expected in this molecule,[4,5] the 6-hydrogen gives rise to a sharp singlet. The 3-CH_3 group shows up as a singlet at $\delta = 1.80$ ppm.

Compound IIIb presents also an easily analyzable spectrum and distinction between IIb and IIIb can be made in a straightforward manner by the absence in the latter of the $J_{5,6}$ coupling. From the nmr point of view it is interesting to note the magnitude (0.7 cps) and clearness with which the long-range coupling $J_{4,6}$ appears.

The case of IIb was the one which was most difficult to study. This compound was always obtained mixed with IIIb (see Experimental Section) and none of the various attempts to separate the two isomers was successful. Nevertheless, by trying different solvent mixtures and with the previous knowledge of the nmr spectrum of IIIb, the spectrum of IIb was analyzed and the assignments were made in an unequivocal way, since none of the other compounds of theoretically possible formation would have shown an nmr spectrum of similar characteristics. All the necessary parameters are given in Table II. Finally, IIc–IIIc also presents two AB-type structures ($J_{4,5}$ and $J_{1,2}$) and two singlets corresponding to the two methyl groups.

Experimental Section[6]

Diels–Alder Adducts Ia, Ib, and Ic.—These were prepared in the usual manner[7] from the corresponding furans and maleic anhydride. The nature of the *exo* adducts obtained was checked by nmr spectroscopy.

***exo-cis*-Endoxo-4,5-*trans*-dibromotetrahydrophthalic Anhydride (IIa–IIIa) and *exo-cis*-3,6-Endoxo-4,5-*cis*-dibromotetrahydrophthalic Anhydride (IVa).**—The method outlined by Berson for the bromination of Ia was followed.[1] The total yield of the bromination reaction was 86%. Product distribution was 34.8 (IVa) and 65.1% (IIa–IIIa).

***exo-cis*-3,6-Endoxo-3-methyl-4,5-*exo-cis*-dibromotetrahydrophthalic Anhydride (IVb).**—To a solution of Ib (10 g, 0.055 mole) in CH_2Cl_2 (250 ml), bromine (3 ml, 0.055 mole) was added in 0.5-ml portions, under diffuse sunlight, with permanent stirring. The white precipitate formed was filtered and washed with a small amount of cold ether to yield 2.74 g (17.3%) of IVb, mp 266–268° dec.

Anal. Calcd for $C_9H_8O_4Br_2$: C, 31.45; H, 2.21; Br, 47.47. Found: C, 31.79; H, 2.37; Br, 47.01.

***exo-cis*-3,6-Endoxo-3-methyl-4-*endo*-5-*exo*-dibromotetrahydrophthalic Anhydride (IIIb).**—The mother liquor of the preceding preparation was kept under refrigeration for 24 hr. The precipitate formed (IIIb) was filtered off and washed with ether (5.30 g, 34%), mp 165–167°.

Anal. Calcd for $C_9H_8O_4Br_2$: C, 31.45; H, 2.21; Br, 47.47. Found: C, 31.50; H, 2.37; Br, 47.11.

***exo-cis*-3,6-Endoxo-3-methyl-4-*exo*-5-*endo*-dibromotetrahydrophthalic Anhydride (IIb).**—The liquid portion left from the preparation of IIIb was evaporated to dryness under reduced pressure to afford 7.6 g (48.7%) of a white solid, mp 125–126°. The nmr spectrum of this product showed it to be a mixture of IIIb (54%) and IIb (46%). The composition of the mixture was determined by comparing the integral values of the 6-H signal for both compounds in their nmr spectrum. Elemental analysis of the mixture confirmed the above statement. None of the various attempts made to separate the two isomers was successful.

***exo-cis*-3,6-Endoxo-3,6-dimethyl-4,5-*trans*-dibromotetrahydrophthalic Anhydride (IIc–IIIc).**—To a solution of Ic (10.7 g, 0.055 mole) in CH_2Cl_2 (200 ml) bromine (3 ml, 0.055 mole) was added in small portions with cooling and permanent stirring. When the addition was completed, the solution was concentrated to 20 ml and ether (100 ml) added. Upon concentration of the solution under reduced pressure, a solid crystallized out. Recrystallization in ether afforded 15.6 g (80%) of IIc–IIIc, mp 127–128°.

Anal. Calcd for $C_{10}H_{10}O_4Br_2$: C, 33.92; H, 3.05; Br, 45.15. Found: C, 33.50; H, 3.17; Br, 44.87.

Registry No.—IIb, 13618-68-3; IIc–IIIc, 13618-69-4; IIIb, 13618-70-7; IVb, 13618-71-8.

Acknowledgments.—We wish to thank Professor J. A. Berson for his valuable criticism and to acknowledge the stimulating comments of one of the referees.

(4) F. A. L. Anet, *Can. J. Chem.*, **39**, 789 (1961).

(5) E. Payo, L. Cortés, J. Mantecón, and C. Piemonti, *J. Org. Chem.*, **31**, 1888 (1966).

(6) All melting points are uncorrected. Microanalyses were performed by F. Pascher, Mikroanalytisches Laboratorium, Bonn, Germany. Nmr spectra were run on a Varian A-60 spectrometer.

(7) O. Diels and K. Alder, *Ber.*, **490**, 243 (1931).

