

**CHEMISTRY OF PYRONES: PART 6. SYNTHESIS OF SOME AMINOXYALKYL DERIVATIVES OF 4-PYRONES<sup>#</sup>****Aziz Shahrisa,\* Reza Tabrizi, Fatemeh Abrishami***Department of Organic Chemistry, Faculty of Chemistry, Tabriz University, Tabriz 51664, Iran**Tel: +98 411 3340081-9, Fax: +98 411 3340191, e-mail: [ashahrisa@yahoo.com](mailto:ashahrisa@yahoo.com)**Received 02-10-2001***Abstract**

Some phthalimidoxymethylpyrones were synthesized by means of reactions of bisbromomethylpyrones and *N*-hydroxyphthalimide and treated with hydrazine in methanol to give bisaminoxymethyl derivatives of 4-pyrones. Reaction of these compounds with arylaldehydes led to six *E,E* and *E,Z* isomers.

**Keywords:** 4*H*-pyran-4-one, bis (aminoxymethyl)pyrone.

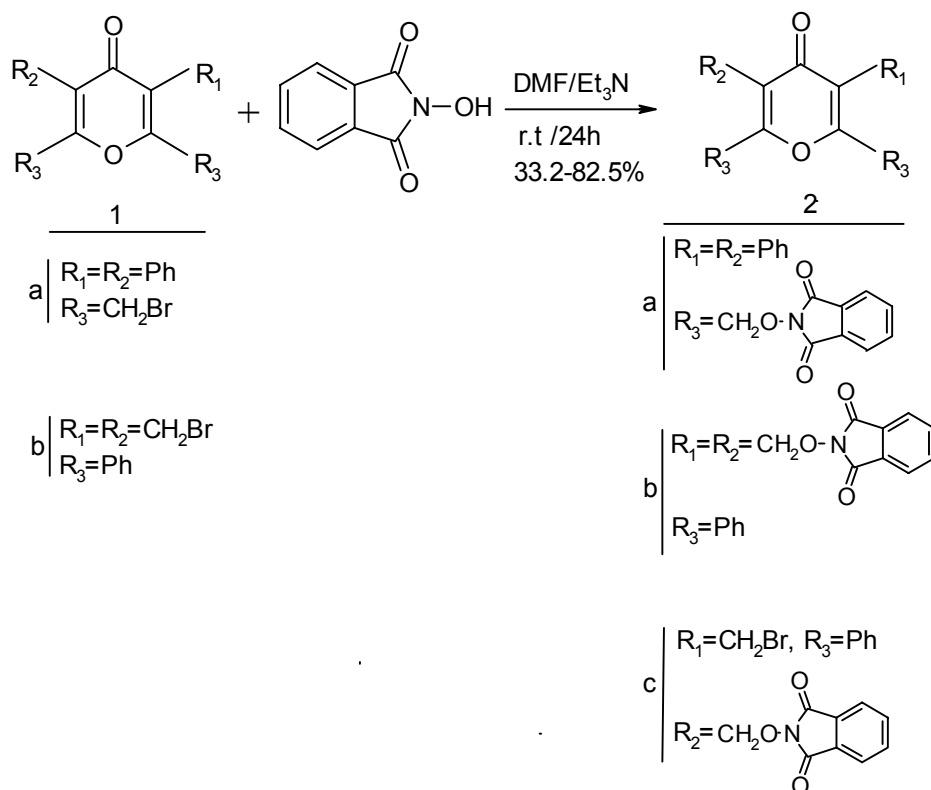
**Introduction**

4-Pyrones and corresponding derivatives have been the subject of much research due to their importance in various applications and their widespread biological significance.<sup>2-12</sup> The synthetic utility would still be enhanced if more pyrones possessing various functional groups could be synthesized.

In the past decade we have been interested in the chemistry of pyrones.<sup>13-16</sup> In continuation of our studies in the chemistry of pyrones we have investigated the reactions for the synthesis of a number of aminoxyalkyl derivatives of 4-pyrones. It should be noted that some aminoxyalkyl derivatives of kojic acid have been prepared and patented.<sup>17</sup>

**Results and Discussion**

Pyrones **1a** and **1b** (prepared according to literature in two and five steps, respectively<sup>18-21</sup>) were treated with *N*-hydroxyphthalimide in DMF and in the presence of triethylamine to give compounds **2a-c** in the range of 52-82.5% yields. In another experiment, starting from **1b** the mixture of **2b** (62.5%) and **2c** (33.2%) was obtained.

