

Studies on the Syntheses of Azole Derivatives. Part IX (1).
 Formation of 2,4-Disubstituted Δ^2 -1,3,4-Oxadiazolin-5-one and 4-Substituted
 1,2,4-Triazolidin-3,5-dione Derivatives by Thermal Reaction of
N-Aryl-*N*-benzylcarbamoyl Azides (2).

T. Kametani (3), S. Shibuya, and M. Shio

Pharmaceutical Institute, Tohoku University (3) and Research Laboratory,
 Taisho Pharmaceutical Co., Ltd., Aobayama, Sendai, Japan

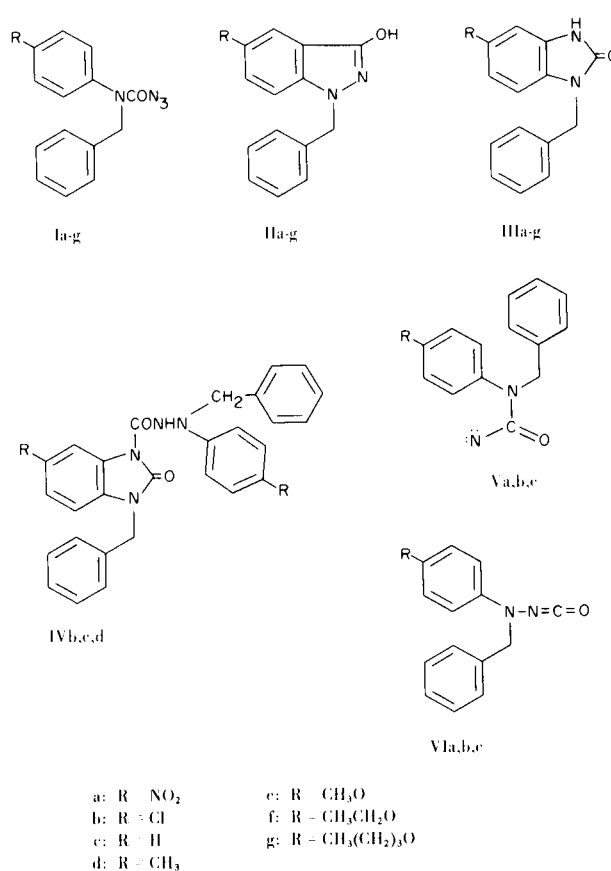
Received May 19, 1971

The structure of the novel products, 2,4-bis-(*N*-benzyl-4-nitroanilino)- Δ^2 -1,3,4-oxadiazolin-5-one (VII), 2-benzyl-1-(*N*-benzyl-4-chloroanilino)-4-(4-chlorophenyl)-1,2,4-triazolidin-3,5-dione (XIVa), and 2-benzyl-1-(*N*-benzylanilino)-4-phenyl-1,2,4-triazolidin-3,5-dione (XIVb), obtained upon thermal reaction of *N*-benzyl-*N*-(4-nitrophenyl)carbamoyl azide (Ia), *N*-benzyl-*N*-(4-chlorophenyl)carbamoyl azide (Ib) and *N*-benzyl-*N*-phenylcarbamoyl azide (Ic), respectively, were determined.

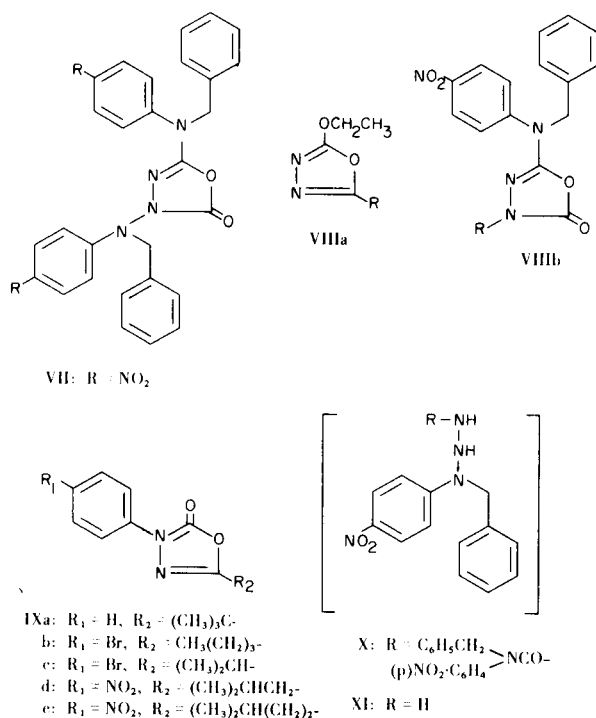
In the previous paper (4), we described the formation of 1-benzyl-3-hydroxy-1*H*-indazoles (IIa-g), 1-benzyl-2-benzimidazolinones (IIIa-g and IVb,c,d) by thermal reaction of *N*-aryl-*N*-benzylcarbamoyl azides (Ia-g). Furthermore, we obtained novel products (VII, XIVa, and XIVb) from Ia (R = NO₂), Ib (R = Cl), and Ic (R = H), respectively (4). We successively investigated the structure of these three compounds and their formation mechanism. The electronegativity of the substituent on the benzene ring was found to be significant in the course of the above reaction. Herein we wish to report our results.

First, microanalysis and molecular weight determination established the empirical formula of C₂₈H₂₂N₆O₆ for the product (VII). The ir spectrum (potassium bromide) exhibited absorption bands due to C=O, C=N, and C-O-C groups at 1753 cm⁻¹, 1645 cm⁻¹, and 968 cm⁻¹, respectively, indicating the presence of an oxadiazolinone system (6,7) in VII. In fact, the ir spectrum of 2-alkyl-5-ethoxy-1,3,4-oxadiazole (VIIIa) showed two C=N bands at 1625 cm⁻¹ and 1570 cm⁻¹ as characteristic absorptions (8). We also observed the absorption bands at 1640 cm⁻¹ and 950-970 cm⁻¹ attributable to C=N and C-O-C groups, respectively, in the ir spectrum of Δ^2 -1,3,4-oxadiazolin-5-one (IX) (9) (cf. Table I). The nmr spectrum (δ in deuteriodimethylsulfoxide) of VII showed aromatic signals as four doublets (*J* = 9 Hz), indicating the presence of two nitrophenyl groups, and two benzyl signals at 5.41 (2H), 4.95 (1H) and 5.26 ppm (1H) as a singlet and AB type doublets, respectively. Since the latter two signals

