One-pot synthesis of *rac*-1,2-diphenylethylene-1,2-diamine

E. A. Mistryukov

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (095) 135 5328. E-mail: secretary@ioc.ac.ru

Derivatives of 1,2-diphenyl-1,2-ethylenediamine enantiomers ((*R*,*R*)- and (*S*,*S*)-**1**) are used as chiral controllers and catalysts in a series of various reactions (see Refs. 1—3 and references cited herein). The main difficulty in obtaining these valuable compounds is to synthesize the corresponding racemic compound (*rac*-**1**), whose enantiomeric splitting as salts of tartaric acids is easy.[3—5] Among numerous published syntheses of diamine *rac*-**1**, the recently modified[2] synthesis from benzaldehyde and liquid ammonium is the best method in the present time. It proceeds through the so-called hydrobenzamide (**2**), amarine (**3**), and isoamarine (**4**). In this work we found that this synthesis can substantially be simplified due to the use of some earlier unknown mechanistic features of the process.

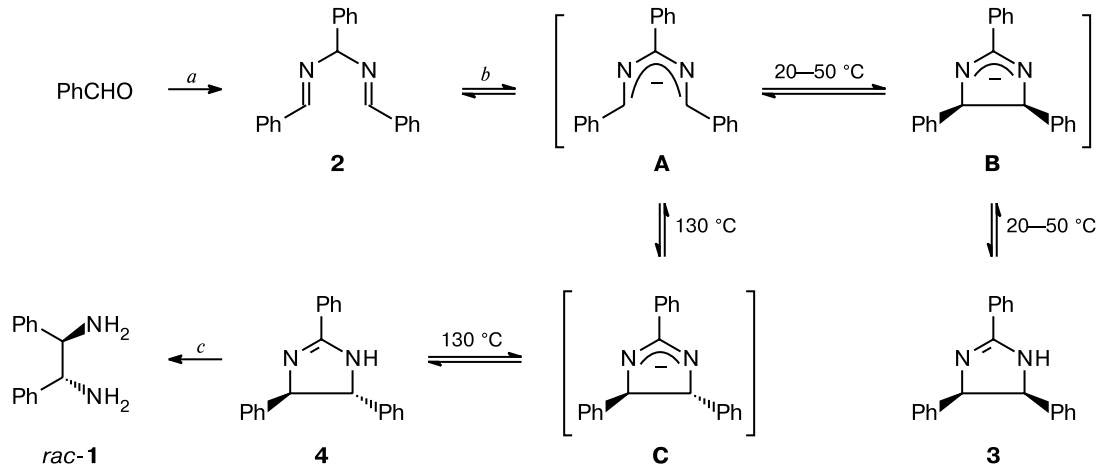
Starting 1,3,5-triphenyl-2,4-diazapenta-1,4-diene (hydrobenzamide, **2**) can most conveniently be obtained in significant amounts from benzaldehyde using ammonia under pressure (~7 atm). This affords an intermediate oily product, presumably 2,4,6-triphenyl-1,3,5-hexahydrotriazine (see Ref. 6), which is transformed into crystalline hydrobenzamide **2** after removal of excessive ammonia.

The cyclization of hydrobenzamide **2** into amarine **3** by thermolysis at 130 °C [7] or treatment with stoichiometric amounts of strong bases was described.[8] We have unexpectedly found that this cyclization occurs exothermically and in ~100% yield when catalytic (5—12 mol.%) quantities of sodium hydroxide in dimethylsulfoxide are used. It is most likely that the cyclization proceeds, under all conditions, through the diazapentadienide anion (**A**), whose formation is favored (under our conditions) by a highly polar solvent (Scheme 1). Anion **A** is rapidly cyclized to diazaallylic anion **B**, whose protonation affords amarine **3**.

In the presence of a catalytic amount of base only, the transformations of compounds **2** and **3** proceeding through anions **A** and **B** are reversible. When the temperature increases to 130 °C, the thermodynamically more stable isoamarine **4** is formed (through the slowly formed anion **C**) (a similar mechanism has been described[9]). Previously,[7,8] the isomerization of amarine **3** to isoamarine **4** by a base at high temperature required a separate step.

Thus, the one-pot transformation of hydrobenzamide **2** into isoamarine **4** was performed. The reductive splitting of isoamarine **4** under the optimized conditions[2] com-

Scheme 1



Reagents and conditions: *a*. NH_3, 20 °C; *b*. NaOH (cat.), DMSO; *c*. Al/Hg, H_2O.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2142—2143, December, 2002.

1066-5285/02/5112-2308 $27.00 © 2002 Plenum Publishing Corporation

pletes the practical method proposed for the synthesis of diamine *rac*-**1** from benzaldehyde in 70% overall yield.

