Studies on the Syntheses of Azole Derivatives. Part IV (1). Novel Syntheses of 1-Benzylbenzimidazolines by Photolysis of *N*-Aryl-*N*-benzylcarbamoyl Azides [Studies on the Syntheses of Heterocyclic Compounds. Part CCCLXXVIII (1)].

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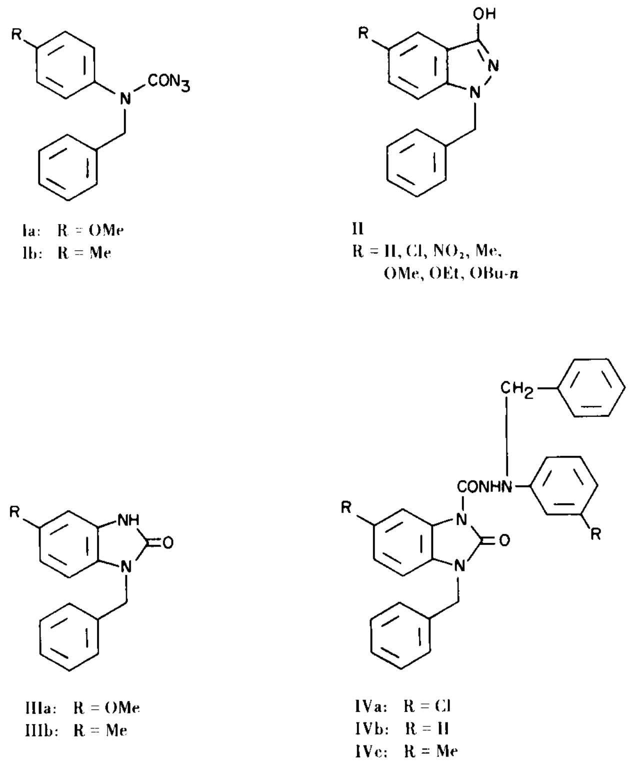
Photolysis of *N*-benzyl-*N*-(4-substituted-phenyl)carbamoyl azides (Ia and Ib) afforded *N*-benzylidene-*N'*-benzylhydrazines (XIIa and XIIb) and the debenzylated benzimidazolines (XIIIa and XIIIb).

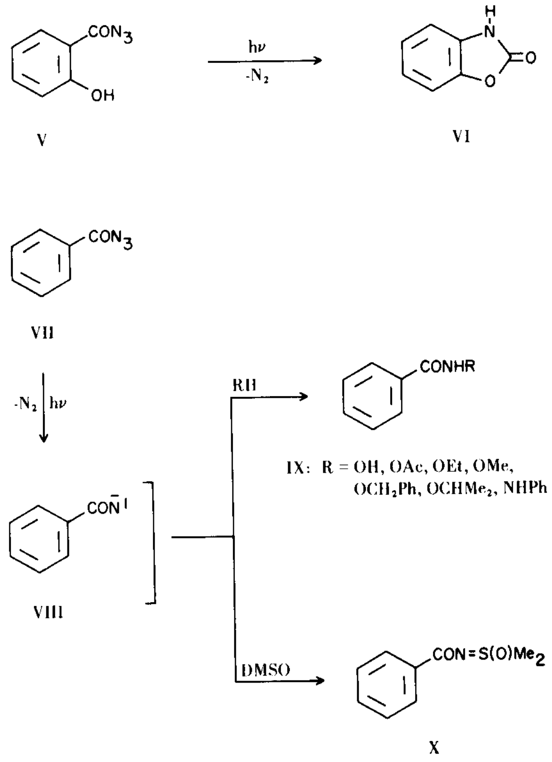
In previous papers (1,4a,4b) the syntheses of a number of 1-benzyl-3-hydroxy-1*H*-indazoles (II) and 1-benzylbenzimidazolin-2-ones (III and IV) by the thermal reaction of *N*-benzyl-*N*-(4-substituted-phenyl)carbamoyl azide (I) were reported. Although some interesting studies on the photolysis of aryl azides and acyl azides have been published (5a), no work on photolysis of carbamoyl azide has been reported.

CHART I



Horner and his co-workers (5b,5c,5d) reported that the irradiation of salicyloyl azide gave the product 2-benzoxazolidinone (VI), which formed by Curtius rearrangement, and, moreover, they described the formation of noncyclized products (IX and X) *via* benzoylnitrene (VIII) on the irradiation of benzoyl azide in the presence of trapping reagent.

