Iodine catalysed synthesis of 5-(arylmethylidene)rhodanines by grinding under solvent-free conditions

Hongshe Wang* and June Zeng

Shaanxi Key Laboratory for Phytochemistry, Department of Chemistry and Chemical Engineering, Baoji University of Arts and Sciences, Baoji, Shaanxi 721013, P. R. China

5-(Arylmethylidene)rhodanines have been synthesised in 88–95% yields by Knoevenagel condensation of various aromatic aldehydes with rhodanine in the presence of a catalytic amount of iodine at room temperature by grinding under solvent-free conditions.

Keywords: 5-(arylmethylidene)rhodanines, iodine, solvent-free, grinding

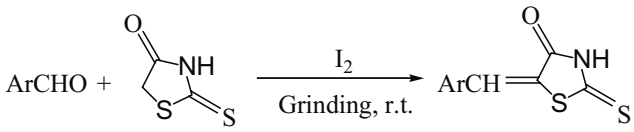
5-(Arylmethylidene)rhodanines are an important class of heterocyclic compounds with different biological and pharmaceutical activities and have been used in qualitative and quantitative analyses of heavy metal ions.[1] 5-(Arylmethylidene)rhodanines are classically obtained in organic solvents.[2,3] However, these methods suffer from several drawbacks such as a long reaction time, an excess of organic solvent and laborious separation techniques. Thus, several more efficient methods have been developed for the synthesis of 5-(arylmethylidene)rhodanines, which include the use of Na_2CO_3/glycine,[4] NaOAc/Bu_4NBr,[5] ionic liquids[6,7] and K_2CO_3/Al_2O_3.[8] However, there are still some disadvantages such as long reaction times, high temperatures and low yields of the products. Thus, there is scope for further improvement involving more environmentally-friendly and milder reaction conditions and higher product yields.

With the increasing public concern over environmental pollution, it is of great importance for chemists to come up with new approaches that are less hazardous to human health and the environment. The use of environmentally benign solvents like water and solvent-free reactions represent very powerful green chemical technology procedures from both the economical and synthetic point of view.[9-11] In recent decades, grinding has been used as an environmentally friendly method for organic synthesis reactions.[12-17]

In recent years, molecular iodine has been considered as an inexpensive, non-toxic and readily available catalyst for a variety of organic transformations.[18-25] In continuation of our work in studying iodine catalysed reactions,[26-28] we report here an efficient and convenient procedure for the synthesis of 5-(arylmethylidene)rhodanines by Knoevenagel condensation of various aromatic aldehydes and rhodanine in the presence of a catalytic amount of iodine at room temperature by grinding under solvent-free conditions (Scheme 1).

To determine the efficiency of this procedure, we carried out the reaction of benzaldehyde with rhodanine using various other Lewis acids such as $InCl_3$, $FeCl_3$, $ZnCl_2$, $(NH_4)_2Fe(SO_4)_2$, $Bi(NO_3)_3$, $Al_2(SO_4)_3$ and $Mg(ClO_4)_2$ at room temperature by grinding for 5 min under solvent-free conditions. Among these catalysts, I_2 was found to be the most effective catalyst for this conversion. As for the amount of the catalyst used, we found that 10 mol% of I_2 is sufficient to promote reaction efficiently. Few desired products would be obtained under similar conditions in the absence of I_2 even after grinding for 2 h. Any excess of I_2 beyond this loading did not show any further increase in conversion and yield. Use of less than the required catalyst loading resulted in poor yields.

To explore the generality of this method, a series of 5-(arylmethylidene)rhodanines was prepared under the optimised reaction conditions. By this method, the reactions were carried out simply by mixing a variety of aromatic aldehydes with rhodanine in the presence of a catalytic amount (10 mol%) of iodine at room temperature by grinding under solvent-free conditions and the results are summarised in Table 1. The mixture was ground together in a mortar with a pestle for 5–10 min. In all the cases, the reactions proceeded smoothly to afford the corresponding products in good to excellent yields. Aromatic aldehydes containing both electron-withdrawing and donating substituents produced satisfactory yields without a distinct difference between them. 2-Furaldehyde also afforded the desired products in excellent yields. However, aromatic ketones and rhodanine did not react under these reaction conditions. This is probably due to the lower general reactivity of aromatic ketones in comparison with aromatic aldehydes.



