Reinvestigation of a 5*H*-Dibenzo[*d,h*][1,3,6]triazonine Synthesis

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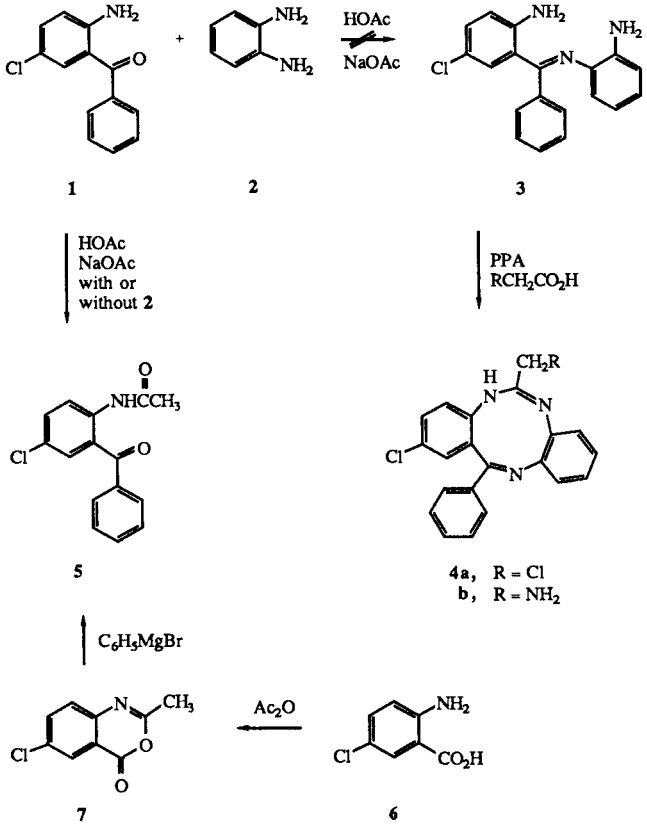
Received June 5, 1989

Treatment of 5-chloro-2-aminobenzophenone (**1**) with *o*-phenylenediamine, sodium acetate, and acetic acid gave 2-(acetyl)amino-5-chlorobenzophenone (**5**) rather than *N*-[(2-amino-5-chlorophenyl)phenylmethylene]-1,2-benzenediamine (**3**), as reported by Kulkarni *et al.* [1]. Authentic **3** was prepared and treated with chloroacetic acid and polyphosphoric acid (PPA) to give **1**, recovered **3**, 2,8-dichloro-6,12-diphenyldibenzo[*b,f*][1,5]diazocine (**9**) and 2-chloro-6-(chloromethyl)-13-phenyl-5*H*-dibenzo[*d,h*][1,3,6]triazonine (**10**). Treatment of **5** with PPA, with or without chloroacetic acid, gave [5-chloro-2-[(6-chloro-4-phenyl-2-quinolinyl)amino]phenyl]phenylmethanone (**11**) as the sole product in 90% yield. Treatment of other benzophenones, acetophenones, and anilines with sodium acetate and acetic acid provided acetanilides in 78-96% yield, with the exception of 2'-aminoacetophenone (**20**), which gave a quantitative yield of 2-[((2-acetyl)phenyl)amino]-4-methylquinoline (**21**). The mechanism of acetanilide formation with sodium acetate and acetic acid is discussed. The structure of **21** was established using high resolution ^{1}H nmr techniques. Attempts to prepare an authentic sample of **21** from 2-chlorolepidine (**26**) and (**20**) gave 4-methyl-*N*-[2-(4-methyl-2-quinolinyl)phenyl]-2-quinolinamine (**29**) as the major product.

J. Heterocyclic Chem., **26**, 1611 (1989).

A recent publication by Kulkarni *et al.* [1] describes the synthesis of 6-substituted 2-chloro-13-phenyl-5*H*-dibenzo-[*d,h*][1,3,6]triazonines [2]. We have reinvestigated this work and obtained discrepant results. This report describes our findings and contrasts them with those reported by Kulkarni *et al.* [1].