CHART 2

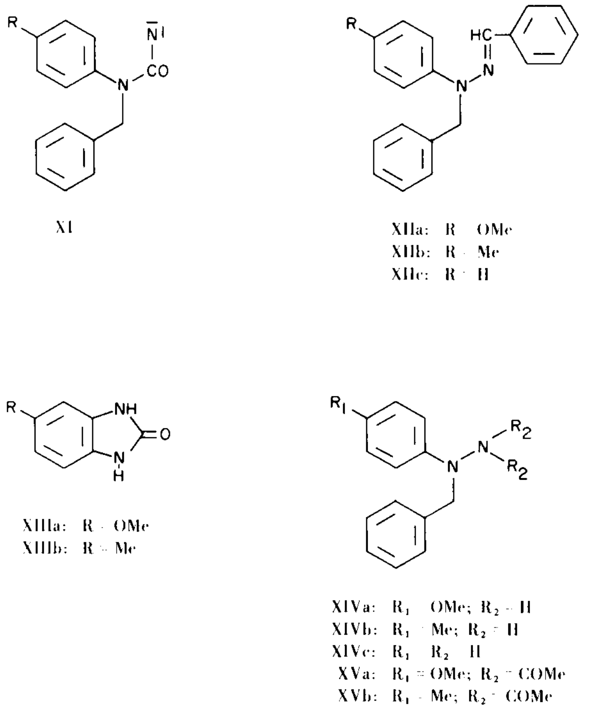


The formation of 1-benzyl-5-substituted-benzimidazolin-2-one (III) *via* the imidogene (XI) (nitrene) could be expected by the photolysis of carbamoyl azide. The present paper describes the results of photolysis of Ia and Ib in tetrahydrofuran as a possible synthesis of III.

N-Benzyl-*N*-(4-methoxyphenyl)carbamoyl azide (Ia) (1), prepared as usual, was irradiated with a Hanovia high pressure mercury lamp for 19.5 hours. After irradiation, the reaction product, obtained by the usual work-up, was chromatographed on silica gel.

Evaporation of the benzene eluate gave *N*-benzyl-*N*′-benzylidene-*N*-(4-methoxyphenyl)hydrazine (XIIa), which was identified by microanalysis and spectra. Its nmr spectrum showed a singlet due to a methoxyl group at 3.89 ppm, a singlet due to methylene protons at 5.12 ppm, and two aromatic protons at 6.88 ppm as a doublet (J = 9.0 cps). The other aromatic and methine protons (13 H) were observed at 7.20-7.70 ppm as a multiplet. These facts indicate that this is a non-cyclized product. The strong absorption at 1510 cm^{-1} in its ir spectrum supported the presence of the conjugated C=N absorption (6). Furthermore, acidic hydrolysis of XIIa with hydrochloric acid in a sealed tube, followed by autoxidation, gave benzoic acid. Accordingly, this product was assigned the structure XIIa and an authentic sample was synthesized by the condensation of *N*-benzyl-*N*-(4-methoxyphenyl)-hydrazine (XIVa) with benzaldehyde. Since Minunni (7) and the other groups (8) had reported the syntheses of *N*-benzyl-*N*-phenylhydrazine (XIVc) and (XIIc) by the condensation of phenylhydrazine (2 mole) with benzyl chloride (1 mole), the condensation of 4-methoxyphenylhydrazine with benzyl chloride in ethanol was carried out successfully to give XIVa. However, when 4-methoxyphenylhydrazine was heated with benzyl chloride without solvent, a severe reaction occurred at 110° (bath) with evolution of a yellowish gas. Furthermore, the formation of XIIa as byproduct was observed as Minunni (7) similarly reported the formation of XIIc. Compound XIVa was also characterized as its *N,N*-diacetyl derivative (XVa). Evaporation of the second chloroform eluate afforded 1-benzyl-5-methoxybenzimidazolin-2-one (IIIa), which was identified by mixed melting point and by comparison of spectroscopic data with those of an authentic sample (4a). Finally, the chloroform-ethanol and ethanol eluates afforded 5-methoxybenzimidazolin-2-one (XIIIa), whose ir spectrum (nujol) showed the absorption bands of NH due to a five-membered ureide at 3250-2700 cm^{-1} and a C=O band at 1755 cm^{-1}. Its nmr spectrum showed three aromatic protons as described in the experimental section and showed no presence of a benzyl group in the molecule. Accordingly, the third product was assigned the structure XIIIa.