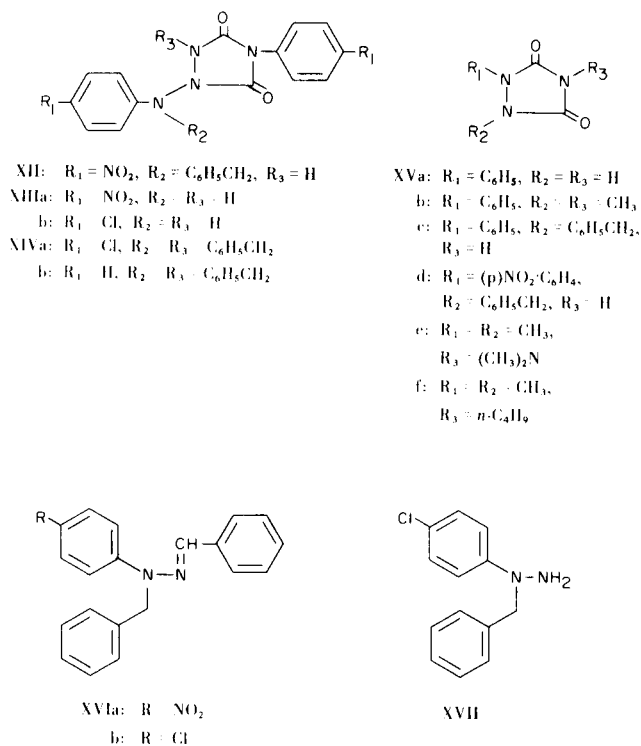
SCHEME 1



SCHEME 2



SCHEME 3



collapsed to a singlet at 5.10 ppm at 100°, the free rotation of one of the benzyl groups seemed to be hindered (10). Therefore, the compound (VII) could be assigned 2,4-bis-(*N*-benzyl-4-nitroanilino)- Δ^2 -1,3,4-oxadiazolin-5-one formed by condensation of the nitrene (Va), derived from Ia, with the isocyanate (VIa) (8,11,12). This structure (VII) was proved to be correct by the following reactions.

TABLE I

Infrared Spectra of 2-Alkyl-4-aryl- Δ^2 -1,2,4-oxadiazolin-5-ones (IX) and 1,3,4-triazolidin-3,5-diones (XV) (a)

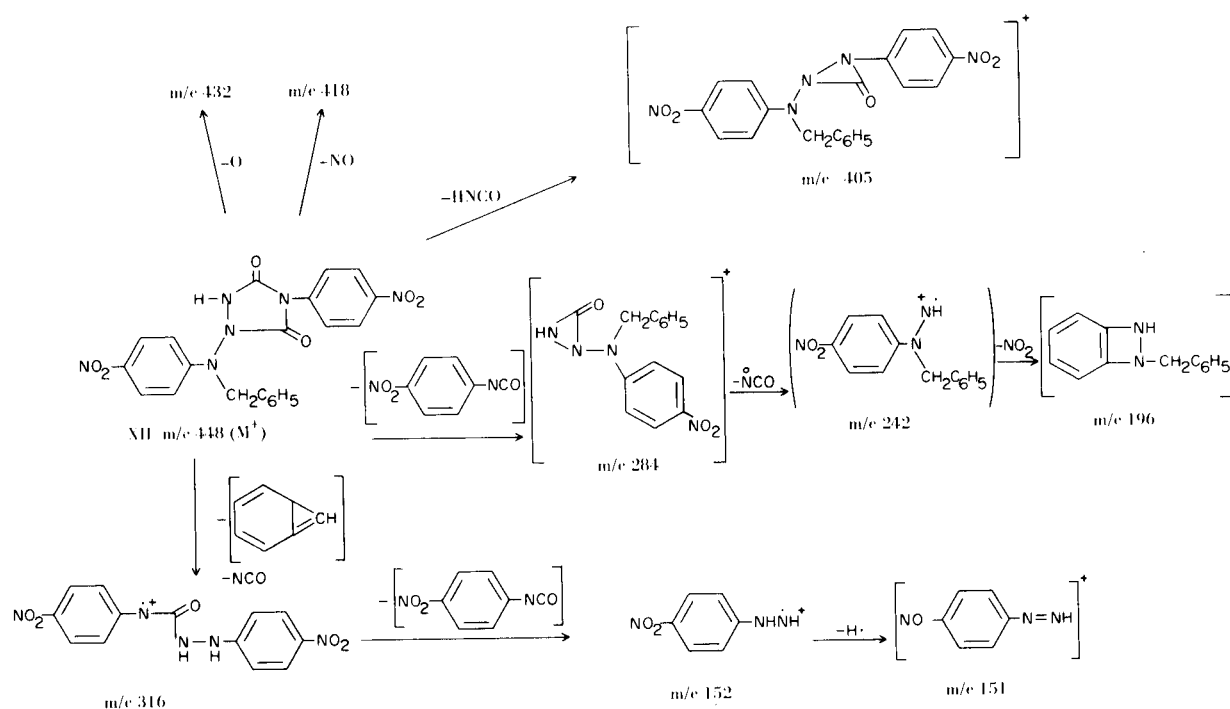
Compound	NH	C=O	C=N	C-O-C
IXa	--	1785	1630	970
IXb	--	1775	1645	960
IXc	--	1780	1640	950
IXd	--	1785	1640	950
IXe	--	1771	1640	953
XVa	3200-2650	1765, 1700	----	---
XVb	--	1760, 1702	----	---
XVc	3250-2650	1790, 1700	----	---
XVd	3250-2650	1783, 1735	----	---
XVe (14)	--	1780, 1730	----	---
XVf (14)	--	1750, 1680	----	---

(a) Potassium bromide disk.

Treatment of VII with potassium hydroxide solution afforded *N*-benzyl-4-nitroaniline, supporting the presence of the VIIIb system in VII as a partial structure. In this reaction, neither X or XI was obtained because of instability.

The oxadiazolin-5-one VII was heated with hydrobromic acid or concentrated hydrochloric acid to give 1-(*N*-benzyl-4-nitroanilino)-4-(4-nitrophenyl)-1,2,4-triazolidin-3,5-dione (XII), the structure of which was confirmed as follows. Microanalysis and mass spectrum revealed the empirical formula C₂₁H₁₆N₆O₆ as shown in Scheme 4. The ir spectrum (potassium bromide) of XII exhibited absorption of NH at 3250-2650 cm⁻¹ and that of C=O group at 1800 and 1730 cm⁻¹, supporting the presence of a five membered imidocarbonyl group. These spectroscopic data are very similar to those of 1,2,4-triazolidin-3,5-diones. XVa (9), XVb (13), XVc, XVd, XVe (14), and XVf (14) (*cf.* Table I). In addition, the nmr spectrum (δ in deuteriodimethylsulfoxide) showed one proton signal at 6.00 ppm as a broad one due to NH, and the presence of two nitrophenyl groups and one benzyl group was indicated by the observation of four doublets (8H) (*J* = 9.0 Hz, 7.02, 7.79, 9.09, 8.33 ppm) and a singlet (2H) at 5.09