Quinazolines and 1,4-Benzodiazepines. XXXVII.[1] Synthesis and Rearrangements of a Substituted 5-Phenyl-1H-1,4-benzodiazepine

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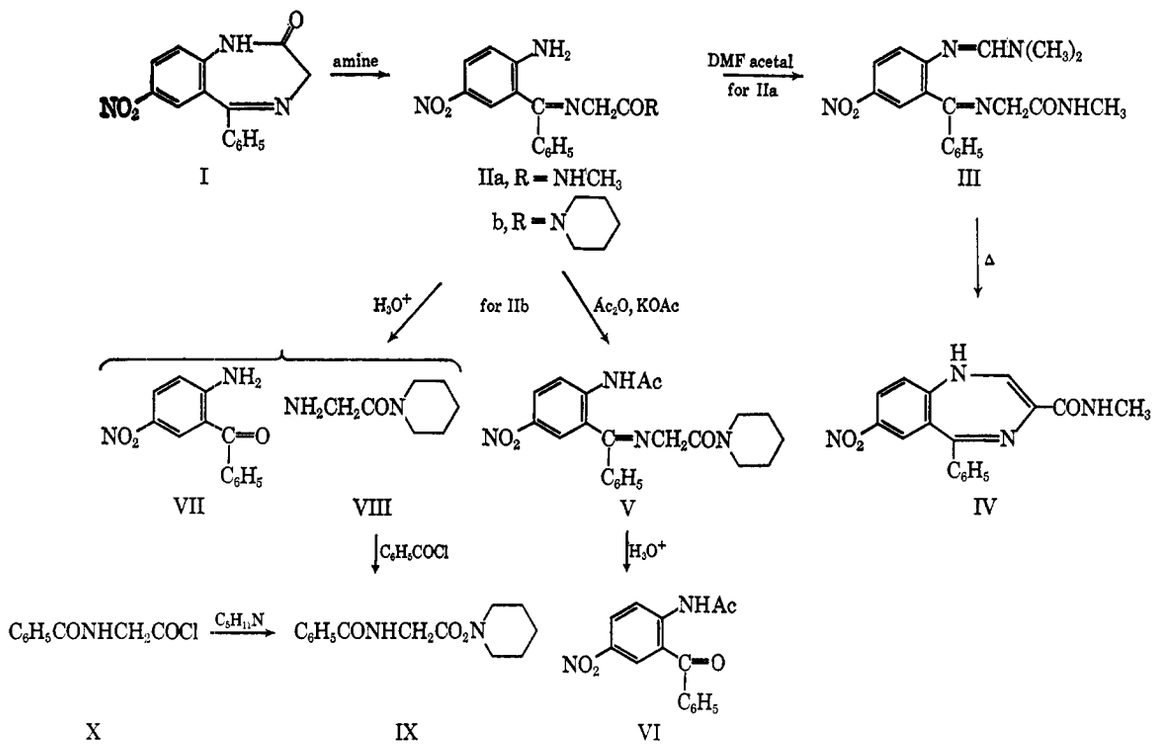
The three-step synthesis of N-methyl-7-nitro-5-phenyl-1H-1,4-benzodiazepine-3-carboxamide (IV) from 1,3-dihydro-7-nitro-5-phenyl-2H-1,4-benzodiazepin-2-one (I) is described. The 1H compound was subsequently oxidized to N-methyl-6-nitro-4-phenyl-2-quinazoline carboxamide (XV) and rearranged in acid to 5-nitro-3-phenylindole (XIX) and N-methyl-5-nitro-3-phenyl-2-indoleglyoxalamide (XVIII). A by-product isolated from the synthesis of the 1H compound was shown to be 3,10b-dihydro-1-methyl-9-nitro-10b-phenylimidazo[1,2-*c*]-quinazolin-2(1H)-one (XXVI). Evidence is given for the structures assigned and possible mechanisms for the formation of these compounds are presented.

As a continuation of our studies on the synthesis and transformations of the 1,4-benzodiazepine ring system, we have prepared the open amides IIa and IIb from 1,3-dihydro-7-nitro-5-phenyl-2H-1,4-benzodiazepin-2-one (I) by means of a transamidation reaction. Compound IIa, on treatment with dimethylformamide acetal, gave the dimethylaminomethylenimino derivative (III) which, on heating in solution, gave the 1H-1,4-benzodiazepine (IV) (Scheme I).

The structure of IIb was confirmed by the series of reactions outlined in Scheme I. On treatment with acetic anhydride and potassium acetate, IIb gave the N-acetyl derivative V. Mild acid hydrolysis of either IIb or V gave the corresponding benzophenones VII and VI in almost quantitative yield. The hydrolysis of IIb also gave an excellent yield of glycylpiperidide

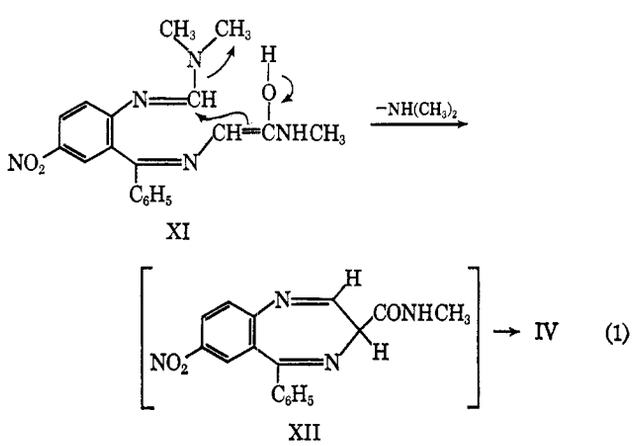
(1) Paper XXXVI: R. I. Fryer, D. Winter, and L. H. Sternbach, *J. Heterocyclic Chem.*, **4**, 355 (1967).

