Synthesis of Pyrano(4,3-b)pyran-4,5-diones

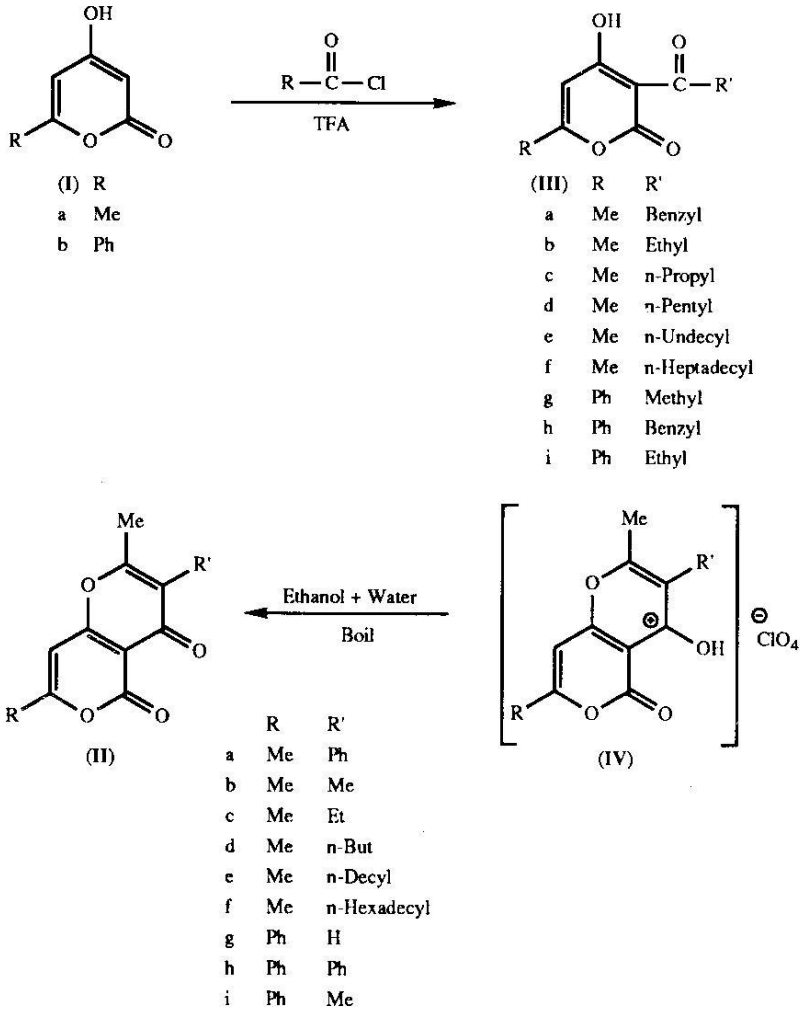
P.F.G. PRAILL, A.W. KHAN AND M. SIDDIQ
Chemistry Department, Islamia University, Bahawalpur, Pakistan

(Received May 20, 1992, revised April 7, 1994)

Summary: 3-Acyl-4-hydroxy-6-methyl(or phenyl)-2H-pyran-2-ones (III) have been converted into 2,3,7-trisubstituted-4H,5H-pyrano-(4,3-b)pyran-4,5-dione perchlorates (IV) using acetic anhydride and perchloric acid mixture. The perchlorates (IV) on boiling with aqueous ethanolic solution gave the corresponding pyranopyran-4,5-diones (II) in moderate to excellent yields