SCHEME 4



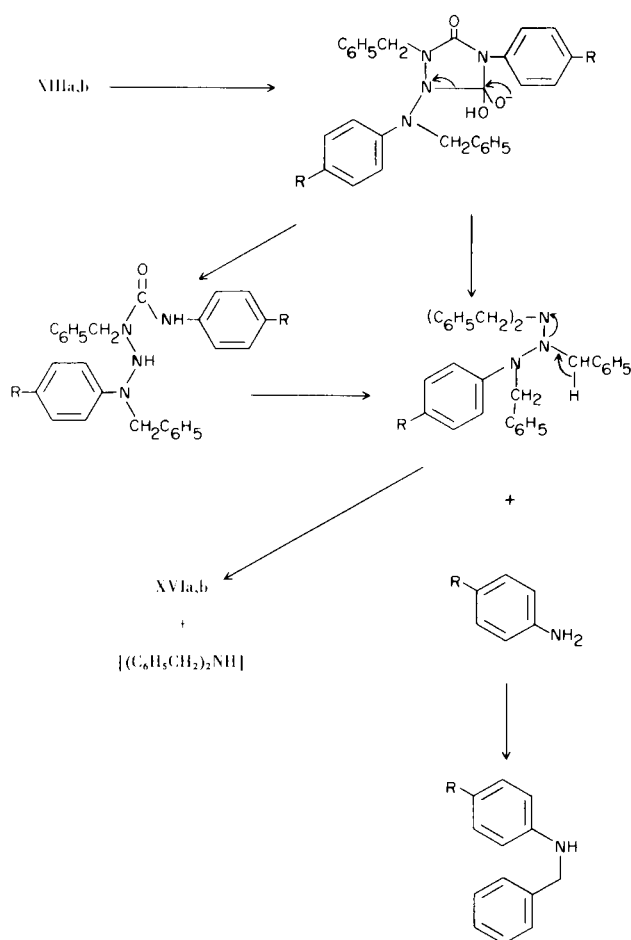
ppm (15). The fragmentation patterns shown in Scheme 4 and 7 also support this structure. On heating VII with sulfuric acid-glacial acetic acid (1:1) 1-(4-nitroanilino)-4-(4-nitrophenyl)-1,3,4-triazolidin-3,5-dione (XIIIa) showing the empirical formula $C_{14}H_{10}N_6O_6$ was obtained; and the spectroscopic data, described in the experimental section, well supported the structure XIIIa. The treatment of XIIIa with benzyl chloride in the presence of sodium hydroxide gave *N*-benzyl-4-nitroaniline and XVIa. In this reaction, a brownish amorphous powder was obtained as the main product. The structure XVIa was identified by a mixed melting point test and comparison of the spectroscopic data with those of an authentic specimen prepared from 4-nitrophenylhydrazine. Acidic hydrolysis of XVIa, followed by air oxidation, gave benzoic acid, indicating the structure XVIa to be correct (16). The mechanism of the formation of XVIa and *N*-benzyl-4-nitroaniline is shown in Scheme 5. Regarding the reaction mechanism of the formation of VII, XII, and XIIIa, three possible routes will be considered: (a) 1,3-dipolar cycloaddition of nitrene (Va) to isocyanate (VIa), (b) through diaziridinone (XVIII) as an intermediate or (c) cyclization of XIXr, one of four resonance structures of azimine (XIX), as shown in Scheme 6 (17).

The formation of 1,3,4-oxadiazole by 1,3-dipolar addition of carboalkoxy nitrene to allene (12b), alkyne (12e,d), and nitrile (12e,f,g and 13) is described in the indicated

literature. The transformation of *N*-acylaziridine to oxazoline by ring expansion (18) and the formation of 1,3,4-oxadiazole by the cyclization of nitrilimine (12e) are also popular reactions. Therefore these three reaction mechanisms were considered. Transformation of VII to XII and XIIIa under acidic conditions would occur through XIXq' or XX as an intermediate (19) as shown in Scheme 6.

We then determined the structure of the products XIVa and XIVb obtained by thermal reaction of Ib and Ic, respectively. The empirical formula $C_{28}H_{22}Cl_2N_4O_2$ (5) for XIVa was determined by microanalyses and mass spectra. Since the ir spectrum (potassium bromide) of XIVa showed C=O absorption at 1790 and 1743 cm^{-1} and exhibited absorption bands similar to those of XII and XIIIa, the presence of the 1,2,4-triazolidin-3,5-dione skeleton in its structure could be presumed. The nmr spectrum (δ in deuteriodimethylsulfoxide) showed three doublets ($J = 9.0$ Hz) at 6.43, 7.17 and 7.57 ppm indicating the presence of two 4-chlorophenyl groups, and two singlets (taken at 80°) at 4.83 (2H) and 4.57 ppm (2H). The latter signal (4.57 ppm) was observed as AB type doublets ($J = 15.0$ Hz) at 4.40 and 4.80 ppm at room temperature. These facts indicate that XIVa possesses two *N*-benzyl groups and that the free rotation of one of them should be hindered (10). Therefore, the compound (XIVa) would be assigned 2-benzyl-1-(*N*-benzyl-4-chloroanilino)-4-(4-chlorophenyl)-1,2,4-triazolidin-3,5-dione. The fragmentation pattern in its mass spectrum is shown in Scheme 7.

SCHEME 5



Debenzylation of XIVa with a mixture of sulfuric acid and glacial acetic acid afforded 1-(4-chloroanilino)-4-(4-chlorophenyl)-1,2,4-triazolidin-3,5-dione (XIIIb), which was treated with benzyl chloride in the presence of sodium hydroxide to give *N*-benzyl-*N'*-benzylidene-*N*-(4-chlorophenyl)hydrazine (XVIb) and *N*-benzyl-4-chloroaniline, as in the case of XIIIa. The structure of XVIb was identified by comparison as spectroscopic data with those of an authentic specimen prepared from *N*-benzyl-*N*-(4-chlorophenyl)hydrazine (XVII). In the case of XIVb, the empirical formula $C_{28}H_{24}N_4O_2$ (5) was established by mass spectra and microanalyses; and the compound (XIVb) could be assigned 2-benzyl-1-(*N*-benzylanilino)-4-phenyl-1,2,4-triazolidin-3,5-dione from the spectroscopic data described in the experimental section.

The reaction mechanism regarding the formation of XIVa and XIVb could be presumed to be that shown in Scheme 8; namely, condensation of the nitrene (Vb and Vc) with isocyanate (VIb and VIc) would afford the diaziridone (XVIII) or azimine (XIX) as possible inter-

mediates. In this case, the lone pair on nitrogen attacks carbon, and then the migration of the benzyl group occurs to form XIVa and XIVb (14,20,21). In the case of the formation of XII, the carbonyl group would attack the carbon of the intermediates (XVIII or XI). In addition, the benzyl group would migrate more easily than the *p*-nitrophenyl group and the phenyl group, as in the general Wittig type anionic migration reaction (21).

As mentioned above, the structures of the novel products (VII, XIVa, and XIVb), obtained on the thermal reaction of *N*-substituted-*N*-arylcabamoyl azides (Ia, Ib, and Ic), were determined. Electronegativity of the substituents on the *N*-phenyl group was found to have a significant effect on these results (22).

