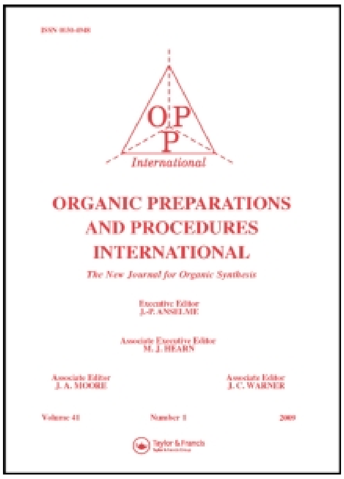

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1,5-DIMETHYLTETRAZOLE

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1,5-DIMETHYLTETRAZOLE

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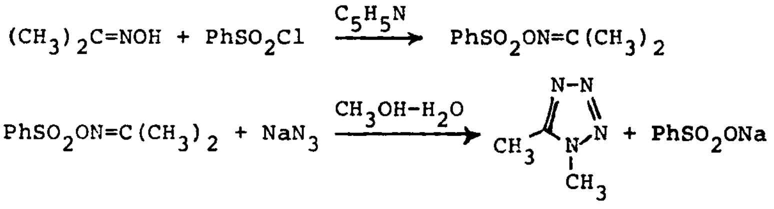
The preparation of 1,5-disubstituted tetrazoles by reaction of O-sulfonyl oximes with sodium azide is described in the patent literature.[1] Details are lacking, however, especially with regard to separation of the product from the large amount of byproduct sodium sulfonate. Later applications to the preparation of 1,5-dimethyltetrazole, in particular, have given erratic results, with reported yields of 56.4% in one case[2] and 6-7% in another.[3,4]

We have obtained 1,5-dimethyltetrazole from acetoxime consistently in yields of 85% by the procedure described below, which involves (1) the use of pyridine in place of



sodium hydroxide in the preparation of O-benzenesulfonyl acetoxime[5] (2) isolation of the O-benzenesulfonyl acetoxime prior to its reaction with sodium azide[6] (3) the use of aqueous methanol to provide a homogeneous mixture for the reaction with sodium azide and (4) the use of hot benzene for extraction of the 1,5-dimethyltetrazole from the sodium benzenesulfonate.[7]

EXPERIMENTAL

Acetoxime Benzenesulfonate.- To a mixture of 365 g. (5 moles) of acetoxime,[8] 410 ml. (395 g., 5 moles) of pyridine, and 1 l. of cold water, contained in a 3-liter, 3-necked flask equipped with a stirrer, dropping funnel and thermometer and cooled in an ice bath, was added over a period of 2 hr. 650 ml. (885 g., 5 moles) of benzenesulfonyl chloride at 15-20°.[9] After the mixture had been cooled to 10°, the white granular solid was collected and washed with cold water. The wet product weighed 1130 g. (106%) and was used in the next step without drying,[10] mp. of a dried sample, 52-53°; lit.[11] mp. 53°.

1,5-Dimethyltetrazole.- One-fourth of the acetoxime benzenesulfonate obtained above (about 280 g., 1.25 mole) and 1100 ml. of cold methanol[12] were placed in a 5-liter 3-necked flask equipped with a reflux condenser and a thermometer reaching into the liquid. A solution of 82 g. (1.25 mole) of sodium azide in 265 ml of water was added and the contents of the flask were mixed well and heated on a steam bath. At about 45°, a homogeneous peach-colored solution was obtained and spontaneous warming began. The flask was set on the bench top and a few Carborundum boiling aids were added. After about five minutes, the mixture began to boil. The reaction was moderated by immersing the flask in an ice-water bath so as to prevent flooding of the water-cooled reflux condenser.[13] After the exotherm subsided, the mixture was transferred to a

2-liter flask and distilled until 1100-1200 ml. of distillate was collected.[14] The residue was evaporated to dryness.[15]

The solids were transferred to a 1-liter 3-necked flask equipped with a stirrer and a condenser arranged for distillation. After addition of 350-400 ml. of benzene, the mixture was heated with stirring so as to distil about 50 ml. of benzene together with remaining water. The residue in the flask was cooled slightly and filtered with suction while still hot.[16] This extraction was repeated four times with 300-350 ml. portions of benzene, except that the distillation of benzene was replaced by simple heating at the boiling point for about 15 minutes.[17] The extracts were concentrated by distillation[18] until a thermometer in the boiling liquid indicated a temperature of 95°.[19] The residue was treated with charcoal and filtered while hot (gravity filtration, stemless funnel). The filtrate chilled thoroughly yielded 104 g. (85%) of 1,5-dimethyltetrazole as white, sugar-like crystals, mp. 70-71°, lit. mp. 71.8-72.6°.[2]

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REFERENCES

1. German Patent 538,981, November 11, 1926, to Knoll A.-G. Chemische Fabriken; British Patent 280,529, November 10, 1926, to A. Boehringer.

