structure that resembled **60** as much as possible: because of the length of the diacetylene group, extra volume in the C_8–C_{10} region of the molecule was unavoidable.

The starting structures for the other compounds were prepared by fusing an MMP2 minimized structure of the C_6–C_{16} region of the molecule with the C_1–C_8 fragment of **16** or **55**. The starting structure of each C_9–C_{16} fragment was built from templates of standard geometry. The starting conformations were chosen as follows: (1) for the dienes **50′–52′**, monoene **51′**, and saturated fragment **9′**, H_{12} was set trans to H_{13}; (2) for **9′** and **50′–54′**, H_{10} was set trans to H_{11}, and for **9′**, **34′**, and **50′–53′**, H_{14} was set trans to H_{15}; and (3) similar rotations about the C_9–C_{10} and C_{15}–C_{16} bonds were selected for all fragments modeled. For certain compounds it was necessary to add parameters: the V_2 torsional parameter for the following bond, C(sp^3)–C(sp^2)–C(sp^2)–C(sp) was set equal to 15.0 kcal/mol while V_1 and V_3 were set at 0.0. For C(sp)–C(sp^3)–O(sp^3)–H and C(sp)–C(sp^3)–O(sp^3)–lone pair all three torsional parameters were set at 0.0. The bending constant for the C(sp^2)–C(sp^2)–C(sp) bond was set at 0.40 kcal/mol with a natural bond angle 120°; the values for C(sp)–C(sp^3)–O(sp^3) were 0.20° and 109.5° and those for C(sp)–C(sp)–C(sp) were 0.40° and 180°. The molecular graphics and manipulation program was written in our laboratory.

Supplementary Material Available: Tables listing Cartesian coordinates for compounds **9**, **12**, **16**, **20**, **34**, **50–56**, and **59–62** (16 pages). Ordering information is given on any current masthead page.

1-[[[5-(Substituted phenyl)-2-oxazolyl]methylene]amino]-2,4-imidazolidinediones, a New Class of Skeletal Muscle Relaxants

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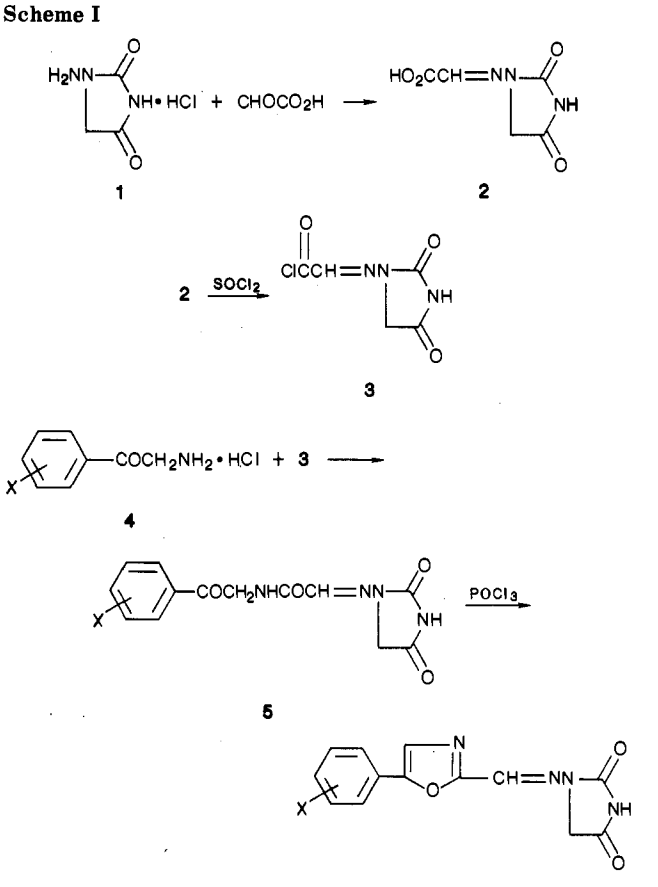
A series of 1-[[[5-(substituted phenyl)-2-oxazolyl]methylene]amino]-2,4-imidazolidinediones (**6a–t**) was synthesized, and the compounds were evaluated for direct skeletal muscle inhibition in the pithed rat gastrocnemius muscle preparation. The correctness of structural assignment of the new series was verified by alternate, unequivocal synthesis of one representative structure (**6f**). The phenyloxazoles **6d**, **6g**, **6j**, **6k**, and **6l** exhibited significant skeletal muscle relaxant activity when administered intravenously and orally. The skeletal muscle relaxant effect of these five compounds is similar to that of other direct-acting skeletal muscle relaxants. The oxazole moiety proved to be an acceptable isosteric replacement for furan, as the biological activity in the oxazole series was retained. The synthesis of this new class of compounds is described, and pharmacologic evaluation data are presented. A discussion of structure–activity relationships is also presented.

