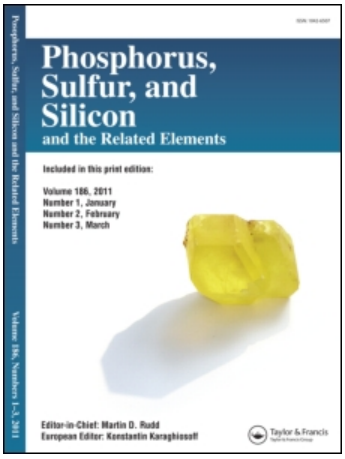

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UNCATALYZED KNOEVENAGEL CONDENSATION OF 2-CYANOMETHYLBENZOTHIAZOLE WITH AROMATIC ALDEHYDES. PREPARATION OF 3-ARYL-2-(2-BENZOTHIAZOLYL)-ACRYLONITRILES AND 3-(2-BENZOTHIAZOLYL)-COUMARIN IMINES[1]

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A series of 3-aryl-2-(2-benzothiazolyl)-acrylonitriles (**3a–n**) and 3-(2-benzothiazolyl)-coumarin imines (**5a–f**) are prepared in good to high yields by refluxing solutions of 2-cyanomethylbenbenzothiazole (**1**) and aromatic aldehydes (**2, 4**) in ethanol.

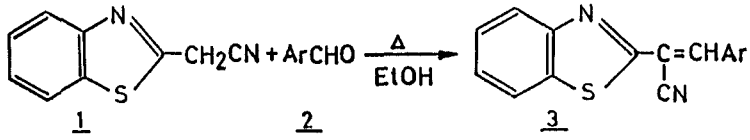
Key words: Uncatalyzed Knoevenagel condensation; 2-cyanomethylbenzothiazole; 3-aryl-2-(2-benzothiazolyl)-acrylonitriles; 3-(2-benzothiazolyl)-coumarin imines.

INTRODUCTION

2-Cyanomethylbenzothiazole (**1**), easily accessible from malononitrile and 2-aminothiophenol,[2] is known to undergo Knoevenagel condensation with aromatic aldehydes to give the corresponding 3-aryl-2-(2-benzothiazolyl)-acrylonitriles (**3**), respectively 3-(2-benzothiazolyl)-coumarin imines (**5**) and 3-(2-benzothiazolyl)-coumarins (**6**), when **1** is reacted with benzaldehydes possessing hydroxyl group at position 2.[2–5] The reaction is usually carried out in the presence of base, triethylamine or piperidine being the most frequently used catalyst.[2–4] Previous reports from this laboratory have demonstrated the synthetic application of aqueous sodium hydroxide as highly effective catalyst for these reactions.[6–8] This procedure, affording a great number of **3, 5**, and **6** in high yields and purity, is simple, fast and general, and quite recently it was successfully applied to the synthesis of some thiosubstituted coumarins.[9] However, this procedure is not applicable for the condensation of **1** with benzaldehydes possessing carboxy group and, on the other hand, the yields and the purity of **3**, prepared by reaction of **1** with some substituted benzaldehydes (2-, 3-, and 4-nitrobenzaldehyde, cinnamaldehyde, and 2,3-dihydroxybenzaldehyde), are low. In this communication we report a new approach to the synthesis of **3** and **5** by performing the condensation of **1** with the aromatic aldehydes **2** and **4** without adding a catalyst.

RESULTS AND DISCUSSION

Refluxing of ethanol solution of **1** with 4-nitrobenzaldehyde resulted in complete crystallization of the reaction mixture in less than one minute and after the usual



1 2 3

2,3	Ar	2,3	Ar
a	C_6H_5	h	4-$CH_3OC_6H_4$
b	$C_6H_5CH=CH$	i	4-$(CH_3)_2NC_6H_4$
c	2-Furyl	j	2-$O_2NC_6H_4$
d	3-Pyridyl	k	3-$O_2NC_6H_4$
e	4-Pyridyl	l	4-$O_2NC_6H_4$
f	4-ClC_6H_4	m	2-$HOCC_6H_4$
g	4-$CH_3C_6H_4$	n	2-$HO_2CC_6H_4$

SCHEME I

TABLE I

3-Aryl-2-(2-benzothiazolyl)-acrylonitriles **3a–n**

Compound	Reaction time (min)[a]	Yield[b,c] (%)	M.p.°C[d]	Literature m.p.
3a	60	65	121–122	121–123[2]
3b	60	60	154–156	155–157[7]
3c	60	50	134–136	136–137[7]
3d	60	88	154–156	155–157[7]
3e	5	86[e]	196–198	196–198[7]
3f	15	95[e]	148–150	148–150[2]
3g	60	66	146–148	147–148[2]
3h	60	48	142–144	143–144[2]
3i	180	13[e]	225–227	228–229[6]
3j	1	85[e]	196–198	197–199[7]
3k	3	74	205–207	205–207[7]
3l	1	90	175–177	175–177[6]
3m	60	35	168–170	[e]
3n	2	96[e,f]	301–302	[f]

[a] Not optimized.
[b] Yield of recrystallized product unless stated otherwise.
[c] Yield of crude product.
[d] All known products exhibit spectral data in agreement with authentic samples.
[e] Recrystallized from ethanol/ethyl acetate;

$C_{17}H_{10}N_2OS$	calc.	C 70.33	H 3.47	N 9.65
(290.4)	found	70.06	3.66	9.48

IR ($CHCl_3$): 1720, 2260 cm^{-1}.
^{1}H-NMR ($CDCl_3$ + TFA): δ 7.0–8.6 (*m*, 8H, arom.), 8.85 (*s*, 1H, C=CH), 9.95 (*s*, 1H, CHO).

