2013 臺灣國際科學展覽會
優勝作品專輯(國外作品)

作品編號 **030033**

參展科別 化學科

作品名稱 **Reactions of Bis(oxy)enamines with Transition Metal Halides**

得獎獎項 一等獎

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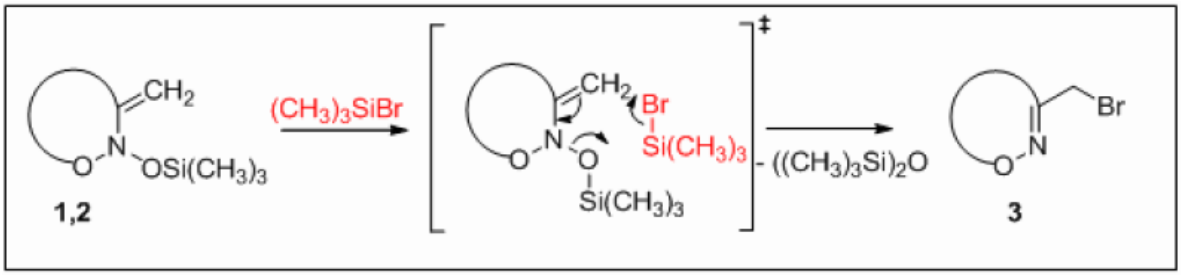
ABSTRACT OF EXHIBIT

TAIWAN INTERNATIONAL SCIENCE FAIR



Synthesis of halooximes has attracted much attention given their importance as precursors to proline derivatives[1], unnatural amino acids[2] and a host of alkaloids[3]. Halooximes have numerous industrial and biological applications [4], for example oxime ethers increases specific channel opening activities, acting as potential targets in drug treatment for various diseases[5], most adrenergic β-receptor blocking compounds also conform to the structure of oxime ethers [6]. They also have vitro antifungal activities against certain plants[7].

A known method for the synthesis of **3** using Me_3SiX as a Lewis acid, via intermediate enamines with acyclic/ cyclic bis(oxy)enamines, gives yields between 21-68%.

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[1] Buchholz, M.; Reissig, H.-U. Eur. J. Org. Chem. 2003, 3524.

[2] Gilchrist, T. L.; Roberts, T. G. J. Chem. Soc., Chem. Commun. 1979, 1090.

[3] Tishkov, A. A.; Reissig, H. U.; Ioffe, S. L. Synlett 2002, 863.

[4] Steven M. J.; Michael H. P.; Satheesh K. P.; Nilofar N. M.; Hans E. P.; Christopher N. Kyle P. C.; Traci W.; James C. S.; K. Barry S.; Jeffery W. K., Bisaryloxime Ethers as Potent Inhibitors of Transthyretin Amyloid Fibril Formation, 2005

[5] Yong-M. C.; Eriko Y.; Yuko O.; Takashi Y.; Katsutoshi I.; Kohei S.; Masatoshi K.; Kentaro Y.; Tomohiko O., Novel oxime and oxime ether derivatives of 12,14-dichlorodehydroabietic acid: Design, synthesis, and BK channel-opening activity, 2008

[6] Gerard L.; Andre M.; Wermuth C., Synthesis and β-adrenergic Blocking Activity of a Novel Class of Aromatic Oxime Ethers, 1998