1 **2** **3**

Scheme 1

Table 1 Synthesis of 5-(arylmethylidene)rhodanines catalysed by iodine[a]

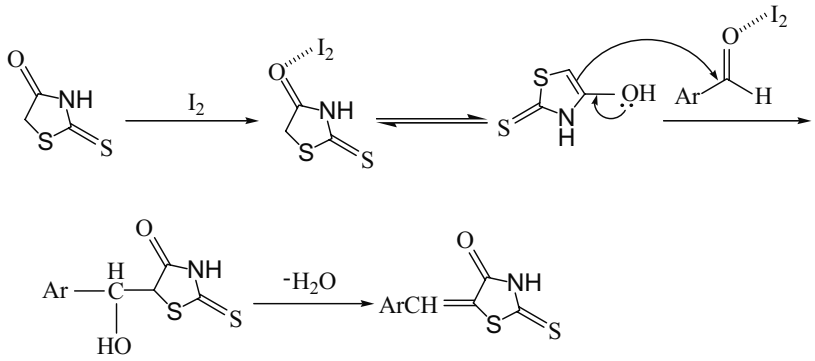
Entry	Ar	Product	Time/min	Yield[b]/%
1	C_6H_5	**3a**	5	93
2	4-ClC_6H_4	**3b**	5	92
3	2-ClC_6H_4	**3c**	8	91
4	4-$CH_3OC_6H_4$	**3d**	8	90
5	4-$CH_3C_6H_4$	**3e**	10	92
6	3-$NO_2C_6H_4$	**3f**	5	93
7	4-$NO_2C_6H_4$	**3g**	5	95
8	4-$(CH_3)_2NC_6H_4$	**3h**	10	88
9	2,4-$Cl_2C_6H_3$	**3i**	8	93
10	2-Furyl	**3j**	5	91

[a]All the reactions were performed with 10 mol% of iodine at room temperature by grinding under solvent-free conditions. [b]Isolated yields.

A possible mechanism for the condensation of aromatic aldehydes with rhodanine is shown in Scheme 2. Iodine activates the carbonyl groups of rhodanine and aromatic aldehyde and facilitates the formation of the enol form of rhodanine.

In summary, we have developed a new methodology to prepare 5-(arylmethylidene)rhodanines by Knoevenagel condensation of aromatic aldehydes and rhodanine in the presence of a catalytic amount of iodine at room temperature by grinding under solvent-free conditions. The advantages of this procedure are shorter reaction times, green environmentally friendly procedures, mild reaction conditions and high yields.

* Correspondent. E-mail: hongshewang@126.com



Scheme 2

Experimental

Melting points were determined on an XT4A electrothermal apparatus equipped with a microscope and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz) in DMSO-d_6 with TMS as an internal standard. IR spectra were determined on a Nicolet FTIR-750 spectrometer. Benzaldehyde and 2-furaldehyde were distilled prior to use. All other reagents were commercially available products and were used without further purification.

General procedure for the synthesis of 5-(arylmethylidene) rhodanines

A mixture of aromatic aldehyde (1 mmol), rhodanine (1 mmol), and iodine (0.1 mmol) was ground in a mortar with a pestle at room temperature until the reaction was completed (monitored by TLC). The reaction mixture was treated with 5% aqueous sodium thiosulfate. The precipitated products were then separated and recrystallised from DMF/H_2O (V:V = 2:1) to afford the pure products.

5-(Phenylmethylene)-2-thioxothiazolidin-4-one (**3a**): M.p. 205–207 °C (lit.,[8] 204.5–206 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.50–7.80 (m, 5H, ArH), 7.65 (s, 1H, CH=), 13.85 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 118.3, 127.2, 128.3, 134.1, 136.6, 150.7, 164.7, 199.2. IR (KBr) ν: 3435 (N–H), 1700 (C=O), 1673 (C=C), 1176 (C=S) cm^{-1}. Anal. Calcd for $C_{10}H_7NOS_2$: C, 54.30; H, 3.17; N, 6.33. Found: C, 54.41; H, 3.26; N, 6.20%.

