Structure Analysis and Refinement. The structure was determined by direct methods and Fourier difference methods. Full-matrix least-squares refinement was done of the position and anisotropic temperature factors of all non-hydrogen atoms (254 variables). The hydrogens were assigned calculated positions. The hydrogens were assigned calculated isotropic temperature factors 1.2 times the equivalent isotropic temperature factor of the associated non-hydrogen atom. Calculated parameters were updated every two refinement cycles. The weighting scheme $W = 1/[\sigma^2(F_o) + 0.000625F_o^2]$ with $\sigma(F_o)$ from counting statistics gave satisfactory agreement between F_o and F_c, with GOF = 1.26. The final R and R_w values were 0.045 and 0.056, respectively. The programs and computers used and sources of scattering factor data are given in ref 15.

Acknowledgment. Ellen Grenci is thanked for typing the manuscript and preparing the figures. Dr. Ignatius Turchi provided valuable insights in oxazole chemistry and nomenclature.

Supplementary Material Available: Details of the data collection and structural analysis, as well as atomic coordinates, positional and thermal parameters, bond lengths and bond angles, and torsional angles for oxidation product **12** (9 pages). Ordering information is given on any current masthead page.

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The Chemistry of 2′-Amino Analogues of 2′-Hydroxychalcone and Its Derivatives

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Received July 18, 1989

The cyclization of 2′-aminochalcone (**2a**) and its side-chain additives has been studied for the development of syntheses of 2-aryl-4-quinolones. **2a** and its 2′-acetamido **2b** and 2′-benzenesulfonamido **2c** derivatives underwent acid- or base-catalyzed cyclization to 1,2,3,4-tetrahydro-4-quinolones. The α,β-dibromides of **2b** and **2c** cyclized to *cis*-3-bromo-4-quinolones as did the corresponding α-bromochalcones and the α-bromo-β-methoxy additive of **2c**. 2′-Acetamido-α-bromochalcone was cyclized by acid to 1,4-dihydro-2-phenyl-4-quinolone. 2′-Aminochalcone formed a stable epoxide which, with acid, gave *cis*-3-hydroxy-1,2,3,4-tetrahydro-3-phenyl-4-quinolone. 2′-Aminochalcones **2a-c** and their additives, such as dibromide and epoxide, are useful, readily available precursors of various 2-aryl-4-quinolones.

Introduction

In 1945, de Diesbach and Kramer[1] noted the similarity between 2-aryl-1,2,3,4-tetrahydro-4-quinolones **1** and flavanones **3**. Yet, except for the base-catalyzed isomerization of 2′-aminochalcone[2] (**2a**) and its *N*-acetyl[3] **2b** and *N*-tosyl[1] **2c** derivatives to the corresponding tetrahydro-4-quinolones **1a-c**, little is known[1-4] of the potential of 2′-aminochalcone (**2a**) and its dihydro derivatives **4** to serve as precursors for 2-aryl-4-quinolones **1**. These 2-aryl-substituted quinolones are difficult to synthesize[5,6] by the usual procedure[6,7] of thermally cyclizing acrylates obtained from the reaction of arylamines with β-keto esters. The opportunity was taken to compare the reactions of 2′-aminochalcone (**2a**) and its derivatives with those of 2′-hydroxychalcone and its corresponding derivatives.

Results and Discussion

2′-Aminochalcone (**2a**), which was conveniently prepared by Murphy and Watanasin's[8] method of aldol condensation, was cyclized by orthophosphoric acid in acetic acid to 1,2,3,4-tetrahydro-2-phenyl-4-quinolone (**1a**), an isomerization analogous to that observed[9] in the synthesis of flavanone **3** from 2′-hydroxychalcone. The same product **1a** was obtained from 2′-acetamidochalcone (**2b**). The *N*-acetyl-4-quinolone **1b** was prepared instead by the reaction of 1,2,3,4-tetrahydro-2-phenyl-4-quinolone (**1a**) with acetic anhydride. 4-Acetoxy-1-acetyl-1,2-dihydro-2-phenylquinoline (**5**) was obtained as a minor product, but, in the presence of sodium acetate, this acetate **5** was the major of the two acetylation products.

2′-(Benzenesulfonamido)chalcone (**2c**) was isomerized to the 1-(phenylsulfonyl)-4-quinolone **1c** by aqueous ethanolic sodium hydroxide. Under similar conditions, 2′-(benzenesulfonamido)-3′,5′-dibromochalcone (**2d**) did not cyclize, probably because of the steric difficulty of accommodating an 8-bromo and a 1-benzenesulfonyl group in a 4-quinolone **1d**.

One of the more effective methods of flavone synthesis is that of Emilewicz and von Kostanecki,[10] in which a 2′-hydroxychalcone dibromide is cyclized by base. For the analogous 4-quinolone synthesis, the *N*-benzenesulfonyl derivative **2c** of 2′-aminochalcone was employed to prevent nuclear halogenation during side-chain bromination and to ensure the availability for cyclization of an ionisable NH function at the 2′-position. Bromination of this chalcone **2c** gave 2′-(benzenesulfonamido)chalcone dibromide (**4a**), which, on reaction with aqueous ethanolic potassium hydroxide, under typical Emilewicz-von Kostanecki reaction

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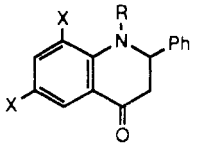

