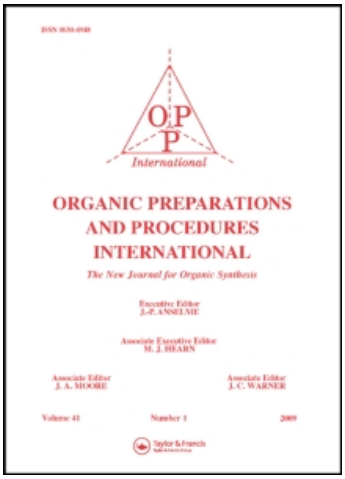

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1,1'-CARBONYLDIBENZOTRIAZOLE AND 1,1'-SULFONYLDIBENZOTRIAZOLE. VERSATILE REAGENTS FOR THE DEHYDRATION OF ALDOXIMES AND AMIDES TO NITRILES

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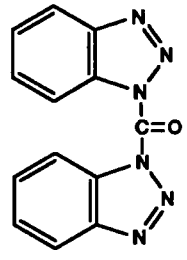
Aldoximes and primary amides can be dehydrated to nitriles in many ways. Effective reagents for the dehydration of aldoximes are acetic anhydride,[1] diphenyl hydrogen phosphonate $(PhO)_2PHO$,[2] 2,4,6-trichloro-s-triazine,[3] N,N'-carbonyldiimidazole,[4] 1-trifluoroacetyl-imidazole,[5] $TiCl_4$ in absolute CCl_4,[6] and dicyclohexylcarbodiimide in the presence of Et_3N and Cu(II) ions,[7] Recently, 2,2'-oxalyldi(o-sulfobenzimide) has also been used.[8] Among these, the mildest procedures for the dehydration of aldoximes to nitriles utilize N,N'-carbonyldiimidazole[4] and trichlorotriazine.[3] Most of the other preparations of nitriles from aldehydes require vigorous acidic or basic conditions,[9-11] tedious work-up procedures, unusual reagents[2,8,12] or pyrolysis.[6] Phosphorus pentoxide has been the most common agent for the dehydration of primary amides to nitriles,[13] but several others, including $POCl_3$ and CCl_4-Ph_3P,[14] $TiCl_4$-Base,[15] phosphorus tris(diethylamide)[16] and HMPT,[17] have also been used. The present paper illustrates 1,1'-carbonyldibenzotriazole (**1**) and 1,1'-sulfonyldibenzotriazole (**2**) to be efficient and versatile agents for the dehydration of both aldoximes and amides under mild and neutral conditions.



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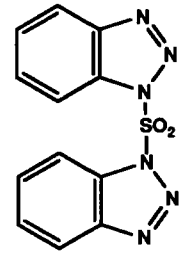

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1,1'-Carbonyldibenzotriazole (**1**) and 1,1'-sulfonyldibenzotriazole (**2**) are readily prepared by the reactions of 1-(trimethylsilyl)benzotriazole with phosgene and sulfuryl chloride, respectively, in excellent yields.[18,19] 1,1'-Carbonyldibenzotriazole has previously found applications in the synthesis of nucleosides and polyprenylpyrophosphate sugars.[20,21] We have recently demonstrated the utility of these two reagents in the preparation of N-alkylbenzotriazoles[22] and N-alkoxycarbonylbenzotriazoles.[23]

3 4 5

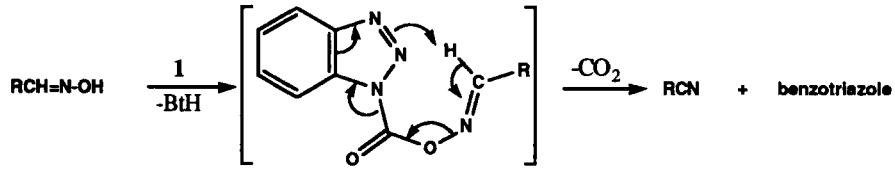
Various aldoximes **3**, prepared from aromatic aldehydes and hydroxylamine as previously described,[24] reacted readily with 1,1'-carbonyldibenzotriazole **1** in refluxing THF to give the corresponding nitriles **4** in 64-84% yields. Similar treatment of 4-chlorobenzaldoxime with 1,1'-sulfonyldibenzotriazole **2** in THF afforded 4-chlorobenzonitrile in 71% yield. Our method gives yields similar to those reported for other dehydrating agents (cf. Table 1); however, the process is quite general and should be particularly useful for acid- and/or base-sensitive aldehydes. For example, trifluoroacetic anhydride requires at least two equivalents of a base to catalyze the reaction and to remove the acid generated,[25] while 2,4,6-trichloro-*s*-triazine and dicyclohexylcarbodiimide are effective only in the presence of pyridine[3] or of triethylamine and Cu(II).[7] Treatment of oximes with *p*-chlorophenyl chlorothionoformate in the presence of pyridine gives moderate yield of nitriles (42-70%).[26] In our reaction, just as for many other dehydrating agents, the stereochemistry of the aldoxime had little effect on the reactionas both Z and E aldoximes gave similar results, and it is likely that the oximes are isomerized under the reaction condition.[4] The oximes used and the yields of the purified nitriles are summarized in Scheme 1 and Table 1.

