Degradation of 3-Aryl-2-hydroxyiminopropionic Acids into Arylacetonitriles Using 1,1′-Carbonyldiimidazole or 2,2′-Oxalyldi(*o*-sulfobenzimide)

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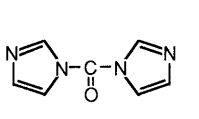
1,1′-Carbonyldiimidazole (1) is a useful reagent for the preparation of arylacetonitriles (9) from 3-aryl-2-hydroxyiminopropionic acids (8), and 2,2′-oxalyldi (*o*-sulfobenzimide) (2) can also be used for this purpose under essentially neutral conditions.

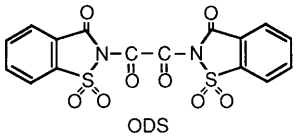
Keywords 1,1′-carbonyldiimidazole; 2,2′-oxalyldi (*o*-sulfobenzimide); arylacetonitrile; 3-aryl-2-hydroxyiminopropionic acid; dehydration; decarboxylation; degradation

1,1′-Carbonyldiimidazole (CDI: **1**)[1] is sometimes utilized for activation of the carbonyl group of carboxylic acids (**3**) in the synthesis of amides (**5**). In addition it can also be applied to the dehydration of aldoximes (**6**) to form nitriles (**7**).[2] In an earlier publication,[3] we showed that 2,2′-oxalyldi (*o*-sulfobenzimide) (ODS: **2**) is an efficient and reliable condensing reagent for the preparation of amides (**5**) under essentially neutral conditions.

The role of arylacetonitriles (**9**) as valuable intermediates for the preparation of 2-arylethylamines[4] and arylacetic acids[5] is well recognized. A well established method for the preparation of **9** is the decarboxylation and dehydration of 3-aryl-2-hydroxyiminopropionic acids (**8**) using acetic anhydride.[5a] However, a disadvantage of this method is the difficulty in separating the desired arylacetonitriles (**9**), which resemble acetic anhydride or aqueous acetic acid very closely in boiling point. To overcome these difficulties in the synthesis of arylacetonitriles (**9**), we examined the ability of CDI (**1**) or ODS (**2**) to degrade 3-aryl-2-hydroxyiminopropionic acids (**8**) into the corresponding arylacetonitriles (**9**).



CDI
1



ODS
2

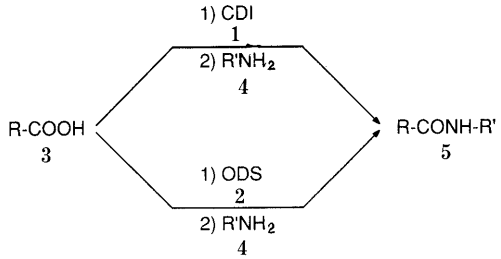


Chart 1

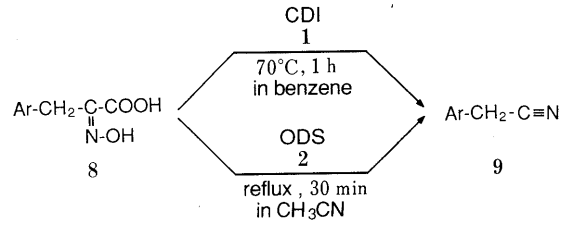


Chart 2

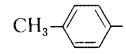
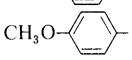
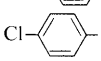
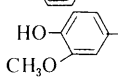
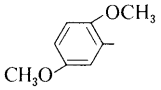
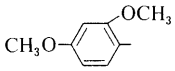
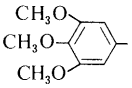
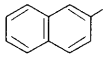
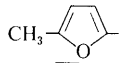
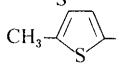
We found that 3-phenyl-2-hydroxyiminopropionic acid (**8a**) reacts readily with CDI (**1**) at 70 °C for 1 h in benzene to afford phenylacetonitrile (**9a**) with accompanying effervescence in 91% yield. This led us to examine the possibility that CDI (**1**) or ODS (**2**) may be generally effective as a reagent for the conversion of **8** into **9** by dehydration and decarboxylation. Incidentally, the critical reagent CDI (**1**) is prepared from the reaction of imidazole with phosgene in tetrahydrofuran.[1b] Unfortunately, the toxicity of phosgene means that the preparation of CDI (**1**) in the average laboratory is quite troublesome. On the other hand, ODS (**2**) is easily prepared from the reaction of *o*-sulfobenzimide (saccharin) in benzene with oxalyl chloride in the presence of triethylamine at room temperature.