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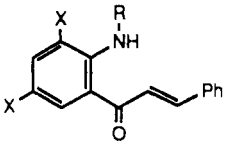
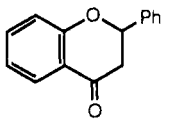


2

a: R = X = H
b: R = Ac, X = H
c: R = SO_2Ph, X = H
d: R = SO_2Ph, X = Br



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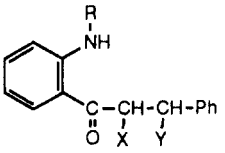

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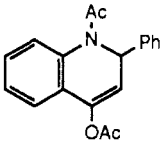


5

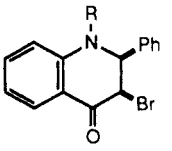
a: R = SO_2Ph, X = Y = Br
b: R = Ac, X = Y = Br
c: R = H, X = Y = Br
d: R = H, X = Br, Y = OEt
e: R = SO_2Ph, X = Br, Y = OMe
f: R = Ac, X = Br, Y = OMe
g: R = H, X = Br, Y = OMe
h: R = H, X = OH, Y = OEt

conditions, gave *cis*-1-(phenylsulfonyl)-3-bromo-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (**6a**). The stereochemical assignment is based on the $J_{2,3}$ coupling constant of 3 Hz in the ^{1}H NMR spectrum of the product. The spectrum of the crude reaction product indicated the presence also of some of the trans isomer, having doublets at δ 5.21 and 6.23 with a coupling constant of 6 Hz. *cis*- and *trans*-3-bromoflavanones have[11] coupling constants of 2 and 8 Hz, respectively. The *trans*-3-bromo-4-quinolone could not be isolated.

The isolation of a 3-bromo heterocycle from the Emilewicz–von Kostanecki reaction is very rare[12] in the O-heterocyclic series; the 3-bromoflavanone intermediates almost always eliminate hydrogen bromide in the basic reaction conditions, forming flavones. The formation of the *cis*-**6a** and *trans*-3-bromo-4-quinolones may occur by direct cyclosubstitution of nitrogen for the β-bromine atom of the dibromide **4a** or, by analogy with their O-heterocyclic counterparts,[13] via the initial formation of an α-bromochalcone **7**,**8** prior to cyclization.

One of the isomers of the α-bromochalcone, (*Z*)-2′-(benzenesulfonamido)-α-bromochalcone (**7a**), was obtained from the chalcone dibromide **4a** by reaction with potassium acetate. The stereochemical assignment is based on the observation[13] that the formation of the *Z* isomer **7** is preferred to that of the *E* isomer **8**. The ^{1}H NMR spectrum of the crude product indicated that as much as 10% of it was comprised of the *E* isomer **8a**. However, the latter **8a** could not be separated chromatographically, and crystallization gave only the *Z* isomer **7a**. This isomer **7a** cyclized to *cis*-1-(phenylsulfonyl)-3-bromo-1,2,3,4-tetrahydro-4-quinolone (**6a**) on reaction with aqueous ethanolic potassium hydroxide.

Bromination of 2′-acetamidochalcone (**2b**) gave the dibromide **4b**, which was dehydrobrominated by potassium acetate to the (*Z*)-**7b** and (*E*)-**8b** isomers of 2′-acetamido-α-bromochalcone. The stereochemical assignment is based on Donnelly and Doran's[13b] observations concerning the multiplicity of the ^{1}H NMR signal of the unsubstituted aromatic ring and the relative chemical shifts of the hydrogens of the 2′-hetero atom. The dibromide **4b** did not react cleanly with aqueous ethanolic potassium hydroxide. In aqueous tetrahydrofuran (THF) it gave, in poor yields, *cis*-1-acetyl-3-bromo-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (**6b**) and (*E*)-2′-acetamido-α-bromochalcone (**8b**); presumably the *Z* isomer **7b** of the α-bromochalcone, usually[13] the more readily formed and the more reactive, cyclized to the 4-quinolone **6b**. Like their parent dibromide **4b**, the α-bromochalcone isomers **7b** and **8b** did not react cleanly with aqueous ethanolic potassium hydroxide and, in aqueous THF, gave the same products, **6b** and **8b**, as the dibromide **4b**.



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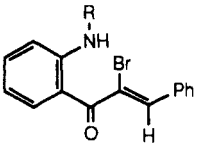

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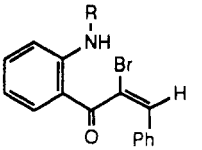
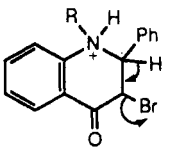


8

a: R = SO_2Ph
b: R = Ac
c: R = H

2′-Acetamido-α-bromochalcone, as a mixture of isomers **7b** and **8b**, underwent acid-catalyzed cyclization to 1,4-dihydro-2-phenyl-4-quinolone (**10**). This reaction is without a counterpart in the O-heterocyclic series. The elimination of hydrogen bromide is possibly due to the acidity of the 2-H in the intermediate **9**.

All the acetamidochalcones showed the anomalous "acylation shift" (greater than 2 ppm downfield) of the ^{1}H NMR signal of the hydrogen ortho to the acetamido group, a phenomenon studied by Sternhell and co-workers.[14] Also of interest is the large "acyl shift" of the 2-H of 1-acetyl-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (**1b**) in comparison with that of the 2-H of the parent 4-quinolone **1a**; the downfield shift was 1.83 ppm.



