, commonly abbreviated as DHA, and its derivatives have been extensively used as important intermediates in organic synthesis particularly for the synthesis of heterocyclic compounds. The reaction of 8-aryloct-7-en-2,4,6-triones (DHA-triones, readily prepared from commercially available DHA by the use of a multistep procedure) with thiosemicarbazide led the formation of some new 2-methyl-5-styryl-7-thioxo-6,7-dihydropyrazolo[1,5-c] pyrimidines.

KEYWORDS 2-Methyl-5-styryl-7-thioxo-6,7-dihydropyrazolo[1,5-c]pyrimidines, 8-Aryloct-7-en-2,4,6-triones, Dehydroacetic acid, Thiosemicarbazide

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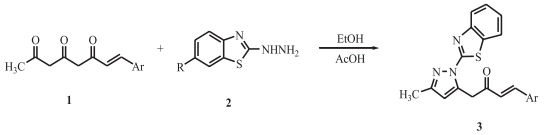
INTRODUCTION

3-Acetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one (DHA) is a versatile molecule for the synthesis of a wide variety of organic compounds particularly heterocyclic compounds. DHA has long been of significance particularly for the biogenetic-type synthesis of natural molecules and heterocyclic compounds of biological importance.[1-10] Dehydroacetic acid and its derivatives can be considered as the important source for a large number of β-polyketones such as β-diketones, triones, and α,β-unsaturated carbonyl compounds.[11-13] Due to the presence of multifunctionality, the α,β-unsaturated tricarbonyl compounds (DHA triones) can be used as important substrates in the area of synthetic organic chemistry.

In a previous report from our laboratory,[14] it has been shown that the reaction of DHA-triones **1** with 2-benzothiazolylhydrazines **2** leads to the formation of benzothiazolylpyrazoles **3** (**Eq 1**).



1 **2** **3** **(Eq 1)**

On the basis of this observation, it was anticipated that the reaction of the 7-en-2,4,6-triones**1** with thiosemicarbazide might lead to the formation of fused pyrazolopyrimidines. Thus, in connection with previous work from our research group on DHA and its derivatives[14-20] and also keeping in mind the biological importance of fused pyrazolopyrimidines,[21-27] it was planned to investigate the reactivity of these triones with thiosemicarbazide with the objective to synthesize some new 2-methyl-5-styryl-7--thioxo-6,7-dihydropyrazolo[1,5-c]pyrimidine derivatives.

RESULTS AND DISCUSSION

To begin with the work, it was considered suitable to carry out the model reaction with trione **1a** and

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mmol) and the mixture was refluxed on water bath for 4–5 h. The reaction mixture was cooled to room temperature after removing about half of the solvent under *vacuum*. A solid product was separated out which was filtered and recrystallized from ethanol.

2-Methyl-5-styryl-7-thioxo-6,7-dihydropyrazolo[1,5-c] pyrimidine (8a)

IR (ν_{max}, KBr): 1260 cm^{-1} (C=S str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.57 (s, 3H, $-CH_3$), 6.36 (s, 1H, C_3-H), 6.77 (s, 1H, C_4-H), 6.79 (d, 1H, -CH=, J = 16.2 Hz), 7.18 (d, 1H, =CH-, J = 16.2 Hz), 7.33–7.54 (m, 5H, Ar-H), 10.34 (s, 1H, -NH); Analysis calculated for $C_{15}H_{13}N_3S$: C, 67.42; H, 4.86; N, 15.73. Found: C, 67.59; H, 4.21; N, 15.69.

2-Methyl-5-(4-methylstyryl)-7-thioxo-6,7-dihydropyrazolo[1,5-c]pyrimidine (8b)

IR (ν_{max}, KBr): 1258 cm^{-1} (C=S str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.48 (s, 3H, $-CH_3$), 2.52 (s, 3H, $-CH_3$), 6.35 (s, 1H, C_3-H), 6.72 (d, 1H, -CH=, J = 16.5 Hz), 6.73 (s, 1H, C_4-H), 7.14 (d, 1H, =CH-, J = 16.5 Hz), 7.21 (d, 2H, Ar-H, J = 7.8 Hz), 7.42 (d, 2H, Ar-H, J = 7.8 Hz), 10.21 (s, 1H, -NH); Analysis calculated for $C_{16}H_{15}N_3S$: C, 68.32; H, 5.33; N, 14.94. Found: C, 68.38; H, 4.69; N, 14.01.

