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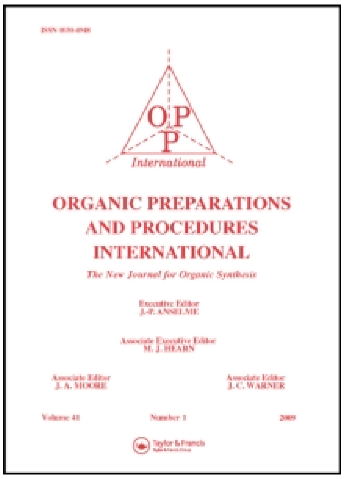

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IMPROVED SYNTHESIS OF DIMETHYLAMINOTHIOACETAMIDE

Kenneth P. Moder[a]; Frank R. Busch[a]; David C. Richter[a]
[a] Lilly Research Laboratories, Eli Lilly and Co., Lafayette, IN

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6. This ratio was determined by the integration of the appropriate peaks in the aromatic region of the nmr spectrum of the crude reaction mixture. It was confirmed by HPLC analysis of the crude mixture.

7. Purity determined by HPLC.

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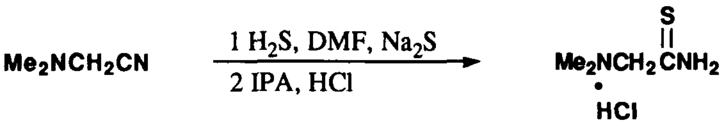
IMPROVED SYNTHESIS OF DIMETHYLAMINOTHIOACETAMIDE

Submitted by (08/29/91) Kenneth P. Moder*, Frank R. Busch and David C. Richter

Lilly Research Laboratories
Eli Lilly and Co., Lafayette, IN 47902

Aminothioamides are useful starting materials in the synthesis of pharmaceutical agents such as, N-alkyl-N'-([2-(aminoalkyl)-4-thiazolylmethyllthioalkyl)guanidines, thioureas, and ethanediamine anti-ulcer agents.[1] Thiation of amides with various phosphorus reagents has been reviewed.[2] However, aminothioamides generally are prepared by reaction of hydrogen sulfide with an aminoamide in the presence of an amine such as ammonia, pyridine, or triethylamine. Vasil'eva's work illustrates this process with the preparation of dimethylaminothioacetamide in 56% non-isolated yield.[3] Unfortunately, the amine often interferes with the isolation of the desired product. If the amine base is removed by distillation, lower yields of the aminothioacetamide product result because of co-distillation of amine and product. If the amine is not distilled and the aminothioacetamide is isolated as its acid salt, the final product is highly impure due to co-precipitation of the acid salt of the amine.The problems encountered with homogeneous amines can be overcome by employing alkali metal sulfide salts such as sodium sulfide or sodium hydrosulfide. These salts may be used in anhydrous or hydrated form but the anhydrous or monohydrate forms are preferred. The alkali metal sulfide or hydrosulfide are used in catalytic amounts, 0.5 to 8.0% on a molar basis.

We now report an efficient process for the synthesis of dimethylaminothioacetamide hydrochloride from the corresponding dimethylaminoacetonitrile, hydrogen sulfide, and sodium sulfide. This method obviates the need for amines and solvent exchanges employed previously and affords the product in 85 to 90% yield.



EXPERMENTAL SECTION

N,N-Dimethylaminothioacetamide.- A 1 L stainless steel Parr reactor vessel was charged with dimethylaminoacetonitrile (53.4 g, 0.636 mol), a catalytic amount of sodium sulfide (5.46 g, 0.07 mol), and dry DMF (100 mL). The reactor vessel was sealed and hydrogen sulfide introduced to 60 psi pressure. The mixture was agitated at ambient temperature for 48 hrs while the reactor pressure was maintained at 60 psi with hydrogen sulfide. The reactor was carefully vented and the contents filtered through filter-aid to remove the catalyst. The filtrate was diluted with isopropyl alcohol (100 mL) and the pH was adjusted to < 1.0 with anhydrous HCl (g) while the temperature of the reaction mixture was maintained below 30°. The resulting slurry was agitated while being cooled to 0° and was maintained at 0° for 2 hrs. The crystals were collected and washed with isopropyl alcohol (100 mL). The product was dried at 50° for 24 hrs to provide 86.9 g (88%) of product (purity 99.2%) as a colorless to light green solid, mp. 171-172°, lit.[3] mp. 169-173°.

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A NEW ROUTE FOR SYNTHESIS OF 1-TRIACONTANOL[†]

Submitted by B. V. S. K. Rao and R. Subbarao*
(05/23/91)

Oils and Fats Division
Indian Institute of Chemical Technology
Hyderabad-500007, INDIA

1-Triacontanol is the principal component of alfalfa *(Medicago sativa* L) which has been