An efficient synthesis of 3,3'-arylmethylenebis(4-hydroxy-6-methyl-2*H*-pyran-2-one)s in aqueous media

Da-Qing Shi[ab]*, Li-Hui Niu[b] and Hao Yao[b]

[a]*College of Chemistry and Chemical Engineering, Key Laboratory of Organic Synthesis of Jiangsu Province, Suzhou University, Suzhou 215123, P. R. China*

[b]*College of Chemistry and Chemical Engineering, Xuzhou Normal University, Xuzhou 221116, P. R. China*

The condensation reactions of aromatic aldehydes and 4-hydroxy-6-methyl-2*H*-pyran-2-one in water in the presence of sodium 1-dodecanesulfonate affords a one-pot synthesis of 3,3'-arylmethylene bis(4-hydroxy-6-methyl-2*H*-pyran-2-one)s.

Keywords: pyrone, aromatic aldehyde, aqueous media, synthesis

The need to reduce the amount of toxic waste arising from chemical processes requires increasing the emphasis on the use of more environmentally compatible materials in the design of new synthetic methods.[1-3] As one of the most promising approaches, water is used as reaction medium.[4-6] Breslow[7,8] showed that hydrophobic effects strongly enhance the rate of several organic reactions. In recent years, there has been increasing recognition that water is an attractive medium for many organic reactions.[9-14] An aqueous medium is less expensive, less dangerous and more environmentally friendly than organic solvents. Generally, the low solubiblity[15] of most reagents in water is not an obstacle to reactivity, which may be reduced with the use of cosolvents.

Many 4-pyrones or compounds containing the 4-pyrone moieties which have been synthesised over the last few decades have biological activities, such as herbicidal, fungicidal, antiallergenic and anticancer activity.[16-18] Based on our previous studies on the use of water as solvent for carrying out carbon–carbon forming reaction under heterogeneous catalysis,[19-22] we report here a novel synthesis of 3,3'-arymethylenebis(4-hydroxy-6-methyl-*2H*-pyran-2-one) using water as the reaction medium.

When aromatic aldehydes **1** and 4-hydroxy-6-methyl-2*H*-pyran-2-one **2** were stirred at 90°C for 4–12 h in water in the presence of sodium 1-dodecanesulfonate, the desired products-3,3'-arylmethylenebis(4-hydroxy-6-methyl-2*H*-pyran-2-one) **3** were obtained in good yields (Scheme 1).

Table 1 summarises the results on this reaction. This protocol did not require the use of any organic solvent. In fact the products 3 were isolated in a practically pure from by simple filtration of the final aqueous mixture. The reactions occurred in a short time. The aqueous phase obtained after filtration can be reused as the reaction medium. The reuse of the aqueous medium was repeated in four subsequent runs and the yields obtained were excellent.

The structures of the compounds **3** were characterised by spectroscopic data and elemental analysis. A reasonable mechanism for the formation of the products **4** is outlined in Scheme 2. The reaction occurs via an initial formation of Knoevenagel condensation product, from the Knoevenagel condensation between the aromatic aldehyde and 4-hydroxy-6-methyl-2*H*-pyran-2-one. Then a Michael addition and isomerisation take place between the Knoevenagel condensation product and another 4-hydroxy-6-methyl-2*H*-pyran-2-one to give product **3**.

In summary, the conversion of aromatic aldehydes and 4-hydroxy-6-methyl-2*H*-pyran-2-one to 3,3'-arylmethylenebis (4-hydroxy-6-methyl-2*H*-pyran-2-one)s can be efficiently performed in water as a solvent using a catalytic amount of SDS. This method has the advantages of good yields, low cost, simple operation and an environmentally benign procedure.