SCHEME I



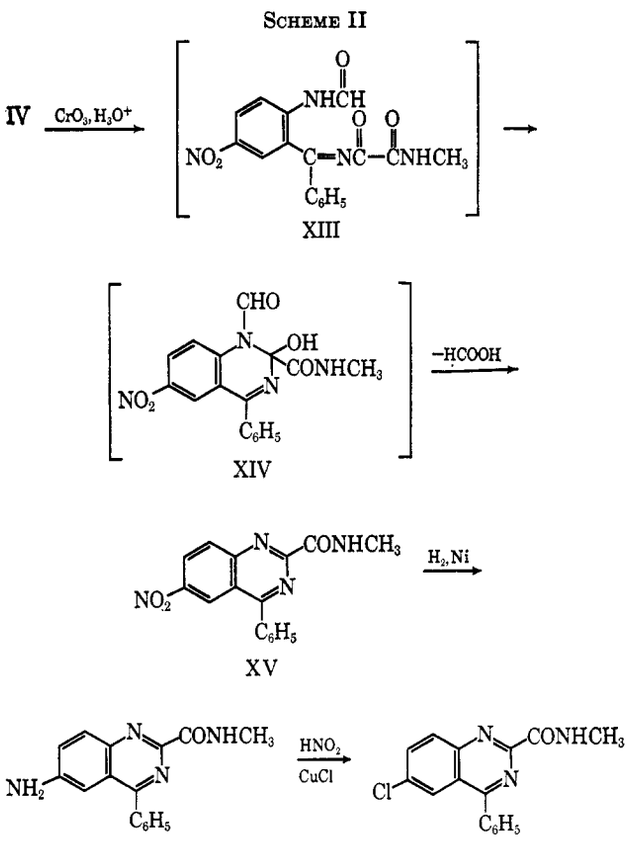
VIII which was characterized as the hippuric acid derivative IX. An authentic sample of IX was prepared from the acid chloride of hippuric acid (X) as shown.

If structure III is written in the tautomeric enol form (XI), it can be seen that condensation with loss of dimethylamine can occur as shown to give XII as an intermediate. A shift of the 1,2 double bond into conjugation with the amide would then give the product IV (eq 1). The chemical transformations of IV (discussed below) and the relatively simple nmr spectrum obtained for the compound gave ample evidence for the assigned structure.



Oxidation of IV with chromic acid resulted in the formation and isolation of the quinazoline derivative XV (Scheme II). The reaction probably proceeds *via* the dicarbonyl intermediate XIII which could then cyclize to the quinazoline XIV. Loss of formic acid from this intermediate would give the product XV. The structure of XV was confirmed by reducing the

SCHEME II

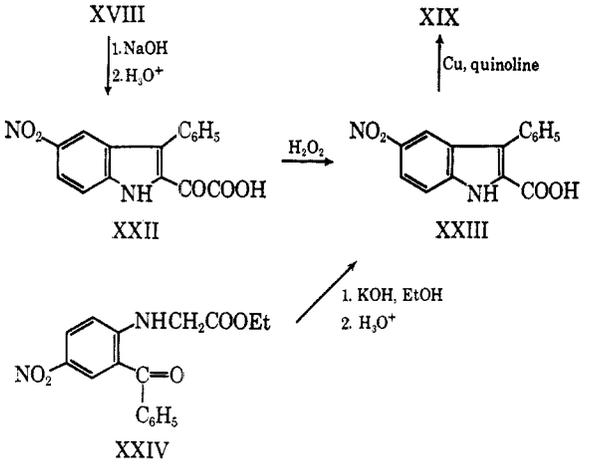


nitro group to the corresponding amine (XVI) and then carrying out a Sandmeyer reaction with nitrous acid and cuprous chloride to give the 6-chloro derivative XVII. A comparison of XVII with an authentic sample prepared by treatment of the known 6-chloro-4-

phenyl-2-quinazolin-2-carboxylic acid[2] with thionyl chloride and then with methylamine showed the two compounds to be identical in all respects.

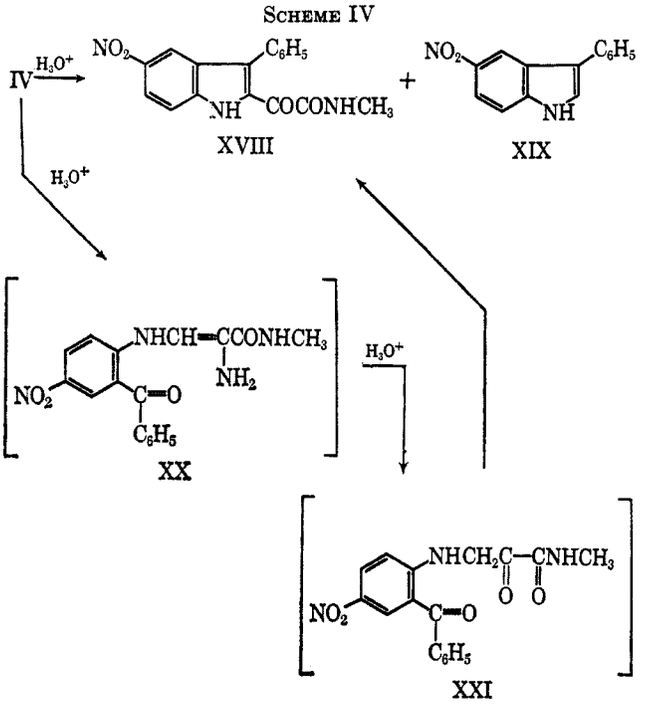
An interesting rearrangement of IV was observed when the compound was treated under mild conditions with dilute mineral acid. After making the reaction mixture basic, an almost quantitative yield of a mixture of the two indole derivatives XVIII and XIX was isolated. While XVIII, the major product, could be isolated directly from the reaction mixture, the mother liquor was difficult to separate into its components. Hydrolysis of this mixture gave the base-soluble salt of the acid XXII (Scheme III) from which the indole

SCHEME III



XIX was readily separated by filtration. The formation of XVIII is relatively easy to justify (Scheme IV).

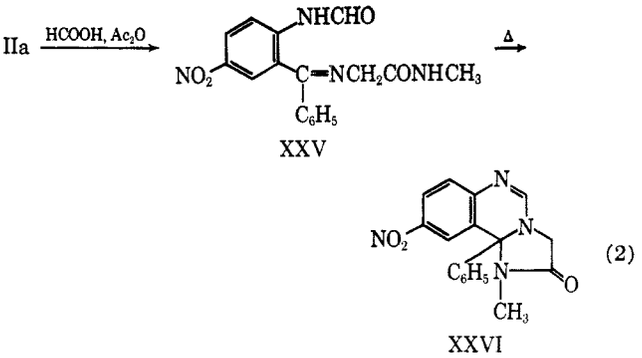
SCHEME IV



If it is assumed that hydrolysis of the azomethine bond is the first step in the rearrangement of IV to XVIII, the enamine XX would readily hydrolyze under these same conditions and give the ketone XXI. The activated methylene group could then condense with the benzophenone carbonyl to give the indole XVIII. The formation of XIX is more difficult to rationalize. It would appear to involve, besides rearrangement, subsequent hydrolysis, oxidation, and decarboxylation steps.

