

A Synthesis of Amphetamine

Amphetamine can be obtained in a 30% yield in a one step synthesis by refluxing phenylacetone in ethanol with ammonia, aluminium grit, and a small quantity of mercuric chloride.

In the course of our educational program in pharmacology, literature research was performed on the synthesis of amphetamine (α -methyl-phenylethylamine) and pervitin (N, α -dimethylphenylethylamine). We were surprised not to find a synthesis for amphetamine similar to the one described for pervitin by "Laboratories Amido."¹ By trying out this reaction procedure for amphetamine it was found that the yield of the reaction was not as high as for pervitin (30% and 70%, respectively). However the easiness of the procedure makes this method worthwhile.

Experimental

A mixture of 40 g (0.3 mole) phenylacetone, 200 ml ethanol, 200 ml 25% ammonia, 40 g (1.5 mole) AL-grit and 0.3 g (0.001 mole) HgCl₂ is warmed with vigorous stirring until reaction takes place, after which warming is stopped immediately. Cooling should be applied if the reaction becomes too violent. When the violence of the reaction has diminished, the mixture is refluxed with vigorous stirring for about 2 hr, concentrated *in vacuo* to 200 ml and poured into ice water, alkalized with 120 g KOH, and extracted with ether. The extractions are treated with 20% HCl, the resulting water layer alkalized and extracted with 150 ml ether. The organic layer is dried over Na₂SO₄, the ether evaporated, and the residue distilled *in vacuo*. Yield: 12.5 g (0.09 mol). n_D^{26} : 1.5182 (lit.²: 1.518). Preparation of amphetaminesulfate yielded 96–98% product with a purity of 99.2–99.8% according to the USP.

¹ Fr. M2.782 (Cl.A 61k, C07c) Oct. 5, 1964, c.f. C.A. 62, 5228c.

² Handbook of Chemistry and Physics, 51st ed, The Chemical Rubber Co., Cleveland, Ohio, 1970–1971.

B. H. Groot Wassink
A. Duijndam
A. C. A. Jansen

Department of Pharmacology
University of Leiden
Leiden, The Netherlands