The purpose of this paper is to describe a simple method for the preparation of arylacetonitriles (**9**) using CDI (**1**) or ODS (**2**). Continuing from the degradation of 3-phenyl-2-hydroxyiminopropionic acid (**8a**) into phenylacetonitrile (**9a**) using CDI (**1**) mentioned above, we prepared **9a** directly from the reaction of **8a** with ODS (**2**). This degradation was performed within 30 min in refluxing acetonitrile and the product (**9a**) was obtained in 77% yield, whereas the reaction giving a 70% yield of **9a** required 2 h at 70 °C in benzene because ODS (**2**) is not sufficiently soluble in benzene.

This degradation method using CDI (**1**) or ODS (**2**) was found to be satisfactory for several structurally different 3-aryl-2-hydroxyiminopropionic acids (**8b—o**). The transformation of 3-(4-substituted phenyl)-, 3-(3,4-, 2,4- or 2,5-disubstituted phenyl)-, 3-(3,4,5-trisubstituted phenyl)-, and 3-(1- or 2-naphthyl)-2-oximinopropionic acids (**8b—k**) into the corresponding acetonitriles (**9a—k**) was also accomplished in acceptable yields as shown in Table I. Moreover, it was ascertained that the heteroaromatic compound 3-(2-furyl)-2-hydroxyiminopropionic acid (**8l**) readily reacted with CDI (**1**) or ODS (**2**) to give 2-furylacetonitrile (**9l**) in 75% or 70% yield, respectively. A similar result was observed with 3-(5-methyl-2-furyl)-, 3-(2-thenyl)-, and 3-(5-methyl-2-thenyl)-2-hydroxyiminopropionic acids (**8m—o**), which were converted into the corresponding arylacetonitriles (**9m—o**) in 71—86% yields.

All of the arylacetonitriles (**9a—o**) prepared in our experiments are known compounds. The structures of **9a—o** were established mainly by infrared (IR) spectroscopic

TABLE I. Substituted Acetonitriles (**9**) Prepared

Product	Ar	Yield (%)[a]		bp (°C)/Torr or [mp (°C)]		IR (cm^{-1}) ν-CN (phase)
		CDI (**1**)	ODS (**2**)	Found	Reported	
9a		91	77	80—81/3	98—100/9[4d]	2254 (neat)
9b		95	84	84—87/3	107—109/9[4d]	2254 (neat)
9c		93	86	105—108/3	74—76/0.2[4d]	2252 (neat)
9d		94	90	117—120/3	140/13[6]	2252 (neat)
9e		90	85	113—116/16	133—143/24[7]	2252 (neat)
9f		83	80	140—143/0.2	135—140/0.05[4c]	2252 (neat)
9g		88	87	[53—54][b]	[56—57][8]	2254 (KBr)
9h		94	89	[74—75][b]	[76][9]	2248 (KBr)
9i		85	83	[75—77][c]	[77][10]	2244 (KBr)
9j		97	87	106—109/0.3	183—187/15[11]	2252 (neat)
9k		97	83	[79—82][d]	[77][11]	2254 (KBr)
9l		75	75	88—90/27	64—65/9[12]	2254 (neat)
9m		86	71	91—93/15	82—85/12[13]	2256 (neat)
9n		88	81	109—111/15	89—100/9[4d]	2254 (neat)
9o		94	86	107—110/17	110—112/20[14]	2252 (neat)

a) Yield of isolated product **9** based on **8**. *b*) Recrystallized from benzene–pet. ether. *c*) Recrystallized from EtOH–water. *d*) Recrystallized from benzene.

studies. The IR spectra of **9a—o** show characteristic absorption bands for the cyano group at near 2250 cm^{-1}. These results, which demonstrate the effectiveness of this method, are summarized in Table I.

Regarding the arylacetonitrile (**9a—o**) yields from our procedure, the data of Table I show that not only CDI (**1**), but also ODS (**2**) can form **9a—o** through degradation of the 3-aryl- or 3-heteroaryl-2-hydroxyiminopropionic acids (**8a—o**). In general, the procedure which utilized CDI (**1**) gave each of the products (**9a—o**) in a slightly higher yield than that which used ODS (**2**). However, CDI (**1**), through commercially available, is too expensive for utilization on a large scale, whereas ODS (**2**) is readily preparable at low cost was nonhygroscopic crystals.[3] With regard to cost and performance relationships, we suggest that ODS (**2**) is more convenient to handle on a laboratory scale than CDI (**1**). In addition, the application of CDI (**1**) to the degradation produces basic imidazole as a by-product, which might cause serious difficulties in the synthesis of base-sensitive arylacetonitriles. In such a case, simple replacement of CDI (**1**) by ODS (**2**) is useful because saccharin formed as a by-product is essentially neutral.