5-(4-Chlorophenylmethylene)-2-thioxothiazolidin-4-one (**3b**)**:** M.p. 229–230 °C (lit.,[6] 227–228 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.66 (s, 4H, ArH), 7.71 (s, 1H, CH=), 13.88 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 119.8, 128.3, 130.9, 134.1, 137.7, 158.9, 166.5, 199.3. IR (KBr) ν: 3439 (N–H), 1708 (C=O), 1601 (C=C), 1180 (C=S) cm^{-1}. Anal. Calcd for $C_{10}H_6ClNOS_2$: C, 46.97; H, 2.35; N, 5.48. Found: C, 46.91; H, 2.43; N, 5.38%.

5-(2-Chlorophenylmethylene)-2-thioxothiazolidin-4-one (**3c**)**:** M.p. 181–182 °C (lit.,[8] 181–182 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.45 (s, 1H, CH=), 7.50–7.59 (m, 3H, ArH), 7.62–7.70 (m, 1H, ArH), 13.95 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 121.8, 125.8, 127.2, 128.1, 132.2, 133, 133.8, 150.3, 164.4, 199.7. IR (KBr) ν: 3436 (N–H), 1703 (C=O), 1597 (C=C), 1193 (C=S) cm^{-1}. Anal. Calcd for $C_{10}H_6ClNOS_2$: C, 46.97; H, 2.35; N, 5.48. Found: C, 46.80; H, 2.46; N, 5.61%.

5-(4-Methoxyphenylmethylene)-2-thioxothiazolidin-4-one (**3d**)**:** M.p. 248–250 °C (lit.,[7] 249–250 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.06 (s, 3H, CH_3), 7.10 (d, J = 8.7 Hz, 2H, ArH), 7.53 (d, J = 8.7 Hz, 2H, ArH), 7.63 (s, 1H, CH=), 13.75 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 56.4, 114.8, 116.0, 126.0, 129.0, 131.6, 134.3, 167.8, 199.1. IR (KBr) ν: 3438 (N–H), 1689 (C=O), 1631 (C=C), 1170 (C=S) cm^{-1}. Anal. Calcd for $C_{11}H_9NO_2S_2$: C, 52.59; H, 3.59; N, 5.58. Found: C, 52.73; H, 3.64; N, 5.47%.

5-(4-Methylphenylmethylene)-2-thioxothiazolidin-4-one (**3e**)**:** M.p. 222–223 °C (lit.,[6] 221–223 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.37 (s, 3H, CH_3), 7.41 (d, J = 8.1 Hz, 2H, ArH), 7.48 (d, J = 8.2 Hz, 2H, ArH), 7.61 (s, 1H, CH=), 13.70 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 22.9, 117.7, 128.6, 129.2, 134.1, 139.9, 144.2, 165.6, 199.1. IR (KBr) ν: 3435 (N–H), 1704 (C=O), 1593 (C=C), 1181 (C=S) cm^{-1}. Anal. Calcd for $C_{11}H_9NOS_2$: C, 56.17; H, 3.83; N, 5.96. Found: C, 56.24; H, 3.96; N, 5.80%.

5-(3-Nitrophenylmethylene)-2-thioxothiazolidin-4-one (**3f**)**:** M.p. 263–264 °C (lit.,[8] 263–265 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.80 (s, 1H, ArH), 7.83–7.90 (m, 1H, ArH), 7.95 (d, J = 7.6 Hz, 1H, ArH), 8.30 (d, J = 8.1 Hz, 1H, ArH), 8.45 (s, 1H, CH=), 13.91 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 123.8, 128.6, 130.4, 133.8, 135.2, 137.5, 145.8, 147.5, 166.6, 199.8. IR (KBr) ν: 3433 (N–H), 1701 (C=O), 1643 (C=C), 1189 (C=S) cm^{-1}. Anal. Calcd for $C_{10}H_6N_2O_3S_2$: C, 45.11; H, 2.26; N, 10.53. Found: C, 45.23; H, 2.14; N, 10.65%.

