lization from ethyl acetate gave **24** as off-white needles: mp 186–188°; ir ($CHCl_3$) 1650 cm^{-1}.

Anal. Calcd for $C_{10}H_{10}Cl_2N_2O$: C, 49.00; H, 4.11. Found: C, 49.21; H, 4.23.

3-Chloromethylene-1,2,3,4-tetrahydro-5*H*-1,4-benzodiazepin-5-one (25).—A solution of **24** (15 g, 61.2 mmol) in dry tetrahydrofuran (350 ml) was cooled in a Dry Ice–acetone bath. To the cold solution was added cautiously potassium *tert*-butoxide (6.7 g, 60 mmol), and the cooling bath was removed. The reaction mixture was then stirred for 17 hr and filtered through Celite. The residue left on concentrating the solution *in vacuo* was crystallized from ether–hexane to give 11 g of tacky solid. Recrystallization from ethyl acetate gave 7.7 g (60%) of **25**, mp 101–103° dec. Careful recrystallization from ethyl acetate gave **25** as off-white prisms: mp 107–108° dec; ir (KBr) 1610 cm^{-1}; nmr (DMSO) δ 3.85 (d, 2, J = 5 Hz, CH_2), 5.67 (s, 1, =CH), 7.00 (t, 1, J = 4 Hz, NH), and 8.51 ppm (s, 1, NH).

Anal. Calcd for $C_{10}H_9ClN_2O$: C, 57.56; H, 4.35. Found: C, 57.64; H, 4.20.

3-Chloromethyl-1,2,3,4-tetrahydro-5*H*-1,4-benzodiazepin-5-one (27).—A solution of **25** (23.5 g, 0.113 mol) in methanol (350 ml) was cooled in an ice bath and treated with tetramethylammonium borohydride (23.5 g, 0.258 mol). The mixture was removed from the ice bath and allowed to stand at room temperature for 20 hr. It was then diluted with several volumes of water, neutralized with glacial acetic acid, and cooled in an ice bath to give **26** (20.1 g, 85%), mp 177–184°. Recrystallization from ethanol gave colorless needles: mp 179–181°; ir ($CHCl_3$) 1635 cm^{-1}; uv max 223 mμ (ϵ 28,000), 250 (7600), and 337 (4200).

Anal. Calcd for $C_{10}H_{11}ClN_2O$: C, 57.02· H, 5.26. Found: C, 56.93 H, 5.15.

Reduction of 25 to 9.—To a solution of **25** (8.35 g) in diglyme (100 ml) which had been cooled to 10° was added sodium borohydride (8.35 g). The reaction mixture was allowed to stand at room temperature overnight, neutralized with acetic acid, diluted with water, and extracted with methylene chloride in four portions. The methylene chloride extracts were combined, dried over sodium sulfate, and concentrated *in vacuo*. The residue was crystallized from ethyl acetate to give crude **9** (5.2 g), mp 195–205°. Recrystallization from ethanol gave colorless plates, mp 210–215°, which had an infrared spectrum identical with that of authentic material.

1,2,3,4-Tetrahydro-3-piperidinomethyl-5*H*-1,4-benzodiazepin-5-one (26a).—A solution of **27** (2.1 g) in piperidine (100 ml) was heated under reflux for 5 hr and cooled. The piperidine hydrochloride was filtered, and the filtrate concentrated to dryness. Crystallization from ethanol of the residue left on evaporation of the solvent *in vacuo* gave **26a** (2 g), mp 174–176°. Recrystallization from ethanol gave colorless plates: mp 175–177° ir ($CHCl_3$) 1630 cm^{-1}.

Anal. Calcd for $C_{15}H_{21}N_3O$: C, 69.46 H, 8.16. Found: C, 69.28; H, 8.48.

1,2,3,4-Tetrahydro-3-*n*-butylaminomethyl-5*H*-1,4-benzodiazepin-5-one (26b).—A solution of **27** (2.1 g, 10 mmol) in *n*-butylamine (100 ml) was heated under reflux for 24 hr and then allowed to stand at room temperature for 24 hr. The reaction mixture was evaporated to dryness *in vacuo*. The residue was partitioned between water and methylene chloride, and the aqueous phase was washed with methylene chloride in three portions. The combined methylene chloride extracts were washed with 10% sodium bicarbonate and then with brine, dried over sodium sulfate, and concentrated *in vacuo* to leave a yellow residue which gave 1.7 g of **26b**, mp 135–147°, on crystallization from ethyl acetate–hexane. Recrystallization from ethyl acetate gave colorless lozenges: mp 145–147°; ir ($CHCl_3$) 1625 cm^{-1}.

Anal. Calcd for $C_{14}H_{21}N_3O$: C, 67.98; H, 8.56. Found: C, 68.36; H, 8.20.

1,2,3,4-Tetrahydro-3-morpholinomethyl-5*H*-1,4-benzodiazepin-5-one (26c).—A solution of **27** (2.1 g) in morpholine (50 ml) was heated under reflux overnight, and the reaction mixture was worked up as for the reaction with *n*-butylamine. This procedure gave crude **26c** (1.8 g), mp 145–150°. Recrystallization from ethyl acetate gave **26c** as off-white plates: mp 151–152.5°; ir ($CHCl_3$) 1630 cm^{-1}.

Anal. Calcd for $C_{14}H_{19}N_3O_2$: C, 64.34; H, 7.33. Found: C, 64.47; H, 7.15.

Registry No.—**5**, 27545-02-4; **6**, 27545-03-5; **7**, 27610-05-5; **8**, 27545-04-6; **9**, 27545-05-7; **10**, 27545-06-8; **11**, 19178-37-1; **12**, 27545-08-10; **13**, 27545-09-1; **14**, 27545-10-4; **15**, 27545-15-9; **17**, 27545-16-0; **18**, 27545-17-1; **19**, 27610-13-5; **20**, 27545-18-2; **21**, 27545-19-3; **22**, 27545-20-6; **23**, 27545-21-7; **24**, 27545-22-8; **25**, 27545-23-9; **26a**, 27537-82-2; **26b**, 27537-83-3; **26c**, 27537-84-4; **27**, 27537-85-5.

