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Bioorganic & Medicinal Chemistry Letters 15 (2005) 1121–1123
Bioorganic & Medicinal Chemistry Letters

Synthesis and antibacterial activity of 2,4,6-tri substituted *s*-triazines☆

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Received 13 October 2004; accepted 6 December 2004
Available online 29 December 2004

Abstract—Various 2,4,6-tri substituted *s*-triazines were synthesized and screened for antibacterial activity against Gram-positive and Gram-negative organisms. These *s*-triazine derivatives displayed high in vitro antibacterial activities comparable to penicillin and streptomycin against tested microorganisms.
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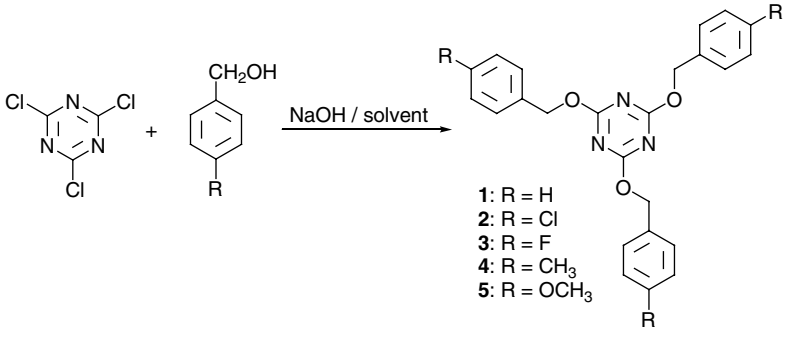
Substituted *s*-triazine derivatives are an important class of compounds having anticancer,[1] antitumor,[2] antiviral[3] and antifungal[4] activities. These compounds have been used in the treatment of depression,[5] and hence received a considerable therapeutic importance. These are valuable bases for estrogen receptor modulators[6a] and also used as bridging agents to synthesize herbicides.[6b] Further substituted *s*-triazines have been used as NLO materials, which have a wide range of applications in optoelectronics and telecommunications.[7] Research on new substances possessing antibacterial activity has considerable attention owing to the continuous increase in bacterial resistance.[8] It has been reported that substituted *s*-triazine derivatives possess antibacterial activity.[4,9] In this article, we illustrate the synthesis and antibacterial activity of a series of *s*-triazine derivatives.

Synthesis of various 2,4,6-tri substituted *s*-triazines is illustrated in Schemes 1–3. Compounds **1**–**5** were synthesized by allowing reaction between benzyl alcohol



Scheme 1.

Keywords: *s*-Triazines; Synthesis; Antibacterial activity; Antifungal activity.
☆Communication No. 041208.
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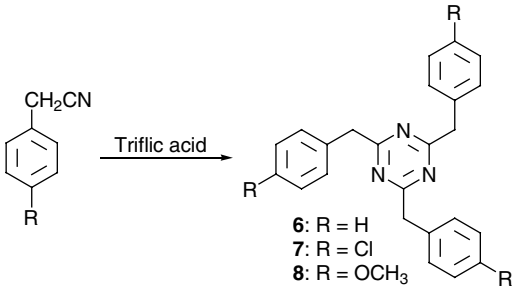
doi:10.1016/j.bmcl.2004.12.020

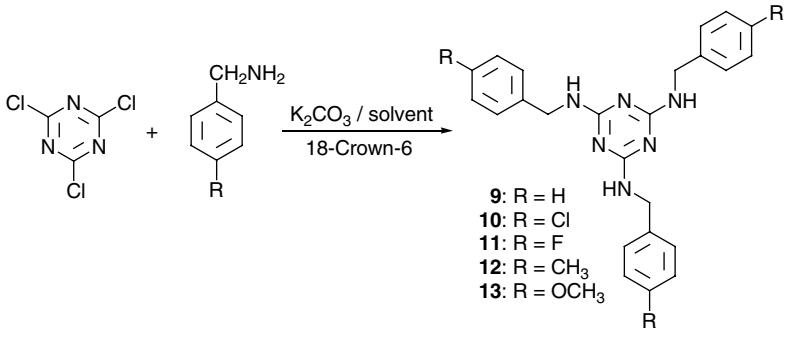


Scheme 2.

derivative and cyanuric chloride in the presence of base (Scheme 1).[10] Compounds **6**–**8** were synthesized using trimerization reaction of phenyl acetonitrile derivative with the use of triflic acid (Scheme 2). Compounds **9**–**13** were synthesized by treating cyanuric chloride with corresponding bezylamine in the presence of K_2CO_3 and 18-Crown-6 as a catalyst in dry toluene (Scheme 3).[11] All compounds were purified by column chromatography followed by recrystallization.

