A Method for the Alkylation at C—3 of 4-Hydroxy-6-methyl-2-pyrone (Triacetic Acid Lactone)

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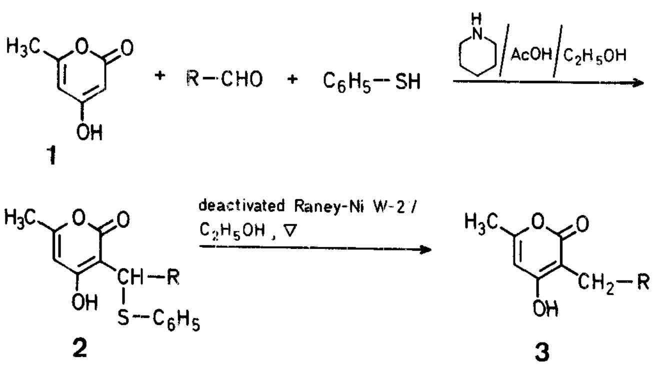
Some important natural products have an alkyl chain at C—3 on a 4-hydroxy(or methoxy)-6-methyl(or alkyl)-2-pyrone nucleus[1,2,3]. 4-Hydroxy-6-methyl-2-pyrone (**1**) is a simple polyketide[4] which is easily prepared from the industrially available 3-acetyl-4-hydroxy-6-methyl-2-pyrone (dehydroacetic acid)[5]. Therefore, the lactone **1** should be an ideal precursor to prepare natural products with the 2-pyrone, dihydro-, and tetrahydro-2-pyrone structures[6,7] were it not for the lack of general methods to functionalize the position C—3. *O*-Methylation is favoured over *C*-methylation under the usual experimental conditions[6,8,9], and only a few particular methods of limited scope have been described for the methylation[10] and for the alkylation at C—3 with reagents which are precursors of stabilized carbenium ions[11,12].

In an effort to solve these problems, we have now found that alkyl-, aryl-, and heteroaryl(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-phenylthiomethanes (**2**), prepared as indicated in the scheme, afford the corresponding 3-alkyl-4-hydroxy-6-methyl-2-pyrones (**3**) in reasonable yields when treated in ethanol with Raney nickel W-2 previously deactivated by boiling in acetone for 45–60 minutes. By using normal Raney nickel W-2, hydrogenation of the pyrone ring is frequently observed.



Products **2d** and **2e** have been previously reported[13]; the other compounds **2** are prepared in a similar manner.

3-(4-Chlorobenzyl)-4-hydroxy-6-methyl-2-pyrone (3f); Typical Procedure:

Raney-Nickel W—2 is boiled in acetone for 45 min, the acetone then being replaced by ethanol. (4-Chlorophenyl)-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-phenylthiomethane (**2f**, 0.60 g, 1.67 mmol) and the above described suspension of Raney nickel (8 ml) are heated in boiling ethanol (27 ml) for 20 min. The mixture is filtered, the nickel is washed with hot ethanol, and the filtrate is evaporated to give **3f**; yield: 0.39 g (93 %); m.p. 210–214 °C (from acetone/pentane).

The same procedure is followed to prepare the other compounds **3**, which in some cases have to be passed through a silica gel column to eliminate traces of nickel.

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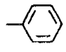
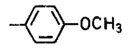
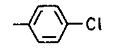
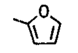
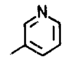
Table. Compounds **2** and **3** prepared

R	Compounds 2			Compounds 3		
	Yield [%]	m.p. [°C]	Molecular formula[a] or Lit. m.p. [°C]	Yield [%]	m.p. [°C]	Molecular formula[a] or Lit. m.p. [°C]
a H	57	151–153°	$C_{13}H_{12}O_3S$ (248.3)	64[b]	209–211°	213°[10]
b n-C_3H_7	38	oil	$C_{16}H_{18}O_3S$ (290.4)	65[b]	132–133°	$C_{10}H_{14}O_3$ (182.2)
c n-C_9H_{19}	71	oil	$C_{22}H_{30}O_3S$ (374.6)	74	103–104°	$C_{16}H_{26}O_3$ (266.4)
d 	89	159–160°	163–164°[13]	88	169–170°	168°[11]
e 	83	oil	oil[13]	85	188–190°	$C_{14}H_{14}O_4$ (246.3)
f 	94	144–146°	$C_{19}H_{15}ClO_3S$ (358.8)	93	210–214°	$C_{13}H_{11}ClO_3$ (250.7)
g 	68	128–130°	$C_{17}H_{14}O_4S$ (314.3)	29	177–178°	$C_{11}H_{10}O_4$ (206.2)
h 	72	170–172°	$C_{18}H_{15}NO_3S$ (325.4)	0		

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[a] Satisfactory microanalyses were obtained for the new compounds: C, ±0.27; H, ±0.19. Exceptions: **2g** was relatively unstable; **3e**, C, −0.52; H, +0.21. Compounds **2** and **3** showed absorptions due to the methyl groups at C-6 and the proton at C-5 in the ranges $\delta = 2.05$–2.17 and 5.67–5.85 ppm, and 2.10–2.22 and 5.96–6.25 ppm, respectively.

[b] Non-deactivated Raney nickel was used.

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[1] S. Omura, A. Nakagawa, H. Ohno, *J. Am. Chem. Soc.* **101**, 4386 (1979).

[2] Y. Koyama et al., *Tetrahedron Lett.* **1969**, 355.

[3] T. Reffstrup, P.M. Boll. *Tetrahedron Lett.* **1976**, 1903.

[4] R. Bentley, P.M. Zwitkowits, *J. Am. Chem. Soc.* **89**, 676, 681 (1967).

[5] J.N. Collie, *J. Chem. Soc.* **59**, 607 (1891).

[6] R. Bacardit, M. Moreno-Mañas, *J. Chem. Ecol.* **9**, 703 (1983).

[7] G.A. Poulton, T.D. Cyr, *Can. J. Chem.* **60**, 2821 (1982).

[8] E. Suzuki, B. Katsuragawa, S. Inoue, *Synthesis* **1978**, 144.

[9] E. Suzuki, B. Katsuragawa, S. Inoue, *J. Chem. Research* [*S*] **1979**, 110.

[10] E. Ziegler, O.S. Wolfbeis, I. Trummer, *Z. Naturforsch.* [b] **37**, 105 (1982).

[11] K.H. Boltze, K. Heidenbluth, *Chem. Ber.* **92**, 982 (1959).

[12] P. de March et al., *An. Quim.* **79C**, 15 (1983).

[13] P. de March, M. Moreno-Mañas, R. Pi, A. Trius, *J. Heterocyclic Chem.* **19**, 335 (1982).