Introduction

A number of methods have been reported for the synthesis of pyrano-pyrandiones which involve the condensation of 4-hydroxy-6-methyl (or phenyl)-2H-pyran-2-one (I) with dicarbonyl compounds such as β-ketoester [1-3], malonic acid [4], malonic ester [4] and malonyl chloride [4,5] or the reaction of the β-diketones with carbon suboxide in the presence of catalytic amount of concentrated sulphuric acid [6]. The pyranopyran (4,3-b)pyran-4,5-diones of type (II) have been reported to a limited extent and are important for the study of biogenetic type synthesis [7] of phenolic compounds. Their synthesis include the oxidation of corresponding 2,3-dihydroderivatives [8], the action of triacetic lactone (Ia) or 3-acyl derivatives (III) with saturated fatty acid chlorides in the presence of $TiCl_4$ [9] and cyclization [10] of 3-cinnamoyl-4-hydroxy-6-methyl-2H-pyran-2-one. A mixture of acetic anhydride and perchloric acid with 3-acyl derivatives of type (III) has also been reported [2,11] to give pyranopyran-4,5-dione (II, R=Me, Ph R'=H). However, the general applicability of this method has not been investigated. In view of the synthetic importance and the utility of the substituted pyranopyrandiones in the biogenetic type synthesis [7] of phenolic compounds, we have prepared a number of substituted pyranopyrandiones (II) by the concomitant acylation and cyclization of 3-acyl-4-hydroxy-6-methyl (or phenyl)-2H-pyran-2-one (III) using a mixture of acetic anhydride and perchloric acid. Method has



been found to be of general applicability and gives moderate to excellent yields (60-94%) of the products.

Addition of perchloric acid to a mixture of appropriate acyl derivative (III) dissolved or suspended in acetic anhydride under the mentioned conditions (Table-1) yielded the corresponding crystalline pyranopyran-4,5-dione perchlorates (IV) from the reaction mixture except the perchlorates (IVd, e). The perchlorates (IVa-c, f-l) were characterised on the basis of their infrared data [12,13] which exhibited peak due to carbonyl group at 1700-1720 cm.$^{-1}$ The shift towards the lower frequency than the anticipated value of 1750 cm^{-1} is attributed to the protonation of the carbonyl group of the 4-pyrone nucleus and resulting hydrogen bonding of the hydroxyl group with the carbonyl of the 2-pyrone ring. All perchlorates (IVa-c, f-l) show absorption maxima [12], expected for the 2- and 4-pyrone rings in the regions 280-333 and 240-262 nm respectively.

The perchlorates (IVa-c, f-l) on boiling with water-ethanol mixture afforded the respective pyranopyran-4,5-diones (IIa-c, f-l). In case of perchlorate (IVe,d) no crystalline solid product was obtained and the reaction mixture on pouring into water gave the corresponding pyranopyran-4,5-diones (IId,e).

The reaction appears to proceed through the C-acylation of the 3-acyl group of (III) followed by the loss of water molecule to form the final pyranopyran-4,5-diones (II). The structure of these compounds is supported by the spectral data which

show the infrared absorptions [2,3,12,13] in the region 1750-1758 cm^{-1} and 1640-1668 cm^{-1} assignable to the carbonyl of 2-pyrone and 4-pyrone ring respectively. Ultraviolet absorption maxima [12] at 285-334 nm and 245-250 nm are in conformity with 2-pyrone and 4-pyrone ring respectively. The ^{1}H-NMR spectra show one-proton singlet at 6.14-6.24 ppm or at 6.65-6.75 ppm when phenyl group is present as the substituent at 7-position. A singlet integrated for six protons at 2.3-2.34 ppm indicates the presence of two chemically equivalent methyl groups at 2- and 7-positions of compounds (**IIa-f**). In addition, the ^{1}H-NMR spectra show the phenyl and alkyl groups signals at their appropriate positions depending upon the length and structure of the side chain. The spectral data reported in the literature [2,8-11] for the analogous compounds is in agreement with that obtained for our products.

The results show that the method is of general applicability and can be used for the synthesis of a variety of substituted pyranopyran-4,5-diones of type (**II**) in high yields.

Experimental

Ultraviolet spectra were recorded on a Unicam SP800 spectrophotometer in ethanol, infrared spectra were determined with Unicam SP200 spectrometer for mulls in Nujol and ^{1}H-NMR spectra were measured with Perkin-Elmer R10 (60 MHz) spectrometer, with deutro-chloroform as solvent, tetramethylsilane as internal reference and are quoted in ppm (δ), unless otherwise stated. Dehydroacetic acid used was from Koch-Light (London). Triacetic lactone (**Ia**) m.p. 187-188°C (lit. [14] m.p. 188-189°C) and 4-hydroxy-6-phenyl-2H-pyran-2-one (**Ib**) m.p. 245-246°C (lit. [15] m.p. 245-246°C) were prepared by the methods given in literature. All melting points are uncorrected.

