with stirring. After 5 min, C_6H_6 was added to the flask and the solution was heated to reflux. When water that formed during the reaction ceased to collect in the Dean–Stark trap, the solution was allowed to cool and was washed successively with 1 N HCl, 5% $NaHCO_3$, and saturated NaCl. The volatiles were evaporated, and the oil that remained was combined with the crude oil from a previous reaction. The crude product was distilled to yield 1.7 g (89%) of 17 as a clear liquid: bp 150–155 °C (0.3 mm); ^1H NMR ($CDCl_3$) δ 0.8–1.2 (m, 3 H), 1.6–2.0 (m, 4 H), 2.8–3.1 (m, 3 H), 3.6–4.6 (m, 8 H), and 7.2 (s, 5 H); IR (film) 2960, 2900, 1700 cm^{-1}. Anal. ($C_{17}H_{23}NO_4$) C, H, N.

6-Benzyl-7-methyl-1,4-dioxa-7-azaspiro[4.5]decane (18). A solution of 17 (1.7 g, 5.6 mmol) in THF (10 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (0.5 g, 13 mmol) in THF (5 mL). After addition was complete, the mixture was heated at reflux for 12 h; then H_2O (0.5 mL), 15% NaOH (0.5 mL), and H_2O (1.5 mL) were added successively to the cooled flask. The solution was filtered, and the volatiles were evaporated to give an oil, which was distilled to yield 1 g (72%) of 18 as a yellow liquid: bp 120–125 °C (0.3 mm); ^1H NMR ($CDCl_3$) δ 1.5.1.9 (m, 4 H), 2.2–2.4 (m and s, 4 H), 2.6–2.9 (m, 4 H), 3.9 (s, 4 H), and 7.2 (s, 5 H). Anal. ($C_{15}H_{21}NO_2$) C, H, N.

Pharmacology. Methods. Cat Cardioaccelerator Nerve Assay. Cats were anesthetized by injection of pentobarbital sodium (30 mg/kg) into the thoracic cavity, and the surgical and experimental procedure was the same as has been published.[12] Experimental compounds were administered intravenously in doses of 0.33 log intervals.

Rotation Assay. Male Sprague–Dawley rats with 6-hydroxydopamine unilateral denervation of the nigrostriatal projection were used to test compounds for circling behavior.[12] Compounds were administered at a dose of 4.0 mg/kg and were also evaluated for their ability to antagonize apomorphine (0.25 mg/kg) induced rotations.

Dopamine Receptor Binding Studies. A method of Seeman et al.[13] was employed using [^3H] spiroperidol (2 nM) and rat striatal tissue.

Acknowledgment. The financial support of an Auburn University Grant-in-Aid is gratefully acknowledged. The author gratefully acknowledges the contribution by Dr. John P. Long, Department of Pharmacology, College of Medicine, The University of Iowa, Iowa City, Iowa, who performed the biological assays for this project.

Registry No. 5, 50606-58-1; 6, 61995-19-5; 8, 78118-62-4; 9, 102520-44-5; 10, 102520-45-6; 11, 102535-14-8; 12, 5379-94-2; 13, 102520-51-4; 14, 102520-46-7; 15, 102520-47-8; 16, 102520-48-9; 17, 102520-49-0; 18, 102520-50-3; $ClCO_2C_2H_5$, 541-41-3; $C_6H_5CH_2Cl$, 100-44-7; pyrrolidine, 123-75-1.

Synthesis and Biological Activity of Benzothiazolo[3,2-*a*]quinolone Antibacterial Agents

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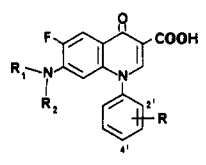
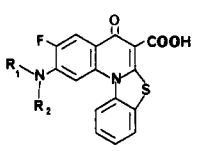
A new class of heterocyclic compounds with potent antibacterial activity, namely, 2-substituted amino-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acids, is described. The compounds are conformationally restricted analogues of 7-substituted amino-6-fluoro-1-aryl-1,4-dihydro-4-oxoquinoline-3-carboxylic acids. Compounds 7 and 10, having a 4-methylpiperazinyl and a piperazinyl substitution at the 2-position, respectively, possess in vitro antibacterial activities comparable to norfloxacin (15). Compound 8, which has a 4-acetylpiperazinyl substitution at the 2-position, is active against Gram-positive organisms and nearly inactive against Gram-negative organisms. An efficient and short synthesis of this novel heterocyclic system via an intramolecular nucleophilic displacement cyclization reaction is reported.