Acknowledgment.—We thank Dr. A. Steyermark for the microanalyses, Mr. S. Traiman for the infrared spectra, Dr. V. Toome for the ultraviolet spectra, Dr. F. Vane and Dr. E. Billeter for the nmr spectra, and Mr. T. Flynn for skillful technical assistance.

3-Amino-3,4-dihydroquinazolines[1]

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The reaction of hydrazine with the 2′-benzoyl-4′-chloroanilides **2** and **3** has been shown to yield the 3-amino-6-chloro-3,4-dihydro-4-hydroxy-4-phenylquinazolines **5** and **6**. Chemical transformations of these compounds to give both cyclic and ring-opened products are discussed.

Our interest in the reaction of amines with amides to give amidines[3] led us to investigate the reaction of hydrazine with amides. The *o*-benzoylanilides chosen for this study contained both amide and ketone functions and were expected to yield heterocyclic products on treatment with hydrazine.

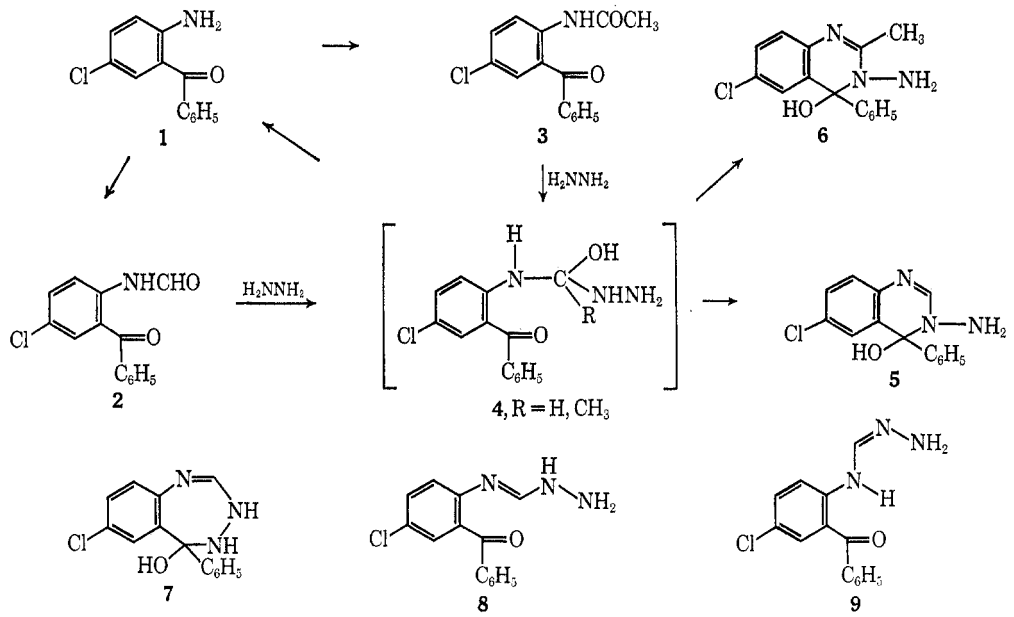
Thus, 2′-benzoyl-4′-chloroformanilide (**2**) [prepared by formylation of the corresponding aminochlorobenzophenone **1** (Scheme I)] gave, on treatment with a 50% excess of hydrazine, a condensation product which was shown by elemental and mass spectral analyses to have lost only one molecule of water. Furthermore, the product did not retain the amide carbonyl group as evidenced by the ir spectrum. Of the possible structures **5**, **7**, **8**, and **9**, the quinazoline **5** seemed most reasonable on chemical and spectral grounds. Structure **7** was rejected since such a carbinolamine would be expected to undergo ready, if not spontaneous, dehydration. Attempts to dehydrate the product led only to a dimer of unknown structure (M^+ at m/e 510), and in no instance were we able to detect a dehydrated monomer. The mass spectral fragmentation pattern[1] of the product was

(1) A part of this work has been reported in preliminary form: M. E. Derieg, J. Blount, R. I. Fryer, and S. S. Hillery, *Tetrahedron Lett.*, 3869 (1970).

(2) To whom inquiries should be addressed.

(3) M. E. Derieg, R. I. Fryer, R. M. Schweininger, and L. H. Sternbach, *J. Med. Chem.*, **11**, 912 (1968).

SCHEME I



incompatible with the open structures **8** and **9** but was quite consistent with that anticipated for the aminoquinazoline structure **5**.

Recently a publication[4] describing the use of diethylmalonate as a leaving group reported that the product of the reaction of hydrazine with 2-(2′,2′-biscarbethoxyvinylamino)-5-chlorobenzophenone was 5-hydroxy-5-phenyl-1,3,4-3*H*-4,5-dihydrobenzotriazepine (**7**).[5] The physical properties of the product were described, the major ir absorptions were presented, and a mechanism was suggested.

When the description of the compound reputed to be **7** was published, the melting point and ir spectral data were observed to be identical with that of the compound to which we had attributed structure **5**. Furthermore, both **5** and the compound purported to be **7** afforded a triacetylated product **25** which exhibited the same ir spectra and melting point.[4] This led us to conclude that the initial condensation products as well as the triacetates were in fact identical. Since an argument defending the assignment of structure **7** had been presented[6] and since the chemical and conventional spectral evidence allowed us little more than a rebuttal in support of structure **5**, X-ray analyses were performed.[1] The structures were thus defined as those depicted by **5** and **25**.