General method for the preparation of (III)

A mixture of (**I**) (0.1 mol), trifluoroacetic acid (20 ml) and appropriate acid chloride (0.1 mol) was refluxed for 2-3 hours and then poured into cold water (100 ml). The resulting oily layer was taken up in a alcohol and reprecipitated by the addition of water. The vacuum dried products were crystallised from *n*-heptane. (**IIIa**) m.p. 150-152°C (60%) (lit. [16] m.p. 151-152°C); (**IIIb**) m.p. 105-106°C (56%) (lit. [17] m.p. 105-107°C); (**IIIc**) m.p. 61-62.5°C (65%) (lit. [17] m.p. 57-59°C); (**IIId**) m.p. 65-67°C (60%) (lit. [18] m.p. 66-67°C); (**IIIf**) (62%) m.p. 94-96°C (lit. [18] m.p. 93-5.94.5°C); (**IIIg**) m.p. 166-167.5°C (58%) (lit. [17] m.p. 169-171°C); (**IIIi**) m.p. 154-155°C (62%) (lit. [17] m.p. 155.5-156.5°C).

Compound (IIIe)

m.p. 80°C (ethanol (60%); IR (cm^{-1}) 1720 (CO ring), 1645 (CO of side chain) 1620 (-C=C-); UV 299 nm (ε log 4.15) ^{1}HNMR 0.9 (m, $-CH_3$, 3H), 1.28 (m, $-CH_2$,18H), 2.25 (s, $-CH_3$, 3H), 2.88-3.2 (t, $-CH_2$,2H), 5.9 (s, -CH=, 1H), 16.92 (s, -OH, 1H). Anal. Calcd for $C_{18}H_{28}O$: C, 70.13; H, 9.09 Found: C, 70.25; H, 8.9.

Compound (IIIh)

m.p. (163-165°C) (ethanol-*n*-heptane) (65%); IR (cm^{-1}) 1709 (CO of ring), 1624 (CO of side chain), 1554 (-C=C-); UV: 347 nm (ε log 4.43); ^{1}HNMR 4.4 (s, $-CH_2$,2H), 6.53 (s, -CH=, 1H), 7.2-7.9 (m, Ph, 10H), 16.44 (s, -OH, 1H). Anal. Calcd for $C_{19}H_{14}O_4$: C, 74.51, H, 4.58. Found C, 74.57; H, 4.62.

General method for the preparation of pyranopyran-4,5-dione perchlorates (IV)

The appropriate 3-acylpyrone (**III**) was dissolved or suspended in acetic anhydride (6-30 ml per gram) and the mixture was cooled below -5°C in an ice-salt freezing mixture. Perchloric acid (72%) (0.5-3 ml per gram) was added dropwise with continuous stirring. During the addition of perchloric acid, the temperature of the reaction mixture was not allowed to rise above 40-45°C. After cooling the clear solution of the reaction mixture was left at room temperature. The solid crystalline product was filtered out and filterate on pouring into dry ether gave more of the product. The perchlorates (**IV**) were crystallized from nitromethane or acetic acid. Experimental conditions for individual compounds are given in the Table-1.

Compound (IVa)

m.p. 188-190 (92%); IR (cm^{-1}) 1715 (CO of 2-pyrone ring), 1615, 1550 (-C=C-); UV 295 nm (ε log 4.0), 250 nm (ε log 4.2). Anal. Calcd for $C_{16}H_{13}ClO_8$: C, 52.1; H, 3.52; Cl, 9.63. Found: C, 52.0; H, 3.5; Cl, 9.50.