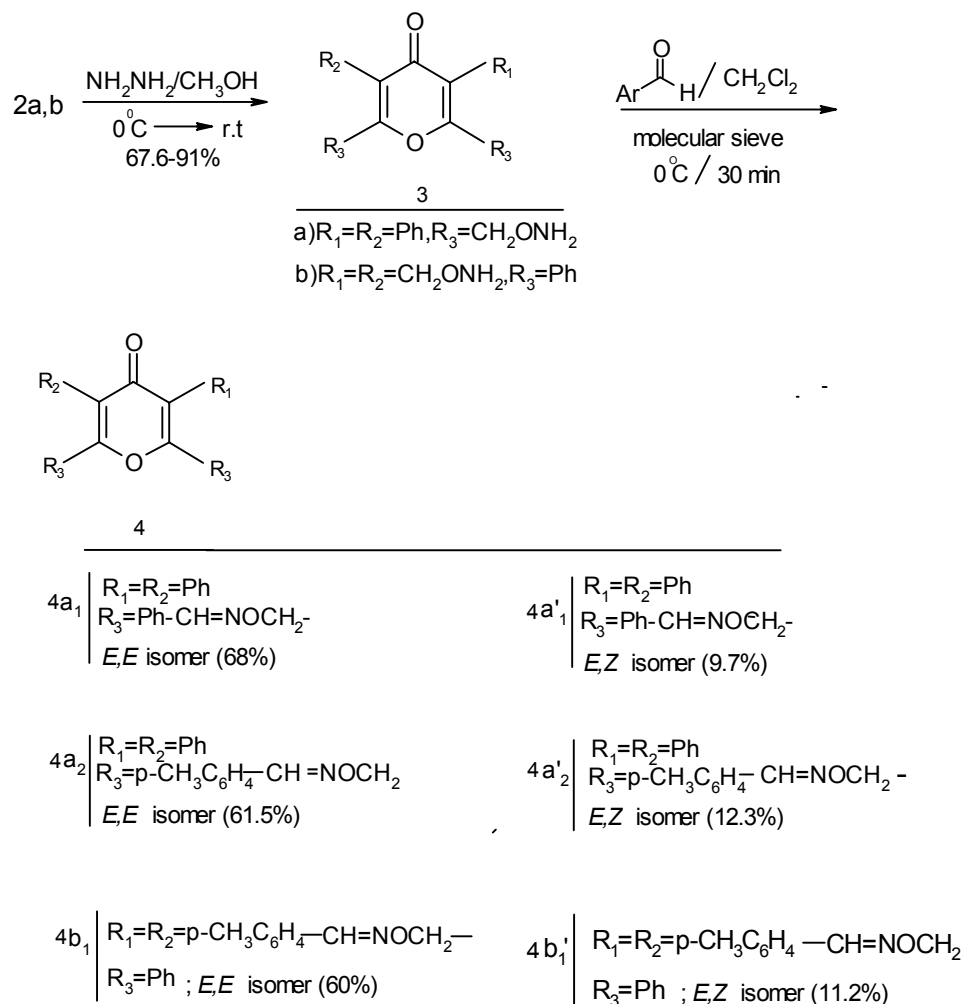


Scheme 1

With the help of IR, <sup>1</sup>H NMR and / or <sup>13</sup>C NMR spectral data and elemental analyses the structures of **2a-c** were established (see experimental section). This is shown in **Scheme 1**, when **2a,b** were reacted with hydrazine in methanol at 0 °C → rt compounds **3a,b** were obtained in 67.6 and 91% yields respectively. Structures of these compounds were established on the basis of physical properties (mp, IR, NMR, deuterium exchange) and elemental analyses.

The reaction of **3a,b** with arylaldehydes in dichloromethane and in the presence of molecular sieves (4Å) at rt leads to the formation of compounds **4** (**Scheme 2**). For instance the reaction of **3a** with benzaldehyde gives the corresponding *E, E* (**4a<sub>1</sub>**) and *E,Z* (**4a'<sub>1</sub>**) isomers in 68 and 9.7% yields respectively. Similarly, compounds **4a<sub>2</sub>** and **4a'<sub>2</sub>** were formed by means of reaction **3a** with *p*-tolualdehyde in 61.5 and 12.3% yields respectively. Treatment of **3b** with *p*-tolualdehyde resulted in the formation of **4b<sub>1</sub>** and **4b'<sub>1</sub>** in 60 and 11.2 % yields respectively (**Scheme 2**). The data obtained from IR,

NMR, mass spectra and elemental analyses are fully consistent with the proposed structures.