In the search for compounds for the treatment of skeletomuscular disorders, a series designed to be direct skeletal muscle relaxants was synthesized and pharmacologically evaluated. Dantrolene sodium[1] and other similar 1-[[[5-(substituted phenyl)-2-furanyl]methylene]amino]-2,4-imidazolidinediones have been found to exhibit direct skeletal muscle relaxant activity.[2,3] It was decided to determine whether structures with an oxazole group would result in compounds that exhibit direct skeletal muscle inhibition. This paper describes the synthesis and pharmacologic evaluation of a series of 1-[[[5-(substituted phenyl)-2-oxazolyl]methylene]amino]-2,4-imidazolidinediones,[4] a new class of skeletal muscle relaxants.

Chemistry

The methodology employed in the past[3] to prepare phenylfuranyliminoimidazolidinediones was not applicable for the proposed corresponding oxazole counterparts. Prior syntheses took advantage of the Meerwein coupling reaction of aryldiazonium salts with 2-furancarboxaldehyde. In this instance, 2-oxazolecarboxaldehyde was not accessible in quantities practical for synthesis, the outcome of a Meerwein reaction was unknown, and 5-phenyl-2-furancarboxaldehydes were nonexistent. Consequently, a new synthetic approach was sought. Two reviews on oxazole chemistry[5,6] yielded useful information on alternative synthetic approaches. The Robinson-Gabriel synthesis[5,6] effects cyclization of α-acylamino carbonyl com-

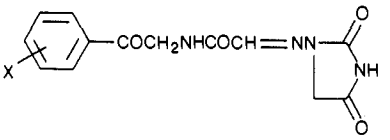
Scheme I



(1) Dantrium, Eaton Laboratories, Inc., a subsidiary of Norwich Eaton Pharmaceuticals, Inc.
(2) Ellis, K. O.; Wessels, F. L. *Arzneim.-Forsch. Drug Res.* **1978**, *28*(11), 7, 1100.
(3) Snyder, H. R., Jr.; Davis, C. S.; Bickerton, R. K.; Halliday, R. P. *J. Med. Chem.* **1967**, *10*, 807.
(4) U.S. Patent 4 049 650, 1977: R. L. White, Jr., Norwich Eaton Pharmaceuticals, Inc.
(5) Lakhan, R.; Ternai, B. *Adv. Heterocycl. Chem.* **1974**, *17*, 99.

0022-2623/87/1830-0263$01.50/0

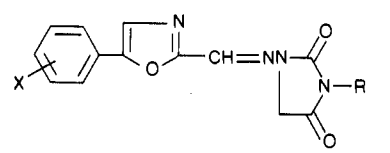
Table I. Synthesis and Analysis of *N*-[2-Oxo-2-(substituted phenyl)ethyl][[(2,4-dioxoimidazolidinyl)imino]methyl]formamides



compd[a]	X	% yield[b]	mp, °C	formula	anal.
5a	H	55	248–253	$C_{13}H_{12}N_4O_4$	C, H, N
5b	4-NO_2	65	279–280	$C_{13}H_{11}N_5O_6$	C, H, N
5c	2-NO_2	50	264–266	$C_{13}H_{11}N_5O_6$	C, H, N
5d	4-Cl	38	267–270	$C_{13}H_{11}ClN_4O_4$	C, H, N
5e	4-Br	45	267–269	$C_{13}H_{11}BrN_4O_4$	C, H, N
5f	4-F	65	281–282	$C_{13}H_{11}FN_4O_4$	C, H, N
5g	4-CH_3O	55	285–287	$C_{14}H_{14}N_4O_5$	C, H, N
5h	4-CH_3	68	269–270	$C_{14}H_{14}N_4O_4$	C, H, N
5i	3-CF_3	79	261–263	$C_{14}H_{11}F_3N_4O_4$	C, H, N
5j	3,4-Cl_2	23	290–293	$C_{13}H_{10}Cl_2N_4O_4$	C, H, N
5k	3-Cl	51	268(dec)	$C_{13}H_{11}ClN_4O_4$	C, H, N

[a] The recrystallization solvent was either *N,N*-dimethylformamide (**5j**, **5b**), acetic acid (**5f**, **5e**, **5g**, **5a**, **5c**), acetonitrile (**5i**, **5h**), or nitromethane (**5d**). [b] Yield was based on conversion of the appropriate amino ketone hydrochloride (**4**) to the corresponding formamide (**5**).

