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# *N,N,N′,N′*-TETRABROMOBENZENE-1,3-DISOLFONAMIDE (TBBDS) AS AN EFFICIENT PROMOTER FOR ONE-POT CONVERSION OF *N*-ARYLGLYCINES TO SYDNONES IN THE PRESENCE OF $NaNO_2/Ac_2O$ UNDER NEUTRAL CONDITIONS

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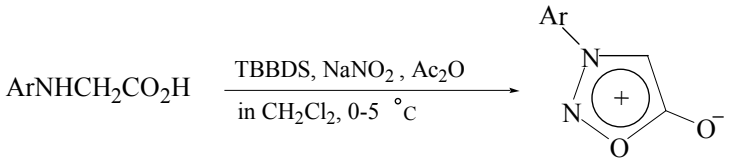
**Abstract**– *N,N,N′,N′*-Tetrabromobenzene-1,3-disolfonamide (TBBDS)-promoted one-pot conversion of various *N*-arylglycines to sydnones using a combination of $NaNO_2$ and $Ac_2O$ has been achieved efficiently through *N*-nitrosation followed by cyclization in high yields (85-95%) under mild and neutral conditions.

Sydnones (*cf.* **2)** are unique members of the class of heterocyclic compounds known as mesoionic.[1] Sydnones were first prepared by Earl and Mackney in 1935,[2] and the greatest interest in them, ever since, stems from their biological activity as antibacterial,[3] antitumour,[4] antimalarial,[5] anti-inflammatory,[6] and antihypertensive[7] agents. Sydnones also undergo a variety of transformations including electrophilic aromatic substitution (at the *4*-position),[8] 1,3-dipolar cycloaddition reactions to form pyrazoles or related species,[9] and cleavage to hydrazines[2] or heterocycles[10] when treated with HCl.

Sydnones are intrinsically neutral substances that are normally prepared by dehydrative cyclization of *N*-nitrosamino acids.[11] *N*-Nitrosamino acids used in the synthesis of sydnones are themselves prepared from *N*-nitrosation of amino acids. *N*-Nitrosation is a well-known reaction in organic synthesis[12] that is usually accomplished by nitrous acid generated from the treatment of sodium nitrite with an aqueous mineral acid.[13]

In continuation of our research on various transformations by halogenating agents[14-16] and sydnones,[17-19] and also in order to avoid the drawbacks generally caused by the use of strong acidic media in nitrosation reactions, we wish, herein, to report on the *N,N,N′,N′*-tetrabromobenzene-1,3-disolfonamide (TBBDS) as

a more robust and efficient promoter for one-pot conversion of *N*-arylglycines to sydnones under neutral conditions. In this work we have observed that *N,N,N′,N′*-tetrabromobenzene-1,3-disolfonamide (TBBDS) can efficiently enhance the conversion of the *N*-arylglycines (**1a-j**) to the sydnones (**2a-j**) using sodium nitrite and acetic anhydride in $CH_2Cl_2$ in satisfactory yields (85-95 %) (**Scheme 1**, **Table 1**). As shown in the table, the reactions occur satisfactorily within 5-8 h at 0-5 ˚C. The experimental results indicated that the most effective conversion occurs if the molar *N*-arylglycines/TBBDS ratio is maintained at 4. Longer reaction times are required when lesser amounts of TBBDS are employed. It is important to note that no sydnones were afforded when the reactions were carried out without using any TBBDS in the reaction. In accordance with the previously reported action of acetic anhydride in the cyclization of *N*-nitrosoglycines to sydnones,[2] and also the crucial role of the acetyl hypobromite, generated from the reaction of acetic anhydride with hypobromous acid during the reaction, in *N*-bromination of sulfonamide,[20] we propose a possible mechanism for these reactions as shown in **Scheme 2,** in which the cyclization of the intermediate *N*-nitrosoglycines is, probably, activated by TBBDS.