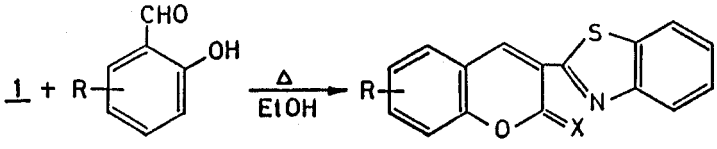
[f] Prepared in 20 ml ethanol; m.p. of the crude **3n** 298–300°C; recrystallization from acetic acid gave analytically pure, colorless crystals.

$C_{17}H_{10}N_2O_2S$	calc.	C 66.65	H 3.29	N 9.14
(306.4)	found	66.25	3.38	9.93

IR (nujol): 1695, 2218, 2560, 2680 cm^{-1}.
^{1}H-NMR (TFA): δ 7.6–8.5 (*m*, 8H, arom.), 8.64 (*s*, 1H, C=CH).

work up the compound **31** was isolated in 90% yield (Scheme I, Table I). Similarly, **1** reacted with 2- and 3-nitrobenzaldehyde after one, respectively three minutes heating, to give the compounds **3j** and **3k** iin 85%, resp. 74% yield. Good to high yields were obtained as well by the reaction of **1** with 3- and 4-pyridinecarbaldehyde, 4-chlorobenzaldehyde, 4-carboxybenzaldehyde, and cinnamaldehyde, the reaction time being 1–15 minutes, or one hour in the cases when it was not observed any crystallization. In general, the yields obtained with benzaldehydes possessing electron-donating groups, i.g., 4-methylbenzaldehyde, 4-methoxybenzaldehyde, and especially 4-dimethylaminobenzaldehyde were low (13% yield of **3i** after 3 hour), and in these cases aq. NaOH/ethanol system is a method of choice.

Similar reaction of **1** with the 2-hydroxybenzaldehydes **4** afforded in one to ten minutes the coumarin imines **5** in moderate to high yields (Table II), which were converted in quantitative yields into the corresponding coumarins (Reference 8). Among the procedures reported for the synthesis of coumarins and coumarin imines, possessing benzothiazolyl cycle at position 3,[4,5,10–12] the Knoevenagel condensation is the most direct route,[4,5] and aq. NaOH/ethanol system gives excellent results.[8] The yields obtained by the reported uncatalyzed procedure are a little lower (55–92%), but it certainly is the method of choice for the preparation of coumarin imines containing hydroxyl groups. For example, 3-(2-benzothiazolyl)-8-hydroxycoumarin imine (**5d**) is prepared in 87% yield. In addition, it should be noted that the purity of the crude **5d**, as well as of all other crude **5** is high (m.p.) and they usually do not need any purification. As far as we know there are only a few examples reported in the literature of uncatalyzed Knoevenagel condensation.[13,14] The uncatalyzed reaction of **1** with 2-hydroxybenzaldehydes provides an excellent route to 3-(2-benzothiazolyl)-coumarins and coumarin imines, which are of special interest because of their numerous uses as laser and fluorescent dyes, photographic sensitizers, optical brighteners, intermediates for dyes, pesticides and pharmaceuticals.[4,5,10,11,15]



5,6	R
a	H
b	5,6-CH=CH-CH=CH
c	6-Br
d	8-OH
e	8-OCH_3
f	5-NO_2

SCHEME II

TABLE II

3-(2-Benzothiazolyl)-coumarin imines **5a–f**

Compound	Aldehyde	Reaction time (min)[a]	Yield[b,c]	M.p.°C (dec)	Literature. (8) m.p.
5a	2-hydroxybenzaldehyde	5	86	194–195[d]	194–195
5b	2-hydroxynaphtal-dehyde	10	55	232–234	234–235
5c	5-bromo-2-hydroxy-benzaldehyde	1	92	242–244	244–245
5d	2,3-dihydroxybenz-aldehyde	10	87	252–254	252–254
5e	2-hydroxy-3-methoxy-benzaldehyde	7	83	187–189	[e]
5f	2-hydroxy-5-nitrobenz-aldehyde	1	87	279–281	281–283

[a] Not optimized.
[b] Yield of pure product based on **1**.
[c] All known products exhibit spectral data in agreement with authentic samples.
[d] Yield of recrystallized (ethanol/benzene) product.
[e] Recrystallized from ethyl acetate.

$C_{17}H_{12}N_2O_2S$	calc.	C 66.19	H 3.92	N 9.08
(308.5)	found	66.35	4.21	8.94

IR ($CHCl_3$): 1660, 3320 cm^{-1}.
^{1}H-NMR ($CDCl_3$): δ 3.89 (*s*, 3H, CH_3O), 6.8–8.1 (*m*, 8H, arom. and C=CH), 8.36 (bs, 1H, NH).

EXPERIMENTAL

Melting points were determined on a Boetius micro melting point apparatus and are uncorrected. The IR spectra were recorded on Specord 71 spectrometer. ^{1}H NMR spectra were obtained on Tesla BS 487-C (80 MHz) and JEOL PS-100 spectrometers in $CDCl_3$ or TFA solutions using TMS as internal standard. 2-Cyanomethylbenzothiazole (**1**) is prepared according to the published procedure.[2] The aldehydes **2** and **4** are commercially available products used without purification.

3-Aryl-2-(2-benzothiazolyl)-acrylonitriles 3 and 3-(2-benzothiazolyl)-coumarin imines **5**. General procedure. A solution of 2-cyanomethylbenzothiazole (**1**, 1.74 g, 10 mmol) and the corresponding aldehyde (10 mmol) in ethanol (10 ml) is heated under reflux until the reaction mixture crystallizes, otherwise for 60 min. After cooling, the crystals are filtered, washed with ethanol, and recrystallized, if necessary.

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