In an earlier paper,[1] we reported the synthesis and antibacterial activity of 7-substituted amino-6-fluoro-1-aryl-1,4-dihydro-4-oxoquinoline-3-carboxylic acids (1), which possess a 1-(substituted phenyl)-1,4-dihydro-4-oxopyridine-3-carboxylic acid moiety. These potent antibacterial agents belong to 4-quinolones, a class of compounds that has attracted increasing attention as a source of new antibacterial agents.[2,3] The mode of action of this class of compounds is the inhibition of bacterial DNA gyrase.[4]



1



2

The optimization of substituents in the field of quinolone antibacterials has recently been reported. Quantitative structure–activity relationship (QSAR) analysis of a set of N-1 allyl and alkyl derivatives suggested an optimum STERIMOL length of 4.2 Å, corresponding approximately to an ethyl group.[5] This generalization obviously does not include aryl substituents, as shown by the high activity reported for N-1 phenyl analogues.[1] The purpose of this work was to determine the effect on antibacterial activity of forcing the N-1 phenyl substituent into rigid planar conformation. This may provide further insight into the importance of the spatial characteristics of 1-phenyl substitution. 5-Oxo-1,2-dihydro-5*H*-thiazolo[3,2-*a*]quinoline-4-carboxylic acid derivatives have recently been reported to be good antibacterial agents.[6] This indicates that substitution of a sulfur atom at the 2-position of 1,4-dihydro-4-oxoquinoline-3-carboxylic acid derivatives can lead to active compounds. Hence, a conformationally restricted rigid analogue formed by bridging the phenyl and quinolone rings by a sulfur atom would

(1) Chu, D. T. W.; Fernandes, P. B.; Claiborne, A. K.; Pihuleac, E.; Nordeen, C. W.; Maleczka, R. E.; Pernet, A. G. *J. Med. Chem.* **1985**, *28*, 1558.
(2) For a review, see Albrecht, R. *Prog. Drug Res.* **1977**, *21*, 9.
(3) Smith, J. T. *Pharm. J.* **1984**, 299.
(4) Cozzarelli, N. R. *Science (Washington, DC)* **1980**, *207*, 953.
(5) Fujita, T. In *Drug Design: Fact or Fantasy*; Jolles, G., Woolridge, K. R. H., Eds.; Academic: New York, 1984; p 19.
(6) Matsumura, S.; Kise, M.; Ozaki, M.; Tada, S.; Kazuno, K.; Watanabe, H.; Kunimoto, K.; Tsuda, M. U.S. Patent 4 426 381, **1984**.

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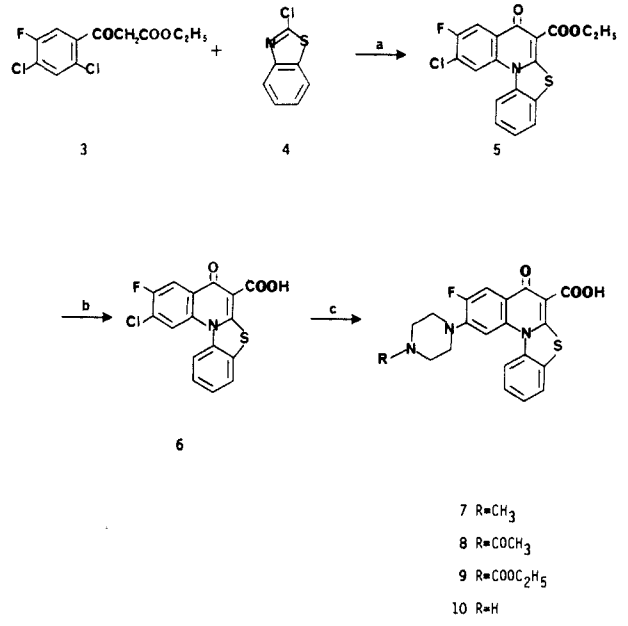
Scheme I



[a] NaH/diglyme. [b] (1) NaOH, (2) CF_3COOH. [c] $HNCH_2CH_2N(R)CH_2CCH_2$/*N*-methyl-2-pyrrolidinone.

provide a useful indication of the relevance of the planarity of the ring system to antibacterial activity. In this paper, we report the synthesis and antibacterial activity of 2-substituted amino-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid derivatives (**2**). These new heterocyclic compounds were found to be very potent broad-spectrum antibacterial agents.