The structure of XVIII was confirmed by its conversion into the indole carboxylic acid XXIII which was compared with and shown to be identical with an authentic sample synthesized from the ester XXIV[3] (Scheme III). Hydrolysis of the amide gave the glyoxylic acid derivative XXII which on treatment with peroxide gave XXIII. Decarboxylation of XXIII with copper and quinoline gave an authentic sample of XIX, which was shown to be identical in all respects with the other rearrangement product.

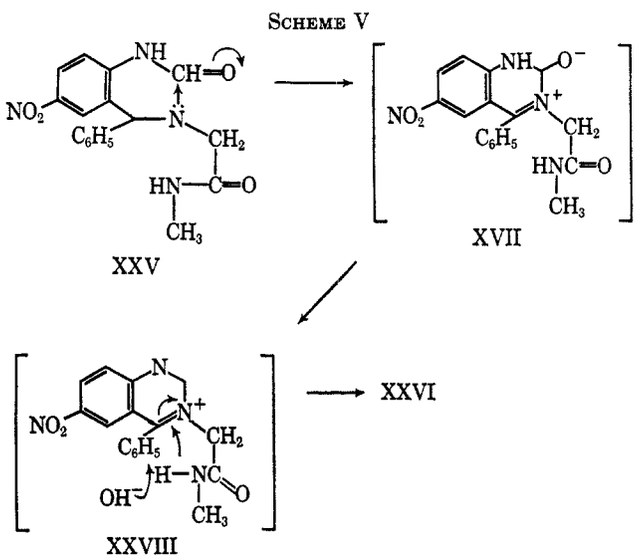
The synthesis of IV from the dimethylaminomethylenimino compound III was accompanied by the formation of varying amounts of a by-product, to which we assign structure XXVI. It was later found that this by-product could be prepared in good yield by cyclization of the N-formyl derivative of IIa, compound XXV (eq 2). In this instance IV was a by-product of the condensation.



(2)

A plausible mechanism for the formation of XXVI from XXV can be postulated as an attack of the formyl group by the unshared pair of electrons on the nitrogen of the Schiff base. This would lead to the intermediate XXVII as shown. Loss of OH^- would give the azomethine and lead to XXVIII which could then lose the proton from the methylamino group to give XXVI (Scheme V).

SCHEME V

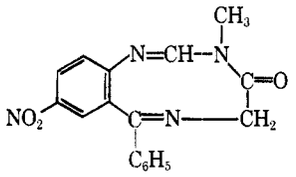


XXVIII

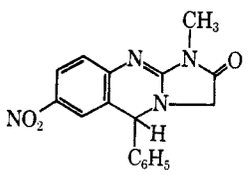
(2) L. H. Sternbach, E. Reeder, A. Stempel, and A. I. Rachlin, *J. Org. Chem.*, **29**, 332 (1964).

(3) Dr. G. A. Archer kindly supplied us with the ester XXIV.

In assigning the structure of XXVI, two other possible isomers, compounds XXIX and XXX, should be considered. Compound XXIX can be discounted, since the reaction product is stable to both acid and base and the infrared carbonyl absorption at 1720 cm^{-1} is indicative of a five-membered cyclic tertiary lactam. For structures XXVI and XXX, however, both compounds would be expected to have an infrared absorption around 1720 cm^{-1} and, in the nmr, both compounds would have a three-proton singlet for the N-methyl group, a two-proton signal for the methylene group, eight aromatic protons, and a low-field proton (aldehydic or benzylic).



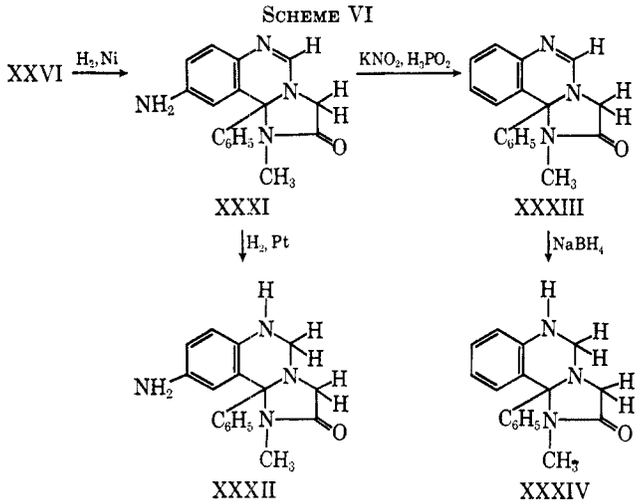
XXIX



XXX

From an examination of the nmr spectra of the reduction products (XXXI, XXXII) and the deaminated derivatives XXXIII and XXXIV, obtained as shown in Scheme VI, it was obvious that XXX could be ruled out and therefore XXVI was assigned as the structure of the product obtained by dehydration of XXV.[4]

SCHEME VI



XXXI XXXIII XXXII XXXIV

Experimental Section

Melting points were determined microscopically on a hot stage and are corrected. Reference spectra were taken on all compounds and are reported in the experimental section only where possible ambiguity exists. The nmr spectra were determined on a Varian A-60 instrument, the infrared spectra were determined on a Beckman IR-9 spectrophotometer, and the ultraviolet spectra were determined on a Cary Model 14 spectrophotometer.

2-[(2-Amino-5-nitrophenyl)phenylmethylenimino]-N-methylacetamide (II).—A stream of methylamine gas was bubbled into a solution of 10 g of I[5] in 100 ml of N,N-dimethylformamide at room temperature. After 30 min the addition of methylamine was stopped and the reaction mixture was allowed to stand overnight. Solvent was removed under reduced pressure and the residue was treated first with 10 ml of methanol and then with 100 ml of ether. The product was filtered (8.6 g, 77.5%), mp 190–192°. Recrystallization from ethanol gave the pure compound as yellow plates, mp 190–193°.

