A Convenient One-Pot Preparation of Nitriles from Aldoximes Using 2,2′-Oxalyldi(*o*-sulfobenzimide)

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Under essentially neutral conditions, alkyl, aryl, and heteroaryl aldoximes (4) readily react with 2,2′-oxalyldi(*o*-sulfobenzimide) (ODS; 6) in refluxing acetonitrile to give the corresponding nitriles (5) in good yields.

Keywords dehydration; 1,1′-carbonyldiimidazole; aldoxime; nitrile; 1,1′-oxalyldiimidazole; saccharin; oxalyl derivative; condensing reagent; dehydrating reagent

Of the many reagents utilized for activation of the carboxyl group of carboxylic acids (**1**) in the synthesis of amides (**3**),[1a] some can also be applied satisfactorily to the dehydration of aldoximes (**4**) into nitriles (**5**).[1b] Examples of reagents, which can be used for the preparation of both amides (**3**) and nitriles (**5**), are 1,1′-carbonyldiimidazole,[2] phosphonitrilic chloride trimer,[3] titanium (IV) chloride,[4] triphenylphosphine,[5] diphenyl phosphite,[6] phosphorus trichloride,[7] cyanuric chloride,[8] diiodotriethoxyphosphorane,[9] fluorosulfonyl chloride,[10] hexamethylphosphoric triamide (HMPA),[11] chlorosulfonylisocyanate,[12] diphosphorus tetraiodide,[13] and 1,1′-oxalyldiimidazole.[14]

During our studies on oxalyl derivatives applicable as activating reagents in the synthesis of carboxylic acid derivatives, we found that 2,2′-oxalyldi(*o*-sulfobenzimide) (ODS; **6**) is a suitable condensing reagent for the preparation of amides (**3**), esters (**7**), and thioesters (**8**) through the reactions of carboxylic acids (**1**) with appropriate nucleophiles.[15] These findings led us to examine the possibility that **6** may be effective as a dehydrating reagent for the conversion of aldoximes (**4**) into nitriles (**5**). It is worth noting that **6** not only is readily preparable at low cost but also is a nonhygroscopic crystalline material, that is convenient to handle on a laboratory scale.

Here, we wish to report the successful application of ODS (**6**) for the dehydration reaction of aldoximes (**4**) into nitriles (**5**). For instance, *n*-heptaldoxime (**4a**) was dehydrated with an equimolar amount of ODS (**6**) in refluxing acetonitrile, with effervescence, to give *n*-heptanenitrile (**5a**) in 78% yield. Similarly, the methodology is also applicable to the transformation of 4-methoxybenzaldoxime (**4f**) into the corresponding nitrile (**5f**) in 96% yield. A heteroaromatic nitro compound, 5-nitro-2-thenaldoxime (**4l**), was successfully converted to 2-cyano-5-nitrothiophene (**5l**) in 84% yield after recrystallization from ethanol. A number of additional examples chosen to show the effectiveness of this method are summarized in Table I. It is clear that ODS (**6**) is very useful as a dehydrating agent for the preparation of nitriles (**5**) from aldoximes (**4**). The following mechanism can be considered for the conversion of **4** to **5**: (i) the formation of an *O*-(2-substituted oxalyl)oxime intermediate (**9**) between the aldoximes (**4**) and ODS (**6**), and (ii) the ensuing concerted elimination of CO_2, CO, and *o*-sulfobenzimide (saccharin) providing the nitriles (**5**), as shown in Chart 2.

In conclusion, the dehydration reaction described herein has the following advantages compared with the previously reported synthesis of nitriles (**5**) from aldoximes (**4**): (i) the reagent ODS (**6**) is simply mixed with aldoximes (**4**) at the beginning with no additive, so this one-pot procedure is quite simple, (ii) the reaction conditions are mild, and (iii) nitriles (**5**) are isolated in good yields after a simple work-up.

