Indian Journal of Chemistry
Vol. 46B, October 2007, pp. 1713-1715

Note

Dehydroacetic acid and its derivatives in organic synthesis: Synthesis of some new 2-substituted-4-(5-bromo-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-yl)thiazoles

Richa Prakash, Ajay Kumar, Shiv P Singh, Ranjana Aggarwal & Om Prakash*

Department of Chemistry, Kurukshetra University, Kurukshetra 136 119, India

E-mail: dromprakash50@rediffmail.com

Received 19 January 2007; accepted (revised) 2 July 2007

Synthesis of 3β,3β,5-tribromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one **2** from the bromination of DHA **1** in chloroform has been reported. The reaction of **2** with various thioureas/thioamides leads to an efficient synthesis of new 2-substituted-4-(5-bromo-4-hydroxy-6-methyl-2*H*-pyran-2-one-3-yl)thiazoles.

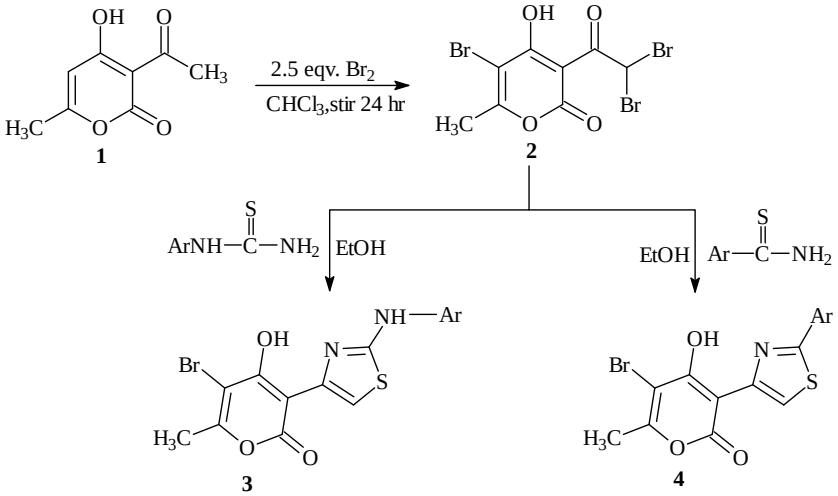
Keywords: Dehydroacetic acid, bromination, thioamides, thioureas, thiazoles

As part of the ongoing studies on the chemistry of 3-acetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one (dehydroacetic acid, DHA, **1**) and its derivatives[1], the synthesis of a new product 3β,3β,5-tribromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one (Tribromo DHA, **2**) from the bromination of **1** involving 2.5 equivalent of Br_2 containing catalytic amount of I_2 in $CHCl_3$ has been reported earlier[2]. In view of the fact that **2** bears α,α-dibromoketone functionality and the compounds possessing such functionality have offered superior alternatives to α-bromoketones in organic syntheses[3-5] especially in Hantzsch thiazole synthesis[6], it was considered worthwhile to investigate the reaction of **2** with various thioureas/thioamides for obtaining new pyranylthiazole derivatives of potential biological interest[7,8].

Results and Discussion

Tribromo DHA **2** was prepared by bromination of DHA **1** employing an improved procedure. The reaction of **2** was carried out with phenylthiourea in ethanol at RT. A solid separated out of the reaction mixture within 10 min, which was characterised as the expected 4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-aminophenylthiazole **3a** as evidenced by spectral and analytical (CHN) data. To assess the generality of the method, a variety of thioureas were treated with **2** in a similar manner to afford 2-arylamino-4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)thiazoles **3a-e**. On replacing thioureas by thioamides, the reaction yielded corresponding 2-aryl-4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)thiazoles **4a-c** (**Scheme I**). The results are summarized in **Table I**.