TABLE 1. Dehydration of Aldoximes and Amides

No.	R	Reactant	Product	Reagent	Yield (%)	mp. (°C)	lit. mp. (°C)
4a	Ph	aldoxime	nitrile	**1**	64	oil	oil
4b	p-ClC_6H_4	aldoxime	nitrile	**1**	84	91-93	91-93
4b	p-ClC_6H_4	aldoxime	nitrile	**2**	71	91-93	91-93[4]
4c	p-$CH_3OC_6H_4$	aldoxime	nitrile	**1**	75	57-59	57-59[4]
4d	3-Py	aldoxime	nitrile	**1**	71	51-52	50-52[4]
4a	Ph	amide	nitrile	**2**	62	oil	oil
4c	p-$CH_3OC_6H_4$	amide	nitrile	**2**	74	57-58	57-59
4e	p-$CH_3OC_6H_4CH_2$	amide	nitrile	**2**	83	oil	286/760mmHg[9]
4f	1-$C_{10}H_7CH_2$	amide	nitrile	**2**	69	oil	183-7/13mmHg[26]

All samples of nitriles were identical (^1H and ^{13}C NMR) to authentic specimens by independent methods.

Aromatic and aliphatic primary amides reacted with 1,1'-sulfonyldibenzotriazole **2** in toluene to give nitriles in good yields (Table 1). Conventional reagents for carrying out the dehydration of amides to nitriles, mainly phosphorus compounds, such as $POCl_3$ and CCl_4-Ph_3P[14] are often toxic and frequently reactive towards other functional groups. Dehydration of amides by hexamethylphosphoric triamide requires heating at 220-240°C.[19] Our method offers possible advantages in the preparation of sensitive nitriles as 1,1'-sulfonyldibenzotriazole and 1,1'-carbonyldibenzotriazole can be used for dehydration under neutral and



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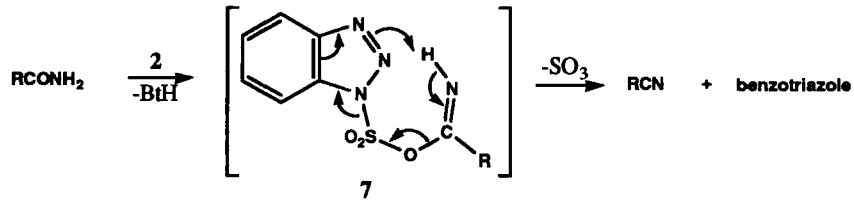

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mild conditions. All cases gave good yields (62-83%). The reactions of primary amides or thioamides with N,N'-sulfinyldiimidazole afforded nitriles in low to moderate yields (11-69%);[27] however, N,N'-carbonyldiimidazole is inert toward amides. Our work shows that 1,1'-sulfonyldibenzotriazole is more reactive than these two imidazole derivatives.

The nitriles prepared were characterized by comparisons (^{1}H NMR and ^{13}C NMR) with authentic specimens (Table 1). The reaction sequence can be rationalized by the formation of intermediate **6** from the reaction of **1** with an aldoxime (or of **7** from **2** with an amide), followed by a ready elimination of benzotriazole to give the nitrile as shown in Scheme 1. This mechanism is supported by the isolation of by-product benzotriazole.

In conclusion, 1,1'-carbonyldibenzotriazole and 1,1'-sulfonyldibenzotriazole are versatile dehydration reagents. They are effective in dehydrations of aldoximes and amides under mild conditions.

EXPERIMENTAL SECTION

Melting points were determined on a Kofler hot stage microscope and are uncorrected. All the ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-300 spectrometer in $CDCl_3$. The IR spectra were obtained on Perkin-Elmer 1640 FTIR spectrophotometer in Nujol. Preparation of 1,1'-carbonyldibenzotriazole and 1,1'-sulfonyldibenzotriazole were reported previously.[22] Aldoximes were prepared using the literature method.[24] THF was dried over sodium and benzophenone and distilled prior to use.

General Procedure for the Dehydration of Aldoximes.- A mixture of an aldoxime (10 mmol) and 1,1'-carbonyldibenzotriazole (2.64 g, 10 mmol) or 1,1'-sulfonyldibenzotriazole (3.00 g, 10 mmol) in THF (20 ml) was stirred under reflux for 24 hrs. The solvent was evaporated and the residue was dissolved in diethyl ether, washed with Na_2CO_3 (5%, 20 ml) and dried over $MgSO_4$. The solvent was removed and the crude nitrile was purified by column chromatography (silica gel, $CHCl_3$).

General Procedure for the Dehydration of Amides.- A mixture of an amide (10 mmol) and 1,1'-sulfonyldibenzotriazole in toluene (20 ml) was refluxed with stirring for 2 hrs. The solvent was removed under vacuum. The residue was poured into Na_2CO_3 solution (5%, 30 ml) and extracted with diethyl ether,

washed with water and dried over $MgSO_4$. The solvent was evaporated and the crude product was purified by column chromatography.

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