August 1994 Communications to the Editor Chem. Pharm. Bull. 42(8) 1697—1699 (1994)

FACILE SYNTHESIS OF 3-SUBSTITUTED CHROMONES FROM AN ENAMINOKETONE

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Utilizing an enaminoketone (**1**) as starting material, 3-substituted chromones were synthesized by the reactions of acid anhydrides derivatives under mild conditions.

KEYWORDS chromone; 3-substituted chromones; 2-N,N-dimethyl-aminoethenyl 2-hydroxyphenyl ketone

The synthesis of 3-substituted chromones appears especially worthy of study because they are important natural products (isoflavones)[1] and some medicines such as ipriflavone (7-isopropoxyisoflavone) used as an antiosteoporosis.[2]

Recently Gammill[3] reported the synthesis of 3-halochromones from enaminoketone (**1**) with halogen-containing reagents. Considering the mechanism of this reaction, 3-substituted chromones would be synthesizable by the reaction with electrophiles having a good leaving group, such as $X^{\delta+}$-$Y^{\delta-}$ (Chart 1). So we first carried out the reactions of **1** with acetic anhydride and obtained 3-acetylchromone in good yield as expected. Now we will report a novel, facile, and practical method for the synthesis of 3-substituted chromones.

To the solution of **1** (190 mg, 1 mmole) in MeCN (30 ml) containing 5 ml of pyridine, acetic anhydride (480 mg, 4 mmole) was added, and the mixture was refluxed for 4 h. The reaction mixture was purified by chromatography to give 3-acetylchromone (**2a**), mp 129 °C (lit.[4] mp 129 °C), and chromone (**3**) in 62% and 16% yields, respectively. Other acid anhydrides also reacted with **1** to afford corresponding 3-acylchromones (**2b, c**)[5] in moderate yields (Table I).

From the reactions of **1** at room temperature with trifluoroacetic anhydride and N-trifluoroacetylimidazole, 3-trifluoroacetylchromone (**4**), mp 125 °C, was formed in the yields of 89% and 93%, respectively, in a very short reaction period. By stirring with trichloroacetic anhydride at room temperature for 6 h, 3-trichloroacetylchromone (**5**), mp 120 °C, was obtained in 65% yield (Chart 2).

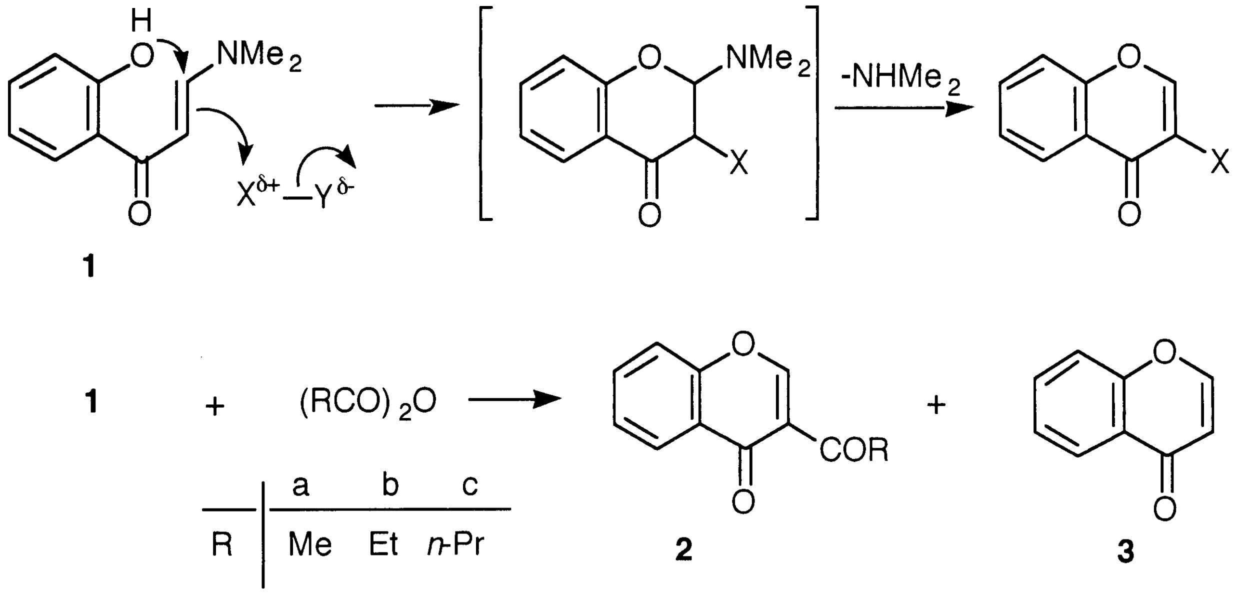

Chart 1

Table I

	R	Reaction time (h)	Yield (%)	mp (°C)
2a	Me	4	62	129
2b	Et	6	45	202
2c	*n*-Pr	8	42	216

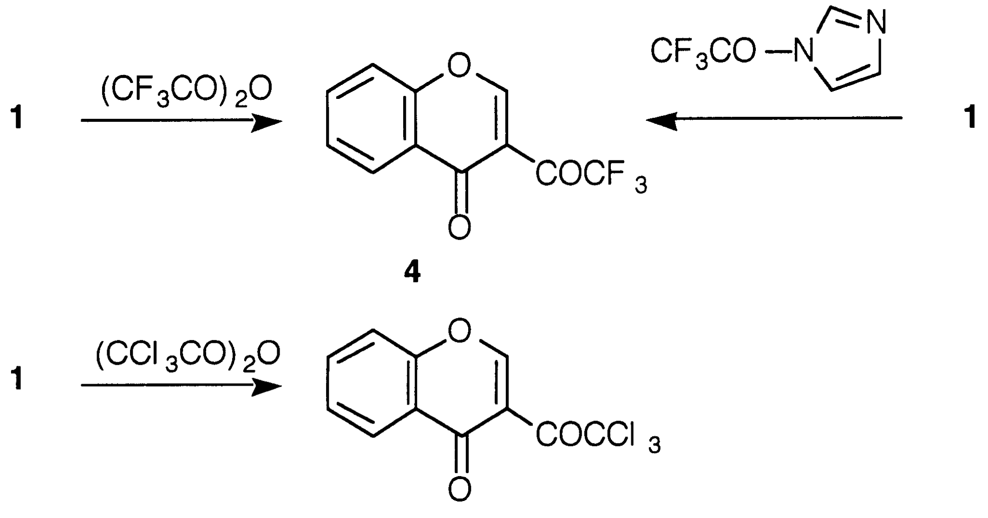

Chart 2

In addition, from N-ethylthiophthalimide 3-ethylthiochromone (**6**), mp 72 °C, was formed in 82% yield. 3-Methythiochromone (**7**),[6] mp 111 °C, was prepared by the reaction of dimethyl(methylthio)sulfonium tetrafluoroborate in 68% yield. 3-Chlorochromone (**8**), mp 115 °C (lit.[7], mp 114-5 °C), was also formed in 95% yield by the reaction of **1** with iodine monochloride (Chart 3). In this reaction iodine ion was a very good leaving group and chloride atom remained at the 3-position of chromone ring.

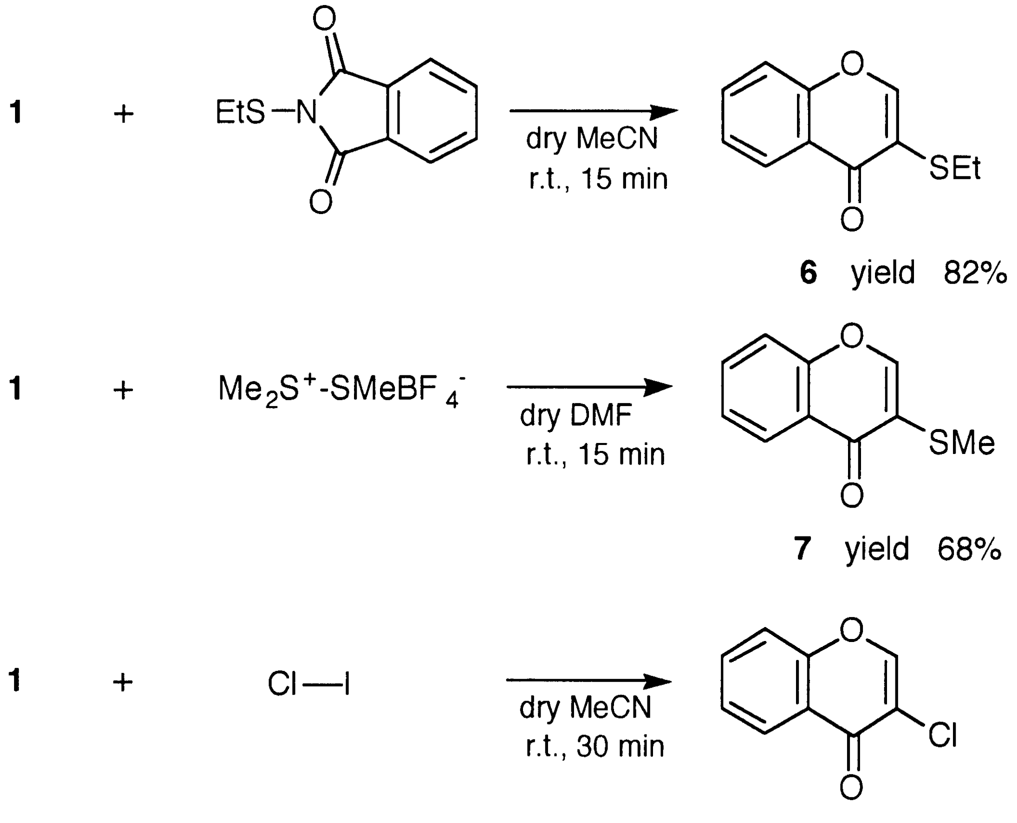

Chart 3

As we would expect, these results demonstrate that enaminoketone (**1**)[8] is reactive enough to prepare 3-substituted chromone under mild condition by using electrophilic reagents possessing a good leaving group.

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(Received May 25, 1994; accepted June 29, 1994)