Chemistry

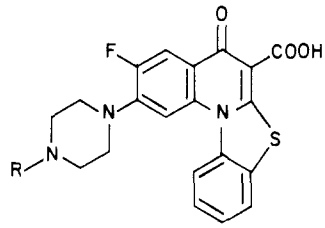
Although the synthesis of benzothiazolo[3,2-*a*]quinolinium salts has been described,[7] the 5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid constitutes a new type of heterocyclic system. We have developed an efficient short synthesis of 2-(substituted amino)-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid derivatives via an intramolecular nucleophilic displacement cyclization reaction as illustrated in Scheme I. In this route, the heterocycle skeleton was synthesized in one synthetic step.

Condensation of ethyl 2,4-dichloro-5-fluorobenzoylacetate (**3**)[8] with 2-chlorobenzothiazole (**4**) in diglyme in the presence of 2 molar equiv of sodium hydride yielded the novel heterocyclic compound ethyl 2-chloro-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylate (**5**) in one step. Hydrolysis of the ester **5** with sodium hydroxide followed by trifluoroacetic acid treatment gave the 2-chloro-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid (**6**). Displacement of the 2-chloro group of **6** with an appropriate amine gave the desired 2-amino derivatives **7–9** (Table I). The 2-piperazin-1-yl-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid (**10**) was prepared by sodium hydroxide hydrolysis of the *N*-carbethoxy derivative **9**.

Results and Discussion

Table III summarizes the in vitro antibacterial activity of the 2-piperazin-1-yl-3-fluorobenzothiazolo[3,2-*a*]-

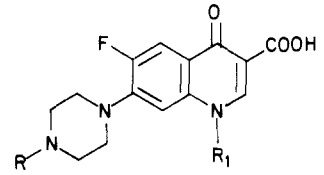
Table I. 2-Piperazin-1-yl-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic Acids



compd	R	yield,[a] %	formula[b,c]
7	CH_3	52	$C_{21}H_{18}FN_3O_3S$·HCl
8	$COCH_3$	56	$C_{22}H_{18}FN_3O_4S$
9	COC_2H_5	67	$C_{23}H_{20}FN_3O_5S$
10	H	36	$C_{20}H_{16}FN_3O_3S$·HCl·$^1/_2H_2O$

[a] Yields are not optimized. [b] C, H, N analyses were within ±0.4% of the theoretical values, except otherwise noted. [c] Melting points of all the compounds listed are >275 °C.

Table II. Structures for Comparative Quinolones



compd	R	R_1
11	H	phenyl
12	CH_3	phenyl
13	CH_3	2-methylphenyl
14	CH_3	2,6-dimethylphenyl
15	H	C_2H_5

quinolones against five Gram-positive bacteria (*Staphylococcus aureus* ATCC 6538P, *Staphylococcus aureus* CMX 686B, *Staphylococcus epidermidis* 3519, *Streptococcus faecium* ATCC 8043, and *Streptococcus pyogenes* 930) and six Gram-negative organisms (*Escherichia coli*, Juhl, *Enterobacter aerogenes* ATCC 13048, *Klebsiella pneumoniae* 8045, *Pseudomonas aeruginosa* 5007, *Pseudomonas aeruginosa* K799/WT, and *Acinetobacter* CMX 669). The data for compounds **11–14**, the nonrigid analogues, and norfloxacin (**15**) are included for comparison. The structures for these compounds are shown in Table II.

The effect of having a conformationally restricted phenyl ring attached to the 6-fluoro-7-piperazinyl-1,4-dihydro-4-oxoquinoline-3-carboxylic acid is shown by the data for compounds **7–10** presented in Table III. The 2-(substituted amino)-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid derivatives are potent antibacterials having activity comparable to norfloxacin, a clinically useful antibacterial agent. Both compounds **7** and **10** possess high inhibitory activity against DNA gyrase.[9] Compounds **11** and **12** are arylquinolones having a conformationally unrestricted N-1 phenyl substituent, and compounds **13** and **14** are arylquinolones having a conformationally partially restricted phenyl substituent. Compound **10** is more potent than compound **11** when tested against *Streptococcus*, but they are equipotent against other organisms. Compounds **7** and **12** (both having a 4-methylpiperazine substituent) are equally potent against both Gram-positive and Gram-negative bacteria, with the exception of *Streptococcus*, against which

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(8) Chu, D. T. W. *J. Heterocycl. Chem.* **1985**, *22*, 1033.
(9) Private communication from Dr. Linus Shen of Abbott Laboratories.