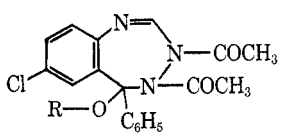
We next examined the products obtained by the treatment of **3**[7] with 1.5 equiv of hydrazine. Under the same conditions which had afforded a 92% yield of **5**, an intractable mixture of compounds **1** and **3** together with a new compound **6** was observed. However, when **3** was warmed in an excess of hydrazine, **6** was isolated in high yield. The ir and mass spectra[8] of **6** were similar to those of **5** and thus the assignment of structure **6** was made by analogy.

It was interesting to note that, in the formation of both **5** and **6**, 2-amino-5-chlorobenzophenone (**1**) was a minor by-product. In no case was the hydrazone of **1** observed nor were the hydrazones of compounds **2** and **3** detected. It thus seems probable that the initial attack of hydrazine occurred at the amide carbonyl of compounds **2** and **3** giving an intermediate of type **4** which could then dehydrate and cyclize to give compounds **5** and **6**, respectively. Podesva, *et al.*, encumbered by the incorrect assignment of structure **7** for compound **5**,[4] had postulated a mechanism for the attack of hydrazine on 2-(2′,2′-biscarbethoxyvinylamino)-5-chlorobenzophenone (**10**). They visualized the attack of hydrazine at the benzophenone carbonyl to yield a carbinol hydrazine intermediate. Since substituted methylene diethylmalonates are known to undergo the addition of hydrazine under these conditions and to subsequently expel diethylmalonate forming the hydrazone,[9] and since we have observed that the reaction of hydrazine with the carbonyl function of 2-aminobenzophenones under the conditions used by Podesva proceeds very slowly, we envisage the most probable mechanism to be the following.

(4) C. Podesva, G. Kohan, and K. Vagi, *Can. J. Chem.*, **47**, 489 (1969).

(5) The 1,3,4-benzotriazepine ring system is described in the literature. See, for example, O. Hromatka, F. Krenmüller, and M. Knollmüller, *Monatsh. Chem.*, **100**, 934 (1969), and references cited therein.

(6) Podesva, *et al.* (see ref 4), argued that solvolysis of the di- and triacetates, assigned by them structures A and B, to give *N*,*N*′-diacetylhydrazine and 6-chloro-4-phenylquinazoline clearly established those assignments. This is a tenuous argument. The *N*,*N*-diacetylhydrazone of



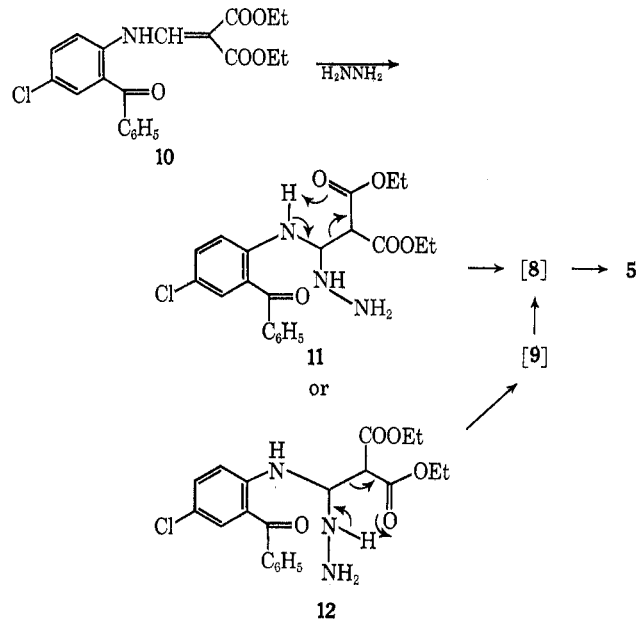
A, R = H
B, R = $COCH_3$

acetone is known to yield *N*,*N*′-diacetylhydrazine on hydrolysis: see R. A. Turner, *J. Amer. Chem. Soc.*, **69**, 875 (1947); M. H. Krackov and B. E. Christensen, *J. Org. Chem.*, **28**, 2677 (1963); H. Fever and J. D. Asunskis, *ibid.*, **27**, 4684 (1962). Thus, *N*,*N*′-diacetylhydrazine would be an explicable if not anticipated product of the *N*,*N*-diacetyl derivatives of **5**, **7**, **8**, and **9** as well as the *N*,*N*-diacetylhydrazone of **2**.

(7) F. D. Chattaway, *J. Chem. Soc.*, **85**, 344 (1904).

(8) Like compound **5**, compound **6** fragments in the mass spectrometer by way of the appropriate quinazoline (mol wt 254). The major ions are *m/e* 287, 254, 253, and 219.

(9) W. Wislicenus, *Justus Liebigs Ann. Chem.*, **279**, 23 (1894).



The cyclic structure of **5** in the crystalline state is now clearly established,[1] and, in the environment of the mass spectrometer, the presence of the cyclic species **5** and **6** is evident. Tautomerism in solution (*e.g.*, **5** ⇌ **8** ⇌ **9**) seems apparent from the isolation of both cyclic and noncyclic derivatives of compounds **5** and **6**.

When **6** was treated with hydrogen chloride in refluxing methanol, a new hydrochloride was obtained (Scheme II). The uv spectrum was only slightly changed from that of the hydrochloride of **6** and the weak ir absorption at 1650 cm^{-1} (C=N) was retained. Elemental analysis indicated that methylation had occurred, and methoxyl analysis showed that the product was an ether. Accordingly, the structure assigned was that of the expected carbinol ether amine **13**.