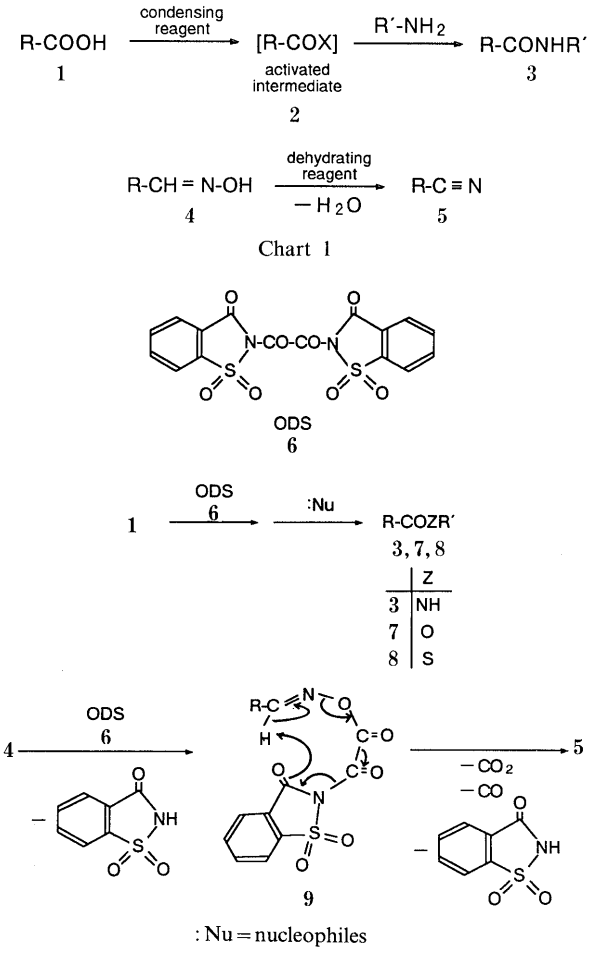


Chart 1

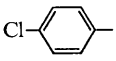
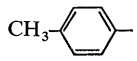
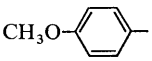
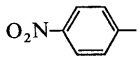
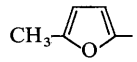
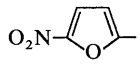
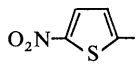
Chart 2

Experimental

Melting points were taken on a Yanagimoto melting point apparatus. All melting and boiling points are uncorrected. Infrared spectra were recorded on a Hitachi 270-30 infrared spectrophotometer.

Materials 2,2′-Oxalyldi(*o*-sulfobenzimide) (ODS; **6**) was prepared by the reaction of saccharin with oxalyl chloride in the presence of triethylamine according to the previous report.[15] Aldoximes (**4**) were prepared by reported methods: heptaldoxime (**4a**),[22] cyclohexylaldoxime (**4b**),[23] benzaldoxime (**4c**),[24] 4-chlorobenzaldoxime (**4d**),[25] 4-nitrobenzaldoxime (**4g**),[26] 2-furaldoxime (**4h**),[27] 5-methyl-2-furaldoxime (**4i**),[28] 5-nitro-2-furaldoxime (**4j**),[29] 2-thenaldoxime (**4k**),[30] and 5-nitro-2-thenaldoxime (**4l**).[31] According to the method previously described for the preparation of benzaldoxime (**4c**),[24] *p*-tolualdoxime (**4e**)[32] and 4-methoxybenzaldoxime (**4f**)[32] were prepared by the reactions of

TABLE I. Preparation of Nitriles (**5**) from Aldoximes (**4**) Using 1,1′-Oxalyldi(*o*-sulfobenzimide) (ODS; **6**)

No.	R	Reaction time[a] (min)	Yield[b] (%)	bp/mmHg (°C) (mp)[c]		IR cm^{-1} $\nu_{-C\equiv N(phase)}$
				Found	Reported	
5a	$CH_3(CH_2)_5$–	10	78	76—78/19	182—182.5/757[16]	2260 (neat)
5b	Cyclohexyl-	90	77	70—73/18	64—66/12[17]	2250 (neat)
5c		60	90	88—90/20	68—69/10[18]	2240 (neat)
5d		90	82	(92—93)[d]	(93—94)[18]	2250 (KBr)
5e		30	75	102—103/20	214—216/760[18]	2230 (neat)
5f		30	96	(57—59)[d]	(58—61)[18]	2200 (KBr)
5g		60	83	(145—147)[e]	(146—147)[18]	2230 (KBr)
5h		30	70	80—82/99	139—140/640[18]	2260 (neat)
5i		30	84	74—76/30	65—67/15[19]	2260 (neat)
5j		120	76	(59—61)[f]	(61—62)[20]	2250 (KBr)
5k		30	83	97—99/30	72—73/10[18]	2240 (neat)
5l		60	84	(44—45)[f]	(45)[21]	2230 (KBr)

a) Heating times under refluxing. *b*) Yields of the products (**5a**—**l**) after purification. Compounds (**5a**—**l**) were characterized by comparison of their melting or boiling points and IR data with those of authentic samples. *c*) All melting points are uncorrected. *d*) Purified by column chromatography on silica-gel with benzene as an eluent. *e*) Recrystallized from ethanol–benzene (4 : 1). *f*) Recrystallized from ethanol.

hydroxylamine with *p*-tolualdehyde and anisaldehyde, respectively. The aldoximes (**4**) used in our experiments are mixtures of (*E*)- and (*Z*)-isomers. Distilled acetonitrile (bp 80—81 °C) was stored over molecular sieves (4Å 1/16) to keep it anhydrous.

Preparation of Nitriles (5) from Aldoximes (4) General Procedure: ODS (**6**) (2.1 g, 5 mmol) was added to a solution of an aldoxime (5 mmol) in acetonitrile (30 ml). The mixture was stirred at room temperature for 15 min, and then refluxed for the time listed in Table I. After removal of the solvent *in vacuo*, the residue was poured into benzene (50 ml), and the resultant mixture was filtered to remove insoluble materials. The filtrate was washed with 1% $HaHCO_3$ and water, then the benzene layer was dried over anhydrous sodium sulfate. The organic solvent was evaporated under reduced pressure to give the crude nitrile (**5**), which was purified by either distillation or recrystallization.

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