Table III. In Vitro Antibiotic Activity of 2-Piperazin-1-ylbenzothiazolo[3,2-*a*]quinolones and Selected Known Quinolones

	minimal inhibitory concentration (MIC),[b] μg/mL										
compd[a]	Sa(A)	Sa	Se	Sf	Sp	Ec	Ea	Kp	Pa(5)	Pa(k)	A
7	0.39	0.39	0.78	1.56	1.56	0.78	1.56	0.39	6.2	6.2	0.39
8	0.2	0.2	0.39	6.2	3.1	6.2	>100	1.56	>100	>100	6.2
9	0.39	0.39	0.39	6.2	3.1	6.2	12.5	1.56	>100	>100	0.1
10	0.39	0.39	0.39	0.78	0.78	0.2	0.78	0.2	1.56	1.56	0.39
11	0.39	0.39	0.78	12.5	1.56	0.2	0.39	0.1	0.78	1.56	0.78
12	0.78	0.78	0.78	12.5	3.1	0.78	1.56	0.2	6.2	3.1	1.56
13	3.1	3.1	3.1	50	50	1.56	3.1	1.56	25	12.5	1.56
14	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100
15[c]	0.78	0.78	1.56	0.78	3.1	0.1	0.2	0.1	0.39	0.39	6.2

[a] Structures are shown in Tables I and II. [b] The MIC were determined by the twofold agar dilution on brain–heart infusion agar. Organisms selected for inclusion in the table are Sa(A), *Staphylococcus aureus* ATCC 6538P; Sa, *Staphylococcus aureus* 686B; Se, *Staphylococcus epidermidis* 3519; Sf, *Streptococcus faecium* ATCC 8043; Sp, *Streptococcus pyrogenes* 930; Ec, *Escherichia coli* Juhl; Ea, *Enterobacter aerogenes* ATCC 13048; Kp, *Klebsiella pneumoniae* 8045; Pa(5), *Pseudomonas aeruginosa* 5007; Pa(K) *Pseudomonas aeruginosa* K799/WT; A, *Acinetobacter* sp. CMX669. [c] Norfloxacin.

compound **7** is more potent. Compounds **7** and **10** are much more potent than compounds **13** and **14**. Compound **14**, which possesses a phenyl ring perpendicular to the quinolone rings due to the steric interaction of the dimethyl and quinolone ring,[10] is essentially inactive. Since the 5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid system has the phenyl ring nearly coplanar with the quinolone ring, these data indicte that the favorable conformation for the inhibitor during its inhibition of DNA gyrase may be that with the phenyl and quinolone rings close to coplanar and not perpendicular to each other.

It is interesting to note that compound **8**, which has a 4-acetylpiperazine substituent, is almost inactive against Gram-negative bacteria while retaining antibacterial activity against Gram-positive organisms. This is not characteristic of the older antibacterial agents of this class (such as nalidixic acid), which are much more active against Gram-negative bacteria than Gram-positive organisms. The fact that the conformationally restricted benzothiazolo[3,2-*a*]quinolones possess high antibacterial potency is of considerable interest since 2-alkyl-substituted 4-quinolone antibacterial agents are generally inactive.[2]

In this study, a new class of heterocyclic compounds with potent antibacterial activity, namely, 2-(substituted amino)-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]-quinoline-6-carboxylic acids, was synthesized by an efficient and short synthetic route via an intramolecular necleophilic displacement cyclization reaction.

Experimental Section

Melting points were taken in a Thomas-Hoover capillary apparatus and are uncorrected. Elemental analyses were obtained for all new compounds reported. Carbon, hydrogen, and nitrogen analyses (unless otherwise specified) were within ±0.4% of the theoretical values. Microanalyses were performed by the Abbott analytical department. The NMR spectra were obtained on Varian T-60 and HA-100 spectrometers using tetramethylsilane as an internal standard. Mass spectra were recorded on a Kratos MS-50 mass spectrometer. The IR spectra were recorded on a Perkin-Elmer Model 710 A infrared spectrometer. The IR, NMR, and MS data of all compounds were consistent with the assigned structures.