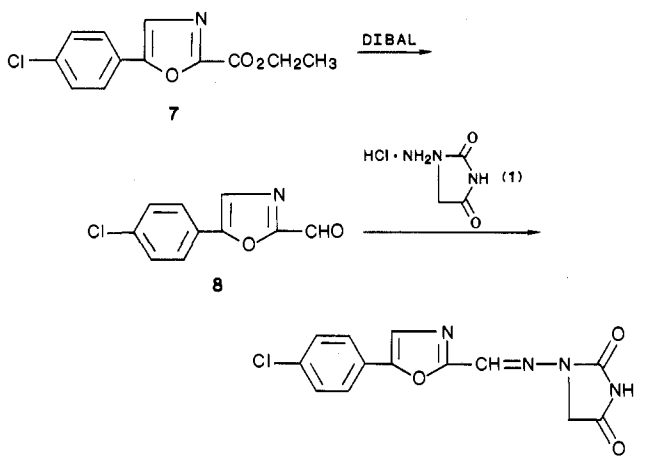
Table II. Synthesis and Analysis of 1-[[[5-(Substituted phenyl)-2-oxazolyl]methylene]amino]-2,4-imidazolidinediones



compd	X	R	% yield[a]	mp, °C	formula	analyses
6a	H	H	78	279–282	$C_{13}H_{10}N_4O_3$	C, H, N
6b	H	Na	56	180	$C_{13}H_9N_4O_3Na{\cdot}H_2O$	C, H, N
6c	4-NO_2	H	42	314–316	$C_{13}H_9N_5O_5$	C, H, N
6d	4-NO_2	Na	64	252	$C_{18}H_8N_5O_5Na{\cdot}2H_2O$	C, H, N
6e	2-NO_2	H	49	261–263	$C_{13}H_9N_5O_5$	C, H, N
6f	4-Cl	H	44	290–293	$C_{13}ClH_9N_4O_3$	C, H, N
6g	4-Cl	Na	81	240–246	$C_{13}H_8ClN_4O_3Na{\cdot}2H_2O$	C, H, N
6h	3-Cl	Na	37	257	$C_{13}H_8ClN_4O_3Na{\cdot}1.25H_2O$	C, H, N
6i	4-Br	H	70	290–292	$C_{13}H_9BrN_4O_3$	C, H, N
6j	4-Br	Na	71	240–242	$C_{13}H_8BrN_4O_3Na{\cdot}2H_2O$	C, H, N
6k	4-F	H	54	281–282	$C_{13}H_9FN_4O_3$	C, H, N
6l	4-F	Na	56	229–234	$C_{13}H_8F_4O_3Na{\cdot}2H_2O$	C, H, N
6m	4-CH_3O	H	28	291–294	$C_{14}H_{12}N_4O_4$	C, H, N
6n	4-CH_3O	Na	41	189–195	$C_{14}H_{11}N_4O_4Na{\cdot}1.75H_2O$	C, H, N
6o	4-CH_3	H	5.5	272–276	$C_{14}H_{12}N_4O_3$	C, H, N
6p	4-CH_3	Na	65	236–288	$C_{14}H_{11}N_4O_3Na{\cdot}1.25H_2O$	C, H, N
6q	3-CF_3	H	76	239–242	$C_{14}H_9F_3N_4O_3$	C, H, N
6r	3-CF_3	Na	86	198	$C_{14}H_8F_3N_4O_3Na{\cdot}1.75H_2O$	C, H, N
6s	3,4-Cl_2	H	45	292–294	$C_{13}H_8Cl_2N_4O_3$	C, H, N
6t	3,4-Cl_2	Na	55	270	$C_{13}H_7Cl_2N_4O_3Na{\cdot}2.5H_2O$	C, H, N

[a] Yield was based on the conversion of structure **5** to **6**.

Scheme II



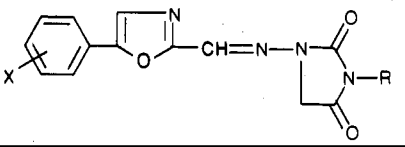
pounds into oxazoles, using sulfuric acid or phosphorus pentachloride. Phosphorus oxychloride is a recent, improved modification in that synthetic approach. The method appeared applicable.