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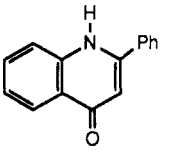

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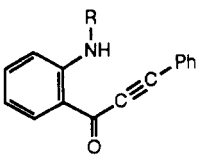

11a: R = H
b: R = Ac

2′-Aminochalcone dibromide (**4c**), prepared by hydrolyzing 2′-acetamidochalcone dibromide (**4b**), reacted with aqueous ethanolic alkali and formed the two diastereomers of 2′-amino-α-bromo-β-ethoxydihydrochalcone (**4d**) and, apparently, the (*Z*)-**7c** and (*E*)-**8c** isomers of 2′-amino-α-bromochalcone together with 2′-amino-3-phenyl-1-propynone (**11a**); the three last-mentioned products could be isolated only as their acetyl derivatives. Lacking a suitably acidic hydrogen in the 2′-position, it is not sur-

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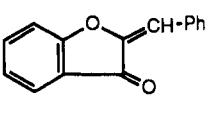
prising that this dibromide gave no heterocyclic products. The 2′-amino substituent also inhibited the elimination of hydrogen bromide by potassium acetate from the side chain of the dibromide **4c**.

The Wheeler synthesis[15] of aurones **12** involves the base-catalyzed cyclization of α-bromo-β-alkoxydihydrochalcones, prepared usually by the reaction of a chalcone with *N*-bromosuccinimide (NBS) in alcohol. 2′-(Benzenesulfonamido)chalcone (**2c**), however, reacted with 1,3-dibromo-5,5-dimethylhydantoin, or NBS, in methanol to give the nuclear brominated chalcone, 2′-(benzenesulfonamido)-3′,5′-dibromochalcone (**2d**). Side-chain bromomethoxylation was not effected even in the presence of an excess of these brominating agents. 2′-(Benzenesulfonamido)-α-bromo-β-methoxydihydrochalcone (**4e**) was, therefore, prepared indirectly. 2′-Acetamidochalcone (**2b**) reacted with NBS in methanol and gave 2′-acetamido-α-bromo-β-methoxydihydrochalcone (**4f**), which was hydrolyzed to 2′-amino-α-bromo-β-methoxydihydrochalcone (**4g**) and converted into the required dihydrochalcone **4e** by reaction with benzenesulfonyl chloride.

2′-(Benzenesulfonamido)-α-bromo-β-methoxydihydrochalcone (**4e**) cyclized on reaction with aqueous ethanolic potassium hydroxide and formed, not a five-membered heterocycle, but *cis*-1-(phenylsulfonyl)-3-bromo-1,2,3,4-tetrahydro-4-quinolone (**6a**). The unexpected formation of the six-membered heterocycle is probably due to a slow rate of formation of the conjugate base of the benzenesulfonamido group which allows side-chain elimination of methanol, forming the 4-quinolone **6a** precursor, the α-bromochalcone **7a**, to predominate over the cyclosubstitution of nitrogen for the α-bromine atom of the dihydrochalcone **4e**. 2′-Acetamido-α-bromo-β-methoxydihydrochalcone (**4b**) formed (*Z*)-2′-acetamido-α-bromochalcone (**7b**) on reaction with aqueous potassium hydroxide in THF; in dioxan it formed 2′-acetamidochalcone (**2b**). When 2′-amino-α-bromo-β-methoxydihydrochalcone (**4g**) reacted with aqueous ethanolic potassium hydroxide, it behaved in a manner similar to the corresponding dibromide **4c** and gave the diastereomers of 2′-amino-α-bromo-β-ethoxydihydrochalcone (**4d**), a mixture of the *Z* and *E* isomers of 2′-amino-α-bromochalcone, **7c** and **8c**, and 1-(2-aminophenyl)-3-phenyl-1-propynone (**11a**).

The epoxides of 2′-hydroxychalcones are extremely difficult to isolate.[16] Indeed, these chalcones are cyclized[17] by alkaline hydrogen peroxide, the Algar–Flynn–Oyamada reaction, to dihydroflavonols without the intermediacy of a chalcone epoxide. In contrast, 2′-aminochalcone (**2a**), on reaction with alkaline methanolic hydrogen peroxide, readily afforded 2′-aminochalcone epoxide (**13**), which, when briefly refluxed in acetic acid, cyclized to *cis*-1,2,3,4-tetrahydro-3-hydroxy-2-phenyl-4-quinolone (**14**). It was not possible to base the stereochemical assignment of this quinolone on its ^{1}H NMR spectrum as the chemical shifts of the 2-H and 3-H were identical. Instead, it was converted by acetic anhydride/sulfuric acid into the *cis*-acetate **15**, the spectrum of which showed $J_{2,3}$ as 2.7 Hz, a typical[11] value for the cis configuration. 2′-Aminochalcone epoxide (**13**) reacted with ethanolic sulfuric acid to give the diastereomers of 2′-amino-α-hydroxy-β-ethoxydihydrochalcone (**4h**).

Acetylation and sulfonylation of 2′-aminochalcone epoxide (**13**) using acetic anhydride/pyridine and benzenesulfonyl chloride/pyridine gave 2′-acetamidochalcone epoxide **16a** and 2′-benzenesulfonamidochalcone epoxide **16b**, respectively, the derivatives required for a study of the base-catalyzed reactions of this epoxide system. Both epoxides, however, on reaction with aqueous ethanolic sodium hydroxide or anhydrous ethanolic potassium acetate, gave inseparable multicomponent mixtures.