The ^{1}H NMR spectrum was recorded on a Bruker AC-200 instrument (200.13 MHz). TLC analyses were carried out on Silufol plates using Et_2O with several droplets of aqueous ammonia (visualized by an aqueous solution of $KMnO_4$). Melting points were determined on a Kofler heating stage. Reaction mixtures were concentrated on a rotary evaporator at 30—40 °C in a vacuum of a water jet pump.

(*E*,*E*)-1,3,5-Triphenyl-2,4-diazapenta-1,4-diene (2). A solution of benzaldehyde (50.7 mL, 53.1 g, 0.50 mol) in THF (50 mL) was placed in a pressure-designed vessel connected through a capillary with the ammonia cylinder. The valve on the cylinder was opened, and the system was left for ~20 h. The vessel was disconnected from the cylinder, and the pressure (~7 atm) was slowly brought to atmospheric. The aqueous (upper) layer was removed from the remaining bilayer mixture. The bottom layer after concentration *in vacuo* crystallized and gave hydrobenzamide **2**. The product thus obtained in ~100% yield (49.7 g) was used in the next step without purification.

***rac-trans*-2,4,5-Triphenyl-4-imidazoline (isoamarine, 4).** Sodium hydroxide in pellets (~0.3 g, 7 mmol) was added (as one portion) to a suspension of hydrobenzamide **2** (16.5 g, 55.3 mmol) in DMSO (25 mL) in argon, and the mixture was vigorously stirred. After ~5 min, the mixture was warmed to ~50 °C, and after ~1 h it cooled to room temperature. According to TLC data, amarine **3** (R_f 0.50) formed in ~100% yield and could be isolated. Then the reaction mixture was heated to 130 °C for 3 h. TLC analysis showed only isoamarine **4** (R_f 0.70). The mixture was cooled to ~80 °C and successively treated with EtOH (30 mL) and a concentrated aqueous solution of NH_4OH (30 mL, gradually poured). The resulting mixture was left for ~20 h. The precipitate of isoamarine **4** was filtered off, washed on the filter with Pr^iOH (30 mL), and dried. The yield was 14.9 g (90%), m.p. 198—200 °C.[7,8] Further the product was used without additional purification.

***rac*-1,2-Diphenylethylene-1,2-diamine (*rac*-1).** A mixture of isoamarine **4** (10 g, 33.5 mmol), an aluminum foil as pieces 0.5 cm^2 each (2.7 g, 100 mmol), $HgCl_2$ (0.6 g, 2.2 mmol), and THF (60 mL) was stirred in an argon atmosphere for 15 min. Then a solution of water (1.8 mL, 100 mmol) in THF (5 mL) was added for 1.5 h. After 2 h, water (5 mL) was added, and the mixture was left for ~20 h. A concentrated aqueous solution of NH_4OH (10 mL) was added to the mixture. After 24 h, the mixture was filtered, and the filtrate was concentrated. The residue on the filter was washed with the distillate obtained by evaporation of the above filtrate, and the new filtrate was also concentrated. The combined residue was concentrated (oil), dissolved on heating in a mixture of MeOH (30 mL), concentrated hydrochloric acid (15 mL), and water (10 mL), and cooled. The crystalline precipitate of diamine dihydrochloride was filtered off, washed on the filter with dioxane, and dried. The yield of *rac*-**1**·2HCl was 7.88 g (82.5%). To isolate the base, the resulting salt in THF was treated with an excess of a 10 *M* aqueous solution of NaOH, the suspension was concentrated to dryness at 80 °C, and the residue was extracted with boiling petroleum ether to obtain *rac*-**1** in 77.6% yield (5.52 g), m.p. 82 °C.[3,7] ^{1}H NMR (DMSO-d_6), δ: 1.70 (s, 4 H, 2 NH_2); 3.90 (s, 2 H, 2 CH); 7.20 (m, 10 H, 2 Ph).

References

1. D. Luset, T. Le Grall, and C. Miosskowski, *Angew. Chem., Int. Ed. Eng.*, 1998, **37**, 2580.
2. E. J. Corey and F. N. M. Kuhnle, *Tetrahedron Lett.*, 1997, **38**, 8631.
3. M. A. Lapitskaya and K. K. Pivnitskii, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 101 [*Russ. Chem. Bull.*, 1997, **46**, 96 (Engl. Transl.)].
4. O. F. Williams and J. C. Bailar, *J. Am. Chem. Soc.*, 1959, **81**, 4464.
5. I. Lifschitz and J. G. Bos, *Rec. Trav. Chim. Pays-Bas*, 1940, **59**, 173.
6. C. Harries and G. Lenart, *Liebigs Ann. Chem.*, 1915, 410.
7. O. F. Williams and J. C. Bailar, *J. Am. Chem. Soc.*, 1959, **81**, 4466.
8. D. H. Hunter and S. K. Sim, *Can. J. Chem.*, 1972, **50**, 669.
9. J. G. Smith and I. Ho, *J. Org. Chem.*, 1972, **37**, 653.

Received September 27, 2002