Anal. Calcd for $C_{16}H_{16}N_4O_3$: C, 61.53; H, 5.16. Found: C, 61.21; H, 5.29.

2-[(Dimethylaminomethylenimino-5-nitrophenyl)phenylmethylenimino]-N-methylacetamide (III).—A solution of 70 g of IIa in 375 ml of N,N-dimethylformamide acetal was stirred at room temperature for 6 days. The precipitated product was obtained by filtration and washed with ether to give 74.9 g (91%) of III as yellow prisms, mp 194–197° dec (sealed capillary).

Anal. Calcd for $C_{19}H_{21}N_5O_3$: C, 62.11; H, 5.76. Found: C, 61.93; H, 5.89.

N-Methyl-7-nitro-5-phenyl-1H-1,4-benzodiazepine-3-carboxamide (IV) and 3,10b-Dihydro-1-methyl-9-nitro-10b-phenylimidazo[1,2-c]quinazolin-2(1H)-one (XXVI). 1. From Compound III.—A solution of 57 g of III in 500 ml of toluene was heated under reflux for 72 hr, cooled slightly, and filtered. The precipitate was washed with ether and dried to give 25.7 g (51.4%) of IV[6] as dark red prisms, mp 278–292°. Recrystallization from a mixture of chloroform and ethanol gave an analytically pure sample: mp 287–292°; infrared absorption (KBr) at 3410 (NH) and at 1660 cm^{-1} (C=O); nmr peaks (DMSO-d_6) at δ 6.24 (1 H doublet, J = 7 cps, >CHCONHCH$_3$), 2.74 (3 H doublet, J = 5 cps, –NHCH$_3$); ultraviolet maxima (2-propanol) at 232 mμ (ϵ 23,500), 260 (18,600), and at 388 (5600).

Anal. Calcd for $C_{17}H_{14}N_4O_3$: C, 63.35; H, 4.38. Found: C, 63.41, 63.55; H, 4.60, 4.55.

Concentration of the mother liquors from IV[6] gave, upon cooling and filtration, 18.2 g of XXVI as yellow prisms, mp 186–193°. Recrystallization from a mixture of chloroform and methanol gave 17.1 g (34.2%) of pure XXVI: mp 194–197°; infrared absorption ($CHCl_3$) at 1720 cm^{-1} (C=O); nmr peaks (DMSO-d_6) at δ 3.02 (3 H singlet, >NCH$_3$), 7.60 (1 H singlet, –CH=N–), and 4.46, 3.94 (2 H, AB quartet, J = 16 cps, –CH$_2$–); ultraviolet maxima (2-propanol) at 238 mμ (ϵ 12,140) and at 354 (12,410).

Anal. Calcd for $C_{17}H_{14}N_4O_3$: C, 63.35; H, 4.38. Found: C, 63.12; H, 4.68.

2. From Compound XXV. A.—A solution of 1 g of XXV in 50 ml of dry toluene was heated under reflux for 7 hr. Solvents were evaporated and the residue was crystallized from a mixture of methanol and ether to give 0.6 g (64%) of XXVI, mp and mmp 189–193°. The mother liquors were evaporated, dissolved in benzene, and chromatographed over silica. Using ethyl acetate as the eluent, 50 mg (5%) of IV was obtained, mp and mmp 285–292°.

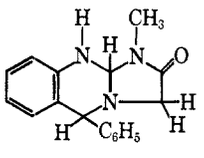
B. A solution of 32.5 g of XXV in 65 ml of acetic anhyride was heated at 65° for 2 hr. This mixture was cooled, poured into 500 ml of water, and the pH was adjusted to approximately 7 with ammonium hydroxide. The products were extracted into three 200-ml portions of dichloromethane. The organic layers were combined, washed with three 100-ml portions of water, dried over anhydrous sodium sulfate, and evaporated to give 38 g of a dark oil. Crystallization from a mixture of dichloromethane and ether gave 17.8 g (57.6%) of the quinazolone XXVI as yellow prisms, mp and mmp 189–194°.

1-{2[(2-Amino-5-nitrophenyl)phenylmethylenimino]acetyl}-piperidine (IIb).—A solution of 10 g of compound I in 50 ml of piperidine was heated under reflux for 1 hr. A total of 35 ml of piperidine was removed by distillation and the residue was poured into 50 ml of methanol. The solution was cooled and the product collected by filtration. Recrystallization of the product from a mixture of chloroform and ethanol gave 10.7 g (82%) of the pure product as yellow prisms, mp 191–196°.

Anal. Calcd for $C_{20}H_{22}N_4O_3$: C, 65.55; H, 6.05; N, 15.29. Found: C, 65.38; H, 5.93; N, 15.15.

1-{2-[(2-Acetamido-5-nitrophenyl)phenylmethylenimino]acetyl}piperidine (V).—A mixture of 5 g of IIb, 25 ml of acetic

(4) For purposes of comparison with XXXIV, compound A would be the product expected to be obtained by reduction of and deamination of structure XXX.



A

(5) L. H. Sternbach, R. I. Fryer, O. Keller, W. Metlesics, G. Sach, and N. Steiger, *J. Med. Chem.*, **6**, 261 (1963).

(6) In several experiments the yield of IV was in the range of 50–70% while the yield of XXVI obtained from the mother liquors varied from trace amounts up to 34%.

anhydride, and 2.5 g of sodium acetate was warmed on a steam bath for 3 hr and then allowed to stand at room temperature for 2 days. The reaction mixture was poured into a mixture of ice and water which was then made basic with ammonium hydroxide and extracted into three 100-ml portions of dichloromethane. The organic layers were combined, washed with three 50-ml portions of water and 100 ml of brine, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was recrystallized from a mixture of benzene and hexane to give 3.2 g (56%) of V as pale yellow prisms, mp 184–186°.