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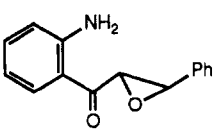

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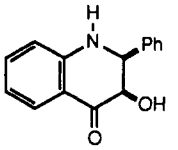

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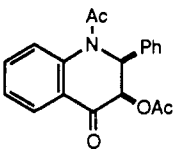

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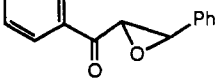

16a: R = Ac
b: R = SO_2Ph

In conclusion, the ease of synthesis of 2′-aminochalcone and its 2′-amido derivatives and the ready cyclization of these compounds to 2-aryl-1,2,3,4-tetrahydro-4-quinolones suggests that this is probably a useful route to related quinolones substituted in either aromatic ring. 4-Quinolones, substituted in the 3-position of the heterocyclic ring by bromine or hydroxy groups, were obtained from side-chain brominated chalcones or chalcone epoxide, respectively. The reactions of 2′-aminochalcones were similar to those of 2′-hydroxychalcone, but the reactions of additives of 2′-aminochalcones gave, as products, compounds related to intermediates for the products obtained from additives of 2′-hydroxychalcone.

Experimental Section

All ^{1}H NMR spectra were recorded at 60 MHz on a Perkin-Elmer R12 spectrometer in $CDCl_3$ solutions containing Me_4Si as an internal standard. Melting points were obtained on a Reichert Thermovar hot-plate apparatus and are uncorrected. Elemental analyses for all new compounds were in satisfactory agreement with the calculated values (C ±0.4, H ±0.2, Br ±0.6, N ±0.4, S ±0.5). Mass spectra were recorded on a VG Micromass 7070H spectrometer. Precoated Merck silica gel $60F_{254}$ plates were used for thin-layer chromatography (TLC). Merck silica gel $PF_{254+366}$ was used for preparative TLC (PLC).

2′-Aminochalcone (2a). 2′-Aminoacetophenone (18.78 g, 139 mmol) was added to a solution of benzaldehyde (14.75 g, 139 mmol) in EtOH (100 mL) containing NaOH (3 pellets) and stirred at 5 °C for 8 h. TLC showed that the resulting orange precipitate was pure **2a**[2] (17.88 g, 59%): mp 71–2 °C; ^{1}H NMR δ 6.20 (brs, NH_2), 6.57–6.91 (m, 3′-H and 5′-H), 7.20–8.08 (m, 9 H).

2′-Acetamidochalcone (2b). Reaction of **2a** (5.0 g) with Ac_2O/C_5H_5N gave **2b**, yellow plates (4.3 g, 72%), mp 92–3 °C, on crystallization from $MeOH/H_2O$: ^{1}H NMR δ 2.28 (s, Ac), 7.07–7.93 (m, 9 H), 7.98–8.22 (m, 6′-H), 8.85 (q, 3′-H, J = 8 and 1.5 Hz), 11.52 (brs, NH).

2′-(Benzenesulfonamido)chalcone (2c). Reaction of **2a** (5.0 g) with $PhSO_2Cl/C_5H_5N$ gave **2c**, yellow needles (6.8 g, 84%), mp 121–2 °C, on crystallization from EtOH: ^{1}H NMR δ 7.03 (m, 16 H), 11.21 (brs, NH).

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2′-(Benzenesulfonamido)-3′,5′-dibromochalcone (2d). NBS (0.44 g, 2 mmol) was added to a solution of **2c** (0.30 g, 0.8 mmol) in MeOH (50 mL). After 3 days, the precipitate of **2d** (0.35 g, 81%) was collected, colorless crystals, mp 279–80 °C, on crystallization from $CHCl_3$. ^1H NMR (DMSO-d_6) δ 7.10–8.10 (m, 14 H); MS m/z 523 (M^+). Similarly, the chalcone **2c** (1.60 g, 4.4 mmol) reacted with 1,3-dibromo-5,5-dimethylhydantoin (1.26 g, 4.4 mmol) to give **2d** (1.19 g, 52%).

2′-(Benzenesulfonamido)chalcone Dibromide (4a). Br_2 (1.44 g, 9 mmol) in $CHCl_3$ (35 mL) was added to **2c** (3.00 g, 8 mmol) in $CHCl_3$ (50 mL). The resulting suspension was stirred for 3 h. Removal of the solvent gave **4a**, yellow crystals (3.59 g, 83%), mp 129–30 °C, on crystallization from EtOH: ^1H NMR δ 5.62 (d, β-H, J = 12.0 Hz), 5.93 (d, α-H, J = 12.0 Hz), 7.09–8.17 (m 14 H), 11.02 (brs, NH).

2′-Acetamidochalcone Dibromide (4b). Similarly, Br_2 (1.83 g, 11 mmol) in CCl_4 (40 mL) reacted with **2b** (3.00 g, 11 mmol) in CCl_4 (120 mL) and gave **4b**, yellow needles (3.35 g, 70%), mp 139–40 °C, on crystallization from MeOH: ^1H NMR δ 2.32 (s, Ac), 5.63 (d, β-H, J = 12.0 Hz), 5.97 (d, α-H, J = 12.0 Hz), 7.12–8.29 (m, 8H), 8.94 (q, 3′-H, J = 8.0 and 1.3 Hz), 11.24 (brs, NH).