EXPERIMENTAL (23)

2,4-Bis(*N*-benzyl-4-nitroanilino)- Δ^2 -1,3,4-oxadiazolin-5-one (VII) (4).

A solution of 15 g. of *N*-benzyl-*N*-(4-nitrophenyl)carbamoyl azide (Ia) in 150 ml. of dry xylene was refluxed for 9 hours. After the usual work-up, the crude product was chromatographed on silica gel to give 4.95 g. (37%) of 1-benzyl-3-hydroxy-5-nitro-1*H*-indazole (IIa), 0.21 g. (0.04%) of 1-benzyl-5-nitro-2-benzimidazolone (IIIa), and 4.8 g. (35.6%) of VII as yellowish prisms, m.p. 189.5-190.5° (from benzene); ν max (potassium bromide) cm^{-1} : 1753 (C=O), 1645 (C=N), 968 (C-O-C); nmr δ (deuteriodimethylsulfoxide): 7.09 (2H, doublet, $J = 9.0$ Hz, C_2 - or N_4 - C_2' , and C_6' -H), 8.15 (2H, doublet, $J = 9.0$ Hz, C_3' - and C_5' -H), 8.10 (2H, doublet, $J = 9.0$ Hz, C_2 - or N_4 - C_2'' - and C_6'' -H), 8.41 (2H, doublet, $J = 9.0$ Hz, C_3'' , C_5'' -H), 7.20-7.66 (10H, multiplet, aromatic protons), 5.41 (2H, singlet, $-CH_2-$), 4.95, 5.26 (2H, each doublet, $J = 15.0$ Hz, $-CH_2-$), the latter signals of which were observed at 5.10 (2H) as a singlet at 100°.

Anal. Calcd. for $C_{28}H_{22}N_6O_6$: C, 62.45; H, 4.12; N, 15.61; Mol. Wt., 538.5. Found: C, 62.86; H, 4.18; N, 15.52; Mol. Wt., 539.3.

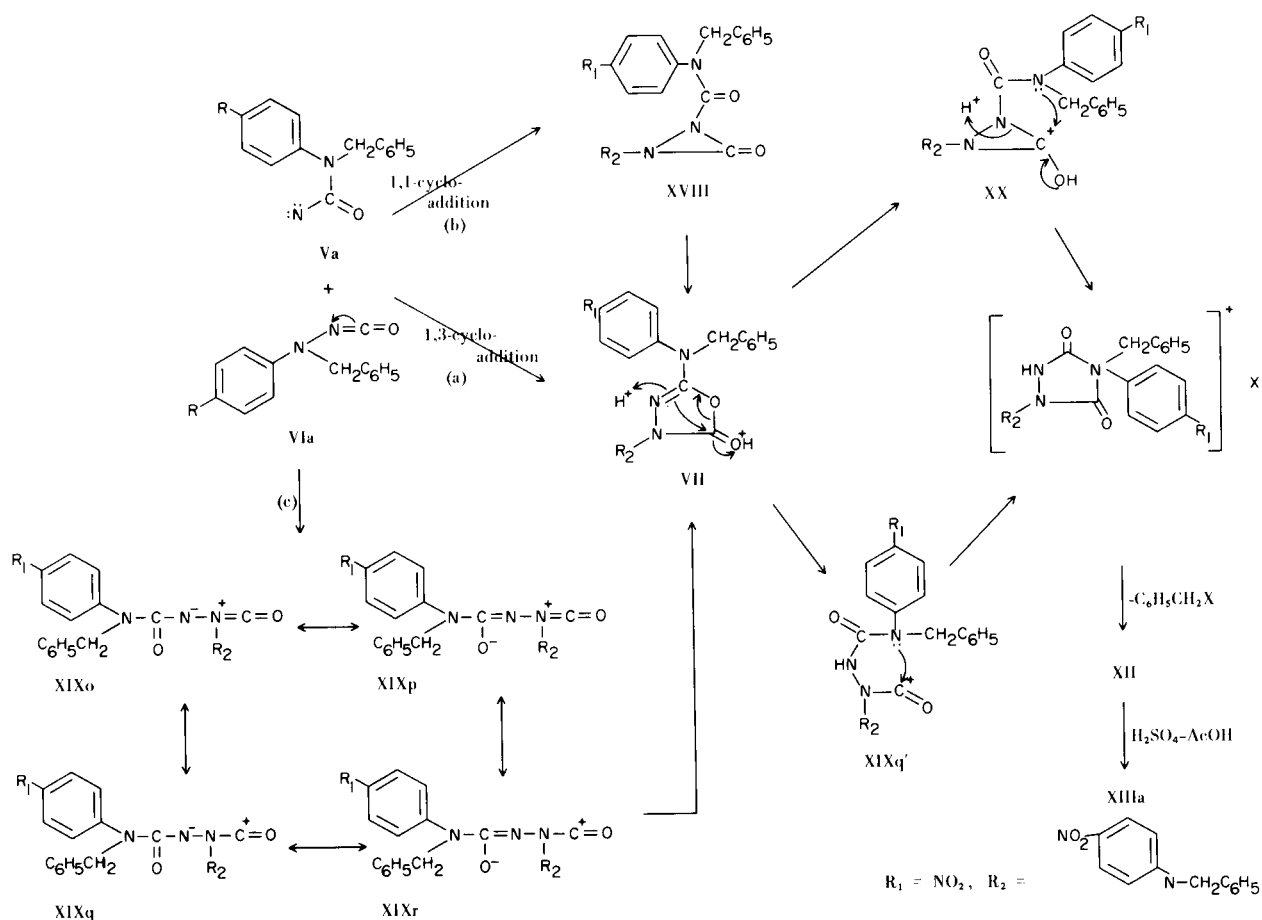
Hydrolysis of VII.

A suspension of 200 mg. of VII, 1 g. of potassium hydroxide, 10 ml. of water, and 5 ml. of ethanol was heated in a sealed tube at 230° for 1 hour. After the reaction, the solvent was evaporated and the remaining residue was extracted with chloroform. The extract and washed with saturated sodium chloride solution and dried. Removal of the solvent afforded 80 mg. of a syrup which was chromatographed on silica gel to give 50 mg. of *N*-benzyl-4-nitroaniline as a pale brownish powder, whose spectroscopic data were identical with those of the authentic specimen.

1-(*N*-Benzyl-4-nitroanilino)-4-(4-nitrophenyl)-1,2,4-triazolidin-3,5-dione (XII)

(a) A mixture of 700 mg. of VII, 10 ml. of 48% hydrobromic acid, and 5 ml. of ethanol was stirred under reflux, and 3 ml. of 48% hydrobromic acid was added each hour to the mixture. After the reflux had been continued for 13 hours, the precipitates were collected by filtration and washed with water, and then ether to give 400 mg. of yellow crystals, which were recrystallized from ethanol-ether (10:1) to afford XII as yellowish needles, m.p. 233-234°.