Anal. Calcd for $C_{22}H_{24}N_4O_4$: C, 64.69; H, 5.92. Found: C, 64.95; H, 5.91.

Hydrolysis of IIb. 1-Hippuroylpiperidine (IX).—A mixture of 12.4 g of IIb, 50 ml of 3 *N* hydrochloric acid, and 25 ml of methanol was heated on a steam bath for 30 min. Methanol was removed under reduced pressure and the resulting mixture was brought to pH 8 with 3 *N* sodium hydroxide solution. The precipitate was removed by filtration, washed well with water, and dried at 110° to give 8.5 g (99.8%) of 2-amino-5-nitrobenzophenone (VII),[5] mp and mmp 150–160°. The original filtrates were placed in a liquid extractor and extracted with ether for 4 days. Removal of the solvent gave 2.4 g of glycylpiperidine as an oil. Treatment of the aqueous layer with benzoyl chloride and sodium hydroxide gave 2.08 g of 1-hippuroylpiperidine, mp 88–91°. A solution of 1.4 g of the extracted glycylpiperidine, dissolved in 20 ml of 10% sodium hydroxide solution, was treated with five 0.29-ml portions of benzoyl chloride with vigorous shaking after the addition of each portion. The reaction mixture was acidified with concentrated hydrochloric acid and extracted with ether. The ether layer was washed with water and brine and was then dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 1.87 g of an oil which was crystallized from a mixture of ether and petroleum ether (bp 30–60°) to give 1.25 g of IX, mp 89–91°. A comparison of IX with an authentic sample prepared as described in the literature[7] showed the two compounds to be identical. The total recovery of VIII, both as glycylpiperidine and as 1-hippuroylpiperidine, amounted to 4.1 g (82%) based on glycylpiperidine.

Hydrolysis of V.—A solution of 0.8 g of V in 50 ml of 1 *N* hydrochloric acid was warmed on a steam bath for 15 min. The solution was cooled and filtered to give 2′-benzoyl-4′-nitroacetanilide (VI) as white needles: melting point and mixture melting point with an authentic sample,[8] 155–158°.

6-Nitro-N-methyl-4-phenyl-2-quinazolinecarboxamide (XV).—A solution of 2.2 g (0.0068 mole) of IV in 25 ml of glacial acetic acid was treated with 2.5 ml (0.0068 mole) of a standard chromate reagent[9] and allowed to stir at room temperature for 5 min. The green reaction mixture was poured onto 300 g of ice and the solution was made basic (pH 7–8) with ammonium hydroxide. Solids were removed by filtration over Celite which was then washed with dichloromethane. The filtrate was extracted with three 50-ml portions of dichloromethane. The organic layers were combined, washed, dried, concentrated to a small volume, and filtered over Woelm grade I neutral alumina. A mixture of ethyl acetate and dichloromethane (1:2) was used as the eluent. Removal of the solvent gave 600 mg (29%) of XV, mp 276–281°. Recrystallization from a mixture of dichloromethane and ethyl acetate gave the pure product as pale yellow rods, mp 285–287°.

Anal. Calcd for $C_{16}H_{12}N_4O_3$: C, 62.33; H, 3.92. Found: C, 62.35; H, 4.15.

6-Amino-N-methyl-4-phenyl-2-quinazolinecarboxamide (XVI).—A suspension of 0.65 g of XV in 200 ml of ethanol was treated with one-half teaspoonful of wet Raney nickel and was hydrogenated at atmospheric pressure until hydrogen uptake ceased. The solution was filtered, the nickel was washed with dichloromethane, and the filtrates were combined and evaporated. Recrystallization of the residue from methanol gave the product, 0.5 g (85%), as yellow prisms, mp 190–193°. The hydrochloride was prepared by dissolving the base in methanol and saturating this solution with dry hydrogen chloride. The solution was then evaporated to dryness and the residue recrystallized from a mixture of methanol and ether to give the salt as red prisms, mp 143–145°.

Anal. Calcd for $C_{16}H_{14}N_4O \cdot HCl$: C, 61.05; H, 4.80. Found: C, 60.88; H, 4.98.

6-Chloro-N-methyl-4-phenyl-2-quinazolincarboxamide (XVII). Method 1.—A solution of 0.3 g (0.001 mole) of XVI in 20 ml of 6 *N* hydrochloric acid was cooled in an ice bath and treated with a solution of 0.08 g (0.0012 mole) of sodium nitrite in 3 ml of water. The diazonium salt was stirred for 15 min and then slowly added to an ice cold solution of 0.24 g (0.0024 mole) of cuprous chloride in 6 ml of 6 *N* hydrochloric acid. The mixture was warmed to 60° and maintained at this temperature for 15 min. After cooling the solution was made basic with ammonium hydroxide and extracted into three 35-ml portions of dichloromethane. The organic layers were combined, washed, dried, and evaporated. The residue was recrystallized twice from methanol to give the product as white prisms, mp 194–197°.

Anal. Calcd for $C_{16}H_{12}ClN_3O$: C, 64.54; H, 4.06; N, 14.11. Found: C, 64.42; H, 4.25; N, 14.70.

Method 2.—A solution of 0.7 g of 6-chloro-4-phenyl-2-quinazolincarboxylic acid[8] in 60 ml of benzene, treated with 5 ml of thionyl chloride, was heated under reflux for 2 hr. Distillation to remove excess thionyl chloride was stopped when the volume of solvent was approximately 20 ml. The solution was cooled and treated with a solution of 4 g of methylamine in 30 ml of benzene. The mixture was stirred for 30 min and then poured into 150 ml of water. The layers were separated and the organic phase was washed with brine, dried over sodium sulfate, and evaporated. Recrystallization of the residue from a mixture of dichloromethane and hexane gave 0.5 g (69%) of XVII as white prisms: melting point and mixture melting point (with a sample prepared by method 1 above), 194–197°.