The problem of generating a 5-(substituted phenyl)-2-oxazolecarboxaldehyde was circumvented by condensing oxoacetic acid with 1-amino-2,4-imidazolidinedione hydrochloride. This derivative (**2**) was then coupled with selected α-amino ketones **4** to form the appropriate α-acylamino carbonyl compound **5** (Table I). Thereafter, application of the Robinson–Gabriel procedure allowed isolation of the targeted oxazoles **6** (Table II). The preferred method for preparing these compounds is shown in Scheme I, and sodium salts were routinely prepared to improve water solubility for biological evaluation.

To demonstrate that the cyclized compounds were in-

(6) Turchi, I. J.; Dewar, M. J. S. *Chem. Rev.* **1975**, *75*, 389.

Table III. Skeletal Muscle Relaxant Activity of 1-[[[5-(Substituted phenyl)-2-oxazolyl]methylene]amino]-2,4-imidazolidinediones



compd	X	R	HTD[a]	muscle relaxant act. grade at HTD	% GTT[b] inhibn	±SE
6a	H	H	>800	0	−41	1.7
6b	H	Na	200	1	−49	4.3
6c	4-NO_2	H	>800	0	−86	2.8
6d	4-NO_2	Na	>800	2	−84	3.3
6e	2-NO_2	H	>800	0	0	13.5
6f	4-Cl	H	>800	0	−80	2.1
6g	4-Cl	Na	400	2	−81	2.7
6h	3-Cl	Na	400	3	−42	7.0
6i	4-Br	H	>800	0	−82	1.9
6j	4-Br	Na	400	3	−83	1.0
6k	4-F	H	>800	2	−70	4.2
6l	4-F	Na	400	2	−75	0.9
6m	4-CH_3O	H	>800	2	−47	2.8
6n	4-CH_3O	Na	>800	0	−58	8.2
6o	4-CH_3	H	>800	0	−65	5.1
6p	4-CH_3	Na	>800	0	−62	1.3
6q	3-CF_3	H	400	0	−56	2.2
6r	3-CF_3	Na	50	1	−69	6.0
6s	3,4-Cl_2	H	>800	0	−82	2.5
6t	3,4-Cl_2	Na	>800	1	−71	3.1
dantrolene sodium[c]			>400	4	−80	1.0

[a] HTD = highest tolerated dose (mg/kg po) in mice; activity was rated as 0 = none, 1 = slight, 2 = moderate, 3 = marked, and 4 = severe. [b] GTT = gastrocnemius twitch tension. Percent inhibition was measured after a cumulative dose of 36.6 mg/kg iv in rats. [c] Dantrolene sodium is 1-[[[5-(4-nitrophenyl)-2-furanyl]methylene]amino]-2,4-imidazolidinedione sodium salt, hydrated; see also ref 3.

deed the proposed structures, one example of the 1-[[(2-oxazolyl)methylene]amino]-2,4-imidazolidinediones was prepared by an alternate route. The known[7] ethyl 5-(4-chlorophenyl)-2-oxazolecarboxylate (**7**) was reduced with diisobutylaluminum hydride (DIBAL) to the corresponding aldehyde **8**. Subsequent condensation of this aldehyde with 1-amino-2,4-imidazolidinedione hydrochloride (**1**) allowed isolation of the imidazolidinedione **6f** (see Scheme II). This same product was also prepared by the general method presented in Scheme I, indicating proper structural assignment of the new oxazole series.

Results and Discussion

The potential skeletal muscle relaxant activity of the target oxazoles listed in Table II was determined by two methods. The pithed rat gastrocnemius muscle preparation described by Ellis and Wessels[2] was used to detect direct skeletal muscle inhibition induced by drug actions on the muscle itself at a site beyond the neuromuscular junction. A gross observation method in mice similar to that described by Irwin[8] was used to detect muscle relaxant activity following oral drug administration. For comparison in both procedures, the results of the reference drug, dantrolene sodium,[1,3] were included. The dual assessment allowed identification and scoring of compounds that are orally active, direct-acting skeletal muscle relaxants.

