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

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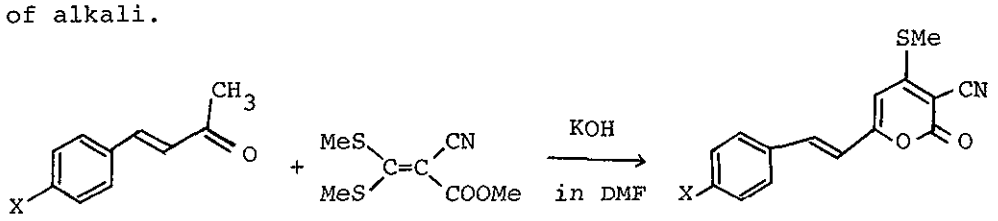
3-Cyano-4-methylthio-6-(2-phenylethenyl)-2H-pyran-2-ones (IIIa, b, c) were synthesized by the reaction of benzalacetone derivatives with methyl 2-cyano-3,3-bis(methylthio)acrylate in the presence of powdered potassium carbonate. Compounds III easily reacted with alkoxy anions and amines to give the corresponding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



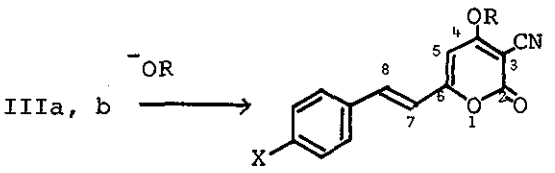
Ia, b, c

a: H
b: MeO
c: Cl

II

IIIa, b, c

a: H
b: MeO
c: Cl



a: X=H, R=Me

b: X=OMe, R=Me

c: X=OMe, R=CH_2CH_2OMe

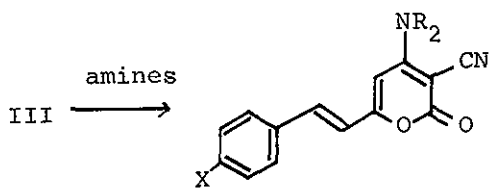
No	mp (°C)	IR(KBr) ν cm^{-1}	UV λ_{max}^{EtOH} nm(log ε)		NMR δ(ppm) C: $CDCl_3$ D: DMSO-D_6 T: CF_3COOH
IIIa	221	CN 2200 CO 1710	235 (*) 279 ( ) 313 ( ) 365 ( ) 395 ( )	C	2.64 (SMe) 6.24 (5-H) 6.28 (7-H, d, J=16 Hz) 7.70 (8-H, d, J=16 Hz)
IIIb	255	CN 2200 CO 1715	242 (4.13) 415 (4.30)	D	2.68 (SMe) 3.76 (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 (*) 284 ( ) 310 ( ) 355 ( ) 390 ( )	T	2.71 (SMe) 6.68 (5-H) 6.74 (7-H, d, J=16 Hz) 7.72 (8-H, d, J=16 Hz)
IVa	281	CN 2200 CO 1710	237 (4.13) 340 (4.37)	D	3.30 (OMe) 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) 415 (4.37)	D	3.86 (OMe) 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) 405 (4.37)	D	3.68 (OMe) 3.78 (OMe) 4.36 - 4.60 (OCH_2CH_2O) 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 pharmarcological 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.



Va - j

	X	NR_2	mp(°C)
a:	H	$NHCH_2$-Ph	235
b:	H	NH-cyclohexyl	219
c:	H	N(piperidine)	199
d:	H	N(morpholine)	204
e:	MeO	$NHCH_2$-Ph	244
f:	MeO	N(piperidine)	199
g:	MeO	N(morpholine)	281
h:	Cl	$NHCH_2$-Ph	270
i:	Cl	$NHCH_2CH_2$-OH	258
j:	Cl	N(morpholine)	311

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