Experimental

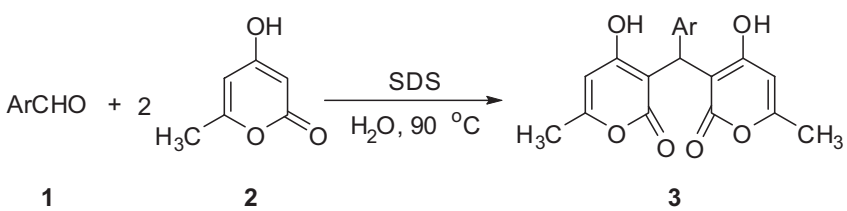
Melting points are uncorrected. IR spectra were recorded on a Tensor 27 spectrometer in KBr with absorptions in cm^{-1}. ^1H NMR spectra were determined on a Bruker-400 MHz spectrometer in DMSO-d_6. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Microanalyses were carried out on a Perkin-Elmer 2400II elemental analyser.

General procedure for the synthesis of 3,3'-arylmethylenebis(4-hydroxy-6-methyl-2H- pyran-2-ones)(**3**)

A mixture of aromatic aldehyde **1** (2 mmol), 4-hydroxy-6-methyl-2*H*-pyran-2-ones **2** (4 mmol) and sodium 1-dodecanesulfonate (0.15 g) in H_2O (10 ml) was stirred for 4–12 h at 90°C, then cooled

Table 1 The synthesis of 3,3'-arylmethylenebis(4-hydroxy-6-methyl-2*H*-pyran-2-one) in aqueous media

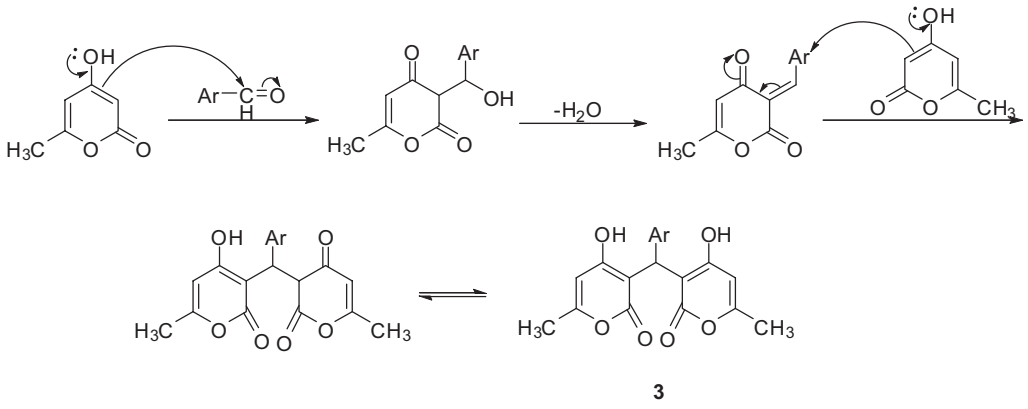
Entry	Product	Ar	Time/h	Isolated yield/%
1	**3a**	2-ClC_6H_4	6	89
2	**3b**	3,4-$Cl_2C_6H_3$	5	95
3	**3c**	3,4-$OCH_2OC_6H_3$	9	96
4	**3d**	4-$CH_3OC_6H_4$	8	90
5	**3e**	3-$NO_2C_6H_4$	6	93
6	**3f**	4-$NO_2C_6H_4$	7	92
7	**3g**	2-$NO_2C_6H_4$	5	91
8	**3h**	2,4-$Cl_2C_6H_3$	4	92
9	**3i**	4-ClC_6H_4	10	88
10	**3j**	4-BrC_6H_4	6	98
11	**3k**	4-$CH_3C_6H_4$	12	86
12	**3l**	3-Pyridyl	6	93



1 **2** **3**

Scheme 1

* Correspondent. E-mail: dqshi@263.net



3

Scheme 2

to room temperature. The crystalline product which formed was collected by filtration, washed with water and recrystallised from DMF to give pure **3**.