Table 1:

Acylderivative III (gm)		Acetic anhydride (ml)	$HClO_4$ (ml)	Time (Hrs)	Product* (IV)
a	1.0	6	0.5	12	a
b	15.0	100	7.5	18	b
c	16.0	100	8.0	24	c
d	2.0	12	2.0	72	-
e	3.0	30	4.0	72	-
f	10.0	300	30.0	72	f
g	1.0	10	1.0	72	g
h	10.0	20	2.0	1.4	h
I	2.5	50	5.0	12	i

*(IVd) and (IVe) did not crystallise out from the reaction mixture.

Compound (IVb)

m.p. 175-177°C (80%); IR (cm^{-1}) 1712 (CO of 2-pyrone), 1618, 1550 (-C=C-); UV 290 nm (ε log 3.96), 246 nm (ε log 4.3). Anal. Calcd. for $C_{11}H_{11}ClO_8$: C, 43.07; H, 3.59; Cl, 11.58. Found: C, 43.2; H, 3.67; Cl, 11.6.

Compound (IVc)

m.p. 245°C (80%); IR (cm^{-1}) 1715 (CO of 2-pyrone), 1610, 1540 (-C=C-); UV 280 nm (ε log 4), 250 nm (ε log 4.2). Anal. Calcd. for $C_{12}H_{13}ClO_8$: C, 44.93; H, 4.05; Cl, 11.08. Found: C, 44.9; H, 3.99; Cl, 11.1.

Compound (IVf)

m.p. 111-113°C (90%); IR (cm^{-1}) 1718 (CO of 2-pyrone), 1620, 1550 (-C=C-); UV 300 nm (ε log 4.0), 244 nm (ε log 4.4). Anal. Calcd. for $C_{26}H_{41}ClO_8$: C, 60.41; H, 7.94; Cl, 6.88. Found: C, 60.57; H, 8.01; Cl, 6.99.

Compound (IVg)

m.p. 230-232°C (60%); IR (cm^{-1}) 1735 (CO of 2-pyrone), 1618, 1540 (-C=C-); UV 330 nm (ε log 4.16); 252 nm (ε log 4.2). Anal. Calcd. for $C_{15}H_{11}ClO_8$: C, 50.78; H, 3.1; Cl, 10.01. Found: C, 50.68; H, 3.2; Cl, 10.06.

Compound (IVh)

m.p. 246-247°C (dec) (60%); IR (cm^{-1}) 1722 (CO of 2-pyrone), 1630, 1598 (-C=C-); UV 333 nm (ε log 4.11), 262 nm (ε log 4.29). Anal. Calcd. for $C_{21}H_{15}ClO_8$: C, 58.54; H, 3.48; Cl, 8.25. Found: C, 58.40; H, 3.46; Cl, 8.04.

Compound (IVi)

m.p. 250°C (70%); IR (cm^{-1}) 1724 CO of 2-pyrone), 1628, 1600 (-C=C-) UV 330 nm (ε log 4.31), 255 nm (ε log 4.32). Anal. Calcd. for $C_{16}H_{13}ClO_8$: C, 52.1; H, 3.53; Cl, 9.63. Found: C, 52.1; H, 3.53; Cl, 9.63. Found: C, 52.1; H, 3.49; Cl, 9.64.

General method for the conversion of perchlorates (IV) into corresponding 4H, 5H-pyranopyran-4,5-diones (II)

The perchlorate **(IVa,b,c,f,g,h,I)** on boiling with ethanol-water mixture gave the corresponding free bases **(IIa,b,c,f,g,h,I)** while in case of **(IVd,e)** where no crystalline solid perchlorate products were obtained, the reaction mixture on pouring into water gave the corresponding free bases **(IId,e).**

Compound (IIa)

m.p. 217-219°C (ethanol-water) (65%); IR (cm^{-1}) 1750 (CO of 2-pyrone ring), 1640 (CO of 4-pyrone ring), 160-0, 1565 (-C=C-); UV 298 nm (ε log 4.3), 235 nm (ε log 4.4); ^{1}H-NMR 2.17-2.39 (m, $-CH_3$,6H), 6.16 (s, -CH=, C, 1H), 7.17-7.43 (m, 5H aromatic). Anal. Calcd. for $C_{16}H_{12}O_4$; C, 71.64; H, 4.48. Found: C, 71.66; H, 4.53.