2. J. M. Markgraf, W. T. Bachman, and D. P. Hollis, J. Org. Chem., 30, 3472 (1965).

3. D. M. Bowers, R. H. Erlich, A. Policec, and A. I. Popov, J. Inorg. Nucl. Chem., 33, 81 (1971).

4. 1,5-Dimethyltetrazole has also been prepared in 24% yield by reaction of hydrazoic acid with the imide chloride, MeC(Cl)=NMe, obtained by reaction of N-methylacetamide with phosphorus pentachloride: E. K. Harvill, R. M. Herbst, E. C. Schreiner, and C. W. Roberts, J. Org. Chem., 15, 662 (1950).

5. In our hands, the use of sodium hydroxide often gave a liquid product containing much unreacted benzenesulfonyl chloride and difficult to crystallize and purify, while with pyridine no such difficulty was encountered.

6. The use of isolated sulfonic acid esters of oximes is described in the patent literature (ref. 1); but later workers (ref. 2,3) have carried out the reaction with the esters generated *in situ*, with fair to poor results.

7. Although the method is claimed to be widely applicable,[1] in our experience marked difference in the stabilities and reactivities of O-sulfonyl oximes make it necessary to work out optimum conditions individually in many cases.

8. W. L. Semon, "Organic Syntheses," Coll. Vol. I, H. Gilman, ed., Second Ed., A. H. Blatt, ed., Wiley, New York, 1932, p. 318. Acetoxime may also be prepared readily from acetone, 18% aqueous sodium hydroxide and commercially available hydroxylamine hydrochloride. An equivalent amount of a wet product (about 95% pure) may be used in this step.

9. If the temperature is allowed to climb much above 30°, an uncontrollable exothermic decomposition sets in.

10. Samples of acetoxime benzenesulfonate kept at room temperature have undergone vigorous exothermic decomposition. While the material may be kept under refrigeration, prolonged storage of large samples is inadvisable.

11. P. Oxley and W. F. Short, J. Chem. Soc., 1948, 1514.

12. Wet methanol recovered from a previous run may be used but then it should be supplemented with 100-150 ml. of fresh methanol, and a correspondingly smaller amount of water should be used with the sodium azide, which may be added as a slurry with 100-150 ml. of water.

13. The use of larger amounts of material than described here is not recommended, because of difficulty in controlling the exothermic reaction.

14. Prior to distillation, the solution should be tested for acidity with pH paper. If acidic, it should be neutralized with sodium hydroxide to prevent the generation of explosive and toxic hydrazoic acid. The volume of distillate (1100-1200 ml.) assumes no vapor loss during the reaction and subsequent distillation. In any case, care should be taken not to overheat the residue in the flask, as some decomposition may occur.

15. Evaporation to dryness may be done on a steam bath and is hastened by occasional thorough cooling of the residue and removal of crystallized solids by filtration with suction and their further drying in the air at ambient temperature. Alternatively, a rotary vacuum evaporator may be used.

16. In the early extractions, there is a tendency for the pores of the Büchner funnel to become clogged through flash evaporation of the hot benzene. This can be prevented by pinching off the hose leading to the aspirator as soon as a vacuum has been established in the filtering flask. The filtration should be done in a hood with care to avoid inhaling vapors of the very toxic benzene.

17. In production of 1,5-dimethyltetrazole on a large scale, the second benzene extract would be used to extract a second 360-g portion of solids (Portion B), and the third benzene extract would be used to extract Portion B a second time and then a third, fresh portion (Portion C), etc., so that each portion of solids is extracted five times, and only the last time with fresh benzene. The senior author has carried out these systematic extractions on kg-sized portions of solids in a 5-l. flask for the production of several kilograms of 1,5-dimethyltetrazole. The extraction might also be carried out with a Soxhlet extractor with an electrically heated solids chamber. Chloroform has been used for the extraction (ref. 2) but seems to have no advantage over the less expensive benzene.

18. The recovered benzene may be reused, if desired.

19. While there have been no reports of explosions from heating 1,5-dimethyltetrazole, suitable precautions should be taken against damage in the event of an explosion at this stage, as benzenesulfonyl azide and other explosive azo compounds are likely contaminants.

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