5-(4-Nitrophenylmethylene)-2-thioxothiazolidin-4-one (**3g**)**:** M.p. 250–251 °C (lit.,[8] 250–251 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.74 (s, 1H, CH=), 7.86 (d, J = 8.8 Hz, 2H, ArH), 8.35 (d, J = 8.8 Hz, 2H, ArH), 13.85 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 122.7, 129.8, 132.9, 145.2, 147.9, 152.4, 167.5, 199.6. IR (KBr) ν: 3439 (N–H), 1723 (C=O), 1641 (C=C), 1192 (C=S) cm^{-1}. Anal. Calcd for $C_{10}H_6N_2O_3S_2$: C, 45.11; H, 2.26; N, 10.53. Found: C, 45.27; H, 2.16; N, 10.70%.

5-(4-Dimethylaminophenylmethylene)-2-thioxothiazolidin-4-one (**3h**)**:** M.p. 269–270 °C (lit.,[6] 270–271 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.03 (s, 6H, $2CH_3$), 6.90 (d, J = 8.9 Hz, 2H, ArH), 7.47 (d, J = 8.8 Hz, 2H, ArH), 7.55 (s, 1H, CH=), 13.66 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 94.9, 109.2, 111.4, 121.2, 140.8, 155.5, 156.2, 167.7, 198.8. IR (KBr) ν: 3439 (N–H), 1687 (C=O), 1583 (C=C), 1171 (C=S) cm^{-1}. Anal. Calcd for $C_{12}H_{12}N_2OS_2$: C, 54.55; H, 4.55; N, 10.61. Found: C, 54.50; H, 4.46; N, 10.68%.

5-(2,4-Dichlorophenylmethylene)-2-thioxothiazolidin-4-one (**3i**)**:** M.p. 235–236 °C (lit.,[7] 234–235 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.50–7.65 (m, 2H, ArH), 7.77 (s, 1H, ArH), 7.89 (s, 1H, CH=), 13.95 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 122.4, 127.3, 128.5, 129.6, 132.2, 133.8, 134.8, 152.6, 163.8, 202.4. IR (KBr) ν: 3433 (N–H), 1702 (C=O), 1645 (C=C), 1192 (C=S) cm^{-1}. Anal. Calcd for $C_{10}H_5Cl_2NOS_2$: C, 41.38; H, 1.72; N, 4.83. Found: C, 41.30; H, 1.83; N, 4.92%.

5-(2-Furylmethylene)-2-thioxothiazolidin-4-one (**3j**)**:** M.p. 229–230 °C (lit.,[7] 228–229 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.73 (s, 1H, ArH), 7.26 (d, J = 3.2 Hz, 1H, ArH), 7.49 (s, 1H, ArH), 8.12 (s, 1H, CH=), 13.75 (br, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 111.4, 119.9, 120.2, 133.3, 142.2, 156.3, 164.6, 198.7. IR (KBr) ν: 3436 (N–H), 1695(C=O), 1602 (C=C), 1180 (C=S) cm^{-1}. Anal. Calcd for $C_8H_5NO_2S_2$: C, 45.50; H, 2.37; N, 6.64. Found: C, 45.61; H, 2.43; N, 6.56%.

This work was financially supported by the Educational Committee of Shaanxi Province (No. 08JZ09) and Baoji University of Arts and Sciences (No.Zk064).