Scheme I

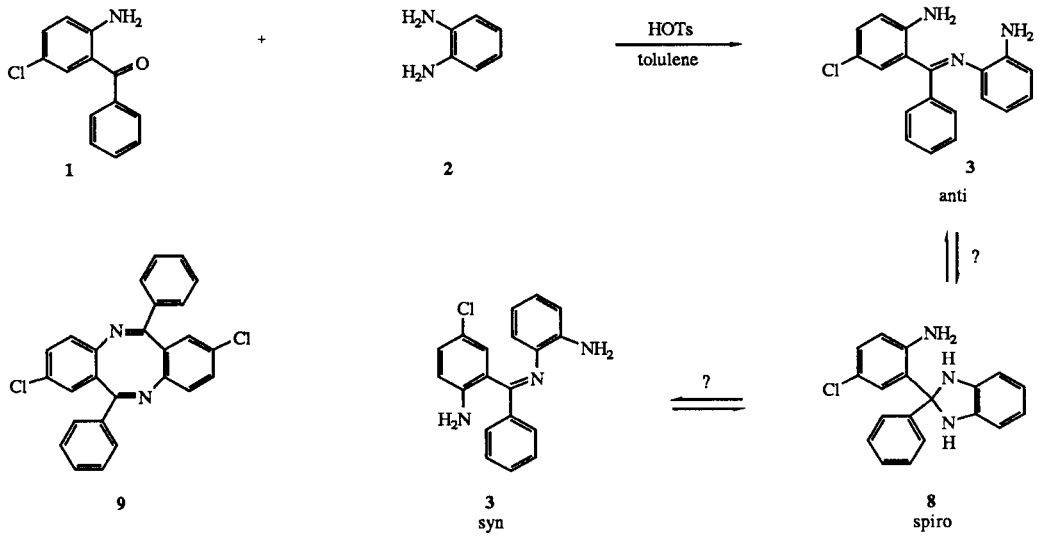


Kulkarni *et al.* [1] report the sequence shown in Scheme I for the preparation of 6-substituted 2-chloro-13-phenyl-5*H*-dibenzo[*d,h*][1,3,6]triazinones **4a** and **4b**. Derivatives of these compounds were also reported in which the chloro group of **4a** was displaced with amines, and the amino functionality of **4b** was acylated. The authors reported the condensation of 5-chloro-2-aminobenzophenone (**1**) with *o*-phenylenediamine (**2**) in acetic acid with added sodium acetate to give the anil **3**, which was dehydratively cyclized with polyphosphoric acid (PPA) and chloroacetic acid or glycine to give **4a** and **4b**, respectively. When the reaction of **1** with **2** in acetic acid with added sodium acetate was repeated exactly as described, a 92% yield of 2-(acetylamino)-5-chlorobenzophenone (**5**) was obtained. The conversion of **1** to **5** also proceeded smoothly in the absence of **2**.

Acetanilide **5**, whose melting point (113-114°) is similar to that of authentic **3** (*vide infra*, 109-110°), has been previously prepared [3] as shown in Scheme I. Treatment of 5-chloroanthranilic acid (**6**) with acetic anhydride gave 6-chloro-2-methyl-4*H*-3,1-benzoxazin-4-one (**7**), which was ring-opened with phenylmagnesium bromide to afford **5**. Our physical constants for **5** prepared from **1** were consistent with those reported for **5** as prepared from **6**. Elemental analysis and all spectral data were consistent with **5** and not **3**.

An authentic sample of anil **3** could be obtained when typical conditions for Schiff base formation were em-

Scheme II

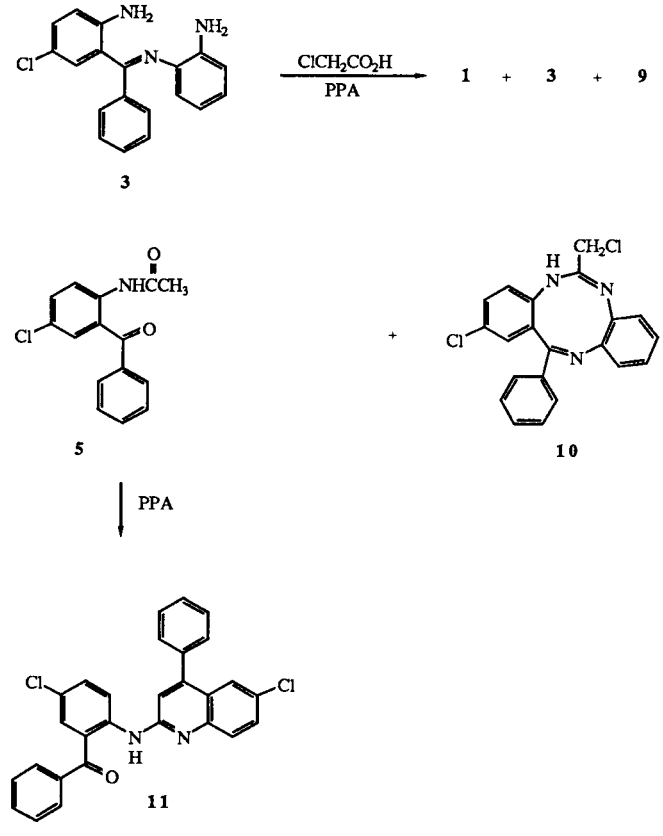


ployed. Thus, when a solution of 2-amino-5-chlorobenzophenone (**1**) and *o*-phenylenediamine (**2**) was heated in toluene with a catalytic amount of *p*-toluenesulfonic acid, a product mixture resulted from which anil **3** was isolated by flash chromatography. Anil **3** was a varnish which slowly crystallized on standing. The melting point was sharp, and similar to that reported by Kulkarni *et al.* [1], but the infrared spectral data were dissimilar. The chemical ionization mass spectrum of **3** displayed an intense protonated molecular ion, and elemental analysis was consistent with the empirical formula. However, both ^{1}H nmr and ^{13}C nmr spectra showed two distinct species in solution [4]. Perhaps anti and syn forms of **3** would account for the nmr spectra, and perhaps the interconversion is mediated by spiro intermediate **8**, as suggested in Scheme II. Interestingly, a coproduct of **3** produced in the reaction of **1** with **2**, also isolated by flash chromatography, was 2,8-dichloro-6,12-diphenyldibenzo[*b*,*f*][1,5]diazocine (**9**). Diazocine **9** is the self-condensation product of **1**.

When anil **3** was subjected to polyphosphoric acid (PPA) in the presence of chloroacetic acid, a mixture of products was obtained (Scheme III) which was separated by flash chromatography. In addition to some recovered starting material **3**, the products isolated were **1**, a product of hydrolysis; dibenzodiazocine **9**, a secondary product of hydrolysis, and 2-chloro-6-(chloromethyl)-13-phenyl-5*H*-dibenzo[*d*,*h*][1,3,6]triazonine (**10**), a product whose structure was fully supported by spectral data and elemental analysis. The melting point obtained for **10** was 199-202° dec, while that reported for **10** by Kulkarni *et al.* [1] was 105°.