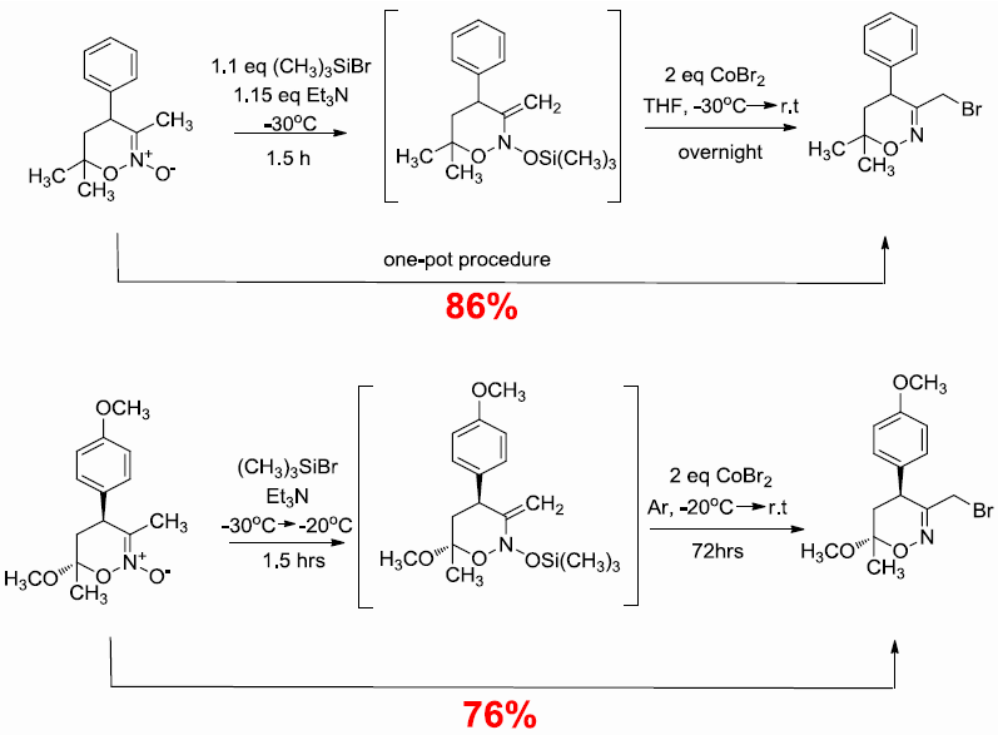
[7] Saeed E.; Mehraban F.; Ali B.; Massoud A.; Abbas S., (*E*)- and (*Z*)-1,2,4-Triazolylchromanone oxime ethers as conformationally constrained antifungals, 2004

Low yield stems from lack of reaction specificity[2]. In this work, we investigate coupling nitrogen-oxides with $CoBr_2$ to synthesise halooximes in high yield.

Initial cyclic/ acyclic bis(oxy)enamines were prepared by reacting 1 equiv. nitro compound with 2.4 equiv. in excess of dichloromethane under argon atmosphere at a temperature of 0℃. 2.2 equiv. of TMS-Br was further added and left to stir till thermal equilibrium with room conditions. The cyclic/ acyclic bis(oxy)enamine was isolated upon aqueous work-up, filtration and evaporation.

Synthesis of halooximes was carried out by reacting 8mL to 1mmol equiv. of THF and 2 equiv. of $CoBr_2$ under argon atmosphere and left to stir till $CoBr_2$ dissolves. 2mL to 1mmol equiv. of CH_2Cl_2 was added to 1 equiv. of bis(oxy)enamines. The reaction mixture was left to stir at room temperature for 2 hours, after which aqueous work-up, filtration and evaporation were carried out. Our results are summarized in **Table 1**.

We also obtained relatively high percentage yields for the direct synthesis of bromooximes from cyclic nitronates via a one-pot procedure:



[8] M. S. Klenox, A. V. Lesiv, Y. A. Khomutova, I. D. Nesterov, S. L. Ioffe; of Substituted 3-α-Haloalkyl-5,6-di-hydro-4H-1,2-oxazines; 2004.

Our work demonstrates a new method for synthesizing bromooxime cyclic ethers **3** from cyclic bis(oxy)enamines **1** and cyclic nitronates, using $CoBr_2$ which acts as a stronger lewis acid. This new method is more efficient both in yield and synthesis time, applying to both six-membered and five-membered cyclic rings. Our work has significant impact in the context of developing precursors to synthesizing a host of important molecules that have specialized application in the biological industry.

評語

The work presents a new method to synthesize Bromooximes cyclic ethers using CoBr2, which acts as a stronger Lewis acid. This work shows significant impact in synthesis of the subject compounds and deserves recommendation.