Synthesis of Bispyranopyran-4,5-diones

M. SIDDIQ AND A.W. KHAN
Chemistry Department, Islamia University, Bahawalpur, Pakistan

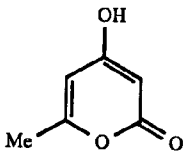
(Received 27th Feburary, 1992)

Summary: Bispyranopyran-4,5-diones (2) have been prepared by the concomitant acetylation and cyclisation of bis-4-hydroxy-6-methyl-2H-pyran-2-ones (3) using a mixture of acetic anhydride and perchloric acid. Reactions of (2c) and (2d) with ammonium acetate afforded the corresponding bispyridopyran-4,5-diones (4) while the hydrolysis of (2c) and (2d) with 20% aqueous sodium hydroxide gave bispyran-4-ones (5a) and (5b) respectively.

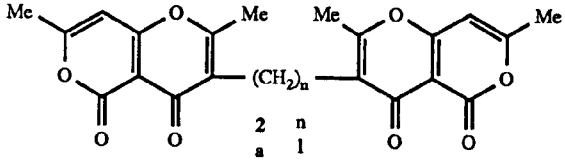
Introduction

Synthesis of pyranopyran-4,5-diones from the reactions of triacetic acid lactone (4-hydroxy-6-methyl-2H-pyran-2-one) (1) with aliphatic monocarboxylic acid chloride [1] or dehydro acetic acid (3-acetyl-4-hydroxy-6-methyl-2H-pyran-2-one) and a mixture of acetic anhydride and perchloric acid [2] are well known. However, no account of the preparation of bispyranopyran-4,5-diones of type (2) is available in literature. In view of the synthetic importance and possible utility of these compounds in the study of biogenetic type synthesis of phenolic compounds [3], a method for the preparation of bis-4-hydroxy-6-methyl-2H-pyran-2-ones (3) and their subsequent conversion to bispyranopyran-4,5-diones (2) has been described.

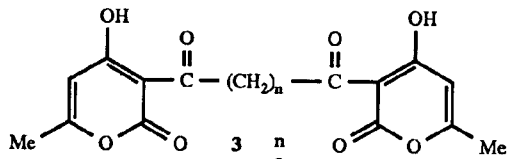
Triacetic acid lactone (1) (1.0 mole) with appropriate aliphatic dicarboxylic acid chloride (2 mole) in trifluoro-acetic acid afforded the corresponding bis-4-hydroxy-6-methyl-2H-pyran-2-one (3) in good yields.



1



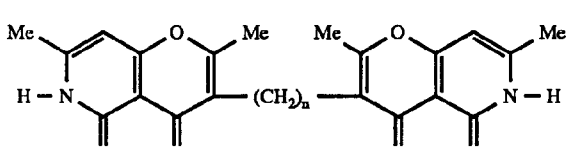
	n
a	1
b	2
c	6
d	8



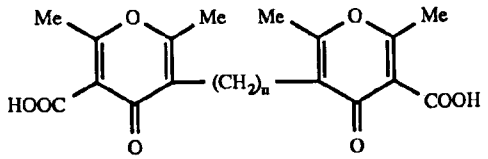
	n
a	3
b	4
c	8
d	10

Initial attempts to convert (3) into (2) using a mixture of acetic anhydride and sodium acetate under Kostanecki-Robinson [4] conditions or aliphatic monocarboxylic acid chlorides in the presence of titanium (IV) chloride (I) or a mixture of aliphatic monocarboxylic acid and phosphoryl chloride (5) were unsuccessful. Alternatively the use of a mixture of acetic anhydride and perchloric acid under the mentioned conditions was found to be a convenient reagent for the conversion of bisacylpyrones (3) to the corresponding bispyranopyran-4,5-diones (2).

The reaction occurs via α-acetylation of bisacylpyrone (3) followed by γ-pyrone ring closure to form (2). All reactions proceeded smoothly and yielded solid products except (2b) which was obtained as a brownish sticky mass. Enhanced yields were obtained with the lengthening of methylene carbon chain, presumably due to the progressive decrease in steric hindrance. Spectral data for all the products are in conformity with their structures.



	n
a	6
b	8



5 n
a 6
b 8

Conversion of the pyrone rings to the corresponding pyridone rings by the action of ammonium salts or ammonia is well known. Similar treatment of compounds (2c) and (2d) with ammonium acetate in acetic acid or storage with ammonia (density 0.880 g/ml) at room temperature resulted in the formation of bispyridopyran-4,5-diones (4a) and (4b) respectively.

Treatment of compounds (2c) and (2d) with 20% aqueous sodium hydroxide at ambient temperature and followed by neutralization with concentrated hydrochloric acid yielded bispyran-4-ones (5a) and (5b) respectively, which shows the greater stability of the 4-pyrone ring as compared to 2-pyrone ring in these compounds. Similar, treatment of bispyridopyran-4,5-diones (4a) and (4b) with sodium hydroxide had no effect and the original compounds were recovered quantitatively.

Experimental

Infrared spectra were recorded with a Unicam SP 200 spectrophtometer for mulls in Nujol, Ultraviolet spectra on Unicam SP 800 and NMR spectra were measured with Perkin-Elmer RIC(60 MHz) spectrometer. Melting points are uncorrected. Dehydroacetic acid used was from Koch Light (London).

4-Hydroxy-6-methyl-2H-pyran-2-one (1) was prepared by the deacetylation of dehydroacetic acid by the method of Collie (6), m.p. 187-188°C.

General method for the preparation of bis-4-hydroxy-6-methyl-2H- pyran-2-ones (3).

A mixture of triacetic acid lactone 1 (0.025 mole), appropriate dicarboxylic acid chloride (0.0175 mole) in trifluoroacetic acid (15 ml) was refluxed for 2-2.5 hours. After cooling, the solid product was filtered out.

Compound (3a) was obtained in 60% yield by the reaction of triacetic lactone 1 and glutyryl chloride, m.p. 135°C (ethanol-pet.ether 60-80°C); ir: 1710 (CO ring), 1645 (CO side chain) cm^{-1}; uv (ethanol) 310 nm (log 4.3); nmr ($CDCl_3$): δ 2.0 (-CH_2,2H), 2.26 (-CH_3,6H), 3.1-3.3 (-CH_2,4H), 5.91 (-CH=2H), 16.88 (-OH,2H). Anal. calcd. for $C_{17}H_{16}O_8$: C, 58.62: H, 4.59. Found: C, 58.8: H, 4.68.

Compound (3b) was obtained from (1) and adipoyl chloride in 50% yield, m.p. 183-184°C (ethanol-chloroform); ir: 1707 (CO of ring), 1640 (CO of side chain) cm^{-1}; uv (ethanol): 310 (ε log 4.3); nmr ($CDCl_3$): δ 1.6 (CH_2, 2H), 2.3 (-CH_3, 6H), 3.1-3.2 (CH_2,6H), 5.9 (-CH=,2H), 16.7 (-OH,2H). Anal. Calcd. for $C_{18}H_{18}O_8$: C, 59.66; H, 4.97. Found: C, 59.52: H, 4.98.

Compound 3c was obtained from (1) and sebacoyl chloride in 70% yield, m.p. 142-143°C (ethanol-chloroform): ir: 1715 (CO of ring), 1640 (CO of side chain) cm^{-1}; uv (ethanol): 308 nm (ε log 4.8); nmr ($CDCl_3$): δ 1.38 (- CH_2,12H), 2.26 (-CH_3,6H), 2.9-3.2 (-CH_2,4H), 5.9 (-CH=, 2H), 16.81 (-OH, 2H). Anal. Calcd. for $C_{22}H_{26}O_8$: C, 63.16; H, 6.22. Found: C 63.39; H, 6.28.

Compound (3d) was obtained from (1) and do-decandioyl chloride in 65% yeild, m.p. 142°C (ethanol-chloroform); ir: 1710 (CO of ring), 1645 (CO of side chain) cm^{-1}; uv (ethanol): 308 nm (ε log 4.47); nmr ($CDCl_3$): δ 1.36 (CH_2, 16H), 2.28 (-CH_3, 6H), 3.0-3.19 (-CH_2, 4H), 5.92 (-CH=, 2H), 16.88 (OH, 2H). Anal. Calcd. for $C_{24}H_{30}O_8$: C, 64.57; H, 6.73. Found: C, 64.69; H, 6.68.