Since acetanilide **5** was the product we obtained from the preparation described for **3** by Kulkarni *et al* [1], and since these authors treated their reaction product with PPA and chloroacetic acid or glycine to supposedly give **4a** or **4b**, respectively, the reactions of **5** with PPA were investigated in the presence of chloroacetic acid and glycine. In both cases a single product was efficiently produced, which was identified as [5-chloro-2-[(6-chloro-4-phenyl-2-quinolinyl)amino]phenyl]phenylmethanone (**11**) (Scheme III). All spectral data, including high resolution

Scheme III



mass spectral data and elemental analysis, were in agreement with this structure. It was also demonstrated that **11** could be produced from **5** in the absence of chloroacetic acid or glycine; quinoline **11** was prepared from **5** and PPA alone in 90% yield. This yield reflects recrystallized, analytically pure material. It should be noted that the melting point we obtained for **11**, 189-192°, also does not coincide with those reported for either **4a** (105°) or **4b** (102-105°) by Kulkarni *et al.* [1].

The synthesis of **11** from **5** with PPA is a variation of the Friedlaender quinoline synthesis [5,6], Quinoline **11** has previously been synthesized using a procedure similar to that of Scheme III [7], and by treating **1** and **5** with phosphorous oxychloride [8].

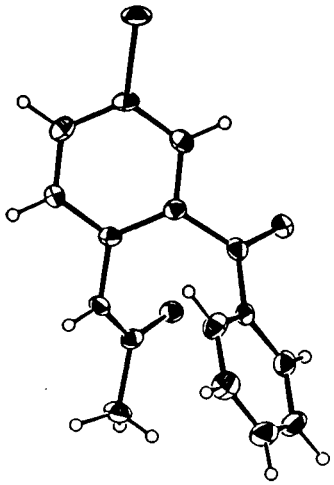


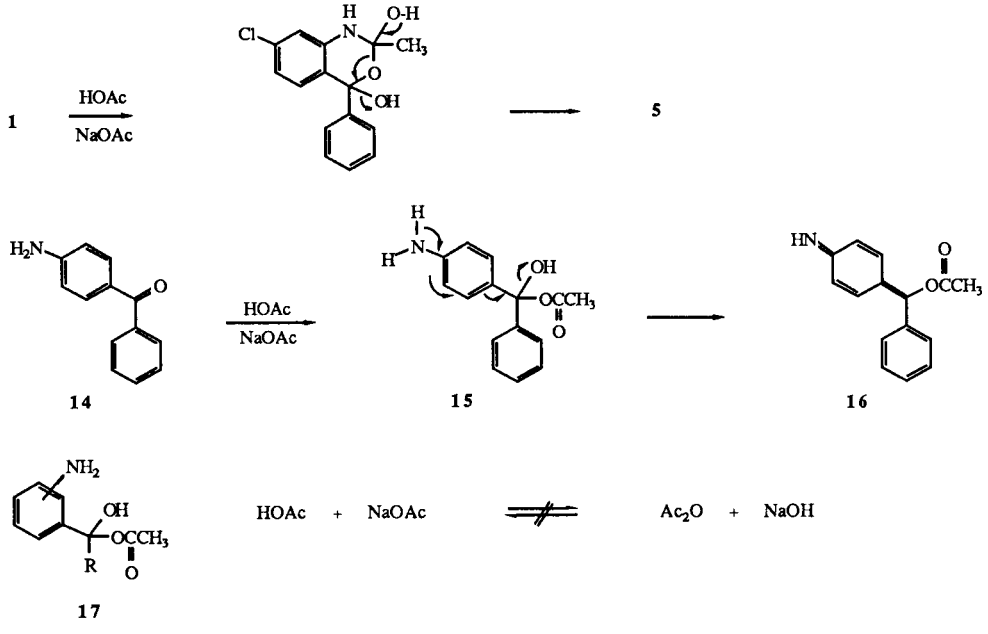
Figure I. ORTEP drawing of 2-(acetyl)aminochlorobenzophenone (**5**).

The ORTEP drawing of 2-(acetyl)amino-5-chlorobenzophenone (**5**) generated from single crystal X-ray crystallography is shown in Figure I. It is interesting to note that the amide hydrogen is not intramolecularly hydrogen-bonded to the benzophenone carbonyl group. Instead, these two groups are directed away from each other. This arrangement is in marked contrast to that of 2-aminobenzophenone, whose ORTEP view shows a strong, intramolecular hydrogen bond between the carbonyl oxygen and an amino hydrogen [10].

The mild conditions (sodium acetate and acetic acid) which led to the acetylation of 2-amino-5-chlorobenzophenone (**1**) were intriguing. Initially, it was felt that the amino group was acetylated by an *ortho*-carbonyl assisted process, as shown in Scheme IV. However, this mechanism was discounted when it was determined that 2-aminobenzophenone, 3-aminobenzophenone, and 4-aminobenzophenone gave acetanilides **12a**, **12c**, and **12b**, respectively, under the same conditions (Table I). The possibility that acetoxy intermediates of general structure **17** were the active acetylating agents was ruled out when it was determined that simple anilines, *e.g.*, aniline, *N*-methylaniline, and 4-aminophenol also underwent efficient acetylation with sodium acetate in acetic acid. Also ruled out, *a priori*, was the possiblity that an appreciable concentration of acetic anhydride was produced in an equilibrium mixture from acetic acid and sodium acetate.