### Scheme 2

### Conclusions

In this research work the synthesis of mono- and bisphthalimidoxymethyl- pyrones **2a-c**, bisaminoxymethylpyrones **3a,3b** and corresponding condensed products with arylaldehydes **4a<sub>1</sub>-a'<sub>1</sub>**; **4a<sub>2</sub>-a'<sub>2</sub>**; **4b<sub>1</sub>-b'<sub>1</sub>** is reported. Reactions of **3a** with other aldehydes

such as pyridin-2-carbaldehyde is under investigation and results will be published elsewhere.

### Experimental

Melting points were determined with an Electrothermal instrument model 9100 and are uncorrected. Infrared (FT-IR) spectra were run on a Shimadzu 8010M Spectrophotometer as KBr disks or as smears between sodium chloride plates. The  $^1\text{H}$  NMR spectra were recorded on a Varian-EM 390 spectrometer. The  $^{13}\text{C}$  NMR spectra were determined on a FT-NMR Bruker 80 MHz spectrometer. Chemical shifts were reported in ppm with TMS as an internal standard. Mass spectra were taken with a Shimadzu MS-QF 1100EX mass spectrometer. Elemental analyses were performed on a Heareus, CHN-O-RAPID analyzer. Starting materials were purchased from commercial sources.

#### General procedure for synthesis of 2a-c.

To a mixture of **1a** or **1b** (1.74 g, 4 mmol), *N*-hydroxyphthalimide<sup>22</sup> (1.32 g, 8 mmol) and DMF (10 mL) triethylamine (8.8 g, 80 mmol) was added. The reaction mixture was stirred at rt for 24 hrs. Water (10 mL) was added and the precipitate was filtered off and washed with water and dried in air to give **2a-c**. Specific detail is given for each compound.

#### 2,6-Bis(phthalimidoxymethyl)-3,5-diphenyl-4*H*-pyran-4-one (**2a**).

Yellow solid, 52% yield, mp 228-229.5 °C. IR (KBr): 3094, 2925, 1790 (phthalimide C=O), 1740 (phthalimide C=O), 1631 (pyrone C=O), 1620 (pyrone C=C), 1579, 1490, 1185, 1120, 876, 760, 700  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  4.95 (s, 4H,  $-\text{CH}_2-$ ), 7.2 (s, 10H, phenyl-**H**), 7.7 (s, 8H, phenylene-**H**).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  74, 123, 127.5, 130.5, 135, 155, 162.5, 172.5. Anal. calcd for  $\text{C}_{35}\text{H}_{22}\text{N}_2\text{O}_4$ : C, 70.23; H, 3.70; N, 4.68. Found: C, 69.80; H, 3.81; N, 4.50%.

**3,5-Bis(phthalimidoxymethyl)-2,6-diphenyl-4H-pyran-4-one (2b).**

Yellow solid, 82.5% yield, mp 233-234 °C. IR: (KBr) 3500, 3075, 2950, 2875, 1790 (phthalimide C=O), 1740 (phthalimide C=O), 1635 (pyrone C=O), 1620 (pyrone C=C), 1575, 1490, 1465, 1250, 1186, 875, 771, 702cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 4.9 (s, 4H, -CH<sub>2</sub>-), 7.15-7.85 (m, 18H, aromatic-H). MS: m/z 599 (M<sup>+</sup>, 2% at sensitivity 16), 436 (80), 273 (32), 105 (100), 77 (25), 76 (24). Anal. calcd for C<sub>35</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>: C, 70.23; H, 3.70; N, 4.68. Found: C, 69.98; H, 3.81; N, 4.55.

**3-Bromomethyl-5-phthalimidoxymethyl-2,6-diphenyl-4H-pyran-one (2c).**

White crystals, 33.2% yield, mp 169.5-170 °C. IR (KBr): 3055, 2962, 2857, 1791 (Phthalimide C=O), 1725 (phthalimide C=O), 1637 (pyrone C=O), 1625 (pyrone C=C), 1446, 1138 (CH<sub>2</sub>-Br), 1187, 1169, 875, 766, 696cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 4.2 (s, 2H, CH<sub>2</sub>-Br), 5.1 (s, 2H, -CH<sub>2</sub>O-), 7.3-7.9 (m, 18H, aromatic-H).

**General procedure for synthesis of 3a,b.**

To a solution of **2** (3.3 mmol) in absolute methanol (20 mL) hydrazine (61.9%, 0.85 mL) at 0 °C was added dropwise with stirring in half an hr. The reaction mixture was stirred at rt for 24 hrs, then filtered. To the filtrate dichloromethane (10 mL) was added and was stirred at 0 °C for 2 hrs, then filtered. Solvent was removed under reduced pressure to give compounds **3a-b**. Specific detail is given for each compound.