N-Methyl-5-nitro-3-phenyl-2-indoleglyoxalamide (XVIII) and 5-Nitro-3-phenylindole (XIX).—A suspension of 20 g of IV in 150 ml of methanol and 150 ml of 6 *N* hydrochloric acid was warmed on a steam bath for 20 min. The solution was adjusted to pH 7 with ammonium hydroxide and the precipitate was collected on a filter. The precipitate was washed with water, cold ethanol, and ether to give 18.1 g of a mixture of XVIII and XIX. The mixture was triturated with three 250-ml portions of boiling dichloromethane and the residue, now almost pure XVIII, was recrystallized from tetrahydrofuran to give 10.0 g (49%) of the pure product as yellow prisms, mp 251–253°.

Anal. Calcd for $C_{17}H_{13}N_3O_4$: C, 63.15; H, 4.05; N, 13.00. Found: C, 62.82; H, 4.19; N, 12.59.

The dichloromethane extracts were combined and evaporated to yield 7.1 g of the mixture. Fraction crystallization of this material from a mixture of the dichloromethane and ethanol gave 0.7 g (4.7%) of XIX as orange prisms, mp 191–200°.

Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.60; H, 4.20; N, 11.76. Found: C, 70.45; H, 4.47; N, 11.51.

Base hydrolysis of the mother liquors as for the preparation of XXII gave, after separation of 1.25 g of the acid, an additional 1.6 g (11%) of XIX.

5-Nitro-3-phenyl-2-indoleglyoxylic Acid (XXII).—A solution of 1 g of XVIII in 20 ml of ethanol was treated with 10 ml of 3 *N* sodium hydroxide solution and heated under reflux for 30 min. Ethanol was removed under reduced pressure and the solution was acidified with dilute hydrochloric acid. The product was obtained by filtration and recrystallized from a mixture of tetrahydrofuran and petroleum ether (bp 30–60°) to give 0.6 g (62.5%) of the pure acid as yellow rods, mp 215–225° dec.

Anal. Calcd for $C_{16}H_{10}N_2O_5$: C, 61.94; H, 3.25; N, 9.03. Found: C, 61.78; H, 3.26; N, 8.78.

5-Nitro-3-phenyl-2-indolecarboxylic Acid (XXIII). Method 1. A solution of 2.0 g of XXII in a mixture of 40 ml of ethanol and 20 ml of 10 *N* sodium hydroxide solution was cooled in an ice bath and treated with 40 ml of 5% hydrogen peroxide solution. The mixture was allowed to stand at room temperature for 5 hr and then acidified with dilute hydrochloric acid. Filtration and recrystallization of the precipitate from a mixture of tetrahydrofuran and hexane gave 1.8 g (99%) of the product as pale yellow prisms, mp 275–295° dec.

Anal. Calcd for $C_{15}H_{10}N_2O_4$: C, 63.83; H, 3.57. Found: C, 63.83; H, 3.72.

Method 2. From N-(2-Benzoyl-4-nitrophenyl)glycine Ethyl Ester (XXIV).—A mixture of 3.0 g of XXIV and 2.2 g of potassium hydroxide in 36 ml of absolute ethanol was heated under reflux for 24 hr. The solution was cooled, acidified with dilute hydrochloric acid, and filtered. The product was separated from a large amount of amorphous material contained in the precipitate by recrystallization from tetrahydrofuran. Recrystallization

(7) D. G. Doherty, E. A. Popenoe, and K. P. Link, *J. Am. Chem. Soc.*, **75**, 3466 (1953).

(8) C. M. Atkinson, J. C. Simpson, and A. Taylor, *J. Chem. Soc.*, 165 (1954).

(9) See C. Djerassi, *et al.*, *J. Org. Chem.*, **21**, 1547 (1956), for the preparation of chromate reagent.

from a mixture of tetrahydrofuran and hexane gave the pure acid, 100 mg (4%), as pale yellow prisms, mp and mmp 275–295° dec.

Decarboxylation of XXIII to Give 5-Nitro-3-phenylindole (XIX).—A mixture of 0.1 g of XXIII and 0.2 g of copper powder in 10 ml of quinoline was heated under reflux for 5 hr and then poured into 100 ml of water. The solution was filtered and acidified with 6 *N* hydrochloric acid. The precipitate was dissolved in dichloromethane and filtered through a column of 10 g of silica gel. The forerun containing about 10 mg of oil was discarded. Removal of solvent from further fractions gave 30 mg of product: mp 187–193°; with material isolated from the rearrangement of IV, mmp 187–195°.

9-Amino-3,10b-dihydro-1-methyl-10b-phenylimidazo[1,2-*c*]quinazolin-2(1H)-one (XXXI).—A solution of 5 g of XXVI in 300 ml of ethanol was treated with 2 tsp of wet Raney nickel and hydrogenated at room temperature and atmospheric pressure until hydrogen uptake stopped. The catalyst was removed by filtration and the solvent was evaporated. The residue was dissolved in 3 *N* hydrochloric acid and the solution was then made basic with ammonium hydroxide. The resulting mixture was extracted into three 50-ml portions of dichloromethane, the organic layers were combined, washed, dried, and evaporated to give the product as an oil. Crystallization and recrystallization from a mixture of dichloromethane and hexane gave 2.9 g (65%) of pure XXXI as white prisms: mp 233–236°; infrared absorption ($CHCl_3$) at 3400, 3450 (NH_2), and at 1710 cm^{-1} (C=O); nmr peaks (DMSO-d_6) at δ 2.86 (3 H, singlet, $CH_3N<$) and 3.50, 415 (2 H, AB quartet, J = 15 cps, $-CH_2-$).

Anal. Calcd for $C_{17}H_{16}N_4O$: C, 69.84; H, 5.52; N, 19.17. Found: C, 69.61; H, 5.48; N, 19.30.