As shown in Chart 3, the mechanism of this degradation most probably involves nucleophilic attack of the hydroxy group of **8** on the carbonyl carbon of CDI (**1**) to give an intermediate (**11**), which undergoes internal rearrangement (path A). In a like manner, the reaction of **8** with ODS (**2**) proceeds *via* the formation of an intermediate (**13**) and the subsequent concerted elimination of CO_2, CO, and saccharin takes place under heating to afford the corresponding arylacetonitrile (**9**) as a final product (path B).

In conclusion, the degradation reaction described herein has the following advantages over the previously reported preparation methods for arylacetonitriles (**9**) using acetic anhydride as the dehydrating reagent: (i), the reagent CDI (**1**) or ODS (**2**) can be employed for the degradation of 3-aryl-2-hydroxyiminopropionic acids (**8a—o**) into **9a—o** with no additive by means of a one-pot procedure, which is simple; (ii), reaction condition are mild with short reaction times, and (iii), using simple chromatographic techniques, the prepared arylacetonitriles (**9**) can usually be isolated in good yields.

Experimental

Melting points were measured on a Yanagimoto melting point apparatus. Boiling points refer to the oven temperature of a Kugelrohr apparatus.

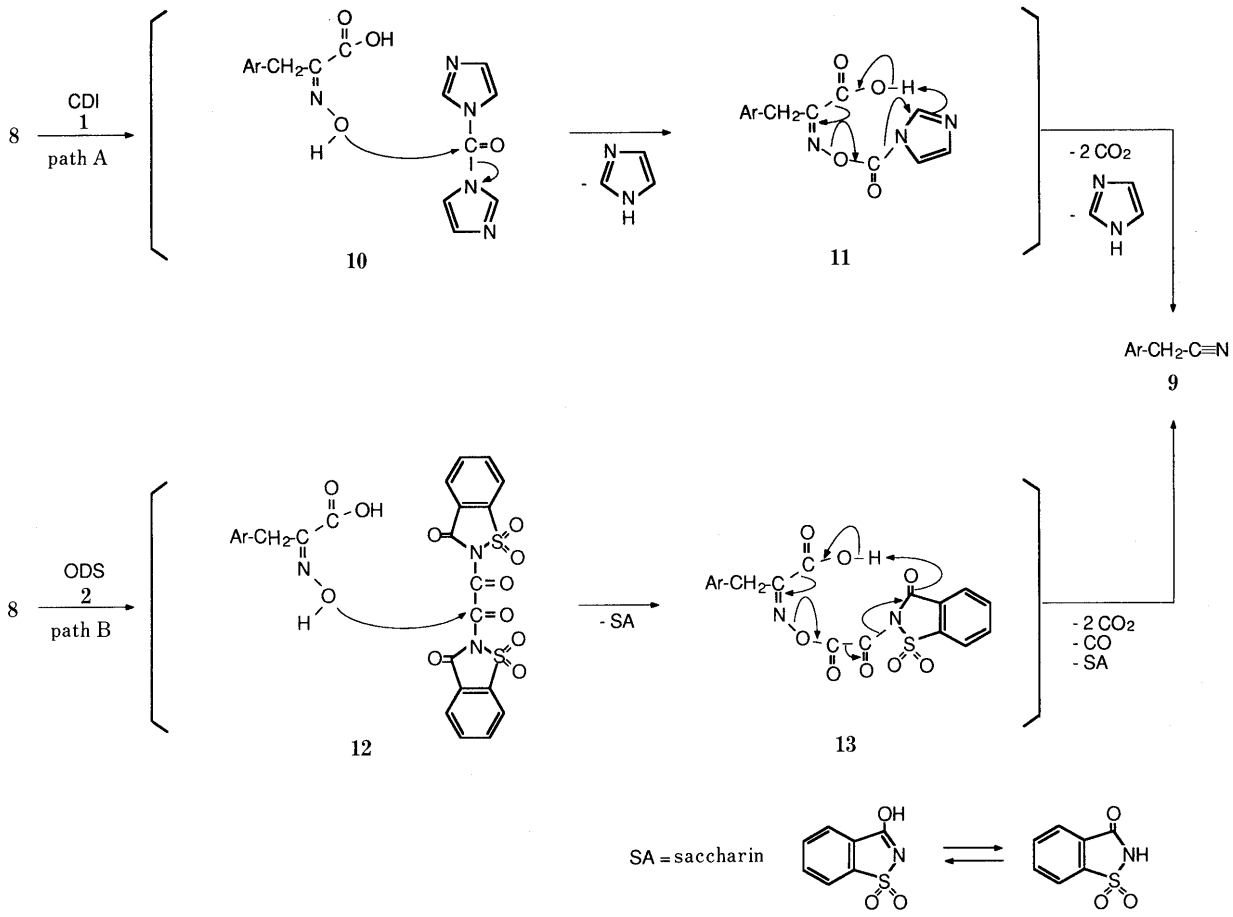


Chart 3

All melting and boiling points are uncorrected. IR spectra were recorded on a Hitachi 270-30 IR spectrophotometer.