Compound (IIb)

m.p. 263-265°C (water-ethanol) 87%); IR (cm^{-1}); 1752 (CO of 2-pyrone), 1640 (CO of 4-pyrone), 1600, 1565 (-C=C); UV 298 nm (ε log 4.11) 246 nm (ε log 4.35); ^{1}H-NMR 1.98 (s, $-CH_3$, 3H), 2.33 (s, $-CH_3$,6H), 6.15 (s, -CH=C, 1H). Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.08; H, 4.86. Found: C, 64.06; H, 5.03.

Compound (IIc)

m.p. 214-216°C (ethanol-water) (60%); IR (cm^{-1}) 1752 (CO of 2-pyrone), 1655 (CO of 4-pyrone), 1626, 1650 (-C=C-); UV 286 nm (ε log 4.1), 248 nm (ε log 4.33); ^{1}H-NMR 0.95-1.18 (t, -=CH_3, 3H), 2.33 (s, $-CH_3$,6H), 2.25-2.5 (q, $-CH_2$,2H), 6.14 (s, -CH=C',1H). Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.46; H.5.4. Found: C, 65.54; H, 5.32.

Compound (IId)

m.p. 166-168°C (ethanol-water) (71%); IR (cm^{-1}) 1750 (CO of 2-pyrone), 1650 (CO of 4-pyrone) 1630, 1560 (-C=C-); UV: 285 nm (ε log 4.1), 250 nm (ε log 4.3); ^{1}H-NMR 0.9 (s, $-CH_3$, 3H), 1.3-1.55 (m, $-CH_2$,4H), 2.28-2.45 (q, CH_2, 2H), 2.34 (s, $-CH_3$, 6H), 6.14 (s, C=CH, 1H). Anal. Calcd. for

$C_{14}H_{16}O_4$: C, 67.74; H, 6.45. Found: C, 67.73; H, 6.48.

Compound (IIe)

m.p. 121-122°C (pet. ether 60-89°C) (60%); IR (cm^{-1}) 1750 (CO of 2-pyrone), 1660 (CO of 4-pyrone), 1640, 1560 (-C=C-); UV: 293 nm (ε log 4.30), 245 nm (ε log 4.4); ^{1}H-NMR 0.88 (s, $-CH_3$, 3H), 1.25 (m, $-CH_2$, 16H), 2.2-2.45 (unresolved, $-CH_2$, 2H), 2.35 (s, $2CH_3$, 6H), 6.16 (s, C=CH, 1H). Anal. Calcd. for $C_{20}H_{30}O_4$: C, 72.29; H, 8.43. Found: C, 72.1; H, 8.5.

Compound (IIf)

m.p. 126°C (ethanol-water) (94%); IR (cm^{-1}) 1750 (CO of 2-pyrone), 1655 (CO of 4-pyrone), 1632, 1562 (-C=C-); UV: 290 nm (ε log 4.). 245 nm (ε log 4.2); ^{1}H-NMR 0.92 ($-CH_3$, 3H), 1.3 (s, $-CH_2$, 28H), 2.38 (s, $-CH_2$,2H and $-CH_3$, 6H), 6.24 (s, -CH=C, 1H). Anal. Calcd. for $C_{26}H_{40}O_4$: C, 75.0, H, 9.6; Found: C, 74.90; H, 9.5.

Compound (IIg)

m.p. 227°C (ethanol-water) 84%); IR (cm^{-1}) 1758 (CO of 2-pyrone), 1668 (CO of 4-pyrone), 1628, 1558 (-C=C-); UV: 333 nm (ε log 4.25), 245 (ε log 4.23); ^{1}H-NMR 2.34 (s, $-CH_3$, 3H), 6.2 (s, HC=C',1H), 6.75 (s, -C=CH,1H), 7.5-8.0 (m, Ph, 5H). Anal. Calcd. for $C_{15}H_{10}O_4$: C, 70.82; H, 3.94 Found: C, 70.85; H, 3.93.