The reaction of *N*-amino compounds with nitrous acid is known to proceed *via* N–N cleavage.[10] Thus, the treatment of **6** with nitrous acid would be expected to lead to a 4-hydroxy-3,4-dihydroquinazoline intermediate which would then readily dehydrate to give the known quinazoline **15**.[11] When, in fact, **6** was treated with sodium nitrite in aqueous acetic acid, compound **15** was isolated together with the by-product **17**. The by-product demonstrated a strong ir absorption at 1675 cm^{-1} and had a molecular weight of 298 (mass spectrum). The elemental composition and spectral data suggested the tetrazolobenzophenone, structure **17**. Treatment of **17** with aqueous sodium hydroxide effected dehydration and gave compound **20**.[12] The alternate synthesis of **20** from the known dichloroquinoline **18**[13] confirmed the structural assignment.

The catalytic hydrogenolysis of carbinolamines is known to afford the corresponding amino derivatives.[14] Treatment of a solution of **6** in acetic acid with hydrogen over a platinum catalyst in the presence of hydrogen chloride gave the expected product **14**. Compound **14** was then treated with nitrous acid to give a product which was assigned structure **16**. This structural assignment was corroborated by the hydrogenation of **15** to give a compound identical in all respects with **16**.

The reactions of compound **5** also gave products derived from both open-chain and quinazoline forms. When **5** was treated with an excess of acetone at reflux, a compound was obtained to which structure **21** was assigned (Scheme III). This structural assignment was based largely on the mass spectral fragmentation pattern which exhibited ions characteristic of the aminobenzophenones,[15] rather than that of the quinazolines. Although the infrared absorption at 1620 cm^{-1} ($CHCl_3$) suggested that the benzophenone carbonyl was influenced by intramolecular hydrogen bonding[16] and that **22** might then best represent the structure of the product, the presence of an excess of triethylamine failed to effect a shift.[17] Thus, we believe that tautomer **21** is the more likely of the two possible structures.

Acetylation of **5** with acetic anhydride in pyridine gave a mixture of acetates in which the previously mentioned triacetate **25** was the major product. Thin layer chromatograms[18] of the reaction mixture indicated the presence of two major by-products. One of these was a diacetate which was much more conveniently prepared by carefully controlling the amount of acetic anhydride in the acetylation mixture. This diacetate exhibited mass spectral character[1] consistent with that of the aminobenzophenones. Upon further acetylation, the diacetate slowly yielded a new triacetate, very similar to, but spectrally nonidentical with, compound **25**. Accordingly, the remaining possible open triacetate structure **24** was assigned and **23** as the structure of the diacetate logically followed.

The remaining by-product of the acetylation of **5** proved to be identical with the compound obtained from the base hydrolysis of **25**. The treatment of compound **25** with methanolic potassium hydroxide gave a monoacetate, the mass spectrum[1] of which clearly indicated the quinazoline structure **26**.[19] The monoacetate **26** readily regenerated **25** under the original acetylation conditions.

Although the slow rate of reaction of acetic anhydride with **23** to give **24** is not surprising, the ease of formation of **25** from **26** under the same conditions merits comment.[20] Of the possible mechanisms[21] which would explain the accelerated formation of the imide **25**, we

(10) E. Fischer, *Justus Liebigs Ann. Chem.*, **199**, 314 (1879).

(11) S. C. Bell and P. H. L. Wei, *J. Org. Chem.*, **30**, 3576 (1965).

(12) The dehydration of *o*-benzoylacetanilides to give quinolones has been reported: R. I. Fryer, B. Brust, and L. H. Sternbach, *J. Chem. Soc.*, 3097, (1964).

(13) A. E. Drukker and C. I. Judd, *J. Heterocycl. Chem.*, **3**, 359 (1966).

(14) W. S. Emerson, *Org. React.*, **4**, 194 (1948).

(15) The mass spectrum of compound **21** was characterized by the following major ions: *m/e* 313, 298, 242, 230, and 105. The ions at *m/e* 242, 230, and 105 are typical of this class of aminobenzophenones.

(16) L. J. Bellamy in "The Infra-red Spectra of Complex Molecules," Wiley, New York, N. Y., 1958, p 144.

(17) N. B. Colthup, L. H. Daly, and S. E. Wiberley in "Introduction to Infrared and Raman Spectroscopy," Academic Press, New York, N. Y., 1964, p 190.

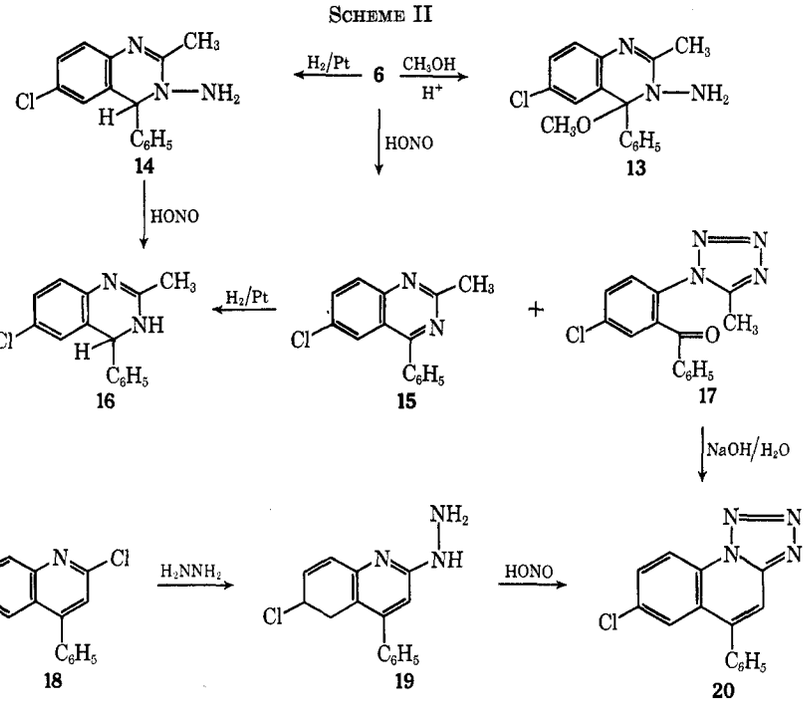
(18) The thin layer chromatograms were prepared as follows. A 1-cc aliquot was removed, mixed with 2 cc of water, and extracted with 1 cc of chloroform, which was washed with water, dried, and applied to a Brinkmann silica plate F 254. The eluent systems were 4:1 and 3:2 hexane–ethyl acetate. Determinations were made by visual comparisons.

