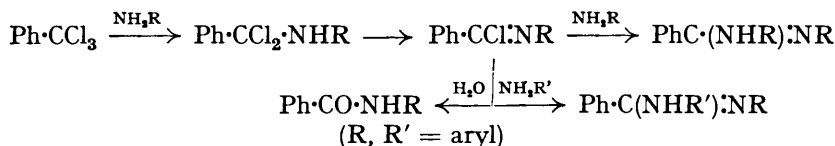


182. Amidines. Part I. The Synthesis of Symmetrical and Unsymmetrical Benzenyldiphenylamidines, and New Reactions of Amidines.

By S. P. JOSHI, A. P. KHANOLKAR, and T. S. WHEELER.

Synthesis of s-Benzyldiphenylamidines.—Limpricht (*Annalen*, 1865, **135**, 82; cf. Doebner, *Ber.*, 1882, **15**, 233; *Annalen*, 1883, **217**, 241) found that s-benzyldiphenylamidine could be obtained directly from benzotrichloride and aniline, but, although the usual methods for the production of amidines involve two or three stages from the initial amines, this reaction does not seem to have been further investigated, possibly because it tends to be vigorous unless properly controlled. It has now been found that, in presence of nitrobenzene, benzotrichloride reacts smoothly with a number of primary arylamines to give the corresponding s-benzyldiphenylamidines in yields which range up to 85%. s-Benzenyldi-p- and -m-nitrophenyl-, -m-tolyl-, -p-chlorophenyl-, and -s-tribromophenyl-amidine have thus been prepared, but satisfactory results could not be obtained with benzidine, m-nitro-p-toluidine, o-nitro-p-toluidine, p-nitro-o-toluidine, and 2:4-dinitroaniline. With o-nitroaniline a product of unknown constitution was obtained which is being further investigated.

The reaction probably involves the intermediate formation of a benzanilideimidochloride, for, if moisture is present, a benzanilide is formed, and further, a small yield of the unsymmetrical amidine, benzenyl-N-p-chlorophenyl-N'-phenylamidine,* has been obtained from benzotrichloride, p-chloroaniline, and aniline.



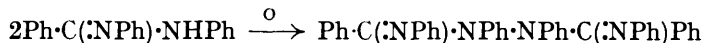
During the work it was observed that benzotrichloride reacts with acetanilide to give s-ethenyldiphenylamidine and benzanilide.

Synthesis of Unsymmetrical Benzenyldiphenylamidines.—For a study of the tautomerism of unsymmetrically substituted benzenylamidines, the following have been synthesised by the method of Hill and Cox (*J. Amer. Chem. Soc.*, 1926, **48**, 3216):—(A) benzenyl-N-p-chlorophenyl-N'-phenylamidine (see above), (B) benzenyl-N-p-bromophenyl-N'-phenylamidine, (C) benzenyl-N-p-chlorophenyl-N'-p-methoxyphenylamidine, (D) benzenyl-N-p-chlorophenyl-N'-p-ethoxyphenylamidine, (E) benzenyl-N-p-chlorophenyl-N'-p-tolylamidine, (F) benzenyl-N-p-nitrophenyl-N'-m-nitrophenylamidine, (G) benzenyl-N-p-nitrophenyl-N'-p-tolylamidine, (H) benzenyl-N-p-nitrophenyl-N'-m-4-xylylamidine, (I) benzenyl-N'-p-chlorophenyl-N-p-nitrophenylamidine, (J) benzenyl-N'-p-bromophenyl-N-p-nitrophenylamidine, and (K) p-nitrobenzenyl-N-p-nitrophenyl-N'-phenylamidine.

* This compound is also obtained by direct chlorination of s-benzyldiphenylamidine.

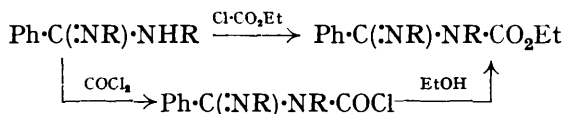
(A) on methylation gives *benzenyl-N-p-chlorophenyl-N'-phenyl-N-methylamidine* and *benzenyl-N'-p-chlorophenyl-N-phenyl-N-methylamidine*; (B) similarly gives *benzenyl-N-p-bromophenyl-N'-phenyl-N-methylamidine* and *benzenyl-N'-p-bromophenyl-N-phenyl-N-methylamidine*. The four methyl-amidines were characterised by their synthesis from the corresponding methylaniline and benzanilideimidochloride.

Oxidation of Amidines.—*s*-Benzenyldiphenylamidine on treatment with acid potassium permanganate gives a well-crystallised product, the analytical results for which show it to be *s-diphenyldi(phenyliminobenzyl)hydrazine* :



s-Benzenyldi-*p*- and -*m*-nitrophenylamidine give similar products.

Condensation of Amidines with Ethyl Chloroformate.—*s*-Benzenyldi-*m*-nitrophenylamidine condenses smoothly with ethyl chloroformate in benzene solution in presence of sodium hydrogen carbonate to give *N-carbethoxy-s-benzenyldi-m-nitrophenylamidine*, the structure of which is confirmed by the fact that it is also obtained by the action of alcohol on the unstable product formed by condensing carbonyl chloride with the amidine :



Similar carbethoxy-compounds were obtained from *s*-benzenyldi-*p*-nitrophenyl, -*m*-tolyl, and -*p*-chlorophenyl-amidines.

EXPERIMENTAL.

* Indicates micro-analysis by Dr. Schoeller. † Indicates crystallisation from alcohol.

Synthesis of s-Benzenyldiphenylamidines.—*s*-Benzenyldi-*p*-nitrophenylamidine. Benzotrichloride (19 g.), *p*-nitroaniline (41 g.), and nitrobenzene (60 c.c.) were heated (calcium chloride guard) at 165° until evolution of hydrogen chloride had ceased. After 12 hours the precipitated hydrochloride was washed with acetone, the residue (34 g.) dissolved in pyridine, and the base precipitated by water; it separated from acetone in yellow crystals, m. p. 190° (Found : N, 15.2. C₁₉H₁₄O₄N₄ requires N, 15.5%). The amidine was also obtained by heating benzo-*p*-nitroanilideimidochloride [from benzo-*p*-nitroanilide (12 g.) and phosphorus pentachloride (11 g.)], *p*-nitroaniline (4.2 g.), and diethylaniline (11.5 g.) at 100° for 3 hours; the product was poured into hydrochloric acid (20%), and the precipitated hydrochloride (7 g.) treated with pyridine. The hydrochloride (action of hydrogen chloride on the amidine in benzene) sintered at 265° (Found : Cl, 8.9. C₁₉H₁₄O₄N₄·HCl requires Cl, 8.9%). The acetyl derivative † (acetic anhydride-fused sodium acetate) had m. p. 182—183° (Found : * N, 14.4. C₂₁H₁₆O₅N₄ requires N, 13.9%). The *N*-methyl derivative was obtained by heating the amidine (5 g.) in a sealed tube for 6 hours at 120° with methyl iodide (5 c.c.). The product was extracted with acetone, and the resulting solution treated with ammonia to give the base (3.8 g.), which was crystallised from benzene-light petroleum; m. p. 188° (Found : * N, 14.9. C₂₀H₁₆O₄N₄ requires N, 14.9%).

s-Benzenyldi-*m*-nitrophenylamidine † (prepared as described for the *p*-derivative) formed yellow needles, m. p. 147—148° (Found : N, 15.2%). The hydrochloride (from the concentrated acid and the amidine in acetone) sintered at 275° (Found : Cl, 9.2%). The sulphate (from the concentrated acid and the amidine in ether) had m. p. 196° (Found : S, 6.9. C₁₉H₁₄O₄N₄·H₂SO₄ requires S, 6.9%), the acetyl derivative † (acetic anhydride) m. p. 135—136° (Found : * N, 14.1%), the benzoyl derivative † (benzoyl chloride-pyridine) m. p. 195—196° (Found : * N, 12.2. C₂₆H₁₈O₅N₄ requires N, 12.0%), and the methyl derivative † (see *p*-compound) m. p. 114—115° (Found : * N, 15.1%).

s-Benzenyldi-*m*-tolylamidine † was prepared (yield, 9 g.) from *m*-toluidine (32 g.), benzotrichloride (19 g.), and nitrobenzene (60 c.c.); m. p. 135° (Found : * N, 9.4. C₂₁H₂₀N₂ requires N, 9.3%). The *N*-methyl derivative † had m. p. 90° (Found : * N, 9.2. C₂₂H₂₂N₂ requires N, 8.9%).