3,3′-((2-chlorophenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3a**): M.p. 144–145°C; IR: ν/cm^{-1} 3200–2500, 1684, 1617, 1558, 1449, 1417, 1306, 1260, 1233, 1205, 1170, 1109, 1090, 1052, 997, 872, 824, 773, 744 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.16 (6H, s, 2 × CH_3), 5.67 (1H, s, CH), 5.96 (2H, s, ArH), 7.11–7.18 (3H, m, ArH), 7.28–7.30 (1H, m, ArH), 11.18 (2H, s, 2 × OH); Anal. calcd for $C_{19}H_{15}ClO_6$: C 60.89, H 4.03; found C 61.15, H 3.92%

3,3′-((3,4-dichlorophenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3b**): M.p. 176–178°C; IR: ν/cm^{-1} 3200–2500, 1681, 1626, 1572, 1447, 1412, 1380, 1350, 1305, 1284, 1193, 1168, 1131, 1056, 1029, 903, 844, 823, 797, 771, 742 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.19 (6H, s, 2 × CH_3), 5.74 (1H, s, CH), 6.03 (2H, s, ArH), 7.02 (1H, d, J = 8.4 Hz, ArH), 7.18 (1H, s ArH), 7.47 (1H, d, J = 8.4 Hz, ArH), 11.23 (2H, s, 2 × OH); Anal. calcd for $C_{19}H_{14}Cl_2O_6$: C 55.77, H 3.45; found C 55.63, H 3.56%

3,3′-((3,4-methylenedioxyphenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3c**): M.p. 183–185°C; IR: ν/cm^{-1} 3500–2500, 1680, 1626, 1575, 1477, 1432, 1413, 1335, 1283, 1246, 1190, 1166, 1135, 1103, 1082, 1034, 990, 925, 833, 780, 763, 751 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.20 (6H, s, 2 × CH_3), 5.86 (1H, s, CH), 5.95 (2H, s, OCH_2O), 6.08 (2H, s, ArH), 6.46 (1H, d, J = 8.0 Hz, ArH), 6.53 (1H, s, ArH), 6.76 (1H, d, J = 8.0 Hz, ArH), 11.63 (2H, s, 2 × OH); Anal. calcd for $C_{20}H_{16}O_8$: C 62.50, H 4.20; found C 62.67, H 4.28%

3,3′-((4-methoxyphenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3d**): M.p. 159–160°C; IR: ν/cm^{-1} 3500-2500, 1683, 1619, 1567, 1509, 1450, 1410, 1350, 1282, 1247, 1178, 1136, 1094, 1036, 997, 870, 827, 799, 773, 762 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.20 (6H, s, 2 × CH_3), 3.71 (3H, s, CH_3O), 5.91(1H, s, CH), 6.08 (2H, s, ArH), 6.79 (2H, d, J = 8.4 Hz, ArH), 6.91 (2H, d, J = 8.4 Hz, ArH), 11.70 (2H, s, 2 × OH); Anal. calcd for $C_{20}H_{18}O_7$: C 64.86, H 4.90; found C 65.04, H 4.75%

3,3′-((3-nitrophenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3e**): M.p. 203–204°C; IR: ν/cm^{-1} 3200–2500, 1680, 1626, 1568, 1453, 1410, 1374, 1349, 1297, 1273, 1196, 1164, 1058, 1038, 993, 918, 840, 812, 789, 772, 754, 726, 701, 691 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.19 (6H, s, 2 × CH_3), 5.81(1H, s, CH), 6.04 (2H, s, ArH), 7.51–7.53 (2H, m, ArH), 7.82 (1H, s, ArH), 8.01–8.03 (1H, m, ArH); Anal. calcd for $C_{19}H_{15}NO_8$: C 59.22, H 3.92, N 3.64; found C 59.35, H 4.01, N 3.70%

3,3′-((4-nitrophenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3f**): M.p. 235–236°C; IR: ν/cm^{-1} 3200–2500, 1675, 1619, 1561, 1507, 1450, 1402, 1373, 1335, 1272, 1191, 1163, 1141, 1110, 1065, 1049, 1040, 994, 875, 846, 787, 754, 725, 701 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.19 (6H, s, 2 × CH_3), 5.84 (1H, s, CH), 6.05 (2H, s, ArH), 7.29 (2H, d, J = 8.4 Hz, ArH), 8.09 (2H, d, J = 8.4 Hz, ArH), 11.16 (2H, s, 2 × OH); Anal. calcd for $C_{19}H_{15}NO_8$: C 59.22, H 3.92, N 3.64; found C 59.16, H 4.05, N 3.57%