Ethyl 2-Chloro-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylate (5). A 60% sodium hydride-in-oil suspension (5.91 g, 148 mmol) was slowly added at room temperature to a solution of ethyl 2,4-dichloro-5-fluorobenzoylacetate (**3**)[8] (20.1 g, 72 mmol) and 2-chlorobenzothiazole (14.6 g, 86.4 mmol) in dry diglyme (200 mL). The mixture was heated at 160 °C for 3 days under nitrogen atmosphere and was cooled. Ice-cold water (1.5 L) was added, and the precipitate was filtered, washed with water, and dried. The solid was purified on a silica gel column with 7% ethyl acetate in methylene chloride as eluent, yielding 13.1 g (48.5%) of **5**, mp 219 °C. Anal. ($C_{18}H_{11}ClFNO_3S$) C, H, N.

2-Chloro-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic Acid (6). A solution of sodium hydroxide (1 g, 25 mmol) in water (15 mL) was added to a hot solution of **5** (3.47 g, 9.24 mmol) in tetrahydrofuran (150 mL). The mixture was heated at 85 °C for 6 h and was cooled. The precipitate was filtered and washed with ether followed by washing with a small amount of cold water. The solid was dissolved in trifluoroacetic acid (15 mL). Water (500 mL) was added and the precipitate was filtered. It was further washed with water and dried, yielding 3.1 g (97%) of **6**, mp >275 °C. Anal. ($C_{16}H_7ClFNO_3S \cdot {}^1/_4H_2O$) C, H, N.

2-(4-Methylpiperazin-1-yl)-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic Acid Hydrochloride (7). *N*-Methylpiperazine (2.9 mL, 26 mmol) was added to a solution of **6** (2 g, 5.76 mmol) in *N*-methyl-2-pyrrolidinone (30 mL) at 115 °C. After being heated at 115 °C under nitrogen atmosphere for 48 h, the reaction mixture was cooled and filtered. The solid obtained was washed with a small amount of cold ethanol and water. The residue was suspended in water (40 mL), and 1 N hydrochloric acid (10 mL) was added and the mixture was heated until all dissolved. After the mixture was allowed to stand and cool for 1 h, precipitate appeared and was filtered, yielding 1.33 g (52%) of **7**, mp >275 °C. Anal. ($C_{21}H_{18}FN_3O_3S \cdot HCl$) C, H, N.

2-(4-Acetylpiperazin-1-yl)-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic Acid (8). *N*-Acetylpiperazine (2.1 g, 16.4 mmol) was added to a solution of **6** (1.85 g, 5.32 mmol) in *N*-methyl-2-pyrrolidinone (26 mL) at 110 °C. After being heated at 110 °C under nitrogen atmosphere for 48 h, the reaction mixture was cooled. Water (250 mL) was added and the precipitate was filtered. The residue was boiled with acetonitrile (30 mL). The mixture was cooled and filtered, yielding 1.6 g (56%) of **8**, mp >275 °C. Anal. ($C_{22}H_{18}FN_3O_4S$) C, H, N.

By use of this procedure, reacting compound **6** with *N*-carbethoxypiperazine, compound **9** was prepared.

2-Piperazin-1-yl-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic Acid Hydrochloride (10). A solution of sodium hydroxide (2 g, 50 mmol) in water (20 mL) was added to a solution of 2-(4-carbethoxypiperazin-1-yl)-3-fluoro-5,12-dihydro-5-oxobenzothiazolo[3,2-*a*]quinoline-6-carboxylic acid (**9**) (0.9 g, 2 mmol) in dioxane (200 mL) at 100 °C. After being heated at 100 °C under nitrogen atmosphere for 2 days, the mixture was cooled and filtered. The solid was dissolved in trifluoroacetic acid (10 mL). Insoluble material was removed by filtration. Water (150 mL) was added to the trifluoroacetic acid solution, and the precipitate was filtered. The solid was suspended in 1 N hydrochloric acid solution (20 mL), and the mixture was heated to dissolve. The solution was evaporated to dryness to yield 0.3 g (36%) of **10**, mp >275 °C. Anal. ($C_{20}H_{16}FN_3O_3S \cdot HCl \cdot {}^1/_2H_2O$) C, H, N.

In Vitro Antibacterial Activity. The in vitro antibacterial activity of the test compounds was tested in a side-by-side comparison with norfloxacin (**15**) and determined by conventional agar dilution procedures. The organisms were grown overnight

(10) Estimated conformation based on molecular models.

in brain-heart infusion (BHI) broth (Difco 0037-01-6) at 36 °C. Twofold dilutions of the stock solution (2000 μg/mL) of the test compound were made in BHI agar to obtain the test concentration ranging from 200 to 0.005 μg/mL. The plate was inoculated with approximately 10^4 organisms. It was then incubated at 36 °C for 18 h. The minimal inhibitory concentration (MIC) was the lowest concentration of the test compound that yielded no visible growth on the plate.