A simple mechanistic possibility which accounts for all of the observations is shown in Scheme V. Interaction of aniline (**18**) with acetic acid could produce a small amount of intermediate adduct **19** in an equilibrium mixture,

Scheme IV



Scheme V

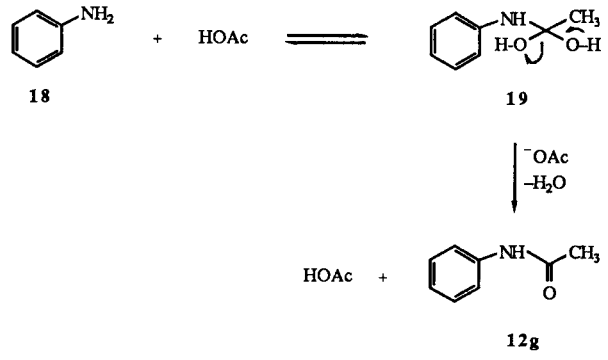
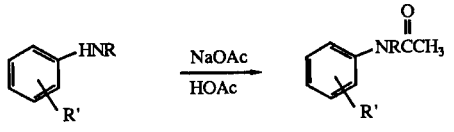


Table 1

Acetanilides Prepared from Anilines, Sodium Acetate, and Acetic Acid



Acetanilide	R	R'	Yield (%)	mp (C°)	lit mp (C°)	DOC ref [a]
5	H	2-benzoyl, 4-chloro	92	113-114 (EtOH)	115-116 [b]	---
12a	H	2-benzoyl	80	81-83 (hexane)	89	1, p 150
12b	H	4-benzoyl	96	151-152	156	1, p 150
12c	H	3-benzoyl	88	104-106 [c] (toluene)	132	1, p 150
12d	H	2-acetyl	0[d]	---	---	---
12e	H	4-acetyl	78	168-170	166-169	1, p 138
12f	H	3-acetyl	84	126-127 (toluene)	128-129	1, p 137
12g	H	H	86	111-113	115-116	1, p 372
12h	CH_3	H	96	93-96 (hexane)	101-102	4, p 3731
12i	H	4-OH	78	165-166	168	1, p 305

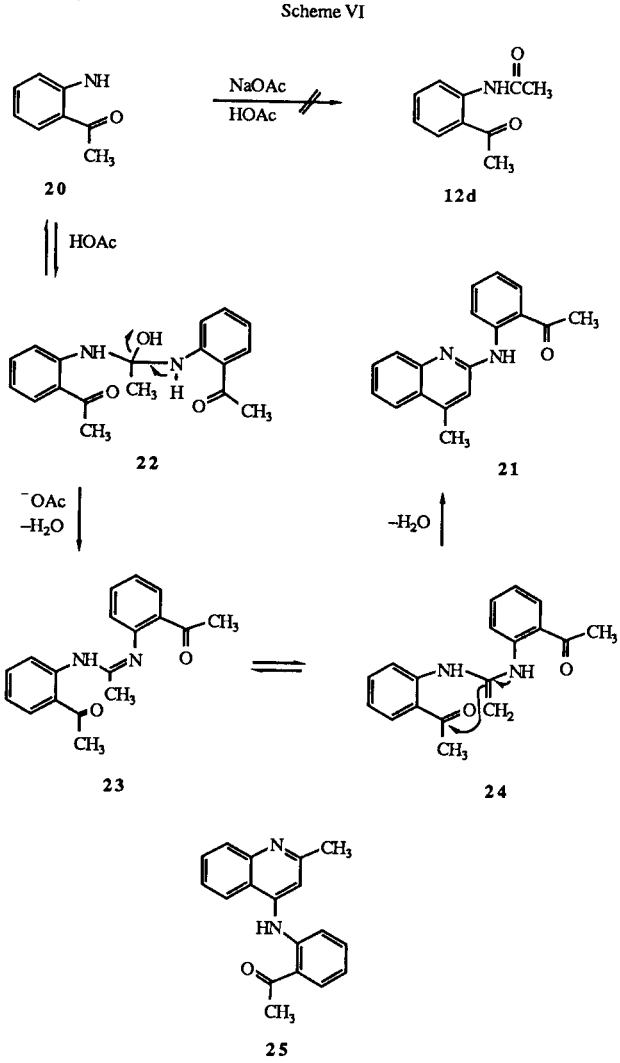
[a] "Dictionary of Organic Compounds", 5th Ed, J. Buckingham, ed, Chapman and Hall, New York, 1982. [b] Ref 3. [c] Since this melting point differed from that reported for 12c in the literature, this material was thoroughly characterized. See Experimental. [d] A quantitative yield of condensation product 21 was produced in this reaction. See Scheme VI.

which then could be dehydrated as shown by sodium acetate. The desiccant action of anhydrous sodium acetate could be a driving force. Moreover, it is known that sodium acetate is a good base in anhydrous acetic acid [11].

4'-Aminoacetophenone and 3'-aminoacetophenone underwent efficient acetylation with sodium acetate in acetic acid (Table I) as did the aminobenzophenones. However, 2'-aminoacetophenone (**20**) under these same conditions gave a quantitative yield of 2-[((2-acetyl)phenyl)amino]-4-methylquinoline (**21**). A proposed mechanism for this interesting transformation is presented in Scheme VI. It is felt that an intermediate corresponding to **19** (Scheme V) may be the first species to form, and interaction of this intermediate with additional **20** may produce **22**. Dehydration of **22** could give amidine **23**, which could equilibrate to provide enamine **24**. Enamine **24** is positioned to undergo an intramolecular condensation to provide quinoline **21**. The production of aromatic quinoline **21** could be a driving force for this efficient process. 2'-Aminoacetophenone (**20**) is the only aniline employed which bears an enolizable ketone at the *o*-position, and thus is the only structure which can undergo the condensation pathway of Scheme VI.