s-Benzenyldi-*p*-chlorophenylamidine, † from *p*-chloroaniline (40 g.), benzotrichloride (30 g.), and nitrobenzene (25 c.c.), had m. p. 143° (Found : * N, 8.0; Cl, 20.8. C₁₉H₁₄N₂Cl₂ requires N, 8.2; Cl, 20.8%); yield, 78%. The amidine was also prepared (1) by Hill and Cox's method (*loc. cit.*) from benzo-*p*-chloroanilide (11.5 g.), phosphorus pentachloride (10 g.), and *p*-chloro-

aniline (6.1 g.); yield, 55%; (2) from *p*-chloroaniline (1 mol.), diethylaniline (2.5 mols.), and benzo-*p*-chloroanilideimidochloride (1 mol.; the imidochloride was prepared from benzo-*p*-chloroanilide and excess of thionyl chloride; b. p. 180—185°/5 mm.). The *amidine hydrochloride* charred above 250° (Found: Cl, 27.9. $C_{19}H_{14}N_2Cl_2 \cdot HCl$ requires Cl, 28.2%). The *sulphate* had m. p. 201° (Found: Cl, 15.9. $C_{19}H_{14}N_2Cl_2 \cdot H_2SO_4$ requires Cl, 16.2%), the *benzoyl derivative* † m. p. 155—156° (Found: Cl, 15.8. $C_{26}H_{18}ON_2Cl_2$ requires Cl, 16.0%), and the *methyl derivative* † m. p. 153—154° (Found: Cl, 19.8. $C_{20}H_{16}N_2Cl_2$ requires Cl, 20.0%).

s-Benzenyldi-*s*-tribromophenylamidine was prepared (yield of hydrochloride, 22 g.) from *s*-tribromoaniline (34 g.), benzotrichloride (10 g.), and nitrobenzene (25 c.c.), and crystallised from acetone and acetic acid; m. p. 196—197° (Found: Br, 64.2. $C_{19}H_{10}N_2Br_6$ requires Br, 64.3%). The *acetyl derivative* (acetic anhydride-pyridine), m. p. 173—174°, was crystallised from acetone (Found: Br, 61.2. $C_{21}H_{18}ON_2Br_6$ requires Br, 60.9%), the *benzoyl derivative* (benzoyl chloride-pyridine), m. p. 235—237°, from acetic acid (Found: Br, 56.8. $C_{26}H_{14}ON_2Br_6$ requires Br, 56.5%), and the *methyl derivative*, m. p. 160—161°, from acetone (Found: Br, 62.9. $C_{20}H_{12}N_2Br_6$ requires Br, 63.2%).

Benzenyl-N-p-chlorophenyl-N'-phenylamidine † was obtained (yield, 0.5 g.) from benzotrichloride (3.9 g.), aniline (1.8 g.), *p*-chloroaniline (2.5 g.), and nitrobenzene (5 c.c.); m. p. 120—122°. Its constitution was confirmed (mixed m. p.) by comparison with the analysed product obtained by the Hill and Cox method (*loc. cit.*) from benzo-*p*-chloroanilide (2.5 g.), phosphorus pentachloride (2.5 g.), and aniline (1 g.) (Found: Cl, 11.4. $C_{19}H_{15}N_2Cl$ requires Cl, 11.6%). The *amidine* was also obtained by this method from benzanilide and *p*-chloroaniline, and by the imidochloride method from benzo-*p*-chloroanilideimidochloride (see above), aniline, and diethylaniline.

Chlorination of s-Benzenyldiphenylamidine.—A chloroform solution of *s*-benzenyldiphenylamidine (5.4 g.) obtained (78% yield) from aniline (27 g.), benzotrichloride (19 g.), and nitrobenzene (60 c.c.) was treated with chlorine (1.4 g.) at 0°. After 12 hours, the solvent was evaporated, and the residual hydrochloride was washed with acetone and treated with ammonia to separate the free base.† A mixed m. p. determination showed it to be the monochloroamidine.

