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One-Pot Synthesis of *N*-Imidoylbenzotriazoles via Benzotriazole-Mediated Beckmann Rearrangement of Oximes

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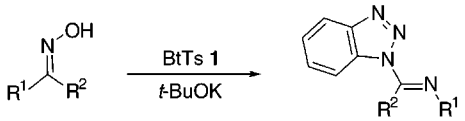
ABSTRACT



2a-l **5a-l**

***N*-Imidoylbenzotriazoles 5a–l are obtained under mild conditions in variable yields (20–87%) by reactions of oximes 2a–l with BtTs 1 via a Beckmann rearrangement.**

The Beckmann rearrangement[1a,b] has been established as a powerful tool with a wide range of applications in organic synthesis for the construction of nitrogen-containing compounds.[2a,b] Among numerous variations, oxime sulfonates, due to their facile preparation, easy handling, and high reactivity have been frequently utilized as versatile intermediates for access to (i) α-alkylated amines via imines,[3a,b] (ii) amidines[4] (iii) thioimidates,[5] (iv) imidoyl halides,[6] (v) imidoyl cyanides,[5] (vi) iminophosphonates,[7] and (vii) enaminones.[8] These methods possess synthetic value, but all reported procedures involve the isolation of the starting oxime sulfonates, some of which lack stability.[5]

Benzotriazole is a versatile synthetic auxiliary for organic synthesis.[9] We have recently demonstrated that *N*-imidoylbenzotriazoles constitute stable and useful substitutes for imidoyl chlorides.[10−12] Previous preparations of such *N*-imidoylbenzotriazoles have required the use of phosphorus oxychloride[10] or the in situ synthesis of the unstable 1,1′-sulfinyldibenzotriazole[11] and sometimes gave low yields and/or *E*/*Z* mixtures. We now report a one-pot synthesis of *N*-imidoylbenzotriazoles from oximes via a 1-[(4-methylphenyl)sulfonyl]-1*H*-1,2,3-benzotriazole (BtTs) induced Beckmann-type rearrangement.

The highly reactive sulfonating agent BtTs[13] **1** (Scheme 1) was obtained solely as the benzotriazol-1-yl isomer in 72%

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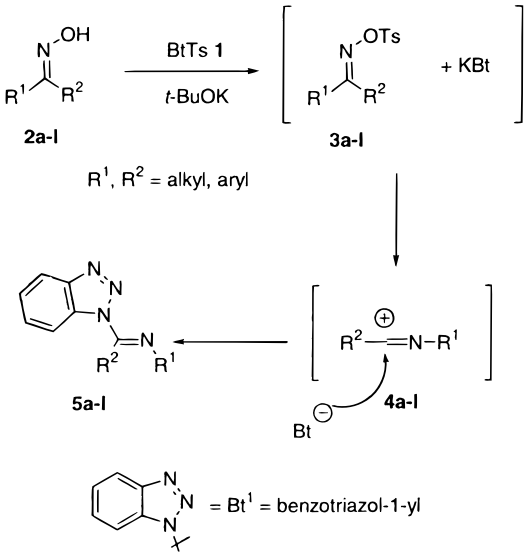
Scheme 1



yield by condensation of benzotriazole with *p*-toluenesulfonyl chloride in toluene in the presence of triethylamine as previously reported.[14] Compound **1** is stable and can be stored for months at room temperature.

N-Imidoylbenzotriazoles **5a**−**l** were then prepared by one-pot reactions of the corresponding oximes **2a**−**l** (commercially available or prepared according to known protocols[15] for **2c**, **2g**, **2k**, and **2l**) with BtTs in the presence of *t*-BuOK as the base. The mechanism probably involves first oxime sulfonates **3** and then iminocarbocations of type **4** which are trapped by the nucleophilic benzotriazole anion (Scheme 1). To the best of our knowledge, these reactions are the first examples of nucleophilic attack of a heterocycle on intermediates **4**. Compounds **5a**−**l** were obtained after purification in moderate to good yields depending essentially on the solvent used (Table 1).