Materials CDI (**1**) from Aldrich Chemical Company, Inc. was used without further purification. ODS (**2**) was prepared from the reaction of saccharin with oxalyl chloride in the presence of triethylamine according to a previous report.[3] Distilled benzene and acetonitrile were subjected to successive drying over 4 Å molecular sieves. 3-Aryl-2-hydroxyiminopropionic acids (**8a—o**) except **8g** and **8k** were prepared as previously described; **8a**,[15] **8b**,[14] **8c**,[16] **8d**,[15] **8e**,[17] **8f**,[5a] **8h**,[18] **8i**,[10] **8j**,[14] **8l**,[12] **8m**,[5b] **8n**,[5b] and **8o**.[14] 3-Aryl-2-hydroxyiminopropionic acids (**8a—o**) used in our experiments are mixtures of (*E*)- and (*Z*)-isomers.

3-(2,5-Dimethoxyphenyl)-2-hydroxyiminopropionic Acid (8g) This compound (**8g**) was prepared according to a published procedure.[5a] Hydroxylamine hydrochloride (4.3 g, 62 mmol) in water (5 ml) was allowed to react with sodium ethoxide [prepared from sodium (1.6 g, 69 mg atom) and anhydrous EtOH (40 ml)]. After removal of inorganic material by filtration, the filtrate containing free hydroxylamine was added to 2,5-dimethoxyphenylthiopyruvic acid (4.8 g, 20 mmol) and the mixture was refluxed for 1 h. The solvent was removed under reduced pressure and the residue was dissolved in 5% NaOH (100 ml). The aqueous phase was filtered through a sintered glass filter and the filtrate was cooled to −15 °C, then acidified with 10% HCl (90 ml). The precipitate was washed with water and dried *in vacuo*; the yield was 4.6 g (96%); crystals (benzene–AcOEt), mp 162—163 °C. *Anal.* Calcd for $C_{11}H_{13}NO_5$: C, 55.23; H, 5.48; N, 5.86. Found: C, 55.05; H, 5.46; N, 5.96. IR ν_{max}^{KBr} cm^{-1}: 1701 (CO).

3-(2-Naphtholyl)-2-hydroxyiminopropionic Acid (8k) Treatment of 2-naphtholylthiopyruvic acid[19] (4.6%, 20 mmol) with hydroxylamine [prepared from hydroxylamine hydrochloride (4.3 g, 62 mmol) and Na metal (1.6 g, 69 mg atom)] as described for the preparation of **8g** gave **8k**; the yield was 3.2 g (69%); crystals (benzene–AcOEt), mp 170—175 °C. *Anal.* Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84; N, 6.11. Found: C, 68.05; H, 4.96; N, 6.04. IR ν_{max}^{KBr} cm^{-1}: 1701 (CO).

Preparation of Arylacetonitriles (9) Using CDI (1) General Procedure CDI (**1**) (3.3 g, 20 mmol) was added to a solution of the appropriate 3-substituted 2-hydroxyiminopropionic acid (**8**) (20 mmol) in benzene (50 ml). The mixture was stirred at room temperature for 15 min, then heated at 68—70 °C for 1 h. After cooling to room temperature, the resultant mixture was poured into ice water (30 ml) and the organic layer was extracted with 50 ml of benzene in several portions. The combined extracts were washed with 1% $NaHCO_3$ (15 ml), 1% HCl (15 ml), and water (15 ml), then dried over anhydrous sodium sulfate. The organic layer was evaporated under reduced pressure to give the crude acetonitrile (**9**), which was developed on a silica gel column with benzene. Concentration of the first eluate (100 ml) gave **9**, which was further purified by distillation or recrystallization.

Preparation of Arylacetonitriles (9) Using ODS (2) General Procedure ODS (**2**) (8.4 g, 20 mmol) was added to a solution of the appropriate 3-substituted 2-hydroxyiminopropionic acid (**8**) (20 mmol) in acetonitrile (70 ml). The mixture was stirred at room temperature for 15 min, then refluxed for 30 min. After cooling to room temperature, the solvent was removed under reduced pressure to give a residue, which was treated with benzene, with stirring. Precipitated saccharin was removed by filtration. Evaporation of the benzene afforded crude **9**, which was purified by column chromatography on silica gel as described for the preparation of **9** using CDI (**1**). The yield, melting point or boiling point, and spectroscopic data for the substituted acetonitriles (**9a—o**) prepared are given in Table I.

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