



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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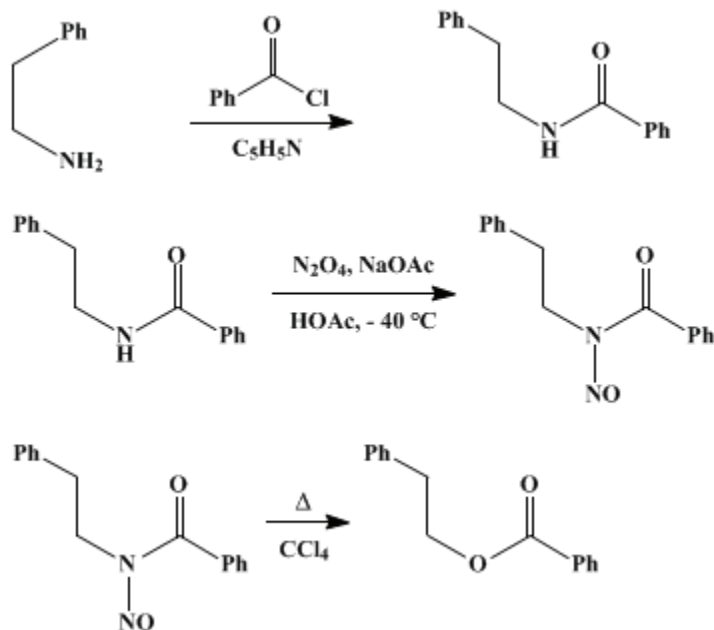
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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DEAMINATION OF AMINES. 2-PHENYLETHYL BENZOATE VIA THE NITROSOAMIDE DECOMPOSITION

[Benzoic acid, 2-phenylethyl ester]



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1. Procedure

Caution! Dinitrogen tetroxide is extremely toxic and should only be handled in an excellent hood.

A. *N*-(2-Phenylethyl)benzamide. To a solution of 12.1 g. (0.10 mole) of 2-phenylethylamine and 7.9 g. (0.10 mole) of pyridine in a 250-ml. Erlenmeyer flask immersed in an ice bath is added, slowly with stirring, 15.5 g. (0.11 mole) of benzoyl chloride. The resulting crystalline mixture is extracted with chloroform and the chloroform solution washed with water, 5% hydrochloric acid, 5% sodium hydroxide, water, and dried. The solvent is removed under reduced pressure to yield 20–22 g. (89–98%) of the crude amide, m.p. 100–110°, which is of sufficient purity for use in the next step. If desired, however, the crude product may be recrystallized from 95% ethanol, m.p. 115–116°.

B. *N*-Nitroso-*N*-(2-phenylethyl)benzamide. A solution of 10.4 g. (0.046 mole) of the crude *N*-(2-phenylethyl)benzamide, 7.36 g. (0.09 mole) of anhydrous sodium acetate, and 50 ml. of glacial acetic acid is placed in a 250-ml. Erlenmeyer flask equipped with a drying tube, and the mixture is cooled to the crystallization point of the acetic acid (Note 1). A solution of dinitrogen tetroxide (Note 2), (Note 3) in glacial acetic acid (85 ml. of a solution approximately 1M in N₂O₄) is then added with stirring. The reaction mixture is allowed to warm to about 15° (15 minutes), and then it is poured into a mixture of ice and water. The yellow solid nitroso derivative is dissolved in 75 ml. of carbon tetrachloride, and this solution is washed with 5% sodium bicarbonate, water, and dried. The solution is used directly in the next step.

If the nitroso derivative is desired, the yellow solid is separated by filtration, washed with water, 5% sodium bicarbonate solution, water, and dried under reduced pressure at room temperature. The solid is recrystallized from ether to give yellow needles of pure nitrosoamide; yield 7.5 g. (64%), m.p. 57–58°

(dec.).