The minimum inhibitory concentrations (MIC) of various substituted *s*-triazines were tested against three representative Gram-positive organisms viz. *Bacillus subtilis* (MTCC 441), *Bacillus sphaericus* (MTCC 11) *Staphylococcus aureus* (MTCC 96) and three Gram-negative organisms viz. *Chromobacterium violaceum* (MTCC 2656), *Klebseilla aerogenes* (MTCC 39), *Pseudomonas aeruginosa* (MTCC 741) by broth dilution method recommended by National Committee for Clinical Laboratory (NCCL) standards.[12]

Standard antibacterial agents like penicillin and streptomycin were also screened under identical conditions for comparison. The minimum inhibitory concentration (MIC) values are presented in Table 1. It has been observed that the test compounds (**1**–**13**) exhibited interesting antibacterial activity, however with a degree of variation. The compound **6**, benzyl substituted triazine, without any substituent at the *para* position of the aryl group exhibited remarkable antibacterial activity against tested organisms comparable to reference agents penicillin and streptomycin. Replacement of hydrogen at the *para* position of the aryl group in benzyl substituted triazines by chloro and methoxy function (**7** and **8**) exhibited moderate activity compared to **6**. Among the benzyloxy substituted triazines, **1**, **2** and **3** (Table 1) displayed moderate activity. Improved activity against *Chromobacterium violaceum* is observed by the introduction of methoxy function in benzyloxy triazine at *para* position, **5** (Table 1). Methyl derivative



Scheme 3.

Table 1. In vitro antibacterial activity of 2,4,6-tri substituted *s*-triazines

Compd. no.	MIC, μg/mL					
	Gram-positive organism			Gram-negative organism		
	B. subtilis	*B. sphaericus*	*S. aureus*	*C. violaceum*	*K. aerogenes*	*P. aeruginosa*
1	25	25	25	25	—	—
2	12.5	12.5	12.5	25	25	—
3	25	12.5	25	12.5	25	—
4	—	—	—	—	—	—
5	25	25	25	6.25	25	—
6	12.5	6.25	12.5	6.25	6.25	—
7	25	25	25	25	25	—
8	50	12.5	25	25	25	—
9	25	25	25	25	25	—
10	—	25	—	25	—	—
11	—	50	—	—	—	—
12	—	50	—	—	—	—
13	25	12.5	25	25	25	—
Penicillin	1.562	3.125	1.562	12.5	6.25	12.5
Streptomycin	6.25	12.5	6.25	3.125	1.562	3.125

of benzyloxy triazine, **4** did not exhibit in vitro antibacterial activity even at the concentration of 200 μg/mL against all the tested organisms. Triazines with benzylamine derivatives showed low activity against all tested organisms. Replacement of hydrogen by fluorine and methyl function in **11** and **12** further suppresses the antibacterial activity. All the compounds **1**–**13** did not exhibit in vitro antibacterial activity against *Pseudomonas aeruginosa* even at the concentration of 200 μg/mL. All these compounds **1**–**13** did not respond to antifungal activity.

In conclusion, a series of 2,4,6-tri substituted *s*-triazines were synthesized and evaluated for antibacterial activity. Most of the compounds showed antibacterial activity. Among them **6** exhibited the most significant activity whereas **2**, **5**, **9** and **13** were displayed moderately large activity against both Gram-positive and Gram-negative microorganisms. Least activity was observed for triazine with benzylamine derivatives.

Acknowledgements

We thank Dr. J. S. Yadav, Director IICT and Head of the Division for the encouragement. K.S. and U.S. thank to CSIR-New Delhi and University Grants Commission-New Delhi for fellowship.

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