9-Amino-3,5,6,10b-tetrahydro-1-methyl-10b-phenylimidazo-[1,2-*c*]quinazolin-2(1H)-one (XXXII).—A solution of 2 g of XXXI in a mixture of 30 ml of acetic acid and 25 ml of water was treated with 0.2 g of platinum oxide and hydrogenated at atmospheric pressure. After hydrogen uptake stopped, the catalyst was removed by filtration and the filtrates were made basic with ammonium hydroxide. The product was extracted into two 75-ml portions of dichloromethane. The organic layers were combined, washed, dried, and evaporated. The residue was crystallized first from methanol and then from a mixture of dichloromethane and hexane to give 0.8 g (40%) of XXXII as white prisms: mp 203–205° dec; infrared absorption ($CHCl_3$) at 3350–3450 (NH, NH_2, broad band) and at 1690 cm^{-1} (C=O); nmr peaks (DMSO-d_6) at δ 2.62 (3 H, $CH_3N<$), 3.75 (2 H, singlet, $-CH_2-$), and 3.30, 3.75 (2 H, AB quartet, J = 14 cps, $-CH_2-$).

Anal. Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.46; N, 19.04. Found: C, 69.31; H, 6.11; N, 18.71.

3,10b-Dihydro-1-methyl-10b-phenylimidazo[1,2-*c*]quinazolin-2-(1H)-one (XXXIII).—A solution of 4 g (0.0137 mole) of XXXI in 2.6 ml (0.0302 mole) of concentrated hydrochloric acid was diluted with 40 ml of water, cooled in an ice bath, and treated with a solution of 1.0 g (0.014 mole) of sodium nitrite in 5 ml of water. The mixture was stirred vigorously for 20 min and then poured onto 32 ml of ice-cold 50% hypophosphorous acid. The mixture was refrigerated overnight and was then made basic with ammonium hydroxide (temperature maintained at 10°). The products were extracted into three 75-ml portions of dichloromethane. The organic layers were combined, washed, dried, and concentrated to an oil. The oil was dissolved in benzene and chromatographed over 150 g of Florisil. The benzene fraction contained 0.7 g of 2-aminobenzophenone and was discarded. The eluent was changed to ethyl acetate and gave 2.2 g of product on removal of solvent. Recrystallization from a mixture of dichloromethane and hexane gave 2.0 g (52.5%) of XXXIII as pale yellow rods, mp 135–145°, which without further purification were converted into the hydrochloride. Recrystallization of the salt from a mixture of methanol and ether gave the pure monohydrochloride as pale yellow prisms: mp 222–226° dec; infrared absorption (KBr) at 1720 cm^{-1} (C=O); nmr peaks (D_2O) at δ 3.33 (3 H, singlet, $-CH_3N<$), 4.77 (2 H, doublet, J = 2 cps, $-CH_2-$), and 8.97 (1 H, singlet, $-CH=N-$).

Anal. Calcd for $C_{17}H_{15}N_3O\cdot HCl$: C, 65.07; H, 5.14; N, 13.39. Found: C, 65.27; H, 5.12; N, 13.38.

3,5,6,10b-Tetrahydro-1-methyl-10b-phenylimidazo[1,2-*c*]quinazolin-2(1H)-one (XXXIV).—A solution of 1.2 g (0.0043 mole) of XXXIII in 5 ml of dry diglyme was treated with 0.2 g (0.0053 mole) of sodium borohydride and stirred at room temperature for 4 hr. Water (50 ml) was added and the mixture was filtered. The precipitate was dissolved in dichloromethane (100 ml) which was then washed with water, dried, and evaporated. The residual oil was dissolved in ether and chromatographed over 50 g of Florisil. The forerun (0.2 g) was discarded and the eluent was changed to ethyl acetate. Removal of the solvent gave 0.7 g of product which was crystallized from a mixture of dichloromethane and hexane to give 0.2 g (16.5%) of XXXIV as pale yellow prisms: mp 150–160°; resolidified, mp 174–178°; infrared absorption ($CHCl_3$) at 3425 (NH) and at 1690 cm^{-1} (C=O); nmr peaks ($CDCl_3$) at δ 2.83 (3 H, singlet, $CH_3N<$), 3.51, 4.02 (2 H, AB quartet, J = 14 cps, $-CH_2-$), and 3.84, 4.16 (2 H, AB quartet, J = 12.5 cps, $-CH_2-$).

Anal. Calcd for $C_{17}H_{17}N_3O$: C, 73.09; H, 6.13; N, 15.04. Found: C, 73.26; H, 6.02; N, 14.77.

2-[(2-Formamido-5-nitrophenyl)phenylmethylenimino]-N-methylacetamide (XXV).—A flask fitted with a stirrer and dropping funnel was cooled externally with an ice bath. Formic acid (94%, 13.6 ml) was added and cooled (0–5°). Acetic anhydride (32.8 mg) was added dropwise and after the addition was complete the reaction mixture was warmed to 50° and maintained at that temperature for 2 hr. The solution was cooled to 0° and 15 g of IIa was added with stirring.

The mixture was allowed to warm to room temperature, stirred for 2 hr, and then poured into 500 ml of water. The aqueous mixture was made basic with ammonium hydroxide and filtered. The precipitate was washed with water, ethanol, and finally with ether to give 15.5 g (94.8%) of product as pale yellow rods. Recrystallization from a mixture of tetrahydrofuran and ether gave the pure compound, mp 179–183°.

Anal. Calcd for $C_{17}H_{16}N_4O_4$: C, 59.99; H, 4.74. Found: C, 60.04, 60.35; H, 5.21, 5.23.

Registry No.—IIa, 14271-30-8; IIb, 14182-29-7; III, 14182-30-0; IV, 14182-31-1; V, 14182-32-2; XV, 14271-31-9; XVI, 14182-33-3; XVI hydrochloride, 14182-44-6; XVII, 14271-32-0; XVIII, 14182-34-4; XIX, 14182-35-5; XXII, 14182-36-6; XXIII, 14182-37-7; XXV, 14182-38-8; XXVI, 14264-69-8; XXXI, 14182-39-9; XXXII, 14182-40-2; XXXIII, 14182-41-3; XXXIII hydrochloride, 14182-45-7; XXXIV, 14182-42-4.

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