(19) The quinazoline products are typified in the mass spectrum by the presence of major fragments at *m/e* 240, 239, and 205. Under these reaction conditions Podesva, *et al.*, reported the isolation of a diacetate.

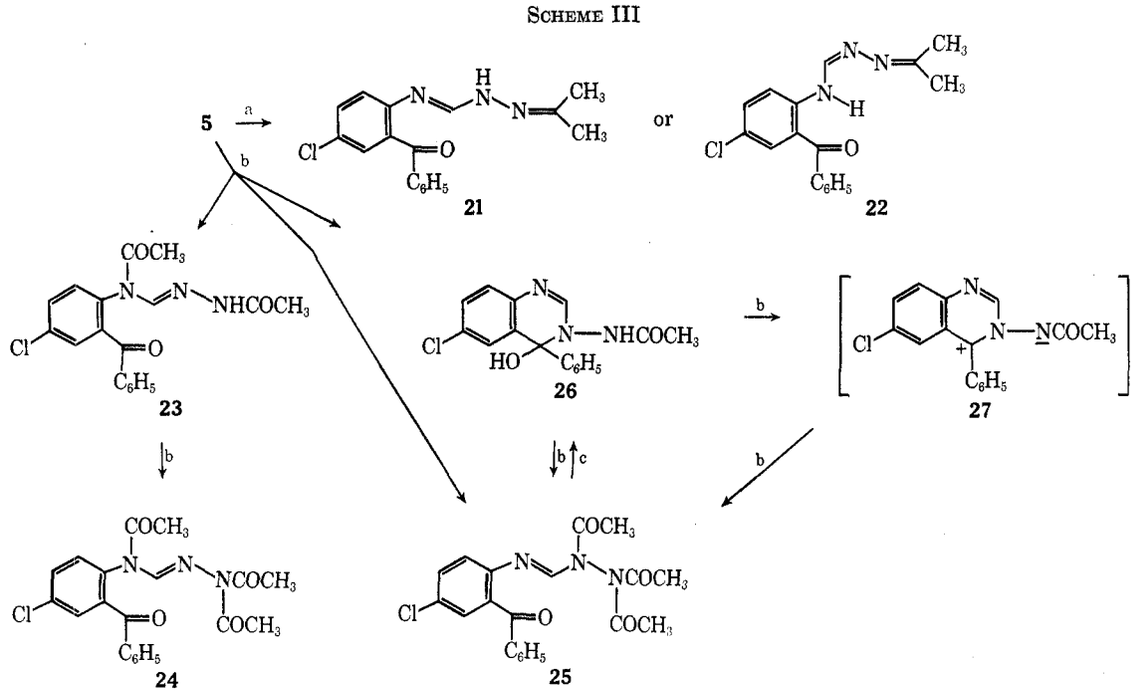
(20) See B. C. Challis and A. R. Butler in "The Chemistry of the Amino Group," S. Patai, Ed., Interscience, New York, N. Y., 1968, p 285, and references cited therein for comments on the introduction of a second acyl group on primary amines.

(21) An alternate mechanism was considered which involved the intramolecular attack of the hydroxy group of **26** at the amide carbonyl to yield a 1,3,4-oxadiazole intermediate. This might then be diacetylated and yield **25** by way of **30**.

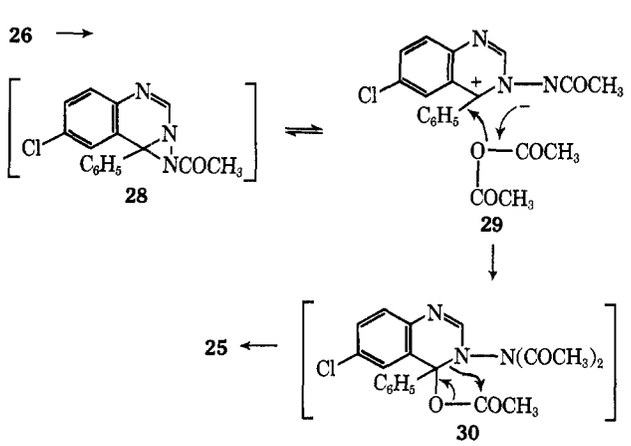
SCHEME II



SCHEME III



(a = acetone, b = acetic anhydride in pyridine, c = KOH in methanol)



favor that shown (**28** → **30**). In the dehydrating environment of the reaction conditions, the formation of the acetylated diaziridine **28** or its 1,3-dipolar isomer **29** might well result. Either **28** or **29** could react with acetic anhydride to give the triacetate **30**, and rearrangement of the sterically crowded **30** to the open product **25** would not be unexpected.

Experimental Section

Melting points were determined microscopically on a hot stage and are corrected. The nmr spectra were determined on a Varian A-60 instrument, the ir spectra were determined on a Cary Model 14 spectrophotometer, and the mass spectra were determined by means of a CEC-21-110B instrument at 70 eV by

direct insertion. Solutions were dried over anhydrous magnesium sulfate. Petroleum ether (bp 30–50°) was used.

2′-Benzoyl-4′-chloroformanilide (2).—A solution of 100 g (0.43 mol) of 2-amino-5-chlorobenzophenone in 500 ml of formic acid (98–100%) was stirred at reflux overnight. The solvent was removed *in vacuo* and the oily residue was crystallized from methylene chloride–hexane to give 103.7 g (92.5%) of crystalline product, mp 85–92°. Recrystallizations from methylene chloride–hexane gave colorless prisms, mp 90–91°.