**2,6-Bis(aminoxymethyl)-3,5-diphenyl-4H-pyran-4-one (3a).**

White crystals 91% yield, mp 128-129 °C. IR: (KBr) 3450, 3300, 3250, 3150, 3050, 2950, 2872, 1634 (pyrone C=O), 1620 (pyrone C=C), 1574, 1495, 1448, 1446, 1184, 731, 700cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 4.65 (s, 4H, -CH<sub>2</sub>O-), 5.3 (broad, 4H, disappeared on shaking with D<sub>2</sub>O, -ONH<sub>2</sub>) 7.35-7.85 (m, 10H, phenyl-H). Anal. calcd for C<sub>19</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>: C, 67.44; H, 5.36; N, 8.28. Found: C, 67.11; H, 5.20; N, 8.31.

**3,5-Bis(aminoxymethyl)-2,6-diphenyl-4H-pyran-4-one (3b).**

White crystals, 67.6% yield, mp 131.5–133 °C. IR (KBr): 3470, 3300, 3250, 3140, 3050, 2960, 1640 (pyrone C=O), 1622 (pyrone C=C), 1570, 1413, 1250, 1180, 773, 696  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  4.64 (s, 4H,  $-\text{CH}_2-$ ), 5.37 (broad, 4H, disappeared on shaking with  $\text{D}_2\text{O}$ ,  $-\text{ONH}_2$ ), 7.33 (m, 10H, phenyl-H); Anal. Calcd for  $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_4$ : C, 67.44; H, 5.36; N, 8.28. Found: C, 67.80; H, 5.11; N, 8.30.

**General procedure for synthesis of compounds 4 ( $\mathbf{a}_1$ - $\mathbf{a}'_1$ ;  $\mathbf{a}_2$ - $\mathbf{a}'_2$ ;  $\mathbf{b}_1$ - $\mathbf{b}'_1$ ).**

To a solution of bis(aminoxymethyl) derivatives **3a** or **3b** (1.47 mmol) in dichloromethane (15 mL), possessing molecular sieves  $4\text{A}^\circ$  (1.5 g) a solution of benzaldehyde or *p*-tolualdehyde (2.9 mmol) in dichloromethane (5 mL) was added dropwise with stirring at 0 °C in half an hr. The reaction mixture was stirred at rt for 24 hr, then filtered. The solvent was removed under reduced pressure and the crude material was purified by column chromatography on silicagel using petroleum ether-ethyl acetate (9:1) as eluent to give *E, E* and *E, Z* isomers. Specific detail is given for each isomer.

***E, E*- $O, O'$ -[(3,5-diphenyl-4H-pyran-4-one-2,6-diyl)bis(methylene)]dioxime benzaldehyde ( $\mathbf{4a}_1$ ).**

Yellow oil, 68% yield. IR (smears): 3050, 3020, 2975, 2880, 1640 (pyrone C=O), 1600 (pyrone C=C), 1480, 1440, 1120, 980, 720  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  5.1 (s, 4H,  $-\text{CH}_2-$ ), 7–7.7 (m, 20H, aromatic-H), 8.1 (s, 2H,  $-\text{CH}=\text{NO}-$ ); MS:  $m/z$  515 ( $\text{M}^+$ , 12%), 410 (12), 394 (18), 291 (18), 273 (42), 115 (100), 89 (50), 77 (28). Anal. calc for  $\text{C}_{33}\text{H}_{26}\text{N}_2\text{O}_4$ : C, 76.96; H, 5.09; N, 5.44. Found: C, 76.75; H, 4.91; N, 5.80.

***E, Z*- $O, O'$ -[(3,5-diphenyl-4H-pyran-4-one-2,6-diyl)bis(methylene)]dioxime benzaldehyde ( $\mathbf{4a}'_1$ ).**

Yellow oil, 9.7% yield. IR ( $\text{CDCl}_3$ ): 3050, 3010, 2895, 2880, 1640 (pyrone C=O), 1600 (pyrone C=C), 1480, 1440, 1050, 905, 700  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  5.14 (s, 4H,  $-\text{CH}_2-$ ), 7–7.7 (m, 20H, aromatic-H), 8.1 (s, 2H,  $-\text{CH}=\text{NO}-$ ); MS:  $m/z$  515 ( $\text{M}^+$ , 12%), 410 (12), 394 (18), 291 (18), 273 (42), 115 (100), 89 (50), 77 (28). Anal. calc for  $\text{C}_{33}\text{H}_{26}\text{N}_2\text{O}_4$ : C, 76.96; H, 5.09; N, 5.44. Found: C, 76.75; H, 4.91; N, 5.80.