Benzenyl-N-p-chlorophenyl-N'-phenylamidine hydrochloride † had m. p. 260—262° (Found: * Cl, 20.7. $C_{19}H_{15}N_2Cl \cdot HCl$ requires Cl, 20.7%), and the *benzoyl derivative* † (benzoyl chloride-pyridine) m. p. 155—156° (Found: * N, 6.4. $C_{26}H_{18}ON_2Cl$ requires N, 6.8%).

Action of Benzotrichloride on Acetanilide.—The product obtained on heating benzotrichloride (90 g.) and acetanilide (135 g.) for 3 hours at 150° was dissolved in hot alcohol, and the solution diluted with water; benzanilide (35 g.; mixed m. p.) then separated. The aqueous-alcoholic filtrate was treated with dilute sodium hydroxide solution to precipitate *s*-ethenyldiphenylamidine (42 g.; mixed m. p.).

Synthesis of Unsymmetrical Benzenyldiphenylamidines.—The Hill and Cox method (*loc. cit.*) was used throughout. Phosphorus pentachloride (1.1 mols.) and a benzanilide derivative (1 mol.) were heated together in dry benzene; when reaction was complete the required arylamine (1—1.5 mols.) was added in the cold, and the mixture boiled under reflux for 4 hours. The amidine hydrochloride which separated (60—70% yield) was converted by means of ammonia into the free base. The hydrochloride was obtained by addition of concentrated hydrochloric acid to an acetone or alcohol solution of the base; the picrate separated from mixed alcoholic solutions of the components.

Benzenyl-N-p-bromophenyl-N'-phenylamidine † (from benzanilide and *p*-bromoaniline) had m. p. 123° (Found: Br, 22.8. $C_{19}H_{15}N_2Br$ requires Br, 22.8%). The *hydrochloride* sintered at 265—266° (Found: Cl + Br, 29.5. $C_{19}H_{15}N_2Br \cdot HCl$ requires Cl + Br, 29.8%).

Benzenyl-N-p-chlorophenyl-N'-p-methoxyphenylamidine † (from benzo-*p*-anisidine and *p*-chloroaniline) had m. p. 117—119° (Found: * C, 71.2; H, 5.1; * N, 8.0; Cl, 10.3. $C_{20}H_{17}ON_2Cl$ requires C, 71.3; H, 5.1; N, 8.3; Cl, 10.6%), the *hydrochloride* m. p. 260 (Found: * Cl, 19.2. $C_{20}H_{17}ON_2Cl \cdot HCl$ requires Cl, 19.0%), and the *picrate* † m. p. 165—166° (Found: * N, 12.1. $C_{30}H_{17}ON_2Cl \cdot C_6H_3O_7N_3$ requires N, 12.4%).

Benzenyl-N-p-chlorophenyl-N'-p-ethoxyphenylamidine † (from benzo-*p*-phenetidine and *p*-chloroaniline) had m. p. 95—98° (Found: Cl, 10.4. $C_{21}H_{19}ON_2Cl$ requires Cl, 10.1%), the *hydrochloride* m. p. 242—244° (Found: Cl, 18.7. $C_{21}H_{19}ON_2Cl \cdot HCl$ requires Cl, 18.3%), and the *picrate* † m. p. 147—148° (Found: * N, 11.9. $C_{21}H_{19}ON_2Cl \cdot C_6H_3O_7N_3$ requires N, 12.1%).

Benzenyl-N-p-chlorophenyl-N'-p-tolylamidine † (from benzo-*p*-toluidide and *p*-chloroaniline) had m. p. 134° (Found: Cl, 10.9. $C_{20}H_{17}N_2Cl$ requires Cl, 11.1%), the *hydrochloride* † m. p.

283° (decomp.) (Found : * Cl, 20.0. $C_{20}H_{17}N_2Cl$, HCl requires Cl, 19.9%), and the *picrate* † m. p. 189—190° (Found : * N, 12.6. $C_{20}H_{17}N_2Cl, C_6H_3O_7N_3$ requires N, 12.7%).

Benzenyl-N-p-nitrophenyl-N'-m-nitrophenylamidine † (from benzo-*m*-nitroanilide and *p*-nitroaniline) had m. p. 170° (Found : * N, 15.1. $C_{19}H_{14}O_4N_4$ requires N, 15.5%); the *hydrochloride* sintered at 238° (Found : Cl, 9.0. $C_{19}H_{14}O_4N_4, HCl$ requires Cl, 8.9%).