CHART 3



XI

XIIa: R = OMe
XIIb: R = Me
XIIc: R = H

XIIIa: R = OMe
XIIIb: R = Me

XIVa: R_1 = OMe; R_2 = H
XIVb: R_1 = Me; R_2 = H
XIVc: R_1 = R_2 = H
XVa: R_1 = OMe; R_2 = COMe
XVb: R_1 = Me; R_2 = COMe

N-Benzyl-*N*-(4-methylphenyl)carbamoyl azide (Ib) (4a) was irradiated and worked up in a similar manner as for Ia. The resulting product was chromatographed on silica gel. Evaporation of the benzene eluate gave *N*-benzylidene-*N*′-benzyl-*N*′-(4-methylphenyl)hydrazine (XIIb), which was identified by mixed melting point and by comparison of spectroscopic data with an authentic sample. In this case XIIb was prepared by the condensation of benzaldehyde with *N*-benzyl-*N*-(4-methylphenyl)hydrazine (XIVb) (7,8), which was characterized as its diacetate (XVb). Acidic hydrolysis of XIIb, followed by autoxidation of the resulting product, also gave benzoic acid. The chloroform eluate afforded 1-benzyl-5-methylbenzimidazolin-2-one (IIIb), which would be formed *via* the imidogene XI. Finally, the chloroform-ethanol and ethanol eluates afforded 5-methylbenzimidazolin-2-one (XIIIb) (9), whose structure was assigned on the basis of microanalysis and spectroscopic data as described in the experimental section. The spectroscopic data of IIIb, XIIb, and XIIIb showed patterns similar to those of IIIa, XIIa, and XIIIa, respectively.

Thus the photolysis of *N*-aryl-*N*-benzylcarbamoyl azide was found to give benzimidazolin-2-ones (IIIa and IIIb) as the main product, formed by the internal condensation of imidogene (nitrene) as an intermediate with the adjacent benzene ring, together with XIIa, b, and XIIIa, b. In addition, extreme differences were observed in the ratio of products formed in the thermal reaction of Ia and Ib (4a).

EXPERIMENTAL (10)

Photolysis of *N*-Benzyl-*N*-(4-methoxyphenyl)carbamoyl Azide (Ia).

A solution of 2.1 g. of carbamoyl azide (Ia) in 700 ml. of tetrahydrofuran was irradiated under a current of nitrogen using a 450 W Hanovia high pressure mercury arc lamp (No. 679 A-36) and VYCOR-7910 ($\lambda > 210$ mμ) filter with water cooling for 19.5 hours. Evaporation of the solvent gave 1.9 g. of a brownish syrup, which was chromatographed on 70 g. of silica gel (*Wakogel*, 100-200 mesh). The first benzene eluate (F_1-F_4, each 30 ml.) gave 320 mg. of a reddish brown amorphous powder. The second benzene eluate (F_5-F_8, each 50 ml.) afforded 100 mg. (4.1%) of *N*-benzylidene-*N'*-benzyl-*N'*-(4-methoxyphenyl)hydrazine (XIIa) as yellowish needles, m.p. 117-118° (from *n*-hexane), which were identified by mixed melting point and by comparison of spectroscopic data with an authentic sample of XIIa [prepared as described later]; ν max (nujol) cm^{-1}: 1510 (C=N); nmr δ (deuteriochloroform): 3.89 (3H, singlet, OCH_3), 5.12 (2H, singlet, $-CH_2-$), 7.38 (5H, singlet, $-CH_2C_6H_5$), 6.88 (2H, doublet, J = 9.0 cps, phenyl-3,5-H), 7.20-7.70 ppm (8H, multiplet, $=CH-C_6H_5$ and phenyl-2,6-H); λ max (ethanol) mμ (log ϵ): 242.5 (5.16), 320.0 (shoulder) (5.16), 345.0 (5.23); mass spectrum m/e 316 (M^+).

Anal. Calcd. for $C_{21}H_{20}N_2O$: C, 79.71; H, 6.37; N, 8.85. Found: C, 79.45; H, 6.44; N, 8.66.