SCHEME 6



(b) A mixture of 200 mg. of VII, 5 ml. of concentrated hydrochloric acid, and 2 ml. of ethanol was refluxed for 15 hours. During the reaction, 1 ml. of concentrated hydrochloric acid was added to the mixture each hour. The mixture was worked up in a similar way as in method (a) to give 130 mg. of XII as yellowish needles, m.p. 233-234°; ν max (potassium bromide) cm^{-1} : 3250-2650 (NH), 1800, 1730 (C=O); nmr δ (deuteriodimethylsulfoxide): 7.02 (2H, doublet, $J = 9.0$ Hz, N_1 - C_2' - and C_6' -H), 8.09 (2H, doublet, $J = 9.0$ Hz, C_3' -, C_5' -H), 7.79 (2H, doublet, $J = 9.0$ Hz, N_4 - C_2'' - and C_6'' -H), 8.33 (2H, doublet, $J = 9.0$ Hz, C_3'' - and C_5'' -H), 7.20-7.67 (5H, multiplet, aromatic protons), 5.09 (2H, singlet, $-\text{CH}_2-$), 6.00 (1H, broad, NH); mass spectrum m/e : 448 (M^+), 227, 226, 196, 179, 122, 91 (base peak).

Anal. Calcd. for $\text{C}_{21}\text{H}_{16}\text{N}_6\text{O}_6$: C, 56.25; H, 3.60; N, 18.74. Found: C, 56.50; H, 3.67; N, 18.91.

1-(4-Nitroanilino)-4-(4-nitrophenyl)-1,2,4-triazolidin-3,5-dione (XIIIa).

A mixture of 740 mg. of VII, 10 ml. of concentrated sulfuric acid, and 10 ml. of glacial acetic acid was heated at 100° for 3 hours. The reaction mixture was diluted with 30 g. of ice-water. The precipitates, collected by filtration, were washed with water and extracted with 30 ml. of 10% sodium hydroxide solution. The extract was made acidic with concentrated hydrochloric acid to give 450 mg. of XIIIa as crystals. Recrystallization from ethanol

afforded XIIIa as yellowish needles, m.p. 270-271°; ν max (potassium bromide) cm^{-1} : 3300, 3200-2600 (NH), 1780, 1715 (C=O); nmr δ (deuteriodimethylsulfoxide): 7.02 (2H, doublet, $J = 9.0$ Hz, N_1 - C_2' - and C_6' -H), 8.13 (2H, doublet, $J = 9.0$ Hz, N_1 - C_3' - and C_5' -H), 7.88 (2H, doublet, $J = 9.0$ Hz, N_4 - C_2'' -, C_6'' -H), 8.48 (2H, doublet, $J = 9.0$ Hz, N_4 - C_3'' - and C_5'' -H), 7.35, 9.75 (2H, each singlet, 2 x NH); mass spectrum m/e : 358 (M^+).

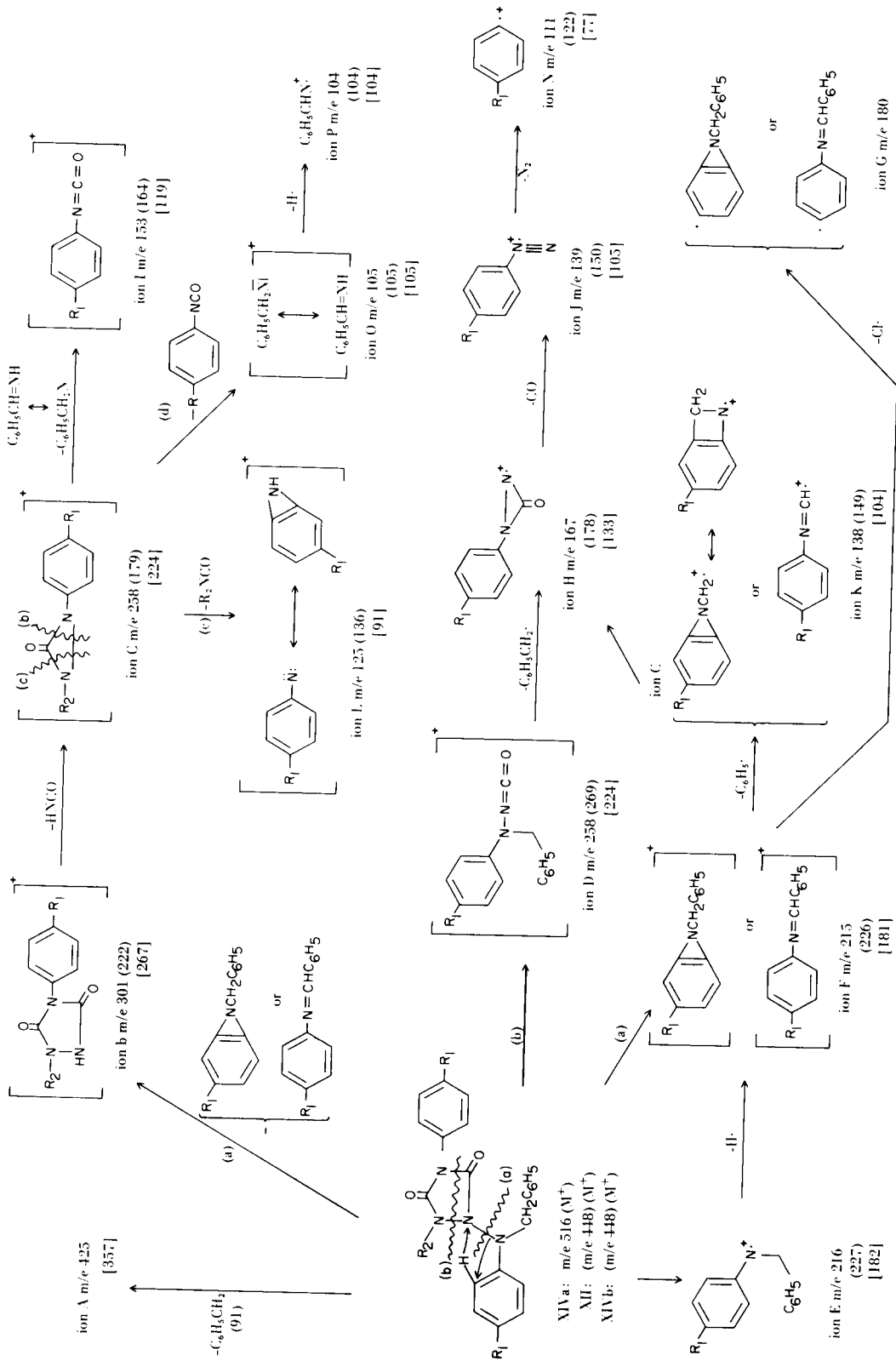
Anal. Calcd. for $\text{C}_{14}\text{H}_{10}\text{N}_6\text{O}_6$: C, 46.93; H, 2.81; N, 23.46. Found: C, 47.27; H, 3.21; N, 23.26.

2-Benzyl-1-phenyl-1,2,4-triazolidin-3,5-dione (XVc).