Since quinoline **25**, isomeric with **21**, was also a potential product of the reaction of **20** with sodium acetate in acetic acid, it was felt that an unequivocal structure deter-

Scheme VI



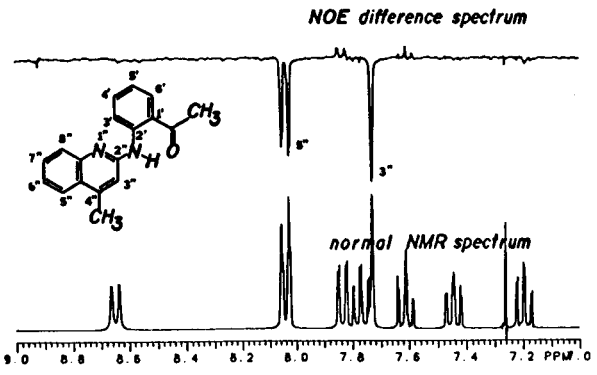
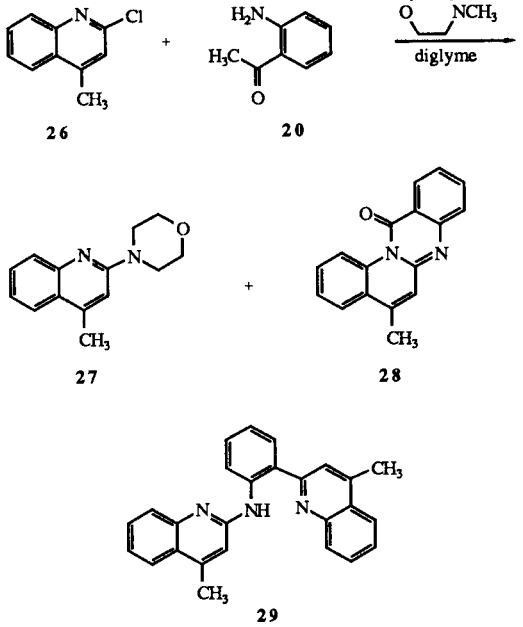


Figure II. NOE difference spectrum of 1-[2-(4-methyl-2-quinolinyl)amino]phenyl]ethanone (**21**) after saturation of quinolinyl methyl group.

mination for **21** was necessary. Quinoline **21** was an ideal candidate for Nuclear Overhauser Enhancement (NOE) [12] difference spectroscopy, which was used to determine the position of the methyl group on the quinoline ring. Figure II shows the NOE difference spectrum (deuteriochloroform) for **21** that results from saturation of the aromatic methyl absorption at δ 2.80. This figure clearly shows NOE's due to H3″ (δ 7.73) and H5″ (δ 8.04). Proton H3″ is adjacent to the methyl group in both **21** and **25** and is therefore expected to give a NOE for either structure.

Scheme VII



However, the observed NOE for H5″ is only expected for **21**. While it is true that H5″ and H8″ are not resolved in the ^{1}H nmr spectrum, in neither structure **21** or **25** is a NOE from the aromatic methyl protons to H8″ anticipated. Therefore, the signal displaying a NOE at δ 8.04 must be due to H5″. Similar NOE observations were made with 2-chlorolepidine (**26**).

The conformation presented for **21** in Scheme VI is also supported by the ^{1}H nmr spectrum. The low field position for H3′ (δ 8.63) is consistent with the deshielding influence of the quinoline nitrogen atom. This deshielding effect has been documented in similar systems [13].

Attempts to prepare an authentic sample of **21** (Scheme VII) by treatment of equivalent amounts of 2-chlorolepidine (**26**), 2′-aminoacetophenone (**20**), and *N*-methylmorpholine in diglyme were unsuccessful. However, **21** was probably an intermediate in the formation of the major product of this reaction, namely, 4-methyl-*N*-[2-(4-methyl-2-quinolinyl)phenyl]-2-quinolinamine (**29**). Also produced was a substantial amount of 4-methyl-2-(4-morpholinyl)quinoline (**27**). The latter product must arise from an initially formed quaternized displacement product which suffers a loss of methyl chloride. The small quantity of 5-methyl-12*H*-quino[2,1-*b*]quinazolin-12-one (**28**) produced in this reaction may have come from an impurity which was present in **20**.

In summary, a reinvestigation of the reaction of 5-chloro-2-aminobenzophenone (**1**) with *o*-phenylenediamine (**2**), sodium acetate, and acetic acid showed that 2-(acetyl)amino-5-chlorobenzophenone (**5**) was produced rather than a triazepinobenzothiazolone. Further study revealed that sodium acetate and acetic acid alone were efficient acetylating conditions for a variety of benzophenones, acetophenones, and anilines. 2′-Aminoacetophenone (**20**), however, produced only 2-[((2-acetyl)phenyl)amino]-4-methylquinoline (**21**) under these conditions. The structure of quinoline **21** was unequivocally assigned using high resolution ^{1}H nmr techniques.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded with a Perkin Elmer Model 710B spectrophotometer, nmr spectra were recorded with Varian EM-360A, VXR-300, and XL-300 (multinuclear probe) spectrometers, and mass spectra with a Finnigan Model 4500 (electron impact and chemical ionization) mass spectrometer. Combustion analyses for C, H, and N were performed by Merrell Dow Analytical Laboratories, Cincinnati, Ohio.

Crystal Data.

Compound **5**, $C_{15}H_{12}ClNO_2$, has a monoclinic space group $P2_1/c$, a = 11.895 (2), b = 14.870 (4), C = 8.220 (1), β = 113.16 (1), V = 1336.82 A^3, Z = 4, D_c = 1.360024 gm/cc. There were 1943 reflections (out of 1760 unique) with $F \geq 3$ (I) collected with a Picker goniostat using graphite-monochromatized molybdenum radiation. The diffractometer, data-handling techniques, and general procedure have been described previously [14]. The structure was solved by direct methods and refined by full-matrix least squares. Final residuals are R = 0.0376 and R_w = 0.0410. Atomic coordinates for this work are available on request from

the Director of Cambridge Crystallographic Data Centre, University Chemical Laboratory, Cambridge CB2 1EN, England. Any request should be accompanied by the full literature citation of this article. Complete crystallographic details are also available in microfiche form from the Chemistry Library, Indiana University, Bloomington, Indiana 47405. Request MSC Report No. 86708.