Bispyranopyran-4,5-dione (2a)

A mixture of bispyrone (3a) (1g, 0.0025 mole) and acetic anhydride (20 ml) was cooled to 0°C Perchloric acid (2 ml) was added dropwise with continuous shaking, the temperature of the reaction mixture rose sharply and a dark brown solution was obtained at 40-45°C. After cooling to 10°C, the reaction mixture was left at room temperature for 16 hours and then poured into ice cold water (150 ml) with stirring. The brownish solid product was filtered out which on crystallisation from petroleum ether (60-80°C) chloroform mixture (1:1) gave white solid (30%), m.p. above 360°C; ir: 1755 (CO of 2-pyrone), 1648 (CO of 4-pyrone), 1620 (- C=C-

), 1555 (-C=C); uv (ethanol): 297 nm (ε log 4.3), 249 nm (ε log 4.4); nmr (TFA, d_1): δ 2.56 (-CH_3, 6H), 2.98(-CH_3,6H), 4.02 (-$CH_2$2H), 6.78 (-CH=,2H). Anal. Calcd. for $C_{21}H_{16}O_8$: C, 63.64; H, 4.04. Found: C, 63.76; H, 4.4

The bispyranopyran-4,5-diones **(2b)**, **(2c)** and **(2d)** were prepared from the bispyrones **(3b)**, **(3c)** and **(3d)** respectively in a similar manner.

Bispyranopyran-4,5-dione **(2b)**

The mixture was left at room temperature for 72 hours which on pouring into water gave brownish sticky mass. Trituration with ether followed by crystallization from chloroform-pet. ether (60- 80°C) mixture gave solid product m.p. 240-242°C. ir: 1750(CO of 2-pyrone), 1650 (CO of 4-pyrone), 1620 (C=C) cm^{-1}; nmr (TFA, d_1): δ 2.5 (CH_3, 6H), 2.98 (-CH_3, 6H), 3.5-4 (-CH_2,4H), 6.8 (-CH=,2H). Anal. Calcd. for $C_{22}H_{18}O_8$: C, 64.39; H, 4.39. Found: C, 64.5; H, 4.42.

Bispyranopyran-4,5-dione **(2c)**

This compound was obtained in a yield of 60% by keeping the reaction mixture at room temperature for 14 hours, m.p. 265-270°C (dec.) from ethanol-chloroform (1:1) mixture. Recrystallisation (thrice) from ethanol-chloroform gave off-white solid m.p. 277°C (dec.); ir: 1744 (CO of 2-pyrone), 1648 (CO of 4-pyrone), 1620, 1555 (-C=C-) cm^{-1}; uv ($CHCl_3$): 289 nm (ε log 4.3), 249 nm (ε log 4.5); nmr (TFA, d_1): δ 1.64 (-CH_2,8H), 2.63 (-CH_3,6H), 2.87 (CH_3, 6H and CH_2,4H), 6.9 (-CH=, 2H). Anal. Calcd. for $C_{26}H_{26}O_8$: C 66.95; H, 5.58. Found: C 67.2; H, 5.66.

Bispyranopyran-4,5-dione **(2d)**

Reaction mixture was left at room temperature for 24 hours. The solid material was filtered out and identified as original bispyrone **(3d)** by the m.p. and mixed m.p. while the filtrate on pouring into water (300 ml) gave product (67%) m.p. 222-224°C (ethanol- benzene); ir: 1747 (CO of 2-pyrone), 1655 (CO of 4-pyrone), 1627, 1560 (-C=C-) cm^{-1}; uv ($CHCl_3$): 288 nm (ε log 4.4), 250 nm (ε log 4.5): nmr ($CDCl_3$): δ 1.52 (-CH_2, 12H), 2.65 (CH_3, 6H), 2.88 (-CH_3, 6H and -CH_2, 4H), 6.94 (-CH=, 2H). Anal. Calcd. for $C_{28}H_{30}O_8$: C, 68.02, H, 6.07. Found: C, 67.7; H, 6.00.

Bispyridopyran-4,5-dione **(4a)**

A mixture of bispyranopyran-4,5-dione **(2c)** (3.0 g, 0.006 mole), ammonium acetate (3g, 0.039 mole) in glacial acetic acid (15 ml) was refluxed for 6 hours. Evaporation of the reaction mixture under reduced pressure gave brownish solid (50%), m.p.315°C from ethanol-benzene mixture (2:1); ir: 1694 (CO of 2-pyrone), 1640 (CO of 4-pyrone), 1605, 1560 (-C=C-) cm^{-1}; uv (ethanol): 310 nm (ε log 4.4), 252 nm (ε log 4.5); nmr (TFA, d_2): δ 1.63 (-CH_2, 8H), 2.7 (CH_3, 6H), 2.84 (CH_3, 6H and CH_2, 4H), 6.96 (-CH=, 2H). Anal. Calcd. for $C_{26}H_{28}N_2O_6$: C, 67.24; H, 6.03; N, 6.03. Found: C, 66.87; H, 6.04; N, 5.98.

