

SYNTHESIS OF 6-(2-PHENYLETHENYL)-2H-PYRAN-2-ONE

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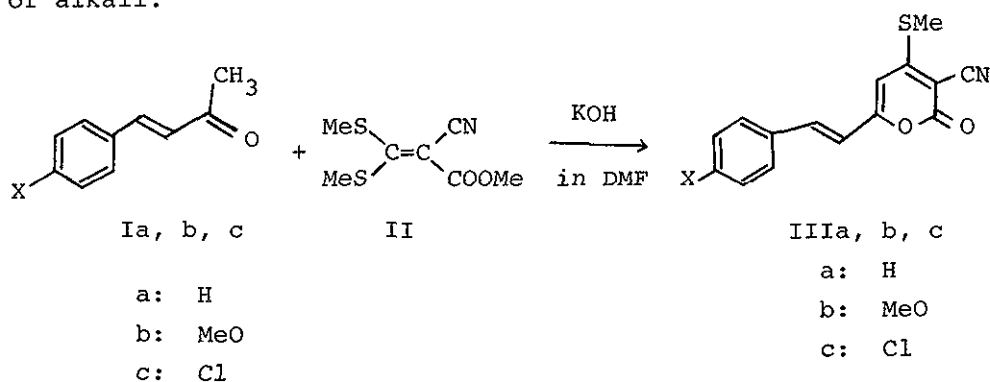
3-Cyano-4-methylthio-6-(2-phenylethenyl)-2H-pyran-2-ones (IIIa, b, c) were synthesized by the reaction of benzalacetone derivatives with methyl 2-cyano-3,3-bis(methylthio)acrylate in the presence of powdered potassium carbonate. Compounds III easily reacted with alkoxy anions and amines to give the corresponding 4-substituted 2H-pyran-2-one derivatives (dehydrokawain and yangonin derivatives).

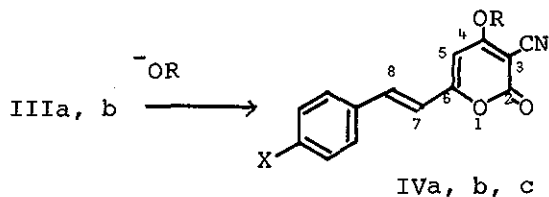
We previously reported a convenient method for the preparation of 6-aryl-3-cyano-4-methylthio-2H-pyran-2-one derivatives in a good yield by the reaction of ketenethioacetals with aryl acetyl compounds in the presence of potassium hydroxide as a base.¹⁾

We then synthesized 6-ethenyl-4-methylthio-2H-pyran-2-ones by the reaction of ketenethioacetal with benzalacetone derivatives. A number of 6-ethenyl-4-hydroxy-2H-pyran-2-ones and their methyl ethers have been isolated from a natural source.²⁾

The reaction of benzalacetone (I) with ketenethioacetal, methyl 2-cyano-3,3-bis(methylthio)acrylate (II), in the presence of powdered potassium hydroxide at room temperature gave a 5,6-dehydrokawain derivative, 3-cyano-4-methylthio-6-(2-phenylethenyl)-2H-pyran-2-one (IIIa), yellow needles, mp 221°, in 35% yield. Similarly, the reaction of other benzalacetone derivatives (p-methoxybenzalacetone (Ib), p-chlorobenzalacetone (Ic)) with II also afforded 6-ethenyl-2H-pyran-2-ones (IIIb, c) in 43% and 45% yield, respectively.

Since the methylthio group on pyran ring is easily substituted by various nucleophilic reagents, the products III would be useful as a synthetic intermediate for 5,6-dehydrokawain and yangonin derivatives. These compounds (IIIa, b) easily converted into alkoxy derivatives (IVa, b, c) when refluxed in alcohol (methanol, Methylcellosolve) in the presence of a small amount of alkali.