2-(Acetyl)amino-5-chlorobenzophenone (**5**).

A mixture of 9.26 g (40.0 mmoles) of 2-amino-5-chlorobenzophenone (**1**), 8.65 g (80.0 mmoles) of *o*-phenylenediamine (**2**), 6.96 g (80.0 mmoles) of anhydrous sodium acetate and 250 ml of acetic acid was heated at reflux for 70 hours. This mixture was cooled, poured into 2 ℓ of cold water, and the white solid was collected, washed with water, and air-dried to give 10.1 g (92%) of **5**, mp 113-114° (ethanol) (lit [3] mp 115-116°); ir (potassium bromide): 3220 (HN), 1665 (ketone C=O), 1640 (amide C=O) cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 10.06 (s, 1H, NH), 7.70-7.60 (m, 4H, aromatic), 7.55-7.45 (m, 4H, aromatic), 7.38 (d, J = 2.8 Hz, 1H, C6-H), 1.72 (s, 3H, CH_3); ms: (70 eV, electron impact) m/e 273 (molecular ion).

Anal. Calcd. for $C_{15}H_{12}ClNO_2$: C, 65.82; H, 4.42; N, 5.12. Found: C, 65.85; H, 4.39; N, 5.07.

The yield of **5** in this experiment was unchanged in the absence of *o*-phenylenediamine.

N-[(2-Amino-5-chlorophenyl)phenylmethylene]-1,2-benzenediamine (**3**).

A solution of 11.6 g (50.0 mmoles) of 2-amino-5-chlorobenzophenone (**1**) and 5.41 g (50.0 mmoles) of *o*-phenylenediamine (**2**) in 200 ml of toluene with 100 mg of added *p*-toluenesulfonic acid (HOTs) was heated at reflux for 138 hours. The solution was washed with water and concentrated to leave a dark viscous liquid. Upon standing, a small amount of solid deposited, which was collected to give 0.92 g of **2**, as identified by infrared spectrometery. The filtrate was flash-chromatographed on silica gel with 8:2::hexane:ethyl acetate to separate three components. Fractions containing the fast-moving component were combined and concentrated to leave 1.00 g (5%) of 2,8-dichloro-6,12-diphenyldibenzo[*b*,*f*][1,5]diazocine (**9**), mp 215-217° (ethanol); ir (potassium bromide): 1615 (C=N) cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 7.67-7.62 (m, 4H, *o*-phenyl protons), 7.57-7.40 (m, 8H), 7.17 (d, J = 2.1 Hz, 2H, C1-H and C7-H), 7.06 (d, J = 8.5 Hz, 2H, C4-H and C10-H); ms: (100 eV, chemical ionization, methane) 427 ($M^+ + 1$), 455 ($M^+ + 29$), 467 ($M^+ + 41$).

Anal. Calcd. for $C_{26}H_{16}Cl_2N_2$: C, 73.08; H, 3.77; N, 6.55. Found: C, 73.06; H, 3.75; N, 6.55.

Fractions containing the second component from the column were combined and concentrated to give 5.68 g (49%) of recovered **1**. Fractions containing the third component were combined and concentrated to give 6.43 g (40%) of **3** as a glass, which crystallized on standing, mp 109-110°; ir (potassium bromide): 3460, 3370 and 3265 (NH), 1610 (C=N) cm^{-1}; nmr spectra were recorded in various solvents [4]; ms: (100 eV, chemical ionization, methane) 322 ($M^+ + 1$), 350 ($M^+ + 29$), 362 ($M^+ + 41$).

Anal. Calcd. for $C_{19}H_{16}ClN_3$: C, 70.91; H, 5.01; N, 13.06. Found: C, 70.84; H, 5.03; N, 12.80.

Treatment of **3** with Chloroacetic Acid and Polyphosphoric Acid (PPA).

A mixture of 3.81 g (11.8 mmoles) of **3**, 2.23 g (23.6 mmoles) of chloroacetic acid and 40 g of PPA was heated at 85-90° for 18 hours. The solution was cooled and poured into sodium bicarbonate solution. The precipitate was collected, washed with water, and dried to give 4.39 g of a mixture of 4 products by thin layer chromatography. A 3.70-g portion of this mixture was flash-chromatographed on silica gel (600 ml dry volume) with 8:2::hexane:ethyl acetate. Fractions containing the fast-moving component were combined and concentrated to give 0.340 g of dibenzodiazocine **9**, as shown by infrared spectrometry. Fractions containing the second component were combined and concentrated to give benzophenone **1**, as also shown by infrared spectrometry. Fractions containing the third component were combined and concentrated to give 0.270 g of 2-chloro-6-(chloromethyl)-13-phenyl-5*H*-dibenzo[*d*,*h*][1,3,6]triazonine (**10**), mp 199-202° dec (ethanol); ir (Nujol): 3170 (NH) cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.47 (d, J = 2.0 Hz, 1H, C1-H), 7.37-7.20 (m, 9H), 7.08-6.93 (m, 3H), 4.79 (broad s, 1H, NH), 4.70 (d, J = 12.7 Hz, 1H, one CH_2 proton), 4.59 (d, J = 12.7 Hz, 1H, one CH_2 proton); ms: (100 eV, chemical ionization, methane) 380 ($M^+ + 1$), 408 ($M^+ + 29$).

Anal. Calcd. for $C_{21}H_{15}Cl_2N_3$: C, 66.32; H, 4.04; N, 11.01. Found: C, 66.35; H, 4.10; N, 11.08.