After the removal of a brownish syrup (343 mg.) from the third eluate composed of benzene-chloroform (1:1) (F_9-F_{15}, each 50 ml.) and chloroform (F_{16}-F_{19}, each 30 ml.), the fourth chloroform eluate (F_{20}-F_{26}, each 100 ml.) was evaporated to afford 570 mg. (30.0%) of 1-benzyl-5-methoxybenzimidazolin-2-one (IIIa) as colorless needles, m.p. 178-179° (from ethyl acetate), which were identified by mixed melting point and by comparison of spectroscopic data with an authentic sample; ν max (nujol) cm^{-1}: 3250-2700 (NH), 1705 (C=O); nmr δ (deuteriochloroform): 3.73 (3H, singlet, OCH_3), 5.06 (2H, singlet, $-CH_2-$), 7.28 (5H, singlet, C_6H_5), 6.40-6.83 ppm (3H, multiplet, C_4–H, C_6–H, C_7–H). The fifth chloroform eluate (F_{27}-F_{31}, each 20 ml.) and chloroform-ethanol (9:1) (F_{32}-F_{33}, each 20 ml.) gave a brownish syrup (170 mg.).

Finally, evaporation of the sixth eluate with chloroform-ethanol (5:1) (F_{34}-F_{38}, each 50 ml.) and ethanol (F_{39}-F_{40}, each 20 ml.) afforded 5-methoxybenzimidazolin-2-one (XIIIa) (175 mg., 14.3%) as colorless needles, m.p. 248-249°; ν max (nujol) cm^{-1}: 3250-2700 (NH), 1755 (C=O); nmr δ (deuteriodimethylsulfoxide), 3.72 (3H, singlet, OCH_3), 9.46 (2H, broad signal, 2 x N*H*), 6.54 (1H, quartet, J = 9.0, 3.0 cps, C_6–H), 6.75 (1H, doublet, J = 3.0 cps, C_4–H), 6.87 ppm (1H, doublet, J = 9.0 cps, C_7–H); λ max (ethanol) mμ (log ϵ): 230.0 (inflection) (5.02), 295.5 (5.07).

Anal. Calcd. for $C_8H_8N_2O_2$: C, 58.53; H, 4.91; N, 17.07. Found: C, 58.27; H, 4.95; N, 16.93.

Photolysis of *N*-Benzyl-*N*-(4-methylphenyl)carbamoyl Azide (Ib).

A solution of 2.5 g. of carbamoyl azide (Ib) in 700 ml. of tetrahydrofuran was irradiated for 36.5 hours under a current of nitrogen in the same way as for Ia. The solvent was evaporated *in vacuo* to give 2.2 g. of a reddish brown syrup which was chromatographed on 80 g. of silica gel (*Wakogel*, 100-200 mesh). After the first benzene eluate (F_1-F_4, each 20 ml.) had been discarded, the second benzene eluate (F_5-F_{14}, each 20 ml.) was evaporated to give 100 mg. (3.3%) of *N*-benzylidene-*N'*-benzyl-*N'*-(4-methylphenyl)hydrazine (XIIb) as pale yellow needles, m.p. 133-134° (from *n*-hexane), which were identified by mixed melting point and by comparison of spectroscopic data with an authentic sample, prepared as described later; ν max (nujol) cm^{-1}: 1515 (>C=N–); mass spectrum: m/e 300 (M^+); nmr δ (deuteriochloroform); 2.30 (3H, singlet, CH_3), 5.13 (2H, singlet, $-CH_2-$), 7.25 (5H, singlet, C_6H_5-), 7.00-7.68 ppm (10H, multiplet, $=CH-C_6H_5$, $CH_3-C_6H_4$); λ max (ethanol) mμ (log ϵ): 240.5 (5.28), 309.0 (shoulder) (5.16), 340.0 (5.42).

Anal. Calcd. for $C_{21}H_{20}N_2$: C, 83.96; H, 6.71; N, 9.33. Found: C, 83.67; H, 6.73; N, 9.27.

