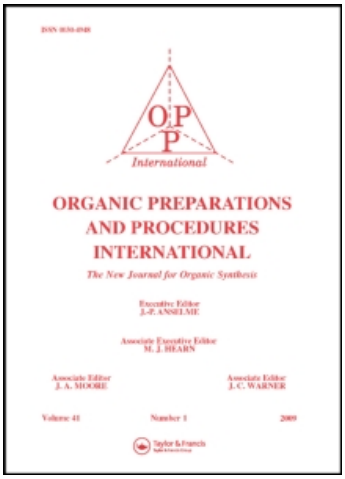

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A CONVENIENT SYNTHESIS OF PHTHALAZINE

S. D. Carter[a]; G. W. H. Cheeseman[a]
[a] Chemistry Department, Queen Elizabeth College, London

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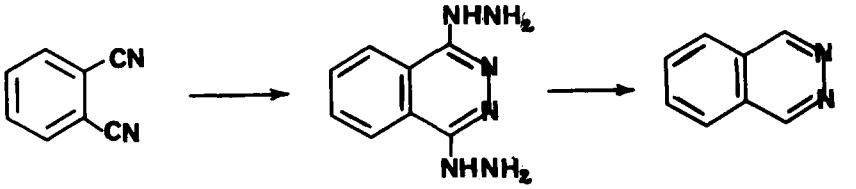
A CONVENIENT SYNTHESIS OF PHTHALAZINE

S. D. Carter and G. W. H. Cheeseman*
Chemistry Department,
Queen Elizabeth College, London W8 7AH

Although phthalazine may be prepared in almost quantitative yield by condensation of phthalaldehyde with hydrazine hydrate,[1] the usefulness of this method of preparation is limited by the availability of the dialdehyde. Phthalaldehyde has been prepared from o-xylene by bromination and hydrolysis of the resulting tetrabromo compound[2] and from naphthalene by ozonolysis.[3]

We now report an alternative two-step synthesis of phthalazine starting from phthalonitrile. Reaction of the dinitrile with hydrazine hydrate in dioxane and acetic acid gives an 82% yield of 1,4-dihydrazinophthalazine[4] which is oxidised to phthalazine with molecular oxygen. The use of cupric sulphate or silver oxide as alternative oxidising agents gives lower yields of product. Our results are therefore in accord with those of Albert and Catterall[5] who recommend oxygen as the best reagent for the oxidation of hydrazino compounds of this type.



The overall yields of phthalazine based on o-xylene, naphthalene or phthalonitrile are in each case about 60%, but we suggest our method is to be preferred in view of its simplicity and the avoidance of noxious chemicals.

EXPERIMENTAL

1,4-Dihydrazinophthalazine. - This was prepared by the method of Reynolds et al.[4] The dihydrazino compound was crystallised from water to give a product, mp. 187-190° (dec.) in 82% yield, lit.[4] mp. 190° (dec.).

Phthalazine. - Oxygen (CO_2 free) was bubbled through a stirred suspension of the dihydrazino compound (19.0 g., 0.1 mole) in ethanol (1250 ml.) and 10N sodium hydroxide (100 ml), until all the orange starting material had disappeared (about 4 hr.). Ethanol was removed from the deep purple reaction mixture under reduced pressure, water (150 ml.) was added to the residue and the pH adjusted to 9 with concentrated hydrochloric acid. The product was extracted into methylene chloride and the combined extracts dried over sodium sulphate. The residue obtained after evaporation of solvent, gave on vacuum sublimation, 9.3 g. (71%) of phthalazine, mp. 88-89°, lit.[1] mp. 90-91°.

An 81% yield of phthalazine was obtained from an oxidation on a 0.01 molar scale. Oxidation with silver oxide[6] or cupric sulphate[5] using literature procedures gave yields of 32 and 27%, respectively.

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