The advantages of the synthesis of new pyranylthiazoles **3a-e** and **4a-c** involving α,α-dibromoketone **2** can be summarized as: (i) The reaction conditions are mild and the reaction time is very short. (ii) The yields are high, the isolation of the products is convenient and crystalline solids obtained



Scheme I

Table I — Physical characterization data of pyranylthiazoles

Compd	Ar	m.p. (°C)	Yield (%)
3a	C_6H_5	240-41	74
3b	*p*-Cl	256	75
3c	*p*-F	250	72
3d	*p*-CH_3	245	71
3e	*p*-OCH_3	230-31	70
4a	C_6H_5	190-91	66
4b	*p*-Cl	212-13	70
4c	*p*-CH_3	180-81	68

do not require purification. (iii) There is no evolution of HBr, unlike Hantzsch thiazole synthesis and therefore acid sensitive moiety *i.e.* pyranyl moiety of DHA remains intact in the reaction[9-12]. (iv) Basification needed in the workup of Hantzsch thiazole synthesis[13] is avoided.

Experimental Section

Melting points were determined in open capillaries and are uncorrected. ^{1}H NMR spectra were recorded on a Brucker 300 MHz instrument using TMS as an internal standard. IR spectra were recorded on a Buck Scientific IR M-500 spectrometer. Elemental analyses were carried out in a Perkin Elmer-2400 instrument and mass spectra were recorded on Kratos MS-50 mass spectrometer. Common chemicals such as dehydroacetic acid, bromine, *etc*. were obtained from commercial suppliers.

3β,3β,5-Tribromoacetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one, 2

To a solution of 3.36 g of dehydroacetic acid **1** in chloroform (20 mL) was added a solution of 2.58 mL of Br_2 in chloroform (20 mL) at RT. The solution was stirred overnight and then it was washed with 5% sodium bisulphite solution, dried with anhydrous sodium sulphate, concentrated and purified by recrystallization from ethanol to give 5.9 g (74%) of **2**.

General procedure for the synthesis of 2-substi-tuted-4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-thiazoles

To a solution of **2 (**10 mmol) in ethanol (10 mL) was added thiourea or thioamide (10 mmol) and the reaction mixture was stirred for 10-20 min. The solid that separated out was filtered and washed with ethanol to give **3** or **4** respectively.

Spectral and analytical characterization data of the products are as follows

4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-aminophenylthiazole, 3a: ^{1}H NMR ($CDCl_3$): δ 2.44 (s, 3H, CH_3), 7.35-7.41 (m, 5H, Ar), 8.03 (s, 1H, C_5-H), 10.81 (s, 1H, NH); IR (KBr): 1703 cm^{-1} (C=O); MS: *m/z* M^+ (378), M^++2 (380). Anal. Found: C, 47.55; H, 2.89; N, 7.35. $C_{15}H_{11}BrN_2O_3S$ requires: C, 47.61; H, 2.91; N, 7.40%.

4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-amino-(4′-chloro)phenylthiazole, 3b: ^{1}H NMR ($CDCl_3$): δ 2.40 (s, 3H, CH_3), 7.34-7.50 (m, 4H, Ar), 7.51 (s, 1H, C_5-H), 10.91 (s, 1H, NH); IR (KBr): 1701 cm^{-1} (C=O); MS: *m/z* M^+ (412), M^++2 (414). Anal. Found: C, 43.64; H, 2.22; N, 6.77. $C_{15}H_{10}BrClN_2O_3S$ requires: C, 43.68; H, 2.42; N, 6.79%.

4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-amino-(4′-fluoro)phenylthiazole, 3c: ^{1}H NMR ($CDCl_3$): δ 2.39 (s, 3H, CH_3), 7.27-7.36 (m, 4H, Ar), 7.39 (s, 1H, C_5-H), 10.82 (s, 1H, NH); IR (KBr): 1700 cm^{-1} (C=O); MS: *m/z* M^+ (396), M^++2 (398). Anal. Found: C, 45.38; H, 2.49; N, 6.99. $C_{15}H_{10}BrFN_2O_3S$ requires: C, 45.45; H, 2.52; N, 7.07%.

4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-amino-(4′-methyl)phenylthiazole, 3d: ^{1}H NMR ($CDCl_3$): δ 2.30 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 7.24-7.38 (m, 4H, Ar), 8.12 (s, 1H, C_5-H), 10.71 (s, 1H, NH); IR (KBr): 1704 cm^{-1} (C=O); MS: *m/z* M^+ (392), M^++2 (394). Anal. Found: C, 48.84; H, 3.27; N, 6.99. $C_{16}H_{13}BrN_2O_3S$ requires: C, 48.97; H, 3.31; N, 7.14%.