**1a-j** **2a-j**

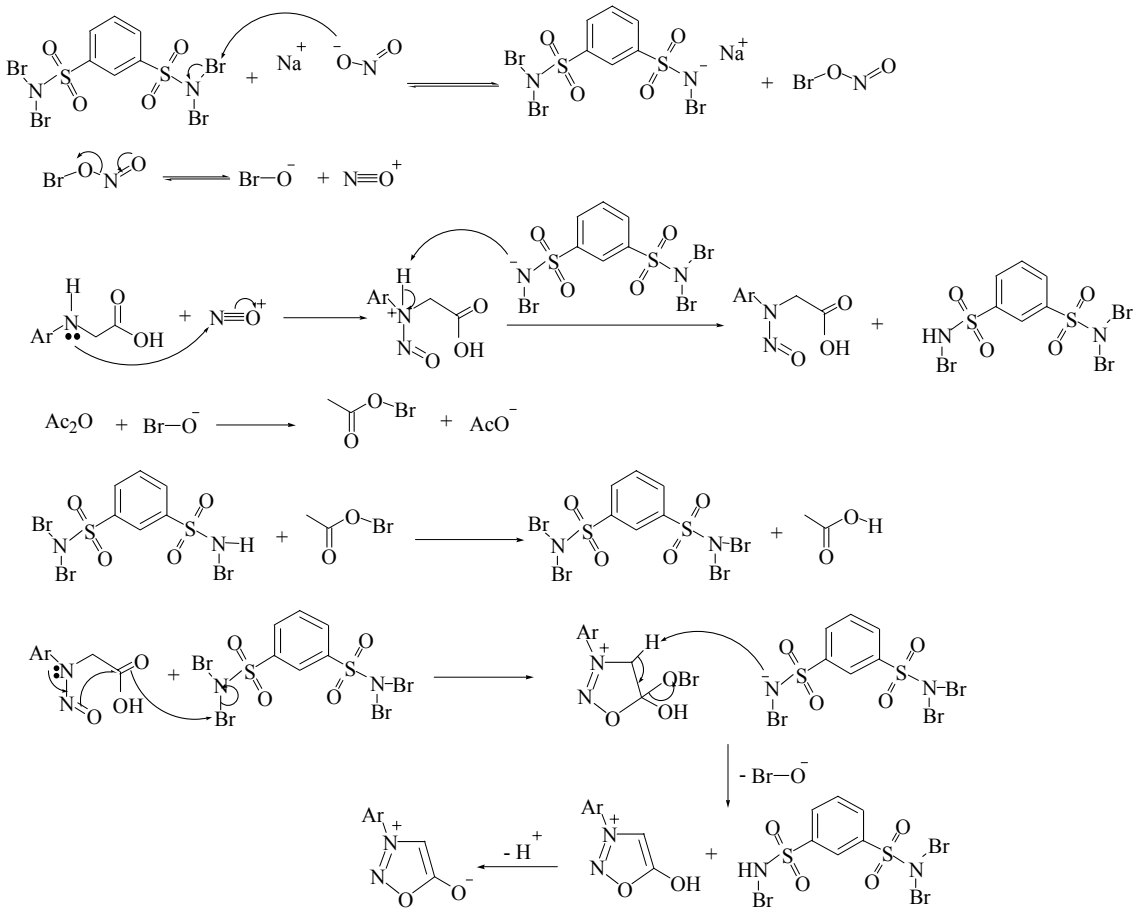
**Scheme 1**

**Table 1** Conversion of the *N*-arylglycines (**1a-j**) to the sydnones (**2a-j**) with a combination of $NaNO_2$ /$Ac_2O$ in $CH_2Cl_2$ promoted by TBBDS.

| Entry | Product[a] | Ar | Time (h) | Yield (%)[b] | mp (˚C) | |
|---|---|---|---|---|---|---|
| | | | | | Found | Reported[20,21] |
| 1 | **2a** | *o*-$CH_3C_6H_4$ | 7.0 | 92 | 98 | 97 |
| 2 | **2b** | *p*-$CH_3C_6H_4$ | 6.0 | 90 | 143 | 145 |
| 3 | **2c** | *o*-$CH_3OC_6H_4$ | 6.0 | 93 | 96 | 97 |
| 4 | **2d** | *p*-$CH_3OC_6H_4$ | 5.5 | 89 | 126 | 125 |
| 5 | **2e** | *p*-$NO_2C_6H_4$ | 6.0 | 88 | 147 | 148 |
| 6 | **2f** | *o*-$NO_2C_6H_4$ | 8.0 | 85 | 184 | 184 |
| 7 | **2g** | *p*-$ClC_6H_4$ | 7.0 | 91 | 114 | 113 |
| 8 | **2h** | *2,4*-$Cl_2C_6H_3$ | 7.8 | 85 | 94 | 96 |
| 9 | **2i** | *p*-$BrC_6H_4$ | 6.2 | 93 | 138 | 137 |
| 10 | **2j** | $C_6H_5$ | 5.0 | 95 | 134 | 135 |

[a]All the isolated products were characterized on the basis of their physical properties and $^1$H NMR, $^{13}$C NMR and IR spectra and by direct comparison with literature data.[2,8,21,22]

[b]Isolated yields.



**Scheme 2**

## EXPERIMENTAL

Chemicals were obtained from Merck and Fluka Chemical Companies. IR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and $^{1}H$ NMR and $^{13}C$ NMR spectra were obtained in $CDCl_3$ using 90 MHz JEOL FT NMR spectrometer. All melting points were determined on a Büchi 530 melting point apparatus, and reported uncorrected.

### Conversion of the *N*-Arylglycines (1a-j) to the Sydnones (2a-j) with $NaNO_2/Ac_2O$ using TBBDS; General Procedure

To a magnetically stirred solution of *N*-arylglycine (**1**) (2 mmol) in $CH_2Cl_2$ (40 mL), was added *N,N,N',N'*-tetrabromobenzene-1,3-disolfonamide (TBBDS) (0.5 mmol), $NaNO_2$ (0.17 g, 2.5 mmol) and $Ac_2O$ (0.31 g, 3 mmol) at 0-5 ˚C. After the complete conversion of the substrate in 5-8 h (Table **1**) as monitored by TLC using AcOEt/hexane mixture (1:1), the reaction mixture was poured into water (5 mL), and then solid $NaHCO_3$ was added cautiously with stirring to remove the remaining glycines. The resulting mixture was filtered, the filtrate was extracted with $CH_2Cl_2$, and then the organic layer was separated, dried and evaporated in *vacuo* to leave the solid product (**2**), which was further purified by

recrystallization from EtOH. These products were characterized on the basis of their physical properties and also their IR and NMR spectra with direct comparison with literature data.[2,8,21,22]

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