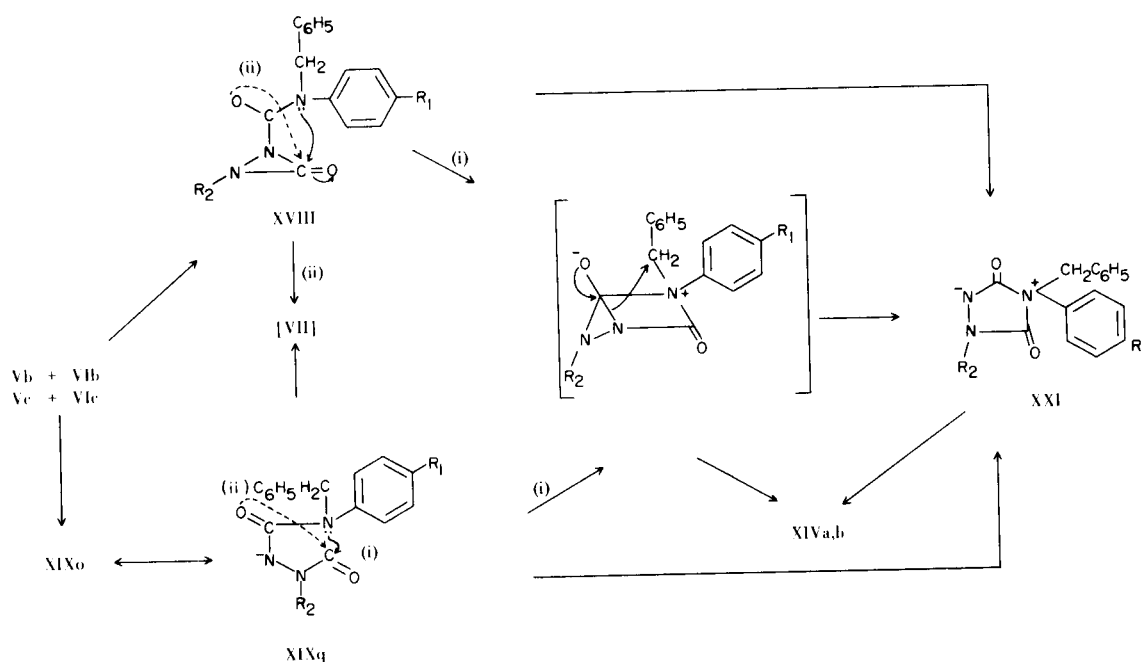
A mixture of 1.8 g. of 1-phenyl-1,2,4-triazolidin-3,5-dione (XVa), 3.1 g. of benzyl chloride, 50 ml. of ethanol, and 1.4 g. of potassium hydroxide was refluxed for 3 hours. The solvent was evaporated; the remaining residue was diluted with 20 ml. of water, and an excess of benzyl chloride was extracted with chloroform. The aqueous layer was acidified with 10% hydrochloric acid to give 800 mg. of precipitate which was collected by filtration. Recrystallization from ethanol afforded XIVc as colorless prisms, m.p. 155-156°; nmr δ (deuteriochloroform): 9.73 (1H, singlet, NH), 4.62 (2H, singlet, $-\text{CH}_2-$), 7.50-6.88 (10H, multiplet, aromatic protons); mass spectrum m/e : 267 (M^+), 91 (base peak).

Anal. Calcd. for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_2$: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.56; H, 4.85; N, 15.96.

SCHEME 7



SCHEME 8



2-Benzyl-1-(4-nitrophenyl)-1,2,4-triazolidin-3,5-dione (XVd).

To a stirred suspension of 300 mg. of XVe in 2 ml. of glacial acetic acid was added 2 ml. of fuming nitric acid under ice-cooling. After the stirring had been continued for 2 hours at room temperature, the mixture was poured into 20 ml. of water and the precipitate of XVd was collected by filtration, washed with water, dried, and recrystallized from ethanol to give 0.38 g. of XVd as pale yellowish needles, m.p. 200-201°; nmr δ (deuteriodimethylsulfoxide): 11.95 (1H, broad, NH), 6.90-7.32 (5H, multiplet, aromatic protons), 7.53 (2H, doublet, $J = 9.0$ Hz, N_1 - C_2' - and C_6' -H), 8.31 (2H, doublet, $J = 9.0$ Hz, N_1 - C_3' and C_5' -H), 4.65 (2H, singlet, $-CH_2-$); mass spectrum m/e : 312 (M^+), 178 (ion H in Scheme 7), 164 (ion I), 150 (ion J), 122 (ion N), 91 (base peak).

Condensation of XIIIa with Benzyl Chloride.

A mixture of 200 mg. of XIIIa, 260 mg. of benzyl chloride, 0.3 g. of potassium hydroxide, and 5 ml. of water was refluxed for 2 hours. An insoluble substance was filtered off, and the filtrate was extracted with chloroform. The extract was washed with water, dried over sodium sulfate, and evaporated. The remaining residue was chromatographed on silica gel. Evaporation of the eluate with benzene gave 30 mg. of *N*-benzyl-*N'*-(4-nitrophenyl)-*N'*-benzylidenehydrazine (XVIa) as yellowish needles, m.p. 156-157° (from hexane), which was identical with the authentic sample of XVIa described later; ν max (potassium bromide) cm^{-1} : 1500, 1325 (NO_2); nmr δ (deuteriochloroform): 8.12 (2H, doublet, $J = 9.0$ Hz, 4-nitrophenyl- C_3' - and C_5' -H), 7.03-7.70 (13H, multiplet, $-CH = N-$ and aromatic protons).

Anal. Calcd. for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.39; H, 5.31; N, 12.42.

Evaporation of the eluate with benzene-chloroform (1:1) afforded 28 mg. of *N*-benzyl-4-nitroaniline as a yellowish powder, whose spectroscopic data were identical with those of an authentic specimen.

Hydrolysis of XVIa.

A mixture of 50 mg. of XVIa and 20 ml. of concentrated hydrochloric acid was heated at 150° in a sealed tube for 4 hours. After cooling, the mixture was extracted with ether. The extract was washed with saturated sodium chloride solution, and a stream of air was introduced under ice-cooling. The solvent was evaporated to a volume of 10 ml., and extracted with 3 ml. of 5% sodium hydroxide. The aqueous layer was made acidic with concentrated hydrochloric acid and extracted with ether. The extract was washed with saturated sodium chloride solution, dried over sodium sulfate, and evaporated to give 7 mg. of benzoic acid, which was identified by comparison of spectroscopic data with those of an authentic sample. The above ethereal extract afforded 18 mg. of XVIa.

N-Benzyl-*N'*-(4-nitrophenyl)-*N'*-benzylidenehydrazine (XVIa).