4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-amino-(4′-methoxy)phenylthiazole, 3e: ^{1}H NMR ($CDCl_3$): δ 2.38 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 7.01-7.28 (m, 4H, Ar), 7.32 (s, 1H, C_5-H), 10.71 (s, 1H, NH); IR (KBr): 1695 cm^{-1} (C=O); MS: *m/z* M^+ (408), M^++2 (410). Anal. Found: C, 47.02; H, 3.17; N, 6.84. $C_{16}H_{13}BrN_2O_4S$ requires: C, 47.05; H, 3.18; N, 6.86%.

4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-phenylthiazole, 4a: ^{1}H NMR ($CDCl_3$): δ 2.51 (s, 3H, CH_3), 7.49-7.91 (m, 5H, Ar), 8.33 (s, 1H, C_5-H); IR (KBr): 1706 cm^{-1} (C=O); MS: *m/z* M^+ (363), M^++2 (365). Anal. Found: C, 49.44; H, 2.73; N, 3.79. $C_{15}H_{10}BrNO_3S$ requires: C, 49.58; H, 2.75; N, 3.85%.

4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-(4′-chloro)phenylthiazole, 4b: ^{1}H NMR ($CDCl_3$): δ 2.51 (s, 3H, CH_3), 7.49-7.89 (m, 4H, Ar), 8.34 (s, 1H, C_5-H); IR (KBr): 1705 cm^{-1} (C=O); MS: *m/z* M^+ (397), M^++2 (399). Anal. Found: C, 45.24; H, 2.22; N, 3.50. $C_{15}H_9BrClNO_3S$ requires: C, 45.34; H, 2.26; N, 3.52%.

4-(5-bromo-4-hydroxy-6-methyl-2-pyran-3-yl)-2-(4′-methyl)phenylthiazole, 4c: ^{1}H NMR ($CDCl_3$): δ 2.38 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 7.38-7.87 (m,

4H, Ar), 8.29 (s, 1H, C_5-H); IR (KBr): 1703 cm^{-1} (C=O); MS: *m/z* M^+ (377), M^++2 (379). Anal. Found: C, 50.80; H, 3.16; N, 3.67. $C_{16}H_{12}BrNO_3S$ requires: C, 50.92; H, 3.18; N, 3.71%.

Acknowledgement

The authors are thankful to DRDO New Delhi for their support through Grant No. ERIP/ER/0303447/M/01 and for the award of Junior Research Fellowship to Richa Prakash to carry out this work and also UCSF mass spectrometry facility, USA for providing mass spectral data.

References

1 Prakash O, Kumar A & Singh S P, *Heterocycles*, 63, **2004**, 1193.

2 Kumar A, Prakash R & Singh S P, *Synth Commun*, 35, **2005**, 461.

3 Prakash O, Sharma N & Pannu K, *Synth Commun*, **2007**, (in press).

4 Ahluwalia V K, Mehta B & Rawat M, *Synth Commun*, 22, **1992**, 2697.

5 Ahluwalia V K, Mehta B & Kumar R, *Synth Commun*, 19, **1989**, 619.

6 Prakash R, Kumar A, Prakash O & Singh S P, *Synth Commun*, **2007**, (in press).

7 Wadodkar S G & Kasturi A V, *J Indian Chem Soc*, 61, **1984**, 374.

8 Sawhney S N, Singh J & Bansal O P, *J Indian Chem Soc*, 51, **1974**, 566.

9 DHA and its derivatives are known to undergo cleavage or rearrangement in presence of acid. For relevant details see reference 10-12.

10 Harris T M, Harris C W & Brush C K, *J Org Chem*, 35, **1970**, 1329.

11 Glein S, Chantergal B & Nadi A I, *J Org Chem*, 48, **1983**, 4078.

12 Singh S P, Prakash O & Vaid R K, *Indian J Chem*, 23B, **1986**, 191.

13 Singh S P, Sehgal S & Sharma P K, *Indian J Chem*, 29B, **1990**, 533.