Anal. Calcd for $C_{14}H_{10}ClNO_2$: C, 64.75; H, 3.88; N, 5.39. Found: C, 64.65; H, 4.17; N, 5.51.

3-Amino-6-chloro-3,4-dihydro-4-hydroxy-4-phenylquinazoline (5).—A mixture of 26 g (0.1 mol) of **2** and 350 ml of ethanol at room temperature was vigorously stirred during the addition of 4.8 g (0.15 mol) of hydrazine. As the exothermic reaction began, solution was effected and the product then precipitated from solution. The reaction mixture was stirred overnight, chilled, and filtered. The precipitate was washed with ethanol and dried to give 25.2 g (92%) of product. Recrystallization from DMF gave colorless prisms: mp 196–198° dec; ir (KBr) 3325, 2780, 2600, 1640, and 1590 cm^{-1}; mass spectrum *m/e* (rel intensity) 273 (15), 254 (90), 240 (64), 239 (100), 205 (99).

Anal. Calcd for $C_{14}H_{12}ClN_3O$: C, 61.43; H, 4.42; N, 15.35. Found: C, 61.73; H, 4.17; N, 15.07.

Dehydration of 3-Amino-6-chloro-3,4-dihydro-4-hydroxy-4-phenylquinazoline (5).—**5** (10 g, 37 mmol) and 350 ml of dry xylene was heated at reflux for 65 hr. The xylene was removed *in vacuo* and the gummy residue was washed with ether, hot DMF, and methanol. The insoluble product, 2.8 g (30%) of orange prisms, mp >350°, was analyzed without further purification: mass spectrum (70 eV) *m/e* (rel intensity) 510 (17), 240 (52), 239 (100), 229 (79), 214 (58), 205 (94); ir (KBr) 1620 cm^{-1}.

Anal. Calcd for $C_{28}H_{20}N_6Cl_2$: C, 65.76; H, 3.94; N, 16.43. Found: C, 66.15; H, 4.06; N, 16.36.

3-Amino-6-chloro-3,4-dihydro-4-hydroxy-2-methyl-4-phenylquinazoline (6).—To 200 ml of 95% hydrazine was added 79 g (0.29 mol) of 2′-benzoyl-4′-chloroacetanilide (**3**). After 1.5 hr, the precipitate was removed by filtration and was washed with water and with ether. Recrystallization from methanol–chloroform gave 53.7 g (64%) of colorless prisms: mp 218–219° dec; ir (KBr) 3325, 2800, 2625, 1630, and 1580 cm^{-1}; mass spectrum *m/e* (rel intensity) 287 (7), 256 (57), 268 (7), 254 (46), 253 (80), 219 (100).

Anal. Calcd for $C_{15}H_{14}ClN_3O$: C, 62.61; H, 4.90; O, 5.56. Found: C, 62.31; H, 5.15; O, 5.72.

Compound **6** formed a salt in aqueous hydrochloric acid, which was recrystallized from aqueous methanol and ether to give colorless prisms, mp 216–220° dec, ir (KBr) 1660 cm^{-1}.

Anal. Calcd for $C_{15}H_{14}ClN_3O \cdot HCl$: C, 55.57; H, 4.66; Cl, 21.87. Found: C, 55.46; H, 4.61; Cl, 21.68.

3-Amino-6-chloro-3,4-dihydro-4-methoxy-2-methyl-4-phenylquinazoline Hydrochloride (13).—A methanolic solution of 8.3 g (29 mmol) of the hydrochloride of **6** was heated at reflux for 5 hr. The solution was concentrated *in vacuo*. Addition of ethereal hydrogen chloride yielded 5 g (58%) of colorless prisms, which after recrystallization from methanol melted at 210–212° dec, ir (KBr) 1650 cm^{-1}.

Anal. Calcd for $C_{16}H_{16}ClN_3O \cdot HCl$: C, 56.81; H, 5.07; Cl, 20.96; OCH_3, 9.18. Found: C, 56.83; H, 5.52; Cl, 20.82; OCH_3, 8.83.

3-Amino-6-chloro-3,4-dihydro-2-methyl-4-phenylquinazoline (14).—A mixture of 6 g (21 mmol) of **6**, 70 ml of acetic acid containing 0.4 g of hydrogen chloride, and 0.15 g of platinum oxide was shaken with hydrogen at room temperature and atmospheric pressure. After 24 hr, a total hydrogen uptake of 800 ml was measured, the catalyst was removed by filtration, and the filtrate was poured over ice and made basic with ammonium hydroxide. The aqueous mixture was extracted with methylene chloride; the extract was washed with water, dried, and concentrated *in vacuo*. Addition of ether gave 3.4 g (56%) of solid which was recrystallized from methylene chloride–ethanol to give colorless prisms: mp 202–207°; uv max (isopropyl alcohol) 227 mμ (ε 16,000), 302 (10,000), and 328 (4600).

Anal. Calcd for $C_{15}H_{14}ClN_3$: C, 66.30; H, 5.19; N, 15.46. Found: C, 66 62; H, 5.02; N, 15.73.

6-Chloro-2-methyl-4-phenylquinazoline (15) and 5-Chloro-2-(5-methyl-1*H*-tetrazol-1-yl)benzophenone (17).—To a solution of 6.34 g (22 mmol) of **6** in 50 ml of acetic acid was added a solution of 1.52 g (22 mmol) of sodium nitrite in 25 ml of water. A mildly exothermic reaction occurred, and after 30 min the reaction mixture was poured into ice and aqueous ammonia. The mixture was extracted with methylene chloride and the extract was washed with water, dried, and concentrated *in vacuo*. Addition of ether and petroleum ether gave 1.6 g (28.5%) of **17** as a crystalline solid which was recrystallized to give colorless prisms: mp 172–174°; ir ($CHCl_3$) 1675 cm^{-1}; uv max (isopropyl alcohol) 253 mμ (ε 18,500), 285 (4000); mass spectrum *m/e* 298, 270, 269, 229, 193, 105.