CH<sub>2</sub>-), 7-7.6 (m, 21H, aromatic-H and Z -CH=NO-), 8.1 (s, 1H, E -CH=NO-). Anal. calcd for C<sub>33</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>: C, 76.96; H, 5.09; N, 5.44. Found: C, 76.81; H, 4.93; N, 5.73.

***E,E-O,O'*-(3,5-diphenyl-4*H*-pyrane-4-one-2,6-diyl)bis(methylene)dioxime-4-methylbenzaldehyde (4a<sub>2</sub>).**

Colorless oil, 61.5% yield. IR (smears): 3050, 3020, 2975, 2880, 1640 (pyrone C=O), 1600 (pyrone C=C) 1480, 1440, 1120, 980, 720 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.2 (s, 6H, -CH<sub>3</sub>), 5.2 (s, 4H, -CH<sub>2</sub>-), 6.9-7.3 (m, 14H, phenyl and phenylene-H), 7.5 (4H, d, J= 8 Hz, phenylene-H), 8.1 (s, 2H, E -CH=NO-) ppm. MS: m/z 543 (M<sup>+</sup>, 25%), 424 (45), 488 (55), 295 (55), 273 (55), 115 (100), 89 (45). Anal calcd for C<sub>35</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub>: C, 77.47; H, 5.57; N, 5.16. Found: C, 77.61; H, 5.41; N, 4.98.

***E,Z-O,O'*-(3,5-diphenyl-4*H*-pyran-4-one-2,6-diyl)bis(methylene)dioxime-4-methylbenzaldehyde (4a'<sub>2</sub>).**

Colorless oil, 12.3% yield. IR (smears): 3010, 2930, 2890, 1645 (pyrone C=O), 1620 (pyrone C=C), 1480, 1040, 930, 770, 700 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.2 (s, 6H, CH<sub>3</sub>), 5.2 (s, 4H, -CH<sub>2</sub>-), 6.9-7.3 (m, 15H, phenyl-H, phenylene-H and Z -CH=NO-), 7.5 (d, 4H, J=8Hz, phenylene-H), 8.1 (s, 1H, E -CH=NO-). Anal. calcd for C<sub>35</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub>: C, 77.47; H, 5.57; N, 5.16. Found: C, 77.58; H, 5.45; N, 4.91.

***E,E-O,O'*-(2,6-diphenyl-3,5-4*H*-pyran-4-one-diyl)bis(methylene)dioxime-4-methylbenzaldehyde (4b<sub>1</sub>).**

White solid, 60% yield, mp 128°C. IR (KBr): 3062, 3035, 2940, 2875, 1642 (pyrone C=O), 1623 (pyrone C=C), 1571, 1509, 1482, 1340, 1174, 1035, 803, 767, 696 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.3 (m, 6H, -CH<sub>3</sub>), 5.2 (s, 4H, -CH<sub>2</sub>-), 6.9-7.6 (m, 18H, aromatic-H), 8.1 (s, 2H, E -CH=NO-), MS: m/z 543 (M<sup>+</sup>, 60%), 424 (15), 408 (20), 289 (15), 273 (19), 159 (14), 105 (100), 77 (31). Anal calcd for C<sub>35</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub>: C, 77.47; H, 5.57; N, 5.16. Found: C, 77.58; H, 5.36; N, 4.94.

***E,Z-O,O'*-(2,6-diphenyl-4*H*-pyran-4-one-3,5-diyl)bis(methylene)]dioxime-4-methylbenzaldehyde (4b'<sub>1</sub>).**

White crystals, 11.2% yield, mp 138° C. IR (KBr): 3052, 3026, 3017, 2941, 2884, 1633 (pyrone C=O), 1610 (pyrone C=C), 1571, 1500, 1180, 1036, 812, 700 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>); δ 2.15-2.3 (m, 6H, -CH<sub>3</sub>), 5.1 (s, 2H, -CH<sub>2</sub>O-), 5.2 (s, 2H, -CH<sub>2</sub>O-) 6.9-7.9 (m, 18H, phenyl and phenylene-H and *Z* -CH=NO-), 8.1 (s, 1H, *E* -CH=NO-). MS: m/z 543 (M<sup>+</sup>, 24%), 424 (14), 408 (31), 289 (17), 273 (24), 159 (14), 105 (100), 77 (36).

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### References and Notes

# For part 5 see reference 1.

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### **Povzetek**

Z reakcijo bisbromometilpyronov z *N*-hidroksiftalimidom ter po obdelavi s hidrazinom v metanolu smo pripravili bisaminooksimetilne derivate of 4-pironov. Pripravljene spojine so v reakcijah z arilaldehidi vodile do *E,E* in *E,Z* izomerov.