a: X=H, R=Me

b: X=OMe, R=Me

c: X=OMe, R=CH₂CH₂OMe

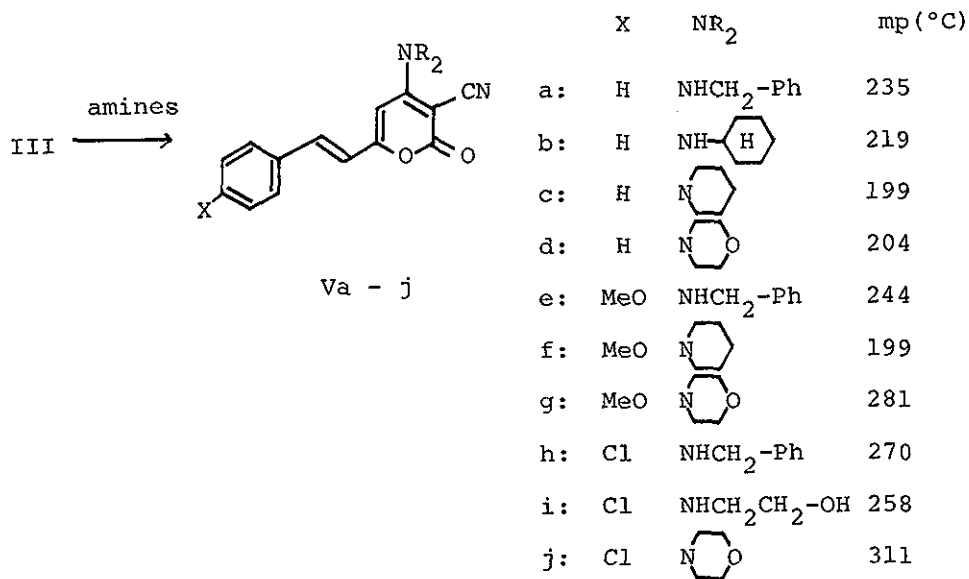
No	mp (°C)	IR(KBr)		UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm(log ϵ)	NMR δ (ppm)	C: CDCl ₃ D: DMSO-D ₆ T: CF ₃ COOH
		ν	cm ⁻¹			
IIIa 221		CN 2200 CO 1710		235 (*)	C	2.64 (SMe)
				279 ()		6.24 (5-H)
				313 ()		6.28 (7-H, d, J=16 Hz)
				365 ()		7.70 (8-H, d, J=16 Hz)
				395 ()		
IIIb 255		CN 2200 CO 1715		242 (4.13)	D	2.68 (SMe)
				415 (4.30)		3.76 (OMe)
						6.76 (5-H)
						6.92 (7-H, d, J=16 Hz)
						7.52 (8-H, d, J=16 Hz)
IIIc 261		CN 2200 CO 1710		228 (*)	T	2.71 (SMe)
				284 ()		6.68 (5-H)
				310 ()		6.74 (7-H, d, J=16 Hz)
				355 ()		7.72 (8-H, d, J=16 Hz)
				390 ()		
IVa 281		CN 2200 CO 1710		237 (4.13)	D	3.30 (OMe)
				340 (4.37)		6.55 (5-H)
						6.99 (7-H, d, J=16 Hz)
						7.39 (8-H, d, J=16 Hz)
IVb 266		CN 2200 CO 1710		230 (4.20)	D	3.86 (OMe)
				415 (4.37)		4.04 (OMe)
						6.77 (5-H)
						6.89 (7-H, d, J=16 Hz)
						7.48 (8-H, d, J=16 Hz)
IVc 201		CN 2200 CO 1710		228 (4.23)	D	3.68 (OMe)
				405 (4.37)		3.78 (OMe)
						4.36 - 4.60 (OCH ₂ CH ₂ O)
						6.83 (5-H)
						7.13 (7-H, d, J=16 Hz)
						7.38 (8-H, d, J=16 Hz)

* Concentration is unknown because of insufficient solubility.

Recently, we reported that the reaction of fused 4-methylthio-2H-pyran-2-one derivatives with nucleophils such as amines and active methylene compounds gave the corresponding substituted products of their methylthio group in a good yield.³⁾

A number of 4-hydroxy-2H-pyran-2-ones and their ethers, which have a variety of pharmacological properties, have been synthesized and their pharmacological activities were studied.⁴⁾ However, synthesis of 4-amino-2H-pyran-2-one had not been reported and we examined the synthesis of 4-amino-6-(2-phenylethenyl)-2H-pyran-2-ones because of pharmacological interest.

The reactions of IIIa, b, c with amines (benzylamine, cyclohexylamine, ethanolamine, morpholine, piperidine) in methanol gave the corresponding amino derivatives (Va, b, c, d, e, f, g h, i, j) in a good yield.



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