Fractions containing the fourth component were combined and concentrated to give 0.490 g of **3** as shown by infrared spectrometry.

Treatment of **5** with PPA.

A mixture of 2.00 g (7.33 mmoles) of benzophenone **5** and 40 g of PPA was heated at 90° for 18 hours. The mixture was cooled and poured into sodium bicarbonate solution. The resulting precipitate was collected, washed with water, dried, and recrystallized from dimethylsulfoxide-water to afford 1.54 g (90%) of [5-(chloro-2-[(6-chloro-4-phenyl-2-quinolinyl)amino]phenyl]phenylmethanone (**11**), mp 189-190° (lit [7] mp 192°); ir (Nujol): 1595 (C=O) cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): [9] δ 9.77 (s, 1H, NH), 7.77 (d, J = 8.7 Hz, 1H, quinolinyl C8-H), 7.67 (dd, J = 8.7 Hz, J = 2.5 Hz, 1H, quinolinyl C7-H), 7.64-7.52 (m, 6H), 7.47 (d, J = 2.5 Hz, 1H, quinolinyl C5-H), 7.46-7.38 (m, 6H), 7.17 (d, J = 9.0 Hz, 1H, C3-H), 6.73 (s, 1H, quinolinyl C3-H); hrms: (70 eV, electron impact) m/e 468.0767 (molecular ion corresponding to $C_{28}H_{18}Cl_2N_2O$).

Anal. Calcd. for $C_{28}H_{18}Cl_2N_2O$: C, 71.65; H, 3.86; N, 5.97. Found: C, 71.44; H, 3.90; N, 5.92.

Similar yields of **11** were obtained in the presence of two equivalents of either chloroacetic acid or glycine.

General Procedure for the Preparation of Acetanilides (Table I) as Illustrated by 3-(Acetylamino)benzophenone (**12c**).

A solution of 3.94 g (20.0 mmoles) of 3'-aminoacetophenone (Pfaltz and Bauer) and 3.48 g (40.0 mmoles) of anhydrous sodium acetate in 50 ml of acetic acid was heated at reflux for 64 hours. The reaction could be followed by tlc by directly spotting onto a silica gel plate and eluting with 1:1::hexane:ethyl acetate. In this system, 3'-aminoacetophenone had an R_f of 0.45 and acetanilide **12c** had an R_f of 0.20. The mixture was concentrated and partitioned between methylene chloride and aqueous sodium carbonate. The organic layer was dried (sodium sulfate) and concentrated to an oil. The oil was extracted with several portions of ether and the concentrated extracts were triturated with ether-

hexane to give 4.24 g (88%) of **12c**, mp 104-106° (toluene), mp 106-107.5° (ethanol-water); ^{1}H nmr (deuteriochloroform): δ 8.52 (br s, 1H, NH), 7.98-7.53 (m, 4H, aromatic), 7.53-7.15 (m, 5H, aromatic), 2.10 (s, 3H, CH_3); ms: (70 eV, electron impact) m/e 239 (molecular ion).

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.74. Found: C, 75.23; H, 5.56; N, 5.74.

1-[2-[(4-Methyl-2-quinolinyl)amino]phenyl]ethanone (**21**).

A solution of 5.41 g (40.0 mmoles) of 4'-aminoacetophenone and 6.96 g (80.0 mmoles) of anhydrous sodium acetate in 50 ml of acetic acid was heated at reflux for 27 hours. The solution was poured into 350 ml of water and stored in the refrigerator. The resulting tan needles were collected and air-dried to give 1.83 g of **21**, mp 130-131°. The filtrate was concentrated, partioned between water and methylene chloride and the organic layer was dried (sodium sulfate) and concentrated to give an additional 4.10 g of **21**. Total yield was 5.93 g (84%) of **21**; ir (potassium bromide): 3440 (NH), 1690 (C=O) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 8.63 (dd, J = 1, 8 Hz, 1H, H-3'), 8.04 (dd's, J = 1, 8 Hz, 2H, H-5" and H-8"), 7.84 (dd, J = 2, 8 Hz, 1H, H-6'), 7.77 (ddd, J = 1, 7, 8 Hz, 1H, H-6"), 7.73 (q, J ~ 1 Hz, 1H, H-3"), 7.61 (ddd, J = 1, 7, 8 Hz, 1H, H-7"), 7.44 (ddd, J = 2, 7, 8 Hz, 1H, H-4'), 7.20 (ddd, J = 1, 7, 8 Hz, 1H, H-5'), 2.80 (d, J ~ 1 Hz, 3H, aromatic CH_3), 2.25 (s, 3H, ethanone CH_3); ms: (70 eV, electron impact) m/e 276 (molecular ion).

Anal. Calcd. for $C_{18}H_{16}N_2O$: C, 78.23; H, 5.84; N, 10.14. Found: C, 78.20; H, 5.90; N, 10.08.

Treatment of 2-Chlorolepidine (**26**) with 2'-Aminoacetophenone (**20**). Preparation of 4-Methyl-*N*-[2-(4-methyl-2-quinolinyl)phenyl]-2-quinolinamine (**29**).