A mixture of 1.5 g. of 4-nitrophenylhydrazine, 1.2 g. of benzyl chloride, 0.8 g. of pyridine and 30 ml. of dry benzene was heated at 120° for 4 hours in a sealed tube. After cooling, the insoluble substance was removed by decantation, and the solvent was washed with water, dried and evaporated. The resulting residue was chromatographed on silica gel using chloroform-benzene (4:1) as an eluant. Removal of the solvent afforded 150 mg. of XVIa as yellow needles, m.p. 156-157° (from ethanol), whose structure was identical with those of the sample obtained from XIIIa as above by comparison of spectroscopic data and mixed melting point determination.

2-Benzyl-1-(*N*-benzyl-4-chloroanilino)-4-(4-chlorophenyl)-1,2,4-triazolidin-3,5-dione (XIVa) (4).

A solution of 12.6 g. of *N*-benzyl-*N'*-(4-chlorophenyl)carbamoyl azide (1b) in 126 ml. of dry xylene was refluxed for 9 hours. After the work-up as described (4), the products obtained were chromatographed on silica gel to give 5.2 g. (46.4%) of 1-benzyl-

5-chloro-3-hydroxy-1*H*-indazole (IIb), 0.6 g. (5.3%) of 1-benzyl-5-chloro-2-benzimidazolinone (IIIb), 0.6 g. (5.3%) of 1-benzyl-3-[β -benzyl- β -(4-chlorophenyl)hydrazocarbonyl]-5-chloro-2-benzimidazolinone (IVb) and 9.4 g. (4.1%) of XIVa as colorless needles, m.p. 176.5-177.5° (from ethanol); ν max (potassium bromide) cm^{-1} : 1790, 1740 (C=O); nmr δ (deuteriodimethylsulfoxide): 6.43 (2H, doublet, $J = 9.0$ Hz, N_1 -C_{2'}- and C_{6'}-H), 7.17 (2H, doublet, $J = 9.0$ Hz, N_1 -C_{3'}- and C_{5'}-H), 7.57 (2H, doublet, $J = 9.0$ Hz, N_4 -C_{2''}- and C_{6''}-H), 7.45-6.90 (12H, multiplet, N_4 -C_{3''}-, C_{5''}-H and the other aromatic protons), 4.83 (2H, singlet, -CH₂-), 4.40 and 4.80 (2H, each doublet, $J = 15.0$ Hz, -CH₂-; these signals were observed at 4.57 (2H) as a singlet at 80°; mass spectrum m/e : 516 (M^+) (cf. Scheme 7).

Anal. Calcd. for C₂₈H₂₂Cl₂N₄O₂: C, 65.00; H, 4.29; N, 10.83. Found: C, 64.84; H, 4.32; N, 11.10.

2-Benzyl-1-(*N*-benzylanilino)-4-phenyl-1,2,4-triazolidin-3,5-dione (XIVb) (4).

A solution of 14.1 g. of *N*-benzyl-*N*-phenylcarbamoyl azide (Ic) in 141 ml. of xylene was refluxed for 9 hours and worked up as described (4). The products obtained were chromatographed on silica gel to give 8.3 g. (66.9%) of 1-benzyl-3-hydroxy-1*H*-indazole (IIc), 0.835 g. (6.7%) of 1-benzyl-2-benzimidazolinone (IIc), 0.65 g. (3.2%) of 1-benzyl-3-(β -benzyl- β -phenylhydrazocarbonyl)-2-benzimidazolinone (IVc), and 0.29 g. (2.3%) of XIVb as colorless needles, m.p. 122-123° (from ethanol); ν max (potassium bromide) cm^{-1} : 1790, 1733 (C=O); nmr δ (deuteriochloroform): 6.54 (2H, two doublet, $J = 9.0$ Hz, 2.5 Hz, N_1 -C_{2'}- and C_{6'}-H), 6.80-7.55 (18H, multiplet, N_1 -C_{3'}- and C_{5'}-H, and the other aromatic protons), 4.79 (2H, singlet, -CH₂-), 4.28 and 4.78 (2H, each doublet, $J = 15$ Hz, -CH₂-), which signal collapsed at 4.53 to a singlet at 65°; mass spectrum m/e : 448 (M^+) (cf. Scheme 7).

Anal. Calcd. for C₂₈H₂₄N₄O₂: C, 74.98; H, 5.39; N, 12.49. Found: C, 75.01; H, 5.54; N, 12.12.

1-(4-Chloroanilino)-4-(4-chlorophenyl)-1,2,4-triazolidin-3,5-dione (XIIIb).

A mixture of 600 mg. of XIVa, 3 ml. of sulfuric acid, and 3 ml. of glacial acetic acid was heated at 100° for 1.5 hours. The mixture was diluted with 20 ml. of ice-water; and the crystals precipitated were collected by filtration, washed with water, and extracted with 20 ml. of 5% sodium hydroxide solution. The extract was made acidic with concentrated hydrochloric acid to give 240 mg. of XIIIb as a precipitate. Recrystallization from ethanol afforded XIIIb as colorless needles, m.p. 242-243°; ν max (potassium bromide) cm^{-1} : 3250-2600 (NH), 1780-1710 (C=O); nmr δ (deuteriodimethylsulfoxide): 11.54, 10.80 (2H, each broad, 2 x NH), 7.49 (8H, singlet, aromatic protons).

Anal. Calcd. for C₁₄H₁₀Cl₂N₄O₂: C, 49.87; H, 2.99; N, 16.62. Found: C, 49.97; H, 3.23; N, 16.87.

The Reaction of XIIIb with Benzyl Chloride.

A mixture of 150 mg. of XIIIb, 200 mg. of benzyl chloride, 7 ml. of water, and 250 mg. of potassium hydroxide was refluxed for 2 hours. After removal of the insoluble substance, the mixture was extracted with chloroform. The extract was washed with water, dried, and evaporated. The resulting residue was chromatographed on silica gel. Evaporation of the eluate with benzene, followed by recrystallization of the remaining residue from hexane, afforded 17 mg. of *N*-benzyl-*N'*-benzylidene-*N*-(4-chlorophenyl)hydrazine (XVIIb) as pale yellowish needles, m.p. 118-119°, whose spectroscopic data were identical with those of the authentic specimen described later. Successive elution with benzene was evaporated to give 30 mg. of *N*-benzyl-4-chloroaniline, whose

spectroscopic data were identical with those of an authentic sample. *N*-Benzyl-*N*-(4-chlorophenyl)hydrazine (XVII).

A mixture of 14.7 g. of 4-chlorophenylhydrazine, 6.3 g. of benzyl chloride and 75 ml. of ethanol was refluxed for 4 hours. The solvent was evaporated and the remaining residue was diluted with 100 ml. of hot water, and extracted with chloroform. The extract was washed, dried over sodium sulfate, and evaporated. The remaining residue was distilled *in vacuo* to give 8.8 g. of XVII as a yellowish oil, b.p. 163-167° (0.7 mm); ν max (liquid) cm^{-1} : 3450, 3400 (NH₂); nmr δ (deuteriochloroform): 3.35 (2H, singlet, NH₂), 4.32 (2H, singlet, -CH₂-), 6.80 (2H, doublet, $J = 9.0$ Hz, C₂- and C₆-H), 7.07 (2H, doublet, $J = 9.0$ Hz, C₃- and C₅-H), 7.15 (5H, singlet, aromatic protons). The hydrochloride prepared as usual was recrystallized from ethanol to give colorless needles, m.p. 157-158°.