2′-Aminochalcone Dibromide (4c). Aqueous HCl (10%; 3 mL) was added to a solution of **4b** (2.00 g, 4.7 mmol) in EtOH (50 mL) and refluxed for 1 h. It was then cooled and neutralized with aqueous NaOH (10%). The precipitate (1.19 g) was filtered off, and the filtrate was extracted with $CHCl_3$. The extract was washed, dried, and evaporated to dryness. The resulting oil (0.65 g) was combined with the precipitate and gave **4c**, yellow needles (1.09 g, 60%), mp 124–5 °C, on crystallization from EtOH: ^1H NMR δ 5.78 (d, β-H, J = 11.0 Hz), 6.06 (d, α-H, J = 11.0 Hz), 6.48 (brs, NH_2), 6.53–7.98 (m, 9 H).

2′-(Benzenesulfonamido)-3′,5′-dibromochalcone Dibromide. Addition of Br_2 (0.33 g, 2 mmol) in $CHCl_3$ (30 mL) dropwise to a refluxing solution of 2′-(benzenesulfonamido)-3′,5′-dibromochalcone **2d** (1.03 g, 2 mmol) in $CHCl_3$ (100 mL) gave the dibromochalcone dibromide, colorless crystals (0.34 g, 25%), mp 179–80 °C, on crystallization from EtOH: ^1H NMR (DMSO-d_6) δ 5.55 (d, β-H, J = 11.0 Hz), 6.26 (d, α-H, J = 11.0 Hz), 7.25–8.14 (m, 12 H).

1-(2-Acetamidophenyl)-2-bromo-3-methoxy-3-phenyl-1-propanone (4f). NBS (2.01 g, 11 mmol) was added to a solution of **2b** (3.00 g, 11 mmol) in MeOH (65 mL). After 3 days, the precipitate was collected. It gave **4f**, yellow needles (2.56 g, 60%), mp 170–1 °C, on crystallization from MeOH: ^1H NMR δ 2.30 (s, Ac), 3.25 (s, OMe), 4.87 (d, β-H, J = 9.3 Hz), 5.26 (d, α-H, J = 9.3 Hz), 6.98–8.17 (m, 8 H), 8.87 (q, 3′-H, J = 8.0 and 1.3 Hz), 11.35 (brs, NH).

1-(2-Aminophenyl)-2-bromo-3-methoxy-3-phenyl-1-propanone (4g). A solution of **4f** (1.36 g, 4 mmol) in MeOH (35 mL) containing aqueous HCl (10%; 4 mL) was refluxed for 4 h and neutralized with aqueous NaOH (10%). Removal of most of the solvent gave **4g**, orange needles (0.71 g, 59%), mp 115–6 °C, on crystallization from MeOH: ^1H NMR δ 3.27 (s, OMe), 4.93 (d, β-H, J = 10.0 Hz), 5.27 (d, α-H, J = 10.0 Hz), 6.04 (brs, NH_2), 6.62–7.03 (m, 3′-H, 5′-H), 7.28-7.79 (m, 6 H), 7.95 (q, 6′-H, J = 8.0 and 1.6 Hz).

1-(2-(Benzenesulfonamido)phenyl)-2-bromo-3-methoxy-3-phenyl-1-propanone (4e). Benzenesulfonyl chloride (0.27 g, 1.5 mmol) was added to a solution of **4g** (0.51 g, 1.5 mmol) in dry pyridine (3 mL). The mixture was stirred for 12 h and poured into iced water (40 mL), and the resulting oily solid was collected. This gave **4e**, orange crystals (0.35 g, 48%), mp 159–60 °C, on crystallization from MeOH: ^1H NMR δ 3.25 (s, OMe), 4.84 (d, β-H, J = 10.0 Hz), 5.18 (d, α-H, J = 10.0 Hz) 6.98–8.08 (m, 9 H), 11.16 (brs, NH).

2′-Aminochalcone Epoxide (13). H_2O_2 (30% w/v; 15 mL) was added to a solution of **2a** (3.65 g, 16 mmol) in MeOH (100 mL) containing aqueous NaOH (20%; 15 mL); the mixture was stirred for 8 h and diluted with H_2O (100 mL). The precipitate gave **13**, yellow crystals (2.74 g, 70%), mp 153–5 °C, on crystallization from EtOH: ^1H NMR δ 4.10 (d, β-H, J = 1.5 Hz), 4.32 (d, α-H, J = 1.5 Hz), 6.43 (brs, NH_2), 6.63–7.95 (m, 9 H).

2′-Acetamidochalcone (16a). A solution of **13** (0.70 g, 3 mmol) in Ac_2O (4 mL) and pyridine (0.5 mL) was stirred for 8 h and diluted with iced water (50 mL). The precipitate gave **16a**, colorless crystals (0.49 g, 60%), mp 140–1 °C, on crystallization from EtOH: ^1H NMR δ 2.24 (s, Ac), 4.12 (d, β-H, J = 1.5 Hz), 4.37 (d, α-H, J = 1.5 Hz), 7.00–8.10 (m, 8 H), 8.83 (q, 3′-H, J = 8.0 and 1.0 Hz), 11.35 (brs, NH).

2′-(Benzenesulfonamido)chalcone Epoxide (16b). Benzenesulfonyl chloride (1.00 g, 5.7 mmol) was added to a solution of **13** (1.25 g, 5 mmol) in dry pyridine (5 mL); the mixture was stirred for 15 h and poured into iced water (50 mL). The precipitate gave **16b**, yellow crystals (0.65 g, 33%), mp 151–5 °C, on crystallization from EtOH: ^1H NMR ($CDCl_3$/CD_3OD) δ 4.01 (d, β-H, J = 1.5 Hz), 4.28 (d, α-H, J = 1.5 Hz), 6.99–8.05 (m, 14 H), 11.00 (brs, NH).