3,3′-((2-nitrophenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3g**): M.p. 237–239°C; IR: ν/cm^{-1} 3200–2500, 1680, 1604, 1522, 1452, 1410, 1357, 1265, 1197, 1168, 1134, 1099, 1059, 1034, 995, 872, 849, 829, 782, 766, 727 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.15 (6H, s, 2 × CH_3), 5.93 (2H, s, ArH), 6.04 (1H, s, CH), 7.25 (1H, d, J = 8.0 Hz, ArH), 7.39 (1H, t, J = 8.0 Hz, ArH), 7.53 (1H, t, J = 8.0 Hz, ArH), 7.73 (1H, d, J = 8.0 Hz, ArH), 11.42 (2H, s, 2 × OH); Anal. calcd for $C_{19}H_{15}NO_8$: C 59.22, H 3.92, N 3.64; found C 59.37, H 3.85, N 3.82%

3,3′-((2,4-dichlorophenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3h**): M.p. 226–229°C; IR: ν/cm^{-1} 3200–2500, 1685, 1633, 1575, 1469, 1447, 1410, 1383, 1363, 1301, 1260, 1224, 1170, 1139, 1108, 1050, 1000, 865, 846, 831, 822, 749 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.14 (6H, s, 2 × CH_3), 5.57 (1H, s, CH), 5.93 (2H, s, ArH), 7.12 (1H, d, J = 8.4 Hz, ArH), 7.26 (1H, dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, ArH), 7.41 (1H, d, J = 2.0 Hz, ArH), 11.20 (2H, s, 2 × OH); Anal. calcd for $C_{19}H_{14}Cl_2O_6$: C 55.77, H 3.45; found C 55.85, H 3.54%

3,3′-((4-chlorophenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3i**): M.p. 206–207°C; IR: ν/cm^{-1} 3200–2500, 1681, 1634, 1581, 1490, 1447, 1413, 1386, 1349, 1313, 1287, 1192, 1168, 1091, 1049, 1014, 996, 868, 844, 829, 784, 768, 726, 690 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.20 (6H, s, 2 × CH_3), 5.86 (1H, s, CH), 6.08 (2H, s, ArH), 7.03 (2H, d, J = 8.0 Hz, ArH), 7.28 (2H, d, J = 8.0 Hz, ArH), 11.32 (2H, s, 2 × OH); Anal. calcd for $C_{19}H_{15}ClO_6$: C 60.89, H 4.03; found C 60.78, H 3.97%

3,3′-((4-bromophenyl)methylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3j**): M.p. 207–208°C; IR: ν/cm^{-1} 3400–2500, 1683, 1634, 1568, 1486, 1445, 1402, 1299, 1253, 1195, 1168, 1131, 1071, 1055, 1042, 1009, 997, 871, 844, 832, 820, 772, 745 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.20 (6H, s, 2 × CH_3), 5.83 (1H, s, CH), 6.06 (2H, s, ArH), 6.97 (2H, d, J = 8.4 Hz, ArH), 7.40 (2H, d, J = 8.4 Hz, ArH), 11.37 (2H, s, 2 × OH); Anal. calcd for $C_{19}H_{15}BrO_6$: C 54.43, H 3.61; found C 54.62, H 3.79%

3,3′-(p-tolylmethylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3k**): M.p. 173–175°C; IR: ν/cm^{-1} 3500–2500, 1689, 1634, 1580, 1510, 1447, 1410, 1350, 1304, 1241, 1193, 1164, 1141, 1097, 1042, 995, 870, 842, 771, 761, 735, 686 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.21 (6H, s, 2 × CH_3), 2.25 (3H, s, CH_3), 5.95 (1H, s, CH), 6.09 (2H, s, ArH), 6.89 (2H, d, J = 8.0 Hz, ArH), 7.04 (2H, d, J = 8.0 Hz, ArH), 11.75 (2H, s, 2 × OH); Anal. calcd for $C_{20}H_{18}O_6$: C 67.79, H 5.12; found C 67.93, H 4.96%