Bispyridopyran-4,5-dione **(4b)**

ZThis compound was also obtained from bispyranopyran-4,5-dione **(2d)** in 60% yield as described in the previous method m.p. 320-322°C from ethanol-benzene mixture; ir: 1694 (CO of pyridone ring), 1642 (CO of 4-pyrone), 1610, 1560 (-CH=C-) cm^{-1}; uv (ethanol): 309 nm (ε log 4.45), 252 nm (ε log 4.5); nmr (TFA, d_1): δ 1.5 (-CH_2, 12H), 2.68 (-CH_3, 6H), 2.9 (CH_3, 6H and CH_2, 4H), 6.94 (-CH=,2H). Anal. Calcd. for $C_{28}H_{32}N_2O_6$: C, 68.29, H, 6.50, N, 5.69. Found: C, 68.3, H, 6.2, N, 5.52.

The products **(4a)** and **(4b)** were also obtained when a mixture of **(2c)** (1 g, 0.0021 moles) or **(2d)** (1g, 0.002 mole) and ammonia (0.88d) (30 ml) was left at room temperature for 15 day and then evaporated to dryness.

Hydrolysis of bispyranopyran-4,5-diones

Bispyranopyran-4,5-dione **(2c)** (1 g, 0.002 mole) was dissolved in 20% aqueous sodium hydroxide (50 ml) at room temperature and then immediately neutralized by concentrated hydrochloric acid. The solid p;roduct **(5a)** was filtered out, m.p. 200-202°C from chloroform-pet.ether 60-80°C mixture (1:1); ir: 1722 (CO of carboxylic group), 1640 (CO of 4-pyrone), 1608, 1573 (-C=C-) cm^{-1}; uv (ethanol): 263 nm (log 4.6); nmr ($CDCl_3$) 1.43 (-CH_2,8H), 2.38 (- CH_3, 6H and -CH_2,4H), 2.83 (-CH_3, 6H), 15.28 (-COOH, 2H). Anal. Calcd. for $C_{22}H_{26}O_8$: C 63.16, H, 6.22. Found: C. 63.37; H, 6.48.

Hydrolysis of bispyranopyran-4,5-dione (**2d**) by the same method gave compound (**5b**), m.p. 150-152°C from ethanol-pet.ether 60-80°C mixture (1:1); ir: 1715 (CO of carboxylic acid), 1638 (CO of 4- pyrone), 1608, 1565 (-C=C-) cm^{-1}; uv (ethanol): 256 nm (ε log 3.6); nmr ($CDCl_3$): δ 1.35 (-CH_2, 12H), 2.39 (CH_3, 6H and -CH_2, 4H), 2.83 (CH_3, 6H), 15.28 (COOH, 2H). Anal. Calcd. for $C_{24}H_{30}O_8$: C, 64.57, H, 6.73. Found: C, 64.57: H, 6.63.

References

1. O. Caputo, L. Cattel, F. Viola and G. Biglino, *Gazz. Chim. Ital.*, **107**, 455 (1977).
2. P.F.G. Prail and A. L. Whitear, *Proc. Chem. Soc.*, London, 112 (1961).
3. (a) T. Money. *Chem. Rev.*, **70**, 553 (1970).
   (b) T.M. Harris, K.B. Hindley, *Fortschr. Chem. Org.* Natur Stoffe ed. by W. Herz, H. Grisebach and G.W. Kirly Springer Verlay, Inc., Wien. Vol. 31, p. 217 (1974).
   (c) N. Takeuchi and S. Tobinaga, *Chem. Pharm. Bull.*, **28**, 2007 (1980).
   (d) F.J. Leaper and J. Staunton, *J. Chem. Soc. Perkin Trans I*, 1053 (1984).
4. (a) M. Blumberg and S. Van Kostanecki, *Ber.*, **36**, 2191 (1903).
   (b) W. Baker and R.Robinson, *J. Chem. Soc.*, 1981 (1925).
5. D.Cook and J.S. Mc Intyre, *J. Org. Chem.*, **33**, 1746 (1968).
6. J. N. Collie, *J. Chem. Soc.*, **59**, 607 (1891).