Compound (IIh)

m.p. 280-281°C (ethanol-water) (60%); IR (cm^{-1}) 1752 (CO of 2-pyrone), 1648 (CO of 4-pyrone) 1620, 1575 (-C=C-); UV : 334 nm (ε log 4.3); 260 nm (ε log 4.36); ^{1}H-NMR 2.27 (s, $-CH_3$, 3H), 6.7 (s, -C=CH-, 1H), 7.3-8.0 (m, Ph. 10H). Anal. Calcd. for $C_{21}H_{14}O_4$: C, 76.36; H, 4.24. Found: C, 76.32; H, 4.22.

Compound (IIi)

m.p. 239-41°C (ethanol-water (92.5%); IR (cm^{-1}) 1753 (CO of 2-pyrone), 1655 (CO of 4-pyrone), 1620, 1561 (-C=C-); UV: 331 nm (ε log 4.36), 254 nm (ε log 4.32); ^{1}H-NMR 1.97 (s, $-CH_3$, 3H), 2.34 (s, $-CH_3$, 3H), 6.65 (s, -C=CH, 1H), 7.407.9 (m, Ph., 5H). Anal. Calcd. for $C_{16}H_{12}O_6$: C, 71.64; H, 4.4 Found: C, 71.68; H, 4.45.

References

1. F.N.A. Fleishman, *J. Chem. Soc.*, **250**, 91 (1907).
2. M. Siddiq and P.F.G. Praill, *J. Chem. Soc. Pak.*, **4**, 205 (1982).
3. A.K. Kiang and S.F. Tan, *J. Chem. Soc.*, 2283 (1965).
4. E. Ziegler and H. Junek, *Monatsh. Chem.*, **323**, 89 (1958).
5. T. Money, I.H. Qureshi, G.B. Webster and A.I. Scott, *J. Am. Chem. Soc.*, **3004**, 87 (1965).
6. F. Hradetzky and E. Ziegler, *Monatsh. Chem.*, **398**, 97 (1966).
7. (a) T. Money, *Chem. Rev.*, **70**, 553 (1970).
   (b) T.M. Harris, C.M. Harris and K.B. Hindley, *Fortschr. Chem. Org. Natur. Stoffe*, Ed. by W. Herz, H. Grisebach, G.W. Kirby Springer Verlag, Inc. Wien 30, p 217 (1974).
   (c) N. Takevchi and S. Tobinaga, *Chem. Pharm. Bull.*, **3007**, 28 (1980).
   (d) F. J. Leaper and J. Staunton, *J. Chem. Soc. Perkin Trans I*, 1053 (1984).
8. L. Cattel, G. Nobibi, O. Caputo and G. Biglino, *Farmaco Ed. Sci.* **26**, 247 (1971)
9. O. Caputo, L Cattel, F. Viola and G. Biglino *Gazetta Chimica Italiana* **107**, 455 (1977).
10. Y. Qamar and M. Siddiq, *Indian J. Chem.*, **27B**, 373 (1988).
11. P.G. Praill, A. L. Whitear, *Proc. Chem. Soc. London*, **112** (1961).
12. K. Yamada, Bull. *Chem. Soc. Japan*, **33**, 1688 (1962).
13. M. Siddiq, *J. Chem. Soc. Pak.*, **5**, 39 (1983).
14. J.N. Collie, *J. Chem. Soc.*, **59**, 609 (1891).
15. F. Arndt, B. Eistert, H. Scholz and E. Aron, *Ber.* **69**, 2373 (1936).
16. L.L. Wood and P.A. Dix, *J. Org. Chem.*, **26**, 2588 (1961).
17. E. Marcus, J.F. Stephen and J.K. Chan, *J. Heterocyclic Chem.*, **6**, 13 (1969).
18. K. Miyaki and S. Yamagishi, *J. Pharm. Soc. Japan*, **75**, 43 (1955).