3,3′-(pyridin-3-ylmethylene)bis(4-hydroxy-6-methyl-2H-pyran-2-one) (**3l**): M.p. 163–165°C; IR: ν/cm^{-1} 3500–2500, 1699, 1626, 1514, 1470, 1417, 1373, 1346, 1291, 1263, 1223, 1198, 1171, 1141, 999, 957, 856, 830, 778, 686 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.13 (6H, s, 2 × CH_3), 5.85 (2H, s, ArH), 5.89 (1H, s, CH), 7.61 (1H, dd, J_1 = 8.0 Hz, J_2 = 5.2 Hz, ArH), 7.84 (1H, d, J = 8.0 Hz, ArH), 8.36 (1H, s, ArH), 8.51 (1H, d, J = 5.2 Hz, ArH), 11.41 (2H, s, 2 × OH); Anal. calcd for $C_{18}H_{15}NO_6$: C 63.34, H 4.43, N 4.10; found C 63.57, H 4.50, N 4.16%

We are grateful to the "Surpassing Project" Foundation of Jiangsu Province and the Foundation of the Key Laboratory of Biotechnology on Medical Plants of Jiangsu Province for financial support.

Received 27 February 2008; accepted 22 March 2008
Paper 08/5125 *doi: 10.3184/030823408X304500*

References

1 J. Amato, *Science*, 1993, **259**, 1538.
2 D. L. Illman, *Chem. Eng. News*, 1993, **71**, 5.
3 D.L. Illman, *Chem. Eng. News*, 1994, **72**, 22.
4 C.J. Li and T.H. Chang, *Organic reactions in aqueous media*, Wiley, New York, 1997.

5 F. Fringuell, O. Piematti, F. Pizzo and L. Vaccaro, *Eur. J. Org. Chem*., 2001, 439.
6 S.C. Stinson, *Chem. Eng. News*, 1996, **74**, 39.
7 R. Breslow and D.C. Rideout, *J. Am. Chem. Soc*., 1980, **102**, 7816.
8 R. Breslow, *Acc. Chem. Res*., 1991, **24**, 159.
9 C.J. Li, *Chem. Rev*., 1993, **93**, 2023.
10 R. Ballini and G. Bosica, *Tetrahedron Lett*., 1996, **37**, 8027.
11 R. Ballini, G. Bosica and T. Mecozzi, *Tetrahedron*, 1997, **53**, 1341.
12 A Meijier, S. Otto and J.B.F.N. Engberts, *J. Org. Chem*., 1998, **63**, 8989.
13 F. Bigi, L. Chesini, R. Maggi and G. Sartori, *J. Org. Chem*., 1999, **64**, 1033.
14 F. Bigi, S. Carloni, L. Ferrari, R. Maggi, A. Mazzacani and G. Sartori, *Tetrahedron Lett*., 2001, **42**, 5203.
15 F. Fringuelli, G. Pani, O. Piermatti and F. Pizzo, *Tetrahedron*, 1994, **50**, 1499.
16 S. Yamamara and S. Nishiyama, *Bull. Chem. Soc. Jpn*., 1997, **70**, 2025.
17 D.C.G.A. Pinto, A.M.S. Silva and J.A.S. Cavaleiro, *J. Heterocycl. Chem*., 1996, **33**, 1887.
18 W.H. Gerwick, A. Lopez, G.D. VanDuyne, J. Clardy, W. Ortiz and A. Baez, *Tetrahedron Lett*., 1986, **27**, 1979.
19 D.Q. Shi, J. Chen, Q.Y. Zhuang, X.S. Wang and H.W. Hu, *J. Chem. Res*., *(S)* 2003, 674.
20 J. Wang, D.Q. Shi, Q.Y. Zhuang, X.S. Wang and H.W. Hu, *J. Chem. Res*., *(S)* 2004, 818.
21 D.Q. Shi, L.H. Niu and Q.Y. Zhuang, *J. Chem. Res*., *(S)* 2005, 648.
22 D.Q. Shi, L.H. Niu, X.S. Wang, Q.Y. Zhuang and Y. Zhang, *J. Chem. Res*., *(S)* 2005, 224.