1,2,3,4-Tetrahydro-2-phenyl-4-quinolone (1a). 2′-Aminochalcone **2a** (6.00 g, 27 mmol) in AcOH (30 mL) and orthophosphoric acid (90%; 30 mL) was refluxed for 2 h, cooled, and poured into iced water (50 mL). The precipitate gave **1a**,[2] pale orange crystals (3.35 g, 56%), mp 149–50 °C, on crystallization from EtOH: ^1H NMR δ 2.72 (q, 3-H, J = −16.4 and 7.4 Hz), 2.90 (q, 3-H, J = −16.4 and 10.6 Hz), 4.75 (q, 2-H, J = 10.6 and 7.4 Hz), 4.75 (brs, NH), 6.70–7.07 (m, 6-H and 8-H), 7.19-7.40 (m, 7-H), 7.45 (s, C_6H_5), 7.93 (q, 5-H, J = 9.0 and 1.5 Hz). **1a** (136 mg, 65%) was also obtained by refluxing **2b** (250 mg, 0.9 mmol) in AcOH (8 mL) and orthophosphoric acid (90%; 8 mL) for 15 min and working up as above.

1-Acetyl-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (1b) and 4-Acetoxy-1-acetyl-1,2-dihydro-2-phenylquinoline (5). **1a** (200 mg, 0.9 mmol) was refluxed in Ac_2O (2 mL) for 2 h, cooled, and poured into iced water (60 mL). The precipitate was fractionated by PLC. Two components were isolated. The one with the smaller R_f value gave **1b**,[3] colorless flakes (114 mg, 48%), mp 166–7 °C, on crystallization from EtOH. The other gave **5**,[2] colorless needles (16 mg, 6%), mp 120–1 °C, on crystallization from EtOH: ^1H NMR (**1b**) δ 2.47 (s, Ac), 3.38 (m, 3-H, 3-H), 6.58 (m, 2-H), 7.20–7.87 (m, 8 H), 8.04 (q, 5-H, J = 7.0 and 1.0 Hz); ^1H NMR (**5**) δ 2.31 (s, Ac), 2.40 (s, Ac), 6.19 (d, 3-H, J = 6.7 Hz), 6.83 (d, 2-H, J = 6.7 Hz), 7.10–7.70 (m, 9 H). The inclusion of anhydrous sodium acetate (200 mg) in the above reaction mixture gave **1b** (31 mg, 13%) and **5** (141 mg, 51%).

1-(Phenylsulfonyl)-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (1c). A mixture of warm (60 °C) aqueous NaOH (1%; 100 mL) and a warm (60 °C) solution of 2′-(benzenesulfonamido)chalcone (**2c**) (3.00 g, 8 mmol) in EtOH (100 mL) was allowed to cool and was stirred for 24 h. Water (30 mL) was added, and the precipitate gave **1c**, orange crystals (1.73 g, 58%), mp 129–30 °C on crystallization from EtOH: ^1H NMR δ 2.63 (q, 3-H, J = −18.0 and 6.3 Hz), 3.12 (q, 3-H, J = −18.0 and 2.0 Hz), 6.06 (q, 2-H, J = 6.3 and 2.0 Hz), 7.09–8.16 (m, 14 H).

(*Z*)-α-Bromo-2′-(benzenesulfonamido)chalcone (7a). Anhydrous KOAc (0.14 g, 1.4 mmol) in a solution of the dibromide **4a** (0.75 g, 1.4 mmol) in acetone (20 mL) was stirred for 2 h and diluted with H_2O (60 mL). The precipitate (0.59 g) gave **7a**, colorless crystals (0.39 g, 62%), mp 122–3 °C, on crystallization from EtOH: ^1H NMR δ 6.95–8.19 (m, 15 H), 11.17 (brs, NH); the initial precipitate had an additional signal at δ 9.40 (brs, NH), assigned to **8a**, one-ninth as intense as that at δ 11.17.

***cis*-1-(Phenylsulfonyl)-3-bromo-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (6a).** Aqueous KOH (4.0 M; 3 mL) was added to a solution of **7a** (250 mg, 0.6 mmol) in EtOH (15 mL); the mixture was stirred for 1 h, diluted with H_2O (20 mL), and extracted with $CHCl_3$ (3 × 50 mL). The extracts gave **6a**, colorless crystals (80 mg, 32%), mp 148–9 °C, on crystallization from EtOH: ^1H NMR δ 5.02 (d, 3-H, J = 3.0 Hz), 6.55 (d, 2-H, J = 3.0 Hz), 7.10–8.34 (m, 14 H).

(*E*)- and (*Z*)-2′-Acetamido-α-bromochalcones (8b and 7b, Respectively). **4b** (200 mg, 0.5 mmol), in acetone (10 mL), on reacting similarly with anhydrous KOAc (47 mg, 0.5 mmol), gave a product which was fractionated by PLC into two components. The one with the larger R_f value gave **8b**, yellow needles (37 mg, 23%), mp 88–9 °C, on crystallization from EtOH. The other gave **7b**, colorless needles (58 mg, 36%), mp 139–40 °C, on crystallization from EtOH: ^1H NMR (**8b**) δ 2.31 (s, Ac), 6.96–8.17 (m, 9 H), 8.93 (q, 3′-H, J = 8.0 and 1.3 Hz), 11.32 (brs, NH); ^1H NMR (**7b**) δ 2.21 (s, Ac), 7.05–8.07 (m, 9 H), 8.67 (q, 3′-H, J = 8.0 and 1.3 Hz), 10.24 (brs, NH).