Generally, increased oral activity was observed when compounds were administered as the sodium salt rather than the free acid form. There were two exceptions: (1) the 3,4-dichloro (**6s** and **6t**) and the 4-CH_3 (**6o** and **6p**) oxazoles, for which oral activity was not evident with either the free acid or the sodium salt, although iv activity was appreciable; and (2) the 4-CH_3O (**6m** and **6n**) oxazoles, for which activity was evident with the free acid but not the sodium salt. However, when these compounds were administered iv, there were no appreciable differences between the free acid and its sodium salt in inhibiting skeletal muscle twitch contractions.

A qualitative structure–activity trend was observed among the oxazole analogues (Table III); i.e., compounds having electron-withdrawing substituents in the phenyl moiety displayed greater iv activity, e.g., **6c**, **6f**, **6i**, **6k**, **6s**. The position of the substituent on the phenyl ring also influenced activity when compounds were administered iv. Isomers substituted in the 4-position were the most active (compare **6c**, **6d** with **6e** and **6f** and **6g** with **6h**). When the substituent was moved to the 2- or 3-position, the observed activity was diminished.

In conclusion, synthesis of compounds having an electron-withdrawing substituent in the phenyl 4-position led to the most potent imidazolidinediones. Thus, in this series the specific 2,5-oxazole moiety proved to be an acceptable isostere for furan. Five compounds (**6d**, **6g**, **6j**, **6k**, and **6l**) that had impressive direct-acting skeletal muscle inhibition (i.e., ≥70% gastrocnemius twitch tension inhibition) also exhibited muscle relaxant activity of 2 or better when given perorally (Table III). These compounds are undergoing further pharmacological evaluation, as they have clear, demonstrable direct skeletal muscle relaxant activity compared to that of the benchmark dantrolene sodium.

Experimental Section

Melting points were taken in a Mel-Temp apparatus in open capillary tubes and are uncorrected. IR spectra were determined as Nujol mulls on a Perkin-Elmer 137B spectrophotometer. All mass spectra were obtained on a Hewlett-Packard 5987A quadrupole mass spectrometer. Compounds were analyzed by 70-eV electron ionization (EI) with a direct insertion probe. Molecular weight information for **5a** was obtained by using methane chemical ionization (CI). The ion source temperature for these experiments

(7) Tanaka, C. *Y. Zasshi* **1965**, *85*, 186–93; *Chem. Abstr.* **1965**, *62*, 16222*d*.
(8) Irwin, S. *Psychopharmacologia* **1968**, *13*, 222.

was 200 °C. Compound **6b** was analyzed by fast atom bombardment mass spectrometry. Xenon atoms at an energy of ~7 keV and a beam current of ~40 mA were used as the primary particles, and **6b** was dispersed in glycerol prior to the analysis. The proton NMR spectra were taken on a Varian A-60A instrument, with Me_4Si as internal standard.

The evaluated compounds were prepared by the procedure shown in Scheme I and exemplified by the preparation of **5a**, **6a**, and **6b**.

[[(2,4-Dioxo-1-imidazolidinyl)imino]methyl]formic Acid (2). Oxoacetic acid (37.0 g, 0.50 mol) was dissolved in 100 mL of water and the solution was filtered into an Erlenmeyer flask. 1-Amino-2,4-imidazolidinedione hydrochloride (1) (75.5 g, 0.50 mol) was dissolved in 400 mL of water and the solution was filtered into the same flask. The two solutions were swirled together, and a white precipitate formed rapidly. The mixture was allowed to stand for 0.5 h and the white solid **2** was then filtered off. A yield of 62 g (73%) was obtained, mp 258–260 °C. Anal. ($C_5H_5N_3O_4$) C, H, N.

[[(2,4-Dioxo-1-imidazolidinyl)imino]methyl]formic Acid Chloride (3). The acid **2** (171 g, 0.30 mol) was combined with 1,4-dioxane (1500 mL) and thionyl chloride (250 mL). The stirred mixture was allowed to reflux for 3.0 h before dissolution occurred and was refluxed for an additional 2.0 h. The solvent was removed under reduced pressure and the remaining solid was recrystallized from nitromethane (1500 mL). A yield of 113.7 g (60%) was isolated, mp 197–207 °C. The product was further characterized by derivatization with 2-amino-1-phenylethanones, exemplified by the following preparation.

***N*-(2-Phenyl-2-oxoethyl)[[(2,4-dioxo-1-imidazolidinyl)imino]methyl]formamide (5a).** To a stirred mixture of 2-amino-1-phenylethanone hydrochloride (4) (50 g, 0.29 mol) and [[(2,4-dioxo-1-imidazolidinyl)imino]methyl]formyl chloride (**3**) