

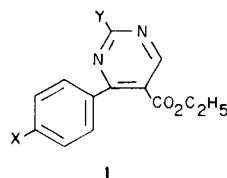
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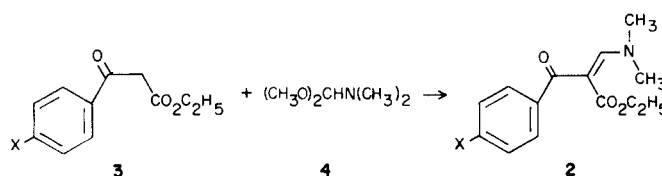
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We wish to report an improved, general synthesis of 4-aryl-5-pyrimidinecarboxylates **1**. Two different routes have previously been reported for the synthesis of examples of this class of pyrimidine carboxylates. The parent compound, ethyl 4-phenyl-5-pyrimidinecarboxylate was prepared in low yield by the reaction of *s*-triazine with ethyl benzoyl acetate. In addition, the enol ether β -ketoaldehyde synthon, ethyl 2-benzoyl-3-ethoxy-2-propenoate, was reported to give **1a** in modest yield when reacted with guanidine (**2**).

J. Heterocyclic Chem., **18**, 183 (1981).



Scheme 1



The new synthetic sequence we have used is shown in Scheme 1. This sequence is based upon the intermediacy of the enaminones such as **2** which are β -ketoaldehyde synthons. These enaminones **2** which were conveniently prepared from the appropriate benzoylacetates **3** and *N,N*-dimethylformamide dimethylacetal **4** are stable, easily purified, yellow crystalline solids (3). We have found

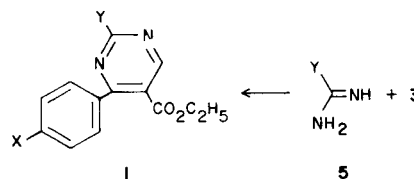


Table I

The preparation of 2-Substituted 4-Aryl *S*-Pyrimidinecarboxylates **1**

Compound No.	X	Y	Yield (%)	°C M.p. (lit)	Analysis				
					C	H	N	S	
1a	H	NH ₂	84	153-154 (156)	Calcd.	64.18	5.39	17.31	---
					Found	64.26	5.40	17.25	---
1b	H	SCH ₃	77	57-58	Calcd.	61.29	5.14	---	11.69
					Found	61.33	5.17	---	11.77
1c	H	C ₆ H ₅	49	58-59	Calcd.	74.98	5.24	9.20	---
					Found	74.96	5.33	9.21	---
1d	H		83	101-103	Calcd.	62.41	4.45	---	8.30
					Found	62.24	4.46	---	8.38
1e	F		66	151-152	Calcd.	59.63	4.00	6.95	---
					Found	59.58	4.03	6.94	---
1f	F	H	35	69-71	Calcd.	63.41	4.50	11.38	---
					Found	63.39	4.62	11.30	---
1g	F	N(CH ₃) ₂	37	94-95	Calcd.	62.27	5.57	14.52	---
					Found	62.23	5.56	14.51	---
1h	F	NHCH ₂ CONH ₂	23	140-141	Calcd.	59.40	4.65	13.85	---
					Found	59.44	4.73	13.94	---
1i	F	NHC ₆ H ₅	39	139-140	Calcd.	67.65	4.78	12.46	---
					Found	67.61	4.78	12.39	---
1j	F	CH ₃	61	78-79	Calcd.	64.61	5.03	10.76	---
					Found	64.59	5.05	10.75	---

that a variety of substituted pyrimidines may be prepared by condensing the appropriate amidine **6** ($Y = \text{NH}_2$; $\text{N}(\text{R})_2$, SR, C_6H_5 , Me) with the enamionone in refluxing ethanol (Scheme 1). The yields are listed in Table I and have not been optimized.

EXPERIMENTAL

The ethyl benzoylacetates, dimethylformamide dimethylacetal, and amidines were purchased from Aldrich Chemical Co. Melting points were determined using a Laboratory Devices Melt-Temp Apparatus and are uncorrected. Nuclear magnetic resonance were recorded using a Varian T-60 with tetramethylsilane as an internal standard. Elemental analyses were performed by Atlantic Microlab, Inc.

Ethyl 2-Benzoyl-3-dimethylaminopropenoate (**2a**).

A solution of ethyl benzoylacetate (9.6 g., 0.05 mole) in benzene (100 ml.) was stirred at room temperature while *N,N*-dimethylformamide dimethylacetal (9.5 g., 0.08 mole) dissolved in 50 ml. of benzene was added dropwise during 0.5 hour. After addition the reaction was brought to completion by refluxing the yellow solution on a steam cone for 0.5 hour. The solution was allowed to cool and the solvent and excess reagent removed by evaporation under reduced pressure. The resulting orange oil was recrystallized from ether-heptane to give 11.5 g. (91%) of the crystalline yellow product, m.p. 63-65°; nmr (deuteriochloroform): δ 1.0 (t, 3H, ethyl CH_3), 3.0 [broad s, 6H, $-\text{N}(\text{CH}_3)_2$], 3.9 (q, 2H, ethyl CH_2), 7.5 (m, 6H, ArH and enamine H).

Anal. Calcd. for $\text{C}_{14}\text{H}_{17}\text{NO}_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.07; H, 6.89; N, 5.63.

Ethyl 2-(4'-Fluorobenzoyl)-3-dimethylaminopropenoate (**2b**).

Compound **3b** was prepared in the same manner as **3a** from ethyl 4'-fluorobenzoylacetate (10.5 g., 0.05 mole). The yellow crystalline pro-

duct (7.0 g., 53%) was obtained by recrystallization from ether-heptane, m.p. 55-57°; nmr (deuteriochloroform): δ 0.95 (t, 3H, ethyl CH_3), 2.9 (broad s, 6H, $\text{N}(\text{CH}_3)_2$), 3.9 (q, 2H, ethyl CH_2), 7.3 (m, 5H Ar and enamine H).

Anal. Calcd. for $\text{C}_{14}\text{H}_{16}\text{NO}_3\text{F}$: C, 63.38; H, 6.08; N, 5.28. Found: C, 63.45; H, 6.11; N, 5.30.

4-Aryl-5-pyrimidinecarboxylates 1.

General Method.

Sodium ethoxide (0.02 mole) and one equivalent of the amidine hydrochloride were suspended in 50 ml. of ethanol. The suspension was stirred for 10 minutes and the sodium chloride was removed by filtration. The neutralized amidine was then added to one equivalent of the appropriate enamionone in 50 ml. of ethanol and the resulting solution was refluxed overnight. The solution was allowed to cool, filtered, and the solvent removed under reduced pressure. The resulting residue was dissolved in ether (200 ml.) washed with 5% sodium bicarbonate solution, water, and then dried with anhydrous magnesium sulfate. The ether was removed *in vacuo* and the residue was recrystallized from a suitable solvent such as methylcyclohexane, ether-pentane, or ethanol.

The progress of the reaction could be followed using proton nmr. The appearance of the pyrimidine C-6 proton absorbance $\delta \cong 9$ was indicative of pyrimidine formation.

The pyrimidines prepared are shown in Table I. The yields have not been optimized.

REFERENCES AND NOTES

- (1) A. Kreutzerberger and C. Grundmann, *J. Org. Chem.*, **26**, 1121 (1961).
- (2) B. R. Baker and H. S. Shapiro, *J. Med. Chem.*, **6**, 664 (1963).
- (3) Technical Information Bulletin, "DMF Acetals", Aldrich Chemical Co., December, 1973.