Anal. Calcd for $C_{15}H_{11}ClN_4O$: C, 60.31; H, 3.71; N, 18.75. Found: C, 60.22; H, 3.55; N, 18.78.

The combined mother liquors were evaporated to dryness *in vacuo* and dissolved in hot petroleum ether, and 0.65 g (10.9%) of **15** crystallized as colorless needles, mp 107–108° (lit.[22] 105–106°).

6-Chloro-3,4-dihydro-2-methyl-4-phenylquinazoline (16). A. From 15.—A solution of 4 g (16 mmol) of **15** in 60 ml of acetic acid was hydrogenated at 25° and 1 atm using 0.1 g of platinum oxide as catalyst. After the uptake of 20 mmol of hydrogen, the mixture was filtered, and the filtrate was poured over ice and made basic with sodium hydroxide. The crystalline precipitate was recrystallized from acetonitrile to give 3.3 g (82%) of colorless plates: mp 211–213°; ir ($CHCl_3$) 1620 cm^{-1}; uv max (isopropyl alcohol) 225 mμ (ε 18,000), 296 (9000), 330 (2000).

Anal. Calcd for $C_{15}H_{13}ClN_2$: C, 70.17; H, 5.10. Found: C, 70.32; H, 5.18.

B. From 14.—To a solution of 0.78 g (3 mmol) of the monohydrochloride of **14** in 25 ml of 2 *N* aqueous hydrochloric acid and 15 ml of acetic acid was carefully added 0.2 g (3 mmol) of sodium nitrite. After 1 hr, the mixture was filtered and the solid was partitioned between 3 *N* sodium hydroxide and ether. The organic phase was separated, washed with water, dried, and concentrated *in vacuo* to a residue which was recrystallized from acetonitrile to give a low yield of product (mp 208–213°) identical with that prepared from **15**.

6-Chloro-2-hydrazino-4-phenylquinoline (19).—A mixture of 4 g (15 mmol) of **18**[13] and 20 ml of hydrazine was heated under reflux for 10 min, cooled, and diluted with water to give 2.2 g (56%) of product, mp 160–163°. Recrystallization from tetrahydrofuran–hexane gave yellow prisms, mp 160–162°.

Anal. Calcd for $C_{15}H_{12}ClN_3$: C, 66.79; H, 4.48; N 15.58. Found: C, 66.79; H, 4.59; N, 15.34.

7-Chloro-5-phenyltetrazolo[1,5-*a*]quinoline (20). From 19.—To a stirred solution of 4 g (15 mmol) of **19** in 75 ml of 50% aqueous acetic acid was added dropwise a solution of 0.98 g (14 mmol) of sodium nitrite in 10 ml of water. The temperature was maintained at 20 ± 5° with an ice bath. The reaction mixture was stirred for 1 hr and filtered, and the solid partitioned between methylene chloride and water. The organic phase was washed with dilute ammonium hydroxide, water, and brine and dried. Evaporation of the solvent *in vacuo* gave 3.14 g (75%) of product, mp 192–196°. Recrystallization from chloroform–ether gave colorless rods, mp 206–209°.

Anal. Calcd for $C_{15}H_9ClN_4$: C, 64.18; H, 3.23; N, 19.96. Found: C, 64.09; H, 3.26; N, 19.96.

From 17.—A solution of 750 mg (2.5 mmol) of **17** in 50 ml of 2 *N* aqueous sodium hydroxide and 50 ml of methanol was heated at the reflux temperature for 15 min. When the solution was chilled, 350 mg (50%) of crystalline product precipitated. Recrystallization from methylene chloride–petroleum ether gave colorless rods, mp 194–195°, identical with **20** prepared from **19**.

5-Chloro-2-(2-isopropylidenehydrazomethyleneamino)benzophenone (21).—A mixture of 5 g (18 mmol) of **5** and 125 ml of acetone was heated at reflux. After 42 hr, the starting material **5** had totally dissolved in the yellow solution. The acetone was removed *in vacuo* and the residue was recrystallized from acetone to give 3.55 g (63%) of yellow crystalline **22**. Recrystallization from acetone gave yellow needles: mp 136–139°; ir (KBr) 1630, 1600 (broad), 1500 cm^{-1}; mass spectrum *m/e* (rel intensity) 313 (16), 300 (37), 298 (100), 242 (21), 230 (25), 105 (21).

Anal. Calcd for $C_{17}H_{16}ClN_3O$: C, 65.07; H, 5.14; N, 13.39. Found: C, 64.92; H, 5.17; N, 13.56.

2′-Benzoyl-4′-chloro-*N*-(2-acetylhydrazono)methylacetanilide (23).—A solution of 27 g (0.1 mol) of **5**, 10.2 g (0.1 mol) of acetic anhydride, and 225 ml of pyridine was stirred overnight at room temperature. The reaction mixture was evaporated *in vacuo* to an oily residue which was partitioned between chloroform and water. The organic layer was washed with 5% sodium bicarbon-

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ate, water, 1.5 *N* hydrochloric acid, and again with water. The chloroform solution was dried and concentrated to 21.9 g of an oil which, when treated with ether, yielded 5 g (14%) of pale yellow prisms. Recrystallizations from methylene chloride–hexane gave colorless prisms: mp 164–166°; mass spectrum *m/e* (rel intensity) 357 (5), 315 (12), 273 (42), 242 (50), 231 (100), 230 (69), 105 (50).