C. *2-Phenylethyl benzoate*. The carbon tetrachloride solution of *N-nitroso-N-(2-phenylethyl)benzamide* (Note 4) and 0.1 g. of sodium carbonate (Note 5) are placed in a 200-ml. round-bottomed flask equipped with a condenser, and the mixture is heated under reflux for 24 hours. The evolution of nitrogen ceases, and the yellow color of the nitrosoamide weakens or disappears near the end of this period. The solution is washed with 5% sodium hydroxide solution, water, and dried. The solvent is removed under reduced pressure and the *2-phenylethyl benzoate* distilled; b.p. 139–142° (1 mm.), yield 5.8–6.1 g. [56–59% based on *N-(2-phenylethyl)benzamide*].

2. Notes

1. Carbon tetrachloride, methylene chloride, and other solvents may be used in this reaction. In these cases it is profitable to cool the reaction mixture to -40° or lower and then allow the mixture to warm to 10° after the dinitrogen tetroxide has been added.
2. Dinitrogen tetroxide (nitrogen dioxide) is available from the Matheson Company, Inc., East Rutherford, New Jersey.
3. Dinitrogen tetroxide is a *poisonous gas* and should only be handled in a well-ventilated hood. The boiling point of dinitrogen tetroxide is 21° , and it is convenient to condense a given volume (or weight, density = 1.5 g./ml. at 0°) from a cylinder of dinitrogen tetroxide and to pour the liquid into the required amount of solvent, or into the reaction mixture directly at temperatures below *ca.* -20° . Impure dinitrogen tetroxide, which is green because of the presence of lower oxides of nitrogen, may also be used.
4. Any nonreactive solvent may be used, but excessive temperatures favor the concurrent elimination reaction.
5. The sodium carbonate may be omitted if it is desired to titrate the acid formed in the reaction. The carbonate prevents denitrosation (observed in a few cases).

3. Discussion

The nitrosation of amides may also be carried out with nitrosyl chloride.² Related methods of deamination of aliphatic amines are the triazene³ and nitrous acid methods.⁴

4. Merits of the Preparation

Dinitrogen tetroxide is the most versatile of the nitrosating reagents and, in addition, it is readily available. The nitrosoamide method of deamination gives far superior yields and much less skeletal isomerization than the nitrous acid method (which is essentially limited to aqueous media), and it leads to a greater retention of optical activity than the triazene method.³ In general, the nitrosoamide decomposition proceeds with retention of configuration.^{5,6}

The method outlined here works well for amides of primary carbinamines. For amides of secondary carbinamines, lower temperatures must be used for the nitrosation step ($\sim 0^{\circ}$), and solvents such as methylene chloride are used in place of the acetic acid (the amide need not be completely soluble in the solvent); the procedure of White and Aufdermarsh⁵ used for a trimethylacetamide is recommended in such a case. Nitrosoamides of tertiary carbinamines are very unstable, and the "salt method" of preparation is suggested for these compounds.⁶

References and Notes

1. Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218.
2. H. France, I. M. Heilbron, and D. H. Hey, *J. Chem. Soc.*, 369 (1940).
3. E. H. White and H. Scherrer, *Tetrahedron Lett.*, 758 (1961).
4. F. C. Whitmore and D. P. Langlois, *J. Am. Chem. Soc.*, **54**, 3441 (1932).
5. E. H. White and C. A. Aufdermarsh, Jr., *J. Am. Chem. Soc.*, **83**, 1174 (1961).
6. E. H. White and J. E. Stuber, *J. Am. Chem. Soc.*, **85**, 2168 (1963).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

dinitrogen tetroxide

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

sodium acetate (127-09-3)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

sodium bicarbonate (144-55-8)

sodium carbonate (497-19-8)

carbon tetrachloride (56-23-5)

nitrogen (7727-37-9)

benzoyl chloride (98-88-4)

pyridine (110-86-1)

nitrogen dioxide (10102-44-0)

methylene chloride (75-09-2)

nitrosyl chloride (2696-92-6)

2-phenylethylamine (64-04-0)

trimethylacetamide (758-96-3)

triazene

2-Phenylethyl benzoate,
Benzoic acid, 2-phenylethyl ester (94-47-3)

N-(2-Phenylethyl)benzamide (3278-14-6)

N-Nitroso-N-(2-phenylethyl)benzamide

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