Anal. Calcd. for C₁₃H₁₃ClN₂·HCl: C, 58.00; H, 5.24; N, 10.41. Found: C, 58.22; H, 5.22; N, 10.41.

The resulting solid, obtained after distillation of XVII, was recrystallized from ethanol-hexane to give 70 mg. of XVIIb, m.p. 118-119°, which was identified by comparison of spectroscopic data with those of the authentic specimen described later.

Thermal Reaction of XVII with Urea (24).

A mixture of 1.2 g. of hydrazine (XVII) and 0.45 g. of urea was heated at 180-190° for 2 hours, and then at 270-280° for 3 minutes. The mixture was extracted with ethanol to remove cyanuric acid. The solvent was evaporated to leave 1.35 g. of colorless crystals which was recrystallized from ethanol to give 1-benzyl-5-chloro-3-hydroxy-1*H*-indazole (IIa) as colorless needles, m.p. 206-207°, whose spectroscopic data were identical with those of the authentic specimen (4).

N-Benzyl-*N'*-benzylidene-*N*-(4-chlorophenyl)hydrazine (XVIIb).

A mixture of 1.2 g. of XVII and 0.55 g. of benzaldehyde was allowed to stand at room temperature for 0.5 hour in a current of nitrogen. The mixture was recrystallized from ethanol to give 1.4 g. of XVIIb as colorless needles, m.p. 118-119°.

Anal. Calcd. for C₂₀H₁₇ClN₂: C, 74.87; H, 5.34; N, 8.73. Found: C, 75.22; H, 5.30; N, 8.86.

Acknowledgments.

We are grateful to Vice President S. Uehara and Director Dr. S. Ikawa, Taisho Pharmaceutical Co., Ltd., for their encouragement. We also thank Dr. I. Tanaka, Dr. T. Seki and Dr. R. Yanase for their helpful suggestions. Further we thank Mr. M. Ohuchi, Miss A. Kawakami, and Miss C. Yoshida for microanalyses and mass spectral measurement.

REFERENCES

- (1) Part VIII, T. Kametani, S. Shibuya, and M. Shio, *J. Heterocyclic Chem.*, **8**, 545 (1971).
- (2) This forms Part CDXLVIII of "Studies on the Syntheses of Heterocyclic Compounds", by T. Kametani.
- (3) Communications concerning this paper should be directed to Professor Tetsuji Kametani.
- (4) T. Kametani, K. Sota, and M. Shio, *J. Heterocyclic Chem.*, **7**, 807 (1970).
- (5) The structures (X, XI, XII, or XIII) assigned for the compound (A, B, and C) (4) should be revised.
- (6) L. J. Bellamy, "Advances in Infrared Group Frequencies", Barnes & Noble, 1968, p. 163.
- (7) T. Shimanouchi, "Analysis of Infrared Spectra", Nankodo,

Tokyo-Kyoto, 1960, p. 65.

(8) W. Lwowski, A. Hartenstein, C. deVita, and R. L. Smick, *Tetrahedron Letters*, 2497 (1964).

(9) T. Kametani, K. Sota, and M. Shio, *J. Heterocyclic Chem.*, 7, 821 (1970).

(10) K-H. Koch and E. Fahr, *Angew. Chem.*, 82, 636 (1970).

(11) S. Ozaki, *J. Synthetic Org. Chem., Japan*, 28, 23 (1970).

(12a) R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, 64, 149 (1964); (b) R. F. Bleiholder and H. Shechter, *J. Am. Chem. Soc.*, 90, 2131 (1968); (c) R. Huisgen and H. Blaschke, *Chem. Ber.*, 98, 2985 (1965); (d) R. Huisgen and H. Blaschke, *Tetrahedron Letters*, 1409 (1964); (e) T. Bacchetti, *Gass. Chim. Ital.*, 91, 866 (1961) [*Chem. Abstr.*, 56, 8708 (1962)]; (f) R. Puttner and K. Hafner, *Tetrahedron Letters*, 3119 (1964); (g) R. Huisgen and H. Blaschke, *Ann. Chem.*, 586, 145 (1965).

(13) M. Bush, *Chem. Ber.*, 35, 1562 (1902).

(14) W. S. Wadsworth and W. D. Emmons, *J. Org. Chem.*, 32, 1279 (1967).

(15) N. S. Bhacca, D. P. Hollis, L. F. Johnson, and E. A. Pier, "NMR Spectra Catalog", Vol. II, 638, Varian, U. S. A., 1963.

(16) T. Kametani and M. Shio, *J. Heterocyclic Chem.*, 7, 831 (1970).

(17) W. Lwowski, "Nitrenes", Interscience Publishers, Inc., New York, 1970, p. 214.

(18a) H. Heine, *Angew. Chem.*, 74, 772 (1962); (b) T. Kato, Y. Yamamoto, and M. Satoh, *Yakugaku Zasshi*, 91, 384 (1971); (c) R. Huisgen, J. Sauer, H. J. Sturm, and J. H. Markgraf, *Chem. Ber.*, 93, 2106 (1960); (d) R. Huisgen, *Angew. Chem.*, 72, 359 (1960); (e) W. Lwowski, and T. J. Maricich, *J. Am. Chem. Soc.*, 86, 3164 (1964); (f) A. Mishra, S. N. Rice, and W. Lwowski, *J. Org. Chem.*, 33, 481 (1968).

(19) c.f. A. R. Katritzky and A. J. Boulton, "Advances in Heterocyclic Chem.", Vol. 7, Academic Press, New York and London, 1966, p. 208.

(20) S. Wawzonek and E. Yeakey, *J. Am. Chem. Soc.*, 82, 5718 (1960).

(21a) G. Witting, *Angew. Chem.*, 66, 10 (1954); (b) C. R. Hauser and S. W. Kantor, *J. Am. Chem. Soc.*, 73, 1437 (1951); (c) D. Y. Curtin and W. R. Proops, *ibid.*, 76, 494 (1954); (d) P. deMayo, "Molecular Rearrangements", Vol. I. Interscience Publisher, Inc., New York-London, 1963, p. 375.

(22) c.f. Y. Yukawa and Y. Tsuno, *J. Am. Chem. Soc.*, 79, 5530 (1957).

(23) All melting points are uncorrected; nmr were taken with a Hitachi R-20 spectrometer; molecular weight was measured with a Hitachi-Perkin-Elmer Molecular Weight Apparatus (Model 115) using chloroform as solvent; and mass spectra were determined with a Hitachi RMU-7-spectrometer.

(24) H. Milrath, *Monatsch. Chem.*, 29, 909 (1908).