Table 1. Preparation of *N*-Imidoylbenzotriazoles **5**

			yield (%)		
product	R^1	R^2	benzene	toluene	xylenes
5a		$-(CH_2)_5-$	55	37	
5b		$-(CH_2)_4-$	50	20	
5c	C_6H_5	CH_3		60	
5d	C_6H_5	C_6H_5		70	
5e	CH_3	CH_3	15	20	84
5f	2-pyridyl	C_6H_5		50	
5g		$-(CH_2)_4CHCH_3$	87	15	
5h	$C(CH_3)_3$	CH_3		60	
5i	C_2H_5	CH_3		30	45
5j	$CH_2C_6H_5$	$CH_2C_6H_5$		20	
5k	$CH(CH_3)_2$	$CH(CH_3)_2$		35	
5l	$-CH(CH_2CH_2)-$	$-CH(CH_2CH_2)-$		64	

For the less reactive oximes **2e** and **2i**, the yield is dramatically improved by using a higher boiling solvent for the reaction. On the other hand, highly reactive oximes (**2a**, **2b,** and **2g**) require a low reaction temperature to avoid decomposition. A solvent effect study suggested that non-polar solvents are more efficient since use of THF gave only starting material. Additionally, the type of base influenced the course of the reaction. Thus, alkylamines (Et_3N), alkyllithiums (*n*-BuLi), or hydrides (NaH) did not permit the synthesis of the desired compounds, while heterogeneous systems using *t*-BuOK or K_2CO_3 were effective.

N-Imidoylbenzotriazoles **5a**−**j** were obtained as single *E*-isomers and as only Bt1 isomers on the basis of their ^1H and ^{13}C NMR data. Interestingly, when oximes **2k** and **2l**, bearing a single hydrogen atom on the α position of bulky substituents, were used as starting materials, the corresponding *N*-imidoylbenzotriazoles **5k** and **5l** were obtained as mixtures of *E*- and *Z*-isomers (*E*/*Z* = 75/25 for both compounds) perhaps because steric effects cause partial isomerization of the intermediates. The regio- and stereochemistry of the unsymmetrical compounds **5f**,**c**[16] were determined by extensive NMR investigations.[17] The regiochemistry for the unsymmetrical *N*-imidoylbenzotriazoles **5h** and **5i** was deduced from the ^{13}C NMR shifts of the methyl groups.

In conclusion, a new method for the synthesis of *N*-imidoylbenzotriazoles has been presented. This approach allows the preparation of such compounds in modest to good yields (average yield in the optimal solvent for twelve compounds is 56%) by using mild reaction conditions.[18]

Acknowledgment. We thank Dr. Ion Ghiviriga for the NMR experiments on compound **5f**.

Supporting Information Available: Full characterization for compounds **5a**−**l**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) Compound **5c** was already described.[10]

(17) The protons on the phenyl group have been identified based on their intensity and multiplicity as 7.38 (d, 2H) *ortho* and 7.32 (t, 2H) *meta*. The *para* proton is at 7.39, as demonstrated by the intensity of the cluster around 7.38 and by the lack of couplings of 7.38−7.39 and 7.32 to any other protons but themselves. The long-range coupling between 7.32 and 130.4 identified the quaternary carbon on the phenyl ring, and the long-range coupling of 7.38 to 156.0 identified the imine carbon and demonstrated that the phenyl is attached to the carbon of the imine group. The quaternary carbon at 146.4 was assigned to position 3a of benzotriazole on the basis of its chemical shift. Long-range couplings identified the protons *meta* to this carbon as 8.53 (d, position 7) and 7.50 (t, position 5). The protons in positions 4 and 6 were identified as 8.14 and 7.62, correspondingly, on the basis of their couplings to the other protons on the Bt. Long-range couplings of 8.14 and 7.62 allowed the assignment of the quaternary carbon in position 7a as 131.8. The CH at 8.34/148.8 was assigned to position 6 of the pyridine, based on the chemical shifts. The tocsy spectrum revealed the sequence 8.34−6.94−7.53−6.73. The H−C long-range couplings confirmed this assignment and revealed the quaternary carbon in position 2 as 159.7.

(18) **General Procedure for the Preparation of Compounds 5.** The corresponding oxime **2** (1 mmol), BtTs (1 mmol), *t*-BuOK (1 mmol), and crown ether 18C6 (0.1 mmol) were stirred and heated in the adequate solvent (10 mL) (see Table 1). After completion of the reaction (TLC), the mixture was allowed to reach room temperature and hydrolyzed by H_2O (10 mL). After extraction, the organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was subjected to purification (method A, extraction with hot hexanes; method B, flash column chromatography).