The third chloroform eluate (F_{15}-F_{19}, each 50 ml.) gave 350 mg. (14.0%) of a reddish brown oil, whose ir spectrum was identical with that of Ib. The fourth chloroform eluate (F_{20}-F_{26}, each 100 ml.) was evaporated to give 710 mg. (31.8%) of 1-benzyl-5-methylbenzimidazolin-2-one (IIIb) as colorless needles, m.p. 185-186° (from ethyl acetate), which were identified by mixed melting point and by comparison of spectroscopic data with an authentic sample (4a); ν max (nujol) cm^{-1}: 3200-2700 (NH), 1703 (C=O); nmr δ (deuteriochloroform): 2.87 (3H, singlet, CH_3), 5.00 (2H, singlet $-CH_2-$), 7.23 (5H, singlet, C_6H_5-), 6.67 (2H, singlet, C_6–H, C_7–H), 6.87 ppm (1H, singlet, C_4–H). After a dark brownish syrup (500 mg.) from the fifth chloroform-ethanol (4:1) eluate (F_{27}-F_{30}, each 50 ml.) had been removed, the sixth eluate (F_{31}-F_{38}, each 50 ml.) with chloroform-ethanol (4:1) was evaporated to give 125 mg. (8.2%) of 5-methylbenzimidazolin-2-one (XIIIb) as colorless needles, m.p. 288-289° (from ethyl acetate) [lit. (9), m.p. 291-292°]; λ max (ethanol) mμ (log ϵ): 230.0 (shoulder) (5.01), 287.5 (5.30); ν max (nujol) cm^{-1}: 3250-2700 (NH), 1756 (C=O); nmr δ (deuteriodimethylsulfoxide): 2.26 (3H, singlet, CH_3), 6.74 (3H, singlet, C_4–H, C_6–H, C_7–H), 10.44 ppm (2H, broad singlet, 2 x NH).

Anal. Calcd. for $C_8H_8N_2O$: C, 64.85; H, 5.44; N, 18.91. Found: C, 64.76; H, 5.42; N, 18.64.

Hydrolysis of XIIa.

A suspension of 40 mg. of XIIa in 20% hydrochloric acid (10 ml.) was heated at 150° in a sealed tube for 3 hours. After cooling, the reaction mixture was extracted with ether. The extract was washed with saturated sodium chloride solution, dried over sodium sulfate, and evaporated to give an oil, whose ir spectrum (chloroform) showed a strong absorption at 1705 cm^{-1} due to the carbonyl group. After exposure to the air, a suspension of the above reaction mixture in 2 ml. of 10% sodium hydroxide solution was extracted with ether. Evaporation of the extract gave 12.4 mg. of starting material, XIIa. The aqueous layer was made acidic with an excess of 10% hydrochloric acid and extracted with ether after addition of an excess of sodium chloride. The ether extract was washed with saturated sodium chloride solution and evaporated to give benzoic acid as a colorless powder, m.p. 122-123°, which was identical to an authentic sample.

Hydrolysis of XIIb.

A suspension of 50 mg. of XIIb in 20 ml. of 20% hydrochloric acid was heated in a sealed tube at 150° for 3 hours. The usual work-up of the reaction mixture afforded 14 mg. of XIIb and benzoic acid as above.

N-Benzyl-*N*-(4-methoxyphenyl)hydrazine (XIVa).

A mixture of 7.3 g. (0.053 mole) of 4-methoxyphenylhydrazine, 3.3 g. (0.026 mole) of benzyl chloride, and 50 ml. of dry ethanol was refluxed for 3 hours. After evaporation of the solvent, the resulting residue was poured into hot water and extracted with benzene. The benzene extract was washed with water, dried over sodium sulfate and evaporated to give an oil, which was distilled *in vacuo* to give 3.4 g. of XIVa as an orange oil, b.p. 159° (0.55

mm.); ν max (liquid) cm^{-1}: 3450, 3400 (NH$_2$); nmr δ (deuteriochloroform), 3.70 (3H, singlet, OCH_3), 4.37 (2H, singlet, –CH_2–), 6.77 (2H, doublet, J = 9.0 cps, C$_2$–H, C$_6$–H), 7.02 (2H, doublet, J = 9.0 cps, C$_3$–H. C$_5$–H), 7.25 (5H, singlet, C$_6H_5$–), 3.42 ppm (2H, broad singlet, NH$_2$). Recrystallization of the hydrochloride gave colorless needles, m.p. 139-140° dec. (ethanol-ether).

Anal. Calcd. for $C_{14}H_{16}N_2O{\cdot}HCl$: C, 63.45; H, 6.47; N, 10.57. Found: C, 63.53; H, 6.52; N, 10.58.

The resulting residue after distillation of XIVa was triturated with ether to give *N*-benzyl-*N'*-benzylidene-*N*-(4-methoxyphenyl)-hydrazine (XIIa) as pale yellowish needles, m.p. 117-118° (from ethanol), which were identical with an authentic sample prepared as described later.

N-Benzyl-*N*-(4-methylphenyl)hydrazine (XIVb).