1,4-Dihydro-2-phenyl-4-quinolone (10). A mixture (1.03 g, 3 mmol) of **7b** and **8b**, obtained from **4b** as above, was dissolved in AcOH (20 mL) and orthophosphoric acid (90%; 20 mL), re-

fluxed for 1 h, cooled, and poured into water (100 mL). The precipitate was collected, washed with water, and dried. Its suspension in warm (70 °C) MeOH was made alkaline (pH 9) with aqueous NaOH (10%) and filtered hot. The filtrate was concentrated and gave **10**[18] (0.51 g, 77%), mp 251–2 °C, on crystallization from MeOH: ^{1}H NMR δ 4.57 (brs, NH), 6.63 (s, 3-H), 7.39–8.03 (m, 8 H), 8.40 (q, 5-H, J = 8.0 and 1.0 Hz).

***cis*-1-Acetyl-3-bromo-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (6b).** Aqueous KOH (4.0 M; 3 mL) was added to a solution in THF (15 mL) of a mixture (207 mg, 0.6 mmol) of **7b** and **8b**, obtained from **4b** as above; the mixture was stirred for 1 h, diluted with H_2O (20 mL), and extracted with $CHCl_3$. The extract was washed, dried, evaporated to dryness, and fractionated by PLC into two components. The one with the larger R_f value gave **8b** (31 mg, 15%). The other gave **6b**, colorless plates (15 mg, 7%), mp 159–60 °C, on crystallization from EtOH: ^{1}H NMR δ 2.55 (s, Ac), 5.13 (d, 3-H, J = 2.7 Hz), 6.47 (d, 2-H, J = 2.7 Hz), 7.12–8.24 (m, 9 H).

***cis*-1-(Phenylsulfonyl)-3-bromo-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (6a).** Aqueous KOH (4.0 M; 3 mL) was added to a solution of **4a** (300 mg, 0.6 mmol) in EtOH (15 mL); the mixture was stirred for 1 h, diluted with H_2O (20 mL), and extracted with $CHCl_3$. The extract was washed, dried, and evaporated to dryness. The residual oil was purified by PLC and gave **6a**, colorless crystals (51 mg, 20%), mp 146–7 °C, on crystallization from EtOH.

Dehydrobromination of 4b. Similarly, the reaction of aqueous KOH (4.0 M; 3 mL) with **4b** (255 mg, 0.6 mmol) in THF solution (15 mL) gave **8b**, yellow needles (26 mg, 13%), mp 88–9 °C, on crystallization from EtOH, the component with the larger R_f value, and **6b**, colorless plates (18 mg, 9%), mp 159–60 °C, on crystallization from EtOH.

1-(2-Aminophenyl)-2-bromo-3-ethoxy-3-phenyl-1-propanone (4d) and 1-(2-Acetamidophenyl)-3-phenyl-1-propynone (11b). Similarly, the reaction of aqueous KOH (4.0 M; 4.5 mL) with **4c** (300 mg, 0.8 mmol) in EtOH solution (20 mL) gave an orange oil (194 mg), which was fractionated by PLC into three components. That with the largest R_f value gave a diastereomer of **4d**, an orange oil (44 mg, 16%): ^{1}H NMR δ 1.04 (t, Me, J = 7.0 Hz), 3.49 (q, CH_2, J = 7.0 Hz), 5.00 (d, β-H, J = 10.0 Hz), 5.30 (d, α-H, J = 10.0 Hz), 6.30 (brs, NH_2), 6.75–6.98 (m, 3′-H, 5′-H), 7.05–8.16 (m, 7 H). The component with the intermediate R_f value gave the other diasteromer of **4d**, an orange oil (39 mg, 14%); ^{1}H NMR δ 1.26 (t, Me, J = 7.0 Hz), 3.48 (q, CH_2, J = 7.0 Hz), 4.92 (d, β-H, J = 10.0 Hz), 5.52 (d, α-H, J = 10.0 Hz), 6.18 (brs, NH_2), 6.43–6.86 (m, 3′-H, 5′-H), 6.93–7.93 (m, 7 H). The component with the smallest R_f value, a yellow oil (97 mg), could not be fractionated; it was dissolved in Ac_2O (1.5 mL) and pyridine (0.2 mL), stirred for 6 h, and diluted with H_2O (30 mL). The yellow precipitate was fractionated by PLC into three components. In order of decreasing R_f values, they were as follows: **8b**, yellow needles (34 mg, 13%), mp 88–9 °C, on crystallization from EtOH; **11b**, yellow needles (10 mg, 21%), mp 77–9 °C, on crystallization from EtOH [^{1}H NMR δ 2.30 (s, Ac), 7.09–8.01 (m, 7 H), 8.54 (q, 6′-H, J = 7.5 and 1.7 Hz), 8.90 (q, 3′-H, J = 7.0 and 1.0 Hz), 11.56 (brs, NH); MS m/z 263]; **7b**, colorless needles (15 mg, 6%), mp 139–40 °C, on crystallization from EtOH.

