A NEW VAPOR-PHASE SYNTHESIS OF THIAZOLES

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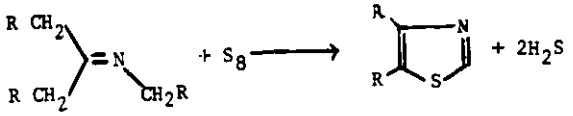
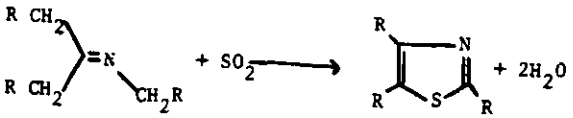
Abstract - The vapor-phase reaction of imines with sulfur dioxide to produce thiazoles has been studied at 450-500°C. Of the imines investigated acetone methyl imine was the most studied which produced 4-methylthiazole in 70% yield.

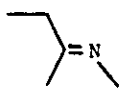
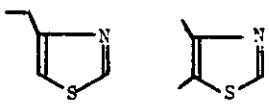
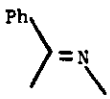
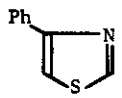
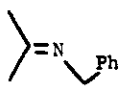
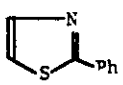
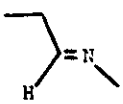
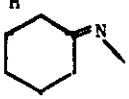
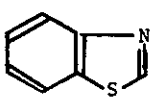
Over the last century numerous syntheses of thiazoles, useful as intermediates for the agricultural and pharmaceutial industry, have been published. One method of potential industrial importance is the vapor-phase reaction of sulfur with imines over suitable catalysts at 300-500°C[1,2]. These reactions are believed to occur via hydrogen abstraction to produce intermediates which give stable thiazoles by aromatisation.



This process yields toxic and odiferous by-products which present environmental problems. The objective of the work reported herein was to find an inexpensive, general route to thiazoles, including 4-methylthiazole, an intermediate in the production of 2-(4-Thiazolyl)-1H-benzimidazole[3]. It appeared to us that sulfur dioxide would be a more practical source of the sulfur atom. The process outlined here, reminiscent of the synthesis of thiophene from butadiene and sulfur dioxide [4], produces only water as a volatile by-product.



The imines for this study were prepared by condensation of a ketone and an amine with 50% caustic followed by purification by distillation. These imines could be stored at -20°C for several weeks without decomposition. The reactions of the imines with SO_2 to form various thiazoles were carried out over a strongly basic catalyst (e.g., CaO, MgO or soda-lime doped with Ca. 1% ZrO_2)[5] in a fixed bed catalytic reactor which consisted of an 8 x 3/8" stainless steel pipe heated with an electric coil heater. The imines were carburated with nitrogen, the vapors mixed with SO_2 and the mixture was passed over the catalyst bed heated to 450°C. The effluent from the reactor was passed through an aqueous HCl scrubber or diverted to a glc equipped with a heated injector valve. The progress of the catalytic reaction was monitored by glc . The scrubber solution was neutralized with NaOH and the products were isolated by extraction with methylene chloride. After concentration in vacuo, the products were identified by ^1H n. m.r. The data in the table illustrate the thiazoles that were produced by this procedure using the zirconium doped soda-lime catalyst.

Imine	Products	Yield[7]
		70%
		30% Total (1:1)
		26%
		40%
		20%
		40%

The conversion of acetone methyl imine to 4-methylthiazole was studied in detail. The efficiency of this condensation is strongly catalyst dependent. Catalysts such as CaO and MgO gave 50% yields of 4-methylthiazole for short periods of time (20 min), producing 0.5 g of 4 methyl thiazole per gram of catalyst. Soda-lime, being more basic, gave a higher yield of 60% and longer lifetime of 1 h, thus producing 1.5 g of 4-methylthiazole per gram of catalyst. Small amounts of transition metal oxides such as 1% ZrO_2 incorporated into the soda lime have been found to raise the yield of the thiazole to greater than 70% for even longer periods (3 hrs), thus producing Ca. 3 g of 4-methylthiazole per gram of catalyst. The catalyst reactivity decreases gradually because of coking and sulfate formation. The coke can be removed by passing steam through the reactor at 400-500°C, leading to reactivation of the catalyst. Slow sulfate formation however, leads to irreversible deactivation of the catalyst.

REFERENCES AND NOTES

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2. Suzuki, U. S. Patent 4,025,526, May 24, 1977.
3. H. D. Brown, A. R. Matzuk, I. R. Ilves, L. H. Peterson, S. A. Harris, L. H. Sarett, J. R. Egerton, J. J. Yakstis, W. C. Cambell, and A. C. Cukler, J. Am. Chem. Soc., 83, 1764 (1961).
4. R. C. Odioso, D. H. Parker, and R. C. Zabor, Industrial and Engineering Chemistry. Vol. 51 (No. 8), 921 (1959).
5. The catalysts were prepared by drying an aqueous slurry of the basic metal oxide to a solid mass. The solid was crushed and passed through 18 and 36 mesh screens followed by heating to 850 C for 14 h. Soda-lime was prepared in the same manner by the addition of 10 mole % NaOH to CaO. The ZrO_2 was introduced to the soda-lime as $Zr(NO_3)_3$ which decomposed to ZrO_2 during the heating.
6. In a typical reaction over 8.7 g of 1% ZrO doped soda lime, 50 mg per min of 4-methylthiazole was produced from 50 mg of acetone methyl-imine. The input composition to the reactor consisted of 4 mole % imine, 4 mole % SO_2 in 150 ml of nitrogen. The effluent concentration of 4-methylthiazole was 2.8 mole % as measured against a known concentration in nitrogen.
7. The yields were calculated on the basis of the amounts of imine carburated into the reactor.

Received, 20th April, 1984