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Convenient Synthesis of Amino-substituted Pyranopyranones

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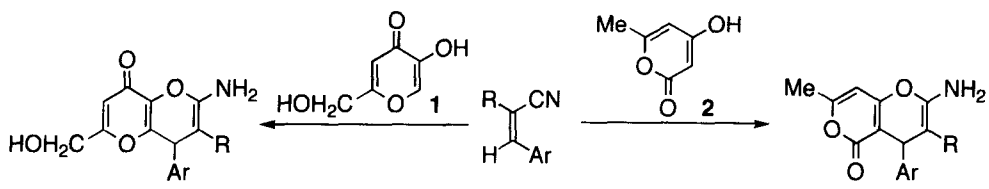
Abstract: Treatment of kojic acid and triacetic acid lactone with arylmethylenemalononitrile derivatives in the presence of piperidine in ethanol, respectively, furnished the corresponding amino-substituted new 4*H*,8*H*-pyrano[3,2-*b*]pyran-4-ones and 4*H*,5*H*-pyrano[4,3-*b*]pyran-5-ones in high yields.

Recently, the synthesis of various derivatives of fused pyran-2-one has attracted great interest, since many of them are nonpeptide human immunodeficiency virus (HIV) protease inhibitors.[1] The fused pyran derivatives have been synthesized by using a number of methods.[2] Arylmethylenemalononitrile derivatives are versatile reagents and have been successfully used as a building block for the synthesis of a variety of amino-substituted fused pyran derivatives.[3] In this communication, we wish to describe our preliminary investigation which is the first example for the reactions of kojic acid, 5-hydroxy-2-(hydroxymethyl)-4*H*-pyran-4-one, and triacetic acid lactone, 4-hydroxy-6-methyl-2*H*-pyran-2-one, with arylmethylenemalononitrile derivatives, providing a convenient method for the synthesis of amino-substituted 4*H*,8*H*-pyrano[3,2-*b*]pyran-4-ones and 4*H*,5*H*-pyrano[4,3-*b*]pyran-5-ones.

When a solution of kojic acid (**1**) (2.0 mmol) and phenylmethylenemalononitrile (**3a**) (2.0 mmol) in absolute ethanol was refluxed for 10 min in the presence of piperidine (1 drop), 6-amino-7-cyano-2-(hydroxymethyl)-8-phenyl-4*H*,8*H*-pyrano[3,2-*b*]pyran-4-one (**4a**) was obtained in 99% yield. Similarly, reactions of compound **1** with a variety of arylmethylenemalononitrile derivatives **3b-k** were carried out to give the corresponding amino-substituted 4*H*,8*H*-pyrano[3,2-*b*]pyran-4-ones **4b-k** in high yields as listed in Table 1. Using triacetic acid lactone (**2**) in a similar manner, the corresponding amino-substituted 4*H*,5*H*-pyrano[4,3-*b*]-pyran-5-ones **5a-k** were obtained in high yields as shown in Table 1.



Scheme 1

Table 1. Reactions of Kojic Acid and Triacetic Acid Lactone with Arylmethylenemalononitrile Derivatives in the Presence of Piperidine

Entry	3			Product (yield / %)[a]			
		Ar	R	4		5	
1	**3a**	C_6H_5	CN	**4a**	99	**5a**	92
2	**3b**	4-MeC_6H_4	CN	**4b**	92	**5b**	91
3	**3c**	4-$MeOC_6H_4$	CN	**4c**	93	**5c**	87
4	**3d**	4-ClC_6H_4	CN	**4d**	99	**5d**	93
5	**3e**	1-Naphthyl	CN	**4e**	89	**5e**	87
6	**3f**	C_6H_5	CO_2Et	**4f**	93	**5f**	80
7	**3g**	4-MeC_6H_4	CO_2Et	**4g**	92	**5g**	78
8	**3h**	4-$MeOC_6H_4$	CO_2Et	**4h**	99	**5h**	77
9	**3i**	4-ClC_6H_4	CO_2Et	**4i**	99	**5i**	75
10	**3j**	2-Naphthyl	CO_2Et	**4j**	84	**5j**	83
11	**3k**	C_6H_5	CO_2Me	**4k**	85	**5k**	83

[a] Isolated yield based on the amount of hydroxypyrone **1** or **2**.

In summary, we have developed a convenient method for the one-step preparation of 4*H*,8*H*-pyrano[3,2-*b*]pyran-4-ones and 4*H*,5*H*-pyrano[4,3-*b*]pyran-5-ones using arylmethylenemalononitirile derivatives as a building block for heteroannulation. Synthetic aspects of the present reactions are presently under investigation. The results will be reported in a forthcoming full paper.

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