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Iodine-catalyzed tandem oxidative coupling reaction: A one-pot strategy for the synthesis of new coumarin-fused pyrroles

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ABSTRACT

The simple and facile strategy for the synthesis of 2,3-disubstituted-chromeno[4,3-*b*]pyrrole-4(1*H*)-ones has been established. This method describes the Kornblum oxidation reaction of acetophenones, followed by the Knoevenagle treatment of the resulted (het)arylglyoxals with active methylene compounds and consequently iodine-activated Michael type reaction with 4-amino coumarin in a one-pot manner to afford disubstituted chromeno[4,3-*b*]pyrrole-4(1*H*)-one derivatives.

Introduction

Chromene and pyrrole are important heterocyclic motifs in biomolecules and setting these rings in one compound creates important systems, which are found as the basic building block in several bioactive compounds including marine alkaloids ningalin B and lamellarin D.[1–3] Many synthetic protocols have been reported for the synthesis of chromeno[4,3-*b*]pyrrole-4(1*H*)-ones, an important fused heterocyclic core consisting chromene and pyrrole, including the reaction of *β*-nitroalkenes and 4-phenylamino coumarins under solvent–free condition[4] and the reaction of amine, glyoxal monohydrate and 4-amino coumarin in the presence of nanocrystalline $CuFe_2O_4$[5] and $KHSO_4$.[6] 4-Chloro coumarin was reported as starting material in literature and reacted with α-amino ketones[7] and α-amino acid derivatives to produce *N*-(α)-(2-oxo-2*H*-1-benzopyran-4-yl)Weinreb-α-aminoamides.[8] In addition, the reaction of 4-*N*-(4′-aryloxybut-2-ynyl)-*N*-methylaminocoumarins with 3-chloroperoxybenzoic acid afforded the desired pyrrolo[3,2-*c*]-coumarin derivatives.[9]

The assembly of N-heterocycles by designing new catalytic systems has attracted the chemists' attention. Since the first application of molecular iodine as a catalytic system in the conversion of diacetone alcohol into mesityl oxide in 1915,[10] the catalytic applications of iodine in organic synthesis and in chemical technology have become the focus of organic chemists in functional group transformation.[11] Two modes of activation have been proposed for iodine-catalyzed reactions, meaning iodine-bond activation and hidden Brønsted acid catalysis.[12] Among these approaches,[13–16] the first one has been favored in catalytic reactions over another pathway, especially in Michael type reactions. By combining the advantageous features of tandem reactions and iodine as a catalyst, a powerful synthetic strategy has been presented in this report for the construction of complex structure, chromeno[4,3-*b*]pyrrole-4(1*H*)-ones, from simple substrates. In continuation of our efforts to introduce economic and environmentally benign methods for the synthesis of heterocyclic compounds,[17] herein, we report a novel I_2-catalyzed, four-component approach towards chromeno[4,3-*b*]pyrrole-4(1*H*)-ones. The reaction entails the *in situ* synthesis of 2-oxo-2-arylacetaldehyde *via* the Kornblum oxidation reaction from the corresponding acetophenone derivatives in the presence of molecular iodine and DMSO.[18]

We started our quest for the *in situ* synthesis of 2-oxo-2-phenylacetaldehyde (phenylglyoxal), by the Kornblum oxidation reaction of acetophenone, according to previously reported procedure.[18] After purification, we performed the one-pot reaction between

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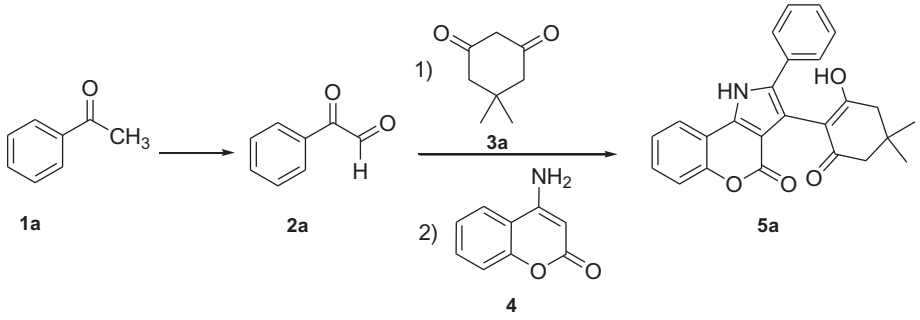
0040-4039/

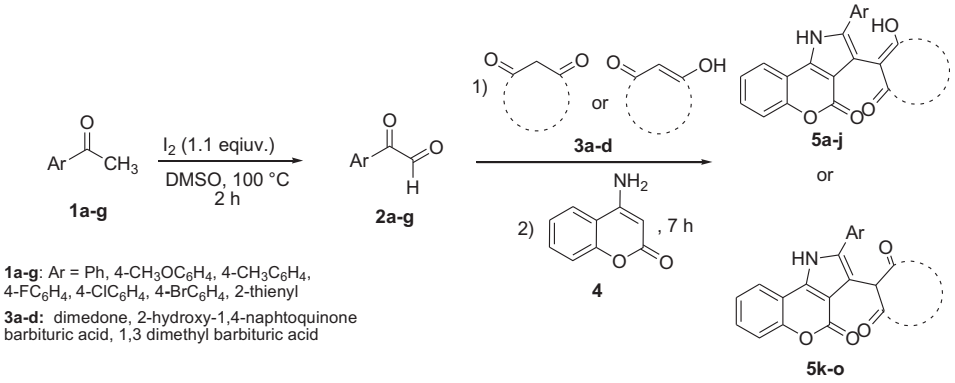
Table 1
Optimization of reaction condition. [a]

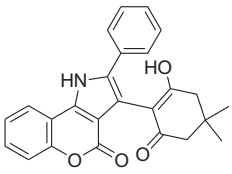
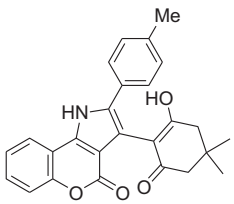
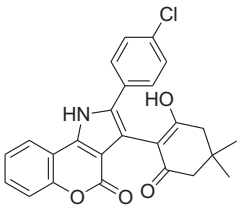
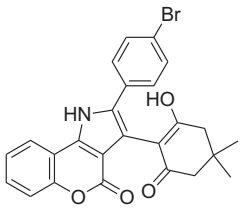


Entry	T (°C)	Catalyst	Yield (%)
1[a]	100	TsOH-H_2O	60[b]
2[a]	100	HOAc	55
3[a]	100	$ZnCl_2$	35
4[a]	100	$FeCl_3$	32
5[a]	100	I_2	79
6[c]	100	I_2	86
7	80	I_2	41
8	90	I_2	65
9	110	I_2	85
10[d]	100	I_2	85

[a] Reaction conditions: phenyl glyoxal (1 mmol), dimedone (1 mmol), 4-amino coumarin (1 mmol) and acidic catalyst (1.1 equiv.) were heated in DMSO at 100 °C for 7 h.
[b] Isolated yields.
[c] Acetophenone (1 mmol) and iodine (1.1 equiv.) were heated in DMSO at 100 °C for 2 h, then dimedone (1 mmol) and 4-amino coumarin (1 mmol) were added and the reaction was continued for 7 h.
[d] 1.2 equiv. of iodine was used.

Table 2
Substrate scope for the one-pot synthesis of chromeno[4,3-*b*]pyrrol-4(1*H*)-ones **5a–o.**



Product	Structure	Yield (%)[a]	Product	Structure	Yield (%)[a]
5a		**86**	**5b**		**78**
5c		**89**	**5d**		**82**

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