Received 6 February 2009; accepted 26 March 2009
Paper 09/0437 doi: 10.3184/030823409X460696
Published online: 3 July 2009

References

1 F.C. Brown, *Chem. Rev.,* 1961, **61,** 463.
2 F.C. Brown, C.K. Bradsher, S.M. Bond and M. Potter, *J. Am. Chem. Soc.*, 1951, **73,** 2357.
3 R.G. Giles, N.J. Lewis, J.K. Quick, M.J. Sasse, M.W.J. Urquhart and L. Youssef, *Tetrahedron,* 2000, **56,** 4531.
4 M.M. Chowdhry, D.M.P. Mingos, A.J.P. White and D.J. Williams, *J. Chem. Soc., Perkin Trans. 1,* 2000, 3495.
5 Y.Q. Zhang, C. Wang, J.J. Ma, J.C. Li, R.X. Tang and Y.P. Wang, *Chin. J. Appl. Chem.*, 2008, **25,** 122.
6 X.Z. Lian, Y.Q. Li and M.Y. Zhou, *Chin. J. Org. Chem.,* 2006, **26,** 1272.

7 J.J. Ma, S.T. Gao, Z. Li, R.X. Tang, H.Y. Liu, C. Wang and Y. Gao, *Chin. J. Org. Chem.,* 2008, **28,** 339.
8 M. Zhang, C.D. Wang, S.L. Yu, Z.B. Tian, L. Zhang, Z.J. Chen and J.G. Li, *Chem. J. Chin. Univ.,* 1994, **15,** 1647.
9 G. Rothenberg, A.P. Downie, C.L. Raston and J.L. Scott, *J. Am. Chem. Soc.,* 2001, **123,** 8701.
10 Y. Liang, Y.X. Xie and J.H. Li, *J. Org. Chem.,* 2006, **71,** 379.
11 S.J. Jeon, H. Li and P.J. Walsh, *J. Am. Chem. Soc.,* 2005, **127,** 16416.
12 G. Cianchetta, R.W. Singleton, M. Zhang, M. Wildgoose, D. Giesing, A. Fravolini, G. Cruciani and R.J. Vaz, *J. Med. Chem.,* 2005, **48,** 2927.
13 F. Toda, K. Tanaka, Y. Kagawn and Y. Sakaino, *Chem. Lett.,* 1990, 373.
14 F. Toda, T. Suzuki and S. Higa, *J. Chem. Soc., Perkin Trans. 1,* 1998, 3521.
15 G.W. Wang and X.L. Wu, *Adv. Synth. Catal.,* 2007, **349,** 1977.
16 H. Wang, Y.L. Wang, G. Zhang, J.P. Li and X.Y. Wang, *Synth. Commun.,* 2000, **30,** 1425.
17 J.P. Li, Y.L. Wang, H. Wang, Q.F. Luo and X.Y. Wang, *Synth. Commun.,* 2001, **31,** 781.
18 G. Sun and Z. Wang, *Tetrahedron Lett.,* 2008, **49,** 4929.
19 B. Liu and S.J. Ji, *Synth. Commun.,* 2008, **38,** 1201.
20 M.L. Deb and P.J. Bhuyan, *Synlett,* 2008, 325.
21 X. Zhang, W. Rao and P.W.H. Chan, *Synlett,* 2008, 2204.
22 R. Lucas, J. Vergnaud, K. Teste, R. Zerrouki, V. Sol and P. Krausz, *Tetrahedron Lett.,* 2008, **49,** 5537.
23 J.S. Yadav, B.V.S. Reddy, G. Narasimhulu and G. Satheesh, *Tetrahedron Lett.,* 2008, **49,** 5683.
24 J. Wang, F.X. Xu, X.F. Lin and Y.G. Wang, *Tetrahedron Lett.,* 2008, **49,** 5208.
25 J.S. Yadav, B.V.S. Reddy, A.V.H. Gopal, G.G.K.S.N. Kumar, C. Madavi and A.C. Kunwar, *Tetrahedron Lett.,* 2008, **49,** 4420.
26 H.S. Wang and J.E. Zeng, *Chin. J. Chem.,* 2008, **26,** 175.
27 H.S. Wang, L.F. Zhao and Z.M. Du, *Chin. J. Chem.,* 2006, **24,** 135.
28 H.S. Wang and J.E. Zeng, *Chin. Chem. Lett.,* 2007, **18,** 1447.