A solution of 3.55 g (20.0 mmoles) of 2-chlorolepidine (Aldrich), 2.70 g (20.0 mmoles) of 2'-aminoacetophenone, and 2.02 g (20.0 mmoles) of *N*-methylmorpholine in 25 ml of diglyme was heated at 100° (oil bath) for 44 hours. The dark solution was concentrated by Kugelrohr distillation and the residue was partitioned between methylene chloride and water. The organic layer was dried (sodium sulfate) and concentrated to leave 5.62 g of a mixture which was applied, with a minimum volume of ethyl acetate, to a 600-ml (dry volume) column of flash chromatography silica gel and eluted with 4:1::hexane:ethyl acetate in 25 75-ml fractions. Fractions 3-10 crystallized on standing to give 3.41 g (45%) of **29**, mp 131° (melt and resolidify, melt again at 143-144°) as bright yellow prisms; ^{1}H nmr (deuteriochloroform): δ 12.44 (broad s, 1H, NH), 9.15 (dd, J = 9, 1 Hz, 1H, H-6'), 8.21 (dd, J = 8, 1, 1 Hz, 1H, H-8"), 8.03 (dd, J = 9, 1 Hz, 1H, H-5"), 7.88-7.77 (m, 4H, H-5, H-7", H-3', and H-8), 7.74 (q, J = 1 Hz, 1H, H-3"), 7.60 (ddd, J = 8, 7, 1 Hz, 1H, H-6"), 7.56 (ddd, J = 8, 7, 1 Hz, 1H, H-6), 7.50 (ddd, J = 9, 7, 1 Hz, 1H, H-5'), 7.30 (ddd, J = 8, 7, 1 Hz, 1H, H-7), 7.11 (ddd, J = 8, 7, 1 Hz, 1H, H-4'), 6.83 (q, J = 1 Hz, 1H, H-3), 2.78 (d, J = 1 Hz, 3H, CH_3 on C-4"), 2.62 (d, J = 1 Hz, 3H, CH_3 on C-4); ^{13}C nmr (deuteriochloroform): δ 158.5, 153.7, 147.6, 146.1, 145.3, 144.6, 141.0, 130.2, 129.7, 129.5, 129.1, 129.0, 127.6, 126.6, 126.3, 124.6, 124.6, 123.8, 123.3, 122.7, 121.6, 120.8, 120.4, 114.7, 19.1, 18.8; ms: (70 eV, electron impact) m/e 375 (molecular ion, 50), 374 (100), 360 (12), 233 (39).

Anal. Calcd. for $C_{26}H_{21}N_3$: C, 83.17; H, 5.64; N, 11.19. Found: C, 83.25; H, 5.77; N, 11.06.

Fractions 11-18 were concentrated to leave 0.68 g (17%) of an oil which was identified as 4-methyl-2-(4-morpholinyl)quinoline (**27**) [15]. Fractions 22-24 were concentrated to leave 50 mg of residue which was triturated with ether to afford 10.6 mg of a solid which was identified as 5-methyl-12*H*-quino[2,1-*b*]quinazolin-12-one (**28**) [16].

Acknowledgement.

The authors thank Professor Hans Zimmer, University of Cincinnati, for helpful discussions regarding the mechanism of acetylation with sodium acetate and acetic acid.

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[3] Netherlands Application 6,604,034, Sept. 30, 1966; *Chem. Abstr.*, **66**, 46441k (1967).

[4] An ^{1}H nmr spectrum in deuteriochloroform indicated two components in a ratio of 1:3; in deuterioacetonitrile the ratio was 1:2; and in dimethyl sulfoxide-d_6 the ratio could not be determined. A ^{13}C nmr spectrum in deuteriochloroform also indicated two components, with respective imino carbon resonances at 172.0 ppm and 165.0 ppm.

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[15] The following spectral data were gathered for **27**: ^{1}H nmr (deuteriochloroform): δ 7.78 (dd, J = 1, 8 Hz, 1H, H-8), 7.72 (ddd, J = 1, 1, 8 Hz, 1H, H-5), 7.54 (ddd, J = 1, 8, 8 Hz, 1H, H-6), 7.27 (ddd, J = 1, 8, 8 Hz, 1H, H-7), 6.82 (s, 1H, H-3), 3.85 (t, J = 7 Hz, 4H, H-3'), 3.70 (t, J = 7 Hz, 4H, H-2'), 2.60 (d, J = 1 Hz, 3H, CH_3); ^{13}C nmr (deuteriochloroform): δ 157.4, 147.7, 145.3, 129.3, 127.2, 123.5, 122.4, 123.7, 109.6, 66.9, 45.5, 19.2; ms: (70 eV, electron impact) m/e 228 (92), 197 (92), 183 (38), 171 (79), 143 (100); hrms: (70 eV, electron impact, resolution = 10,000) calculated M^+ is 228.1263 for $C_{14}H_{16}N_2O$, the actual M^+ is 228.1264.

[16] The following spectral data were gathered for **28**: ^{1}H nmr (deuteriochloroform): δ 9.58 (dd, J = 1, 9 Hz, 1H, H-1), 8.44 (dd, J = 2, 8 Hz, 1H, H-11), 7.80, 7.78 (m, 2H, H-4 and H-9), 7.72 (dd, J = 8, 1 Hz, 1H, H-8), 7.64 (ddd, J = 9, 7, 2 Hz, 1H, H-2), 7.51 (ddd, J = 7, 7, 1 Hz, 1H, H-3), 7.48 (ddd, J = 7, 7, 1 Hz, 1H, H-10), 7.02 (q, J = 1 Hz, 1H, H-6), 2.55 (d, J = 1 Hz, 3H, CH_3); ^{13}C nmr (deuteriochloroform): δ 163.0, 147.8, 146.8, 142.2, 135.3, 134.6, 129.1, 127.5, 126.2, 126.2, 125.7, 125.2, 124.2, 124.1, 121.8, 119.9, 19.2; ms: (70 eV, electron impact) m/e 260 (100), 232 (16), 231 (16); hrms: (70 eV, electron impact, resolution = 10,000) calculated M^+ is 260.0950 for $C_{17}H_{12}N_2O$, the actual M^+ is 260.0934.