Acknowledgment. We thank the staff of the microbiological team for biological testings, Akiyo Claiborne for her expert technical assistance, and the staff of the Analytical Department for microanalyses.

Registry No. 3, 86483-51-4; 4, 615-20-3; 5, 102614-42-6; 6, 102614-43-7; 7, 102614-44-8; 7 (free base), 102614-48-2; 8, 102614-45-9; 9, 102614-46-0; 10, 102614-47-1; 10 (free base), 102614-49-3; 11, 98106-13-9; 12, 98106-14-0; 13, 98106-25-3; 14, 98106-26-4; *N*-carbethoxypiperazine, 120-43-4; *N*-methylpiperazine, 109-01-3; *N*-acetylpiperazine, 13889-98-0.

Anticonvulsant Activity of 2- and 3-Aminobenzanilides

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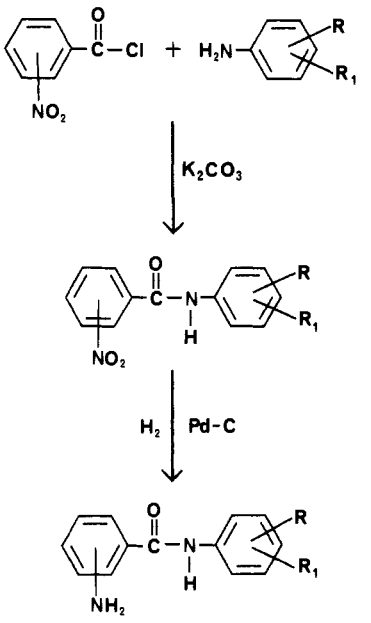
A series of 2- and 3-aminobenzanilides derived from ring-alkylated anilines were prepared and evaluated for anticonvulsant activity. These benzanilides were prepared in the course of studies designed to determine the relationship between the benzamide structure and anticonvulsant effects. The compounds were tested in mice against seizures induced by maximal electroshock (MES) and pentylenetetrazole and in the rotorod assay for neurologic deficit. The 3-aminobenzanilide derived from 2,6-dimethylaniline, **21**, was the most potent anti-MES compound, with an ED50 of 13.48 mg/kg and a protective index of 21.11 (PI = TD50/ED50). The activity profile for **21** compares favorably with that for phenobarbital and phenytoin.

Recent reports[1,2] from this laboratory described the anticonvulsant activity for numerous 4-aminobenzamides of alkyl- and arylamines. Several of these amides show a high level of protection against maximal electroshock (MES) induced convulsions in animal models. These compounds are less effective against subcutaneous pentylenetetrazole (scMet) induced convulsions, and the profile of anticonvulsant activity and toxicity for the more potent analogues resembles that for phenobarbital and phenytoin.

Structurally, some of the simplest compounds possessing anticonvulsant properties are carboxylic acids and their amides.[3] Valproic acid is perhaps the best known example of this class of compounds.[4] Half the dose of valproic acid amide has been shown[5] to be as effective as the dose of valproic acid. Various reports[6,7] have described the anticonvulsant effects of substituted cinnamamides. Cinromide, 3-bromo-*N*-ethylcinnamamide, has been evaluated as a broad-spectrum anticonvulsant and has a reported anti-MES ED50 of 60 mg/kg when administered intraperitoneally (ip) in mice.[7] Several derivatives of 3-phenyl-2-piperidinone have been shown to possess anti-MES and anti-scMet activity in animal models.[8]

The unique behavioral profile produced in animals by substituted benzamide neuroleptics such as metoclopramide has generated considerable interest in recent years.[9]

Scheme I



The benzamide neuroleptics are useful in the treatment of schizophrenia and appear to exert their neuroleptic action selectively at a subpopulation of the D-2 type dopamine receptors.[10] The aminobenzanilides reported in this paper were prepared in an effort to determine the optimal disubstitution pattern in the aminobenzoyl moiety and are a continuation of our studies on the relationship between benzamide structure and anticonvulsant activity.

Results and Discussion

A series of 2- and 3-aminobenzanilides were prepared and evaluated for anticonvulsant activity. The study was conducted in an effort to further elucidate the relationship between benzamide structure and anticonvulsant activity. Previous studies[1,2] demonstrated the potent anticonvulsant properties of several 4-aminobenzamides. The amino-

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