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### ***N*- And *S*-Alkylation of 3-(1-Adamantyl)-4-methyl-1,2,4-triazole-5-thiol and 2-(1-Adamantyl)-1,3,4-oxadiazole-5-thiol**

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## *N*- And *S*-Alkylation of 3-(1-Adamantyl)-4-methyl-1,2,4-triazole-5-thiol and 2-(1-Adamantyl)-1,3,4-oxadiazole-5-thiol

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**ABSTRACT** - The reaction of 3-(1-adamantyl)-4-methyl-1,2,4-triazole-5-thiol **1** with certain 2-aminoethyl chlorides in alkaline medium yielded a separable mixture of the *S*-(2-aminoethyl) derivatives **2** and the *N*-(2-aminoethyl) derivatives **3**. Meanwhile, alkylation of 2-(1-adamantyl)-1,3,4-oxadiazole-5-thiol **4** with 2-aminoethyl chlorides under the same conditions yielded only the *S*-alkyl derivatives **5**. Interaction of **4** with primary or secondary amines and formaldehyde solution yielded the corresponding *N*-aminomethyl derivatives in high yields.

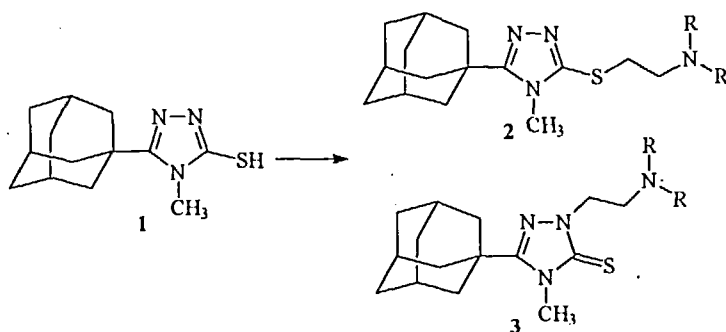
**KEY WORDS** - Adamantane Derivatives, 1,2,4-Triazoles-5-thiol, 1,3,4-Oxadiazole-5-thiol.

### INTRODUCTION

Several adamantane derivatives have long been known for their antiviral<sup>1-4</sup> and antimicrobial<sup>4-6</sup> activities. In addition certain adamantane derivatives were found clinically useful in the control of certain central nervous disorders<sup>7-10</sup>. In a previous work<sup>11</sup>, we observed that the compound 3-(1-adamantyl)-4-methyl-5-ethylthio-1,2,4-triazole produced significant central nervous stimulant activity in rats. In continuation to our studies on the chemistry and biological properties of adamantane derivatives<sup>11-14</sup>, we report herein the alkylation pattern of 3-(1-adamantyl)-4-methyl-1,2,4-triazole-5-thiol and 2-(1-adamantyl)-1,3,4-oxadiazole-5-thiol.

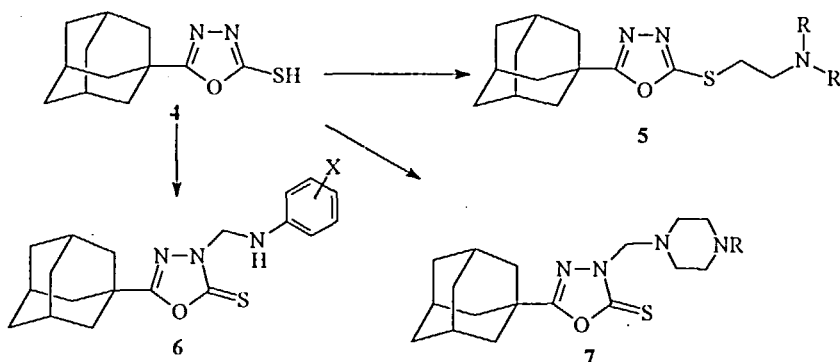
### RESULTS

The reaction of 3,4-disubstituted-1,2,4-triazole-5-thiols with alkyl halides in alkaline media was reported to yield the *S*-alkyl derivatives as the sole product<sup>15-18</sup>. In our laboratory, we reacted 3-(1-adamantyl)-4-methyl-1,2,4-triazole-5-thiol **1** with certain 2-aminoethyl chlorides in ethanol in the presence of potassium hydroxide to get the target compounds **2**. This reaction yielded reasonable amounts of the *N*-alkyl derivatives **3** in addition to the target compounds **2** (Scheme 1). The two products were separated by column chromatography.



Scheme 1

On the other hand, the reaction of 2-(1-adamantyl)-1,3,4-oxadiazole-5-thiol **4** with 2-aminoethyl chlorides under the same conditions yields only the *S*-alkyl products **5**. The reaction of **4** with several substituted anilines or 1-substituted piperazines and formaldehyde solution in ethanol, at ambient temperatures, yielded high yields of the *N*-aminomethyl derivatives **6** & **7**, respectively (Scheme 2). The structural assignment of the synthesized compounds was based on IR,  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$  and mass spectroscopy. The synthesized compounds were tested for their activity against certain strains of gram-positive, gram-negative bacteria and pathogenic fungi, the derivatives **6** & **7** proved to be highly active.



Scheme 2

## REFERENCES

1. V. G. Vernier, J. B. Harmon, J. M. Stump, T. E. Lynes, J. O. Marvel, and D. H. Smith, *Toxicol. Appl. Pharmacol.*, **15**, 642 (1969).
2. A. Scherm, and D. Peteri, *Ger. Offen.*, 1,941,21 (1971).
3. S. Rabinovich, J. T. Baldini, and R. Bannister, *Am. J. Med. Sci.*, **257**, 328 (1969).
4. V. L. Narayanan, *US Pat.*, 3,471,491 (1969).
5. V. L. Narayanan, *US Pat.*, 3,501,511 (1970).
6. C. P. Krimmel, *US Pat.*, 3,565,942 (1971).
7. B. Cox, and S. J. Tha, *Eur. J. Pharmacol.*, **30**, 344 (1975).
8. J. Maj, H. Sowinska, L. Baran, and J. Sarneck, *Eur. J. Pharmacol.*, **26**, 9 (1974).
9. E. Mariani, P. Schenone, F. Bondavalli, E. Lampa, and E. Marmo, *Farmaco Ed. Sci.*, **35**, 430 (1980).
10. Delmar Chem. Ltd., *Brit. Pat.*, 1,347,871 (1974).
11. A. A. El-Emam, and T. M. Ibrahim, *Arzneim.-Forsch./Drug Res.*, **41**, 1260 (1991).
12. A. A. El-Emam, and J. Lehmann, *Monatsh. Chem.*, **125**, 587 (1994).
13. A. A. El-Emam, *Chin. Pharm. J.*, **42**, 309 (1990).
14. A. A. El-Emam, A. M. Abdelal, M. A. Moustafa, and M. B. El-Ashrawy, *Chin. Pharm. J.*, **45**, 101 (1993).
15. J. R. Maxwell, D. A. Wasdahl, A. C. Wolfson, and V. I. Stenberg, *J. Med. Chem.*, **27**, 1565 (1984).
16. T. George, D. V. Mehta, R. Tahilramani, J. David, and P. K. Talwalker, *J. Med. Chem.*, **14**, 335 (1971).
17. P. J. Kothari, M. A. Mehloff, S. P. Singh, S. S. Parmar, and V. I. Stenberg, *J. Heterocycl. Chem.*, **17**, 1369 (1980).
18. B. N. Gosowami, J. C. S. Katakya, and J. N. Baruah, *J. Heterocycl. Chem.*, **21**, 1225 (1984).