A Novel Method for the Synthesis of Substituted and Fused 3-Cyano-4-methylmercapto-2(1*H*)-pyridones Using α-Oxoketen *S,S*-Diacetals

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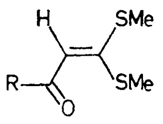
Summary α-Oxoketen *S,S*-diacetals (**1**), (**4**), and (**6**) react readily with cyanoacetamide in the presence of sodium isopropoxide in boiling propan-2-ol to give substituted and fused 3-cyano-4-methylmercapto-2(1*H*)-pyridones (**2**), (**5**), and (**7**) respectively.

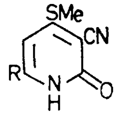
The keten *S,S*-diacetals (**1**), which are prepared from various ketones in one step, in good yields,[1] have not been explored as a three carbon fragment for the synthesis of pyridones.[2] We now report a new synthesis, with excellent overall yields of the title compounds by the reaction of (**1**) (**4**), and (**6**) with cyanoacetamide.

In a typical experiment, equimolar quantities of (**1**), cyanoacetamide, and $NaOPr^i$ were refluxed in Pr^iOH for 0·5 h. The residue, after removal of the solvent, was acidified to give (**2**) (65—85%). Under identical conditions, with ethanolic NaOEt an inseparable mixture of (**2**) and (**3**) was obtained in the ratio 95:5 (estimated by n.m.r. spectroscopy). An attempt to convert (**2**) completely into (**3**) by prolonging the reaction time (10 h) produced (**3**) in only slightly improved (15%) yield. The fused pyridones (**5**) and (**7**) were similarly prepared from (**4**) and (**6**). The m.p.s. and yields of all compounds prepared are as follows:† compound (**2a**), m.p. 325 °C (65%); (**2b**) 282 °C (82); (**2c**) 291 °C (85); (**2d**) 300 °C (80); (**2e**) 320 °C (65); (**2f**) 318 °C (65); (**5a**) 259 °C (77); (**5b**) 272 °C (76); (**7**) 268 °C (65).

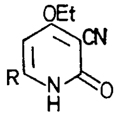
Very few methylmercaptopyridones have been prepared previously. Compounds (**5a**), (**5b**), and (**7**) are reported[3] to be formed in unspecified yields, when (**8**) is refluxed in dioxan with enamines of cyclopentanone, cyclohexanone, and α-tetralone respectively. We repeated the reaction of the morpholine enamine of cyclohexanone with (**8**) and isolated (**5b**) (m.p., and i.r. and n.m.r. spectra identical with our compound) in poor yields. The simplicity of our procedure, and higher yields obtained, make it more attractive than the enamine route. Besides, our method is more general and can be extended to keten *S,S*-diacetals of other active methylene compounds having nitrile as well as ethoxycarbonyl groups to give the corresponding amino- and hydroxy-substituted methylmercaptopyridones respectively.



(1)

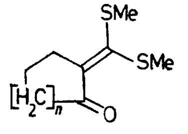


(2)

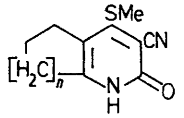


(3)

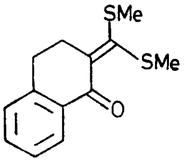
(a) R = Me
(b) R = Ph
(c) R = C_6H_4-*p*-Me
(d) R = C_6H_4-*p*-OMe
(e) R = 3-pyridyl
(f) R = 4-pyridyl



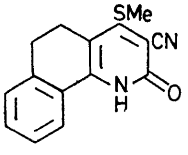
(4)
(a) *n* = 1
(b) *n* = 2



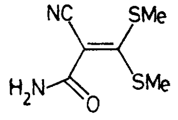
(5)
(a) *n* = 1
(b) *n* = 2



(6)



(7)



(8)

One of us (R.R.R) thanks the C.S.I.R., New Delhi, for a Junior Fellowship.

(*Received, 9th June* 1975; *Com.* 650.)

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† All new compounds gave satisfactory elemental analysis and were characterized by n.m.r. and i.r. spectroscopy.

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