Base-Initiated Reactions of 4f, 4e, and 4g. Aqueous KOH (4.0 M; 3 mL) was added to a solution of **4f** (200 mg, 0.5 mmol) in THF (15 mL); the mixture was stirred for 1 h, diluted with H_2O (20 mL), and extracted with $CHCl_3$. The extract was washed, dried, and evaporated to dryness. Purification of the residual oil by PLC gave **7b**, colorless needles (27 mg, 15%), mp 139–40 °C, on crystallization from EtOH. A solution of **4f** (200 mg, 0.5 mmol) in dioxan (10 mL) was refluxed for 8 h, diluted with H_2O (25 mL), and extracted with $CHCl_3$. The extract was washed, dried, and evaporated to dryness. The residual oil was fractionated by PLC into two components. The one with the larger R_f value gave **4f** (44 mg, 22%). The other gave **2b**, yellow plates (49 mg, 34%), mp 92–3 °C, on crystallization from MeOH/H_2O.

Aqueous KOH (4.0 M; 3 mL) was added to a solution of **4e** (290 mg, 0.6 mmol) in EtOH (15 mL), stirred for 1 h, diluted with H_2O (20 mL), and extracted with $CHCl_3$. The extract was washed, dried, and evaporated to dryness. The residual oil was purified by PLC and gave **6a**, colorless crystals (47 mg, 17%), mp 148–9 °C, on crystallization from EtOH.

Aqueous KOH (4.0 M; 2 mL) was added to a solution of **4g** (200 mg, 0.6 mmol) in EtOH (15 mL), and the reaction was carried out as above. The resulting oil was fractionated by PLC into three components. In order of decreasing R_f value, they were as follows: The two diastereomers of **4d**, both orange oils (47 mg, 23%, and 37 mg, 18%). The third component, a yellow oil (48 mg), was identical with the yellow oil obtained above from the reaction of **4c** with aqueous ethanolic KOH and shown to be a mixture of (*E*)-**8c** and (*Z*)-**7c** 2′-amino-α-bromochalcone and 1-(2-aminophenyl)-3-phenyl-2-propyn-1-one (**11a**).

***cis*-1,2,3,4-Tetrahydro-3-hydroxy-2-phenyl-4-quinolone (14).** The epoxide **13** (0.75 g, 3 mmol) in AcOH (15 mL) was refluxed for 10 min, diluted with H_2O (20 mL), and extracted with $CHCl_3$. The extract was washed, dried, and evaporated to dryness. The residual orange oil (0.75 g) gave **14**, orange crystals (0.32 g, 43%), mp 188–91 °C, on crystallization from EtOH: ^{1}H NMR δ 4.57 (s, 2-H, 3-H), 6.36 (brs, NH), 6.62–7.07 (m, 6-H, 8-H), 6.88 (brs, OH), 7.20–8.00 (m, 7 H); MS m/z 239.

***cis*-3-Acetoxy-1-acetyl-1,2,3,4-tetrahydro-2-phenyl-4-quinolone (15).** A solution of **14** (0.93 g, 4 mmol) in Ac_2O (10 mL) and H_2SO_4 (1 mL) was diluted with iced H_2O (100 mL) after 30 min. The precipitate gave **15**, colorless crystals (0.57 g, 45%), mp 140–1 °C, on crystallization from EtOH: ^{1}H NMR δ 2.17 (s, OAc), 2.46 (s, NAc), 5.87 (d, 3-H, J = 2.7 Hz), 6.55 (d, 2-H, J = 2.7 Hz), 7.18–7.92 (m, 3 H), 7.26 (s, Ph), 8.13 (q, 5-H, J = 8.0 and 1.5 Hz).

2′-Amino-α-hydroxy-β-ethoxydihydrochalcone (4h). A solution of the epoxide **13** (0.75 g, 3 mmol) in EtOH (15 mL) and H_2SO_4 (1 mL) was diluted with H_2O (30 mL) after 1 h and extracted with $CHCl_3$. The extract was washed, dried, and evaporated to dryness. A sample (180 mg) of the residual orange oil (0.63 g) was purified by PLC and gave the inseparable diastereomers of **4h**, an orange oil (110 mg, 43%): ^{1}H NMR δ 0.83–1.42 (m, Me), 3.18–3.80 (m, CH_2), 4.65 (d, β-H, J = 4.0 Hz), 4.72 (d, β-H, J = 4.0 Hz), 5.25 (d, α-H, J = 3.5 Hz), 5.45 (d, α-H, J = 3.5 Hz), 5.40 (brs, OH), 6.22 (brs, NH_2), 6.50–6.92 (m, 3′-H and 5′-H), 7.00–7.60 (m, 6 H), 7.81 (q, 6′-H, J = 8.0 and 1.5 Hz); MS m/z 285.

Registry No. **1a**, 16619-14-0; **1b**, 60355-81-9; **1c**, 124857-02-9; **2a**, 78396-00-6; **2b**, 16619-52-6; **2c**, 124856-90-2; **2d**, 124856-91-3; **4a**, 124856-92-4; **4b**, 124856-93-5; **4c**, 124856-94-6; (*R**,*S**)-**4d**, 124857-08-5; (*R**,*R**)-**4d**, 124890-66-0; **4e**, 124856-98-0; **4f**, 124856-96-8; **4g**, 124856-97-9; (*R**,*S**)-**4h**, 124857-16-5; (*R**,*R**)-**4h**, 124857-17-6; **5**, 60355-89-7; **6a**, 124857-04-1; **6b**, 124857-07-4.

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