Anal. Calcd for $C_{18}H_{16}ClN_3O_3$: C, 60.42; H, 4.51; N, 11.74. Found: C, 60.37; H, 4.60; N, 11.62.

2′-Benzoyl-4′-chloro-*N*-(2,2-diacetylhydrazono)methylacetanilide (24).—A solution of 800 mg (2 mmol) of **23**, 7 ml of acetic anhydride, and 10 ml of pyridine was stirred overnight at room temperature. The reaction mixture was poured over ice and extracted with chloroform. The organic extract was washed with water, dried, and concentrated *in vacuo*. The residue was washed with chloroform leaving 250 mg (44%) of the dimeric orange product from **5** (*vide supra*). The chloroform wash was treated with hexane and yielded 125 mg (14%) of colorless prisms: mp 134–136°; mass spectrum *m/e* (rel intensity) 399 (3), 357 (14), 315 (7), 298 (20), 273 (34), 242 (43), 231 (100), 230 (50), 105 (24).

Anal. Calcd for $C_{20}H_{18}ClN_3O_4$: C, 60.08; H, 4.54; N, 10.51. Found: C, 59.83; H, 4.58; N, 10.50.

5-Chloro-2-(1,2,2-triacetyl-1-hydrazinylmethyleneamino)benzophenone (25).—A mixture of 50 g (0.18 mol) of **5**, 100 ml of pyridine, and 200 ml of acetic anhydride was stirred at room temperature for 41 hr. The volatile materials were removed *in vacuo* leaving an oil which was partitioned between chloroform and water. The organic phase was washed with water, 5% sodium bicarbonate, water, 1.5 *N* hydrochloric acid, and again with water. The chloroform was removed *in vacuo* yielding an oily residue which was crystallized from ethanol to give 37.3 g (51.8%) of colorless crystals, mp 101–104°. Recrystallizations from ethanol gave colorless blocks: mp 105–107°; ir (KBr) 1730, 1672, 1647 cm^{-1}; mass spectrum *m/e* (rel intensity) 399 (18), 357 (22), 315 (29), 298 (57), 273 (76), 242 (86), 231 (100), 230 (80), 105 (55).

Anal. Calcd for $C_{20}H_{18}ClN_3O_4$: C, 60.08; H, 4.54; N, 10.51. Found: C, 60.13; H, 4.46; N, 10.52.

3-Acetamido-6-chloro-3,4-dihydro-4-hydroxy-4-phenylquinazoline (26).—A solution of 10% potassium hydroxide in methanol was added dropwise to a solution of 8 g (20 mmol) of **25** and 20 ml of methanol at 45°.

When the solution had maintained a pH of 10, it was allowed to stand for 30 min and was then diluted with 300 ml of water. The precipitate was removed by filtration, washed with water, and dried at 65–70° *in vacuo* (5 g, 79.3%). Recrystallizations from THF–ether gave colorless prisms: mp 160–162°; ir (KBr) 3240, 1670, 1610 cm^{-1}; nmr (DMSO) 1.60 (s, 3, $NCOCH_3$); mass spectrum *m/e* (rel intensity) 315 (2), 297 (35), 282 (36), 254 (70), 240 (33), 239 (55), 220 (100), 205 (44).

Anal. Calcd for $C_{16}H_{14}ClN_3O$: C, 60.86; H, 4.47; N, 13.31. Found: C, 60.75; H, 4.46; N, 13.19.

Registry No.—**2**, 10352-28-0; **5**, 27610-14-6; **6**, 27537-87-7; **6** HCl, 27537-88-8; **13** HCl, 27537-89-9; **14**, 27537-90-2; **16**, 17433-16-8; **17**, 27537-92-4; **19**, 27537-93-5; **20**, 27537-94-6; **21**, 27537-95-7; **23**, 27537-96-8; **24**, 27537-97-9; **25**, 27537-98-0; **26**, 27537-99-1.

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1,2,4-Triazines. IV. Synthesis and Characterization of 1,2,4-Triazine *N*-Oxides

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The N-oxidation of 1,2,4-triazines affords the 1-oxides when C_3 is either unsubstituted or is substituted by a methoxyl group. It has been shown that N-oxidation of 3-amino-1,2,4-triazines affords the 2-oxides as major products. This is in contrast to some of the reported data which suggested that oxidation of 3-amino-5,6-diphenyl-1,2,4-triazine yields the 1-oxide.

Recent developments of new syntheses of 1,2,4-triazines[1-3] have made this ring system readily available and permit its study in some detail.

We now wish to describe the preparation and structure elucidation of some 1,2,4-triazine *N*-oxides.

Several papers[4-7] have dealt with the N-oxidation of some 3-amino- and 3-methoxy-1,2,4-triazines with alkyl and aryl substituents in the 5 and 5,6 positions of the 1,2,4-triazine ring. The only all-alkyl or all-aryl substituted 1,2,4-triazine that has been N-oxidized is the 3,5,6-triphenyl compound,[8] where the 1-oxide is formed as the major product (33%) and the 2-oxide as the minor one (8%).

The N-oxidation of 1,2,4-triazines can, *a priori*, occur at either N-1, N-2, or N-4. In order to establish the position of N-oxidation one can, in theory, determine the dipole moments of these substances and thus elucidate their structures, or one can examine the differences in proton chemical shifts between the N-oxidized compounds and the appropriate bases themselves.

The oxidation with perbenzoic acid of compounds **1a–d** (see Scheme I) afforded mono-*N*-oxides in 15–40% yields after chromatography on neutral grade III alumina.

The mass spectra of these compounds clearly indicate the presence of an *N*-oxide function by the appearance of a P − 16 peak. In addition to this fragmentation process, all compounds (including those with no substituents at C-3) having a methyl or a phenyl group substituted at C-6 give rise to a P − 17 peak which is more abundant than the P − 16 ion. This observation suggests that we are dealing with the 1- rather than the 2-

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