2-Methyl-5-(4-methoxylstyryl)-7-thioxo-6,7-dihydropyrazolo[1,5-c]pyrimidine (8c)

IR (ν_{max}, KBr): 1259 cm^{-1} (C=S str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.51 (s, 3H, $-CH_3$), 3.85 (s, 3H, $-OCH_3$), 6.32 (s, 1H, C_3-H), 6.64 (d, 1H, -CH=, J = 16.5 Hz), 6.72 (s, 1H, C_4-H), 6.92 (d, 2H, Ar-H, J = 8.7 Hz), 7.11 (d, 1H, =CH-, J = 16.5 Hz), 7.46 (d, 2H, Ar-H, J = 8.7 Hz), 10.26 (s, 1H, -NH); Analysis calculated for $C_{16}H_{15}N_3OS$: C, 64.64; H, 5.05; N, 14.14. Found: C, 64.80; H, 4.86; N, 14.34.

2-Methyl-5-(4-chlorostyryl)-7-thioxo-6,7-dihydropyrazolo[1,5-c]pyrimidine (8d)

IR (ν_{max}, KBr): 1246 cm^{-1} (C=S str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.60 (s, 3H, $-CH_3$), 6.37 (s, 1H, C_3-H), 6.73 (d, 1H, -CH=, J = 16.2 Hz), 6.75 (s, 1H, C_4-H), 7.10 (d, 1H, =CH-, J = 16.2 Hz), 7.37 (d, 2H, Ar-H, J = 8.7 Hz), 7.44 (d, 2H, Ar-H, J = 8.7 Hz), 10.03 (s, 1H, -NH); Analysis calculated for $C_{15}H_{12}N_3SCl$: C, 59.80; H, 3.98; N, 13.95. Found: C, 60.22; H, 3.48; N, 14.02.

2-Methyl-5-(4-bromostyryl)-7-thioxo-6,7-dihydropyrazolo[1,5-c]pyrimidine (8e)

IR (ν_{max}, KBr): 1248 cm^{-1} (C=S str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.53 (s, 3H, $-CH_3$), 6.39 (s, 1H, C_3-H), 6.76 (d, 1H, -CH=, J = 16.5 Hz), 6.77 (s, 1H, C_4-H), 7.09 (d, 1H, =CH-, J = 16.5 Hz), 7.39 (d, 2H, Ar-H, J = 8.4 Hz), 7.54 (d, 2H, Ar-H, J = 8.4 Hz), 10.01 (s, 1H, -NH); Analysis calculated for $C_{15}H_{12}N_3SBr$: C, 52.02; H, 3.47; N, 12.14. Found: C, 52.35; H, 3.12; N, 12.50.

2-Methyl-5-(4-fluorostyryl)-7-thioxo-6,7-dihydropyrazolo[1,5-c]pyrimidine (8f)

IR (ν_{max}, KBr): 1257 cm^{-1} (C=S str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.55 (s, 3H, $-CH_3$), 6.40 (s, 1H, C_3-H), 6.75 (d, 1H, -CH=, J = 16.5 Hz), 6.79 (s, 1H, C_4-H), 7.07 (d, 1H, =CH-, J = 16.5 Hz), 7.40 (d, 2H, Ar-H, J = 8.4 Hz), 7.55 (d, 2H, Ar-H, J = 8.4 Hz), 10.03 (s, 1H, -NH); Analysis calculated for $C_{15}H_{12}N_3SF$: C, 63.16; H, 4.21; N, 14.74. Found: C, 63.47; H, 4.08; N, 14.95.

CONCLUSION

The present study involving the reaction of 8-aryloct-7-ene-2,4,6-triones (DHA-triones) with thiosemicarbazide provides a regioselective way for synthesizing new pyrazolopyrimidines of the type **8**. The new synthesis of fused compounds containing pyrazole and pyrimidine moieties may find interesting applications in synthetic and therapeutic areas.

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