A mixture of 6.7 g. (0.054 mole) of 4-methylphenylhydrazine and 3.3 g. (0.026 mole) of benzyl chloride was heated at 120° for 4 hours. After the same treatment as above, the residue was distilled to give 1 g. of XIVb as an orange oil, b.p. 130° (1 mm.); ν max (liquid) cm^{-1}: 3450, 3400 (NH), nmr δ (deuteriochloroform): 2.22 (3H, singlet, CH_3), 4.20 (2H, singlet, –CH_2–), 6.49 (2H, doublet, J = 9.0 cps, C$_2$–H, C$_6$–H), 6.98 (2H, doublet, J = 9.0 cps, C$_3$–H, C$_5$–H), 7.28 (5H, singlet, C$_6H_5$–), 3.13 ppm (2H, broad singlet, NH$_2$). The hydrochloride prepared as usual was recrystallized from ethanol-ether to give colorless needles, m.p. 174-176° dec.

Anal. Calcd. for $C_{14}H_{16}N_2{\cdot}HCl$: C, 67.60; H, 6.89; N, 11.26. Found: C, 67.41; H, 6.98; N, 11.39.

After XIVb had been distilled off, the resulting residue was triturated with ether to give XIIb as pale yellowish needles, m.p. 133-134° (from ethanol), which were identical with an authentic sample described later.

N,N-Diacetyl-*N'*-benzyl-*N'*-(4-methoxyphenyl)hydrazine (XVa).

A mixture of 600 mg. of XIVa and 5 ml. of acetic anhydride was heated in an oil-bath at 130° for 3 hours. The excess acetic anhydride was evaporated *in vacuo* and the resulting residue was recrystallized from ethanol to give 800 mg. of XVa as colorless needles, m.p. 116-117°; ν max (nujol) cm^{-1}: 1735, 1702 (C=O); ν max (chloroform) cm^{-1}: 1720 (C=O); nmr δ (deuteriochloroform): 2.31 (6H, singlet, 2 x COCH_3), 3.73 (3H, singlet, OCH_3), 4.75 (2H, singlet, –CH_2–), 6.78 (4H, singlet, –C$_6H_4$–N), 7.30 ppm (5H, singlet, C$_6H_5$–).

Anal. Calcd. for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97. Found: C, 69.24; H, 6.54; N, 8.93.

N,N-Diacetyl-*N'*-benzyl-*N'*-(4-methylphenyl)hydrazine (XVb).

A mixture of 700 mg. of XIVb and 7 ml. of acetic anhydride was heated at 130° for 3 hours. The same treatment as above afforded 930 mg. of XVb as colorless needles, m.p. 130-131° (from ethanol); ν max (nujol) cm^{-1}: 1730, 1702 (C=O); ν max (chloroform) cm^{-1}: 1720 (C=O); nmr δ (deuteriochloroform): 2.28 (9H, singlet, CH_3, 2 x COCH_3), 4.73 (2H, singlet, –CH_2–), 6.64 (2H, doublet, J = 9.0 cps, C$_2$–H, C$_6$–H), 7.07 (2H, doublet, J = 9.0 cps, C$_3$–H and C$_5$–H), 7.28 ppm (5H, singlet, C$_6H_5$–).

Anal. Calcd. for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 73.03; H, 6.92; N, 9.32.

N-Benzyl-*N'*-benzylidene-*N*-(4-methoxyphenyl)hydrazine (XIIa).

A mixture of 228 mg. of the above hydrazine (XIVa) and 106 mg. of benzaldehyde was shaken under a current of nitrogen and the mixture was allowed to stand for 0.5 hours. The crude product which separated was recrystallized from ethanol to give 270 mg. of XIIa as pale yellowish needles, m.p. 117-118°.

Anal. Calcd. for $C_{21}H_{20}N_2O$: C, 79.71; H, 6.37; N, 8.85. Found: C, 79.65; H, 6.42; N, 8.84.

N-Benzyl-*N'*-benzylidene-*N*-(4-methylphenyl)hydrazine (XIIb).

The treatment of 300 mg. of the above hydrazine (XIVb) with 150 mg. of benzaldehyde as above gave 330 mg. of XIIb as pale yellowish needles, m.p. 133-134° (from ethanol).

Anal. Calcd. for $C_{21}H_{20}N_2$: C, 83.96; H, 6.71; N, 9.33. Found: C, 84.00; H, 6.93; N, 9.20.

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((2) Communications concerning this paper should be directed to Professor T. Kametani.

(3) Communications concerning this paper should be directed to Professor T. Kametani.

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