Benzenyl-N-p-nitrophenyl-N'-p-tolylamidine † (from benzo-*p*-toluidide and *p*-nitroaniline) had m. p. 159—160° (Found : * N, 12.8. $C_{20}H_{17}O_2N_3$ requires N, 12.7%); the *hydrochloride* † sintered at 258° (Found : Cl, 9.6. $C_{20}H_{17}O_2N_3, HCl$ requires Cl, 9.7%).

Benzenyl-N-p-nitrophenyl-N'-m-4-xylylamidine † (from benzo-*m-4*-xylidide and *p*-nitroaniline) had m. p. 143—144° (Found : * N, 12.1. $C_{21}H_{19}O_2N_3$ requires N, 12.2%); the *hydrochloride* sintered at 237° (Found : Cl, 9.6. $C_{21}H_{19}O_2N_3, HCl$ requires Cl, 9.3%).

Benzenyl-N'-p-chlorophenyl-N-p-nitrophenylamidine † (from benzo-*p*-chloroanilide and *p*-nitroaniline) had m. p. 174—175° (Found : * N, 11.8. $C_{19}H_{14}O_2N_3Cl$ requires N, 11.9%); the *hydrochloride* sintered at 272° (Found : Cl, 18.4. $C_{19}H_{14}O_2N_3Cl, HCl$ requires Cl, 18.3%).

Benzenyl-N'-p-bromophenyl-N-p-nitrophenylamidine † (from benzo-*p*-nitroanilide and *p*-bromoaniline) had m. p. 170—171° (Found : Br, 20.6. $C_{19}H_{14}O_2N_3Br$ requires Br, 20.2%); the *hydrochloride* sintered at 270° (Found : Cl + Br, 27.1. $C_{19}H_{14}O_2N_3Br, HCl$ requires Cl + Br, 26.7%).

p-Nitrobenzenyl-N-p-nitrophenyl-N'-phenylamidine (from *p*-nitrobenzanilide and *p*-nitroaniline) was crystallised from acetone-alcohol; m. p. 223° (Found : * N, 15.5. $C_{19}H_{14}O_4N_4$ requires N, 15.5%). The *hydrochloride* sintered at 250° (Found : Cl, 8.6. $C_{19}H_{14}O_4N_4, HCl$ requires Cl, 8.9%).

Methylation of Benzenyl-N-p-chlorophenyl-N'-phenylamidine.—The product obtained by heating the amidine (15 g.) and methyl iodide (15 c.c.) in a sealed tube for 6 hours at 105° was extracted with boiling acetone (200 c.c.), and the residue was dissolved in pyridine; *benzenyl-N-p-chlorophenyl-N'-phenyl-N-methylamidine*, † needles, m. p. 112°, was precipitated by addition of water to the pyridine solution. The constitution of the base was established by its synthesis from *p*-chloromethylaniline and benzanilideimidochloride in presence of diethylaniline; the m. p. of the separated methylation product was unchanged by addition of the synthetic product (Found : * C, 74.8; H, 5.4; * N, 8.4; Cl, 11.0. $C_{20}H_{17}N_2Cl$ requires C, 74.9; H, 5.3; N, 8.7; Cl, 11.1%). The *hydrochloride* † had m. p. 226° (Found : * Cl, 19.4. $C_{20}H_{17}N_2Cl, HCl$ requires Cl, 19.9%), and the *picrate* † m. p. 157—158° (Found : N, * 12.3; Cl, 6.6. $C_{20}H_{17}N_2Cl, C_6H_3O_7N_3$ requires N, 12.7; Cl, 6.5%).

Ammonia precipitated *benzenyl-N'-p-chlorophenyl-N-phenyl-N-methylamidine* from the acetone filtrate as an oil which solidified; after repeated crystallisation from alcohol to free it from its isomeride, it formed hexagonal plates, m. p. 102°, depressed to 83—95° on admixture with the isomeride of m. p. 112°. Its constitution was established by its synthesis (mixed m. p. comparison) from methylaniline and benzo-*p*-chloroanilideimidochloride in presence of diethylaniline (Found : * C, 74.8; 5.3; * N, 8.3%). The *picrate* † had m. p. 150—151° (Found : * N, 12.3%).

Methylation of Benzenyl-N-p-bromophenyl-N'-phenylamidine.—The procedure was the same as for the chloro-amidine. The hydriodide insoluble in acetone yielded *benzenyl-N-p-bromophenyl-N'-phenyl-N-methylamidine* † (constitution established by synthesis from *p*-bromomethylaniline and benzanilideimidochloride); needles, m. p. 123—124° (Found : * C, 65.9; H, 4.8; Br, 21.6. $C_{20}H_{17}N_2Br$ requires C, 65.8; H, 4.7; Br, 21.9%). The *picrate* † had m. p. 179—180° (Found : * N, 11.3. $C_{20}H_{17}N_2Br, C_6H_3O_7N_3$ requires N, 11.8%).

The acetone filtrate on basification gave *benzenyl-N'-p-bromophenyl-N-phenyl-N-methylamidine*, which after repeated crystallisation from alcohol formed sugar-like crystals, m. p. 120—121°, depressed to 98—112° by admixture with its isomeride. Its constitution was established by its synthesis from methylaniline and benzo-*p*-bromoanilideimidochloride (Found : * C, 65.5; H, 4.7; Br, 21.6%). The *picrate* † had m. p. 158—159° (Found : * N, 11.4%).

Oxidation of Amidines.—*s-Diphenyldi(phenyliminobenzyl)hydrazine.* Aqueous potassium permanganate (1% ; 450 c.c.) was added in small portions at 100° to *s*-benzenyldiphenylamidine (2.7 g.) dissolved in sulphuric acid (70% ; 175 c.c.). The resulting solution was diluted with water, and basified with aqueous ammonia to precipitate a mixture of the oxidation product and manganese hydroxide, from which the hydrazine *derivative* (1 g.) was extracted with acetone; m. p. 112° (Found : * C, 84.0; H, 5.0; * N, 10.6. $C_{38}H_{30}N_4$ requires C, 84.2; H, 5.5; N, 10.3%).

s-Di-p-nitrophenyldi-(p-nitrophenyliminobenzyl)hydrazine was similarly prepared. Most of the oxidation product separated on dilution of the reaction mixture with water, and was re-

crystallised from alcohol-acetone; m. p. 236° (Found : * C, 63.1; H, 3.4; N, 15.6. $C_{38}H_{26}O_8N_8$ requires C, 63.2; H, 3.6; N, 15.5%).

s-Di-*m*-nitrophenyldi-(*m*-nitrophenyliminobenzyl)hydrazine, crystallised from alcohol-acetone, had m. p. 262—264° (Found : * C, 63.5; H, 3.4%).

Condensation of Amidines with Ethyl Chloroformate.—*N*-Carbethoxy-*s*-benzenyldi-*m*-nitrophenylamidine.† (1) A solution (prepared at 0°) of ethyl chloroformate (2.2 g.) and benzenyldi-*m*-nitrophenylamidine (7.2 g.) in benzene with sodium hydrogen carbonate (2.4 g.) in suspension was kept for 12 hours at room temperature and filtered. The crude product (4.2 g.) which remained on evaporation of the filtrate had, after recrystallisation, m. p. 153° (Found : N, 13.1. $C_{22}H_{18}O_6N_4$ requires N, 12.9%).

(2) A solution (prepared at 0°) of carbonyl chloride (0.5 g.) and *s*-benzenyldi-*m*-nitrophenylamidine (2 g.) in toluene was kept for 12 hours and filtered from the separated amidine hydrochloride. The pasty residue obtained on evaporation of the filtrate gave on recrystallisation from alcohol the same carbethoxy-derivative (mixed m. p.) as was obtained by method (1).

N-Carbethoxy-*s*-benzenyldi-*p*-nitrophenylamidine † (method 1) had m. p. 169—170° (Found : * N, 12.8%), *N*-carbethoxy-*s*-benzenyldi-*m*-tolylamidine † (method 1) m. p. 94—95° (Found : * N, 7.8. $C_{24}H_{24}O_2N_2$ requires N, 7.5%), and *N*-carbethoxy-*s*-benzenyldi-*p*-chlorophenylamidine † (method 1) m. p. 118—119° (Found : Cl, 17.0. $C_{22}H_{16}O_2N_2Cl_2$ requires Cl, 17.2%).

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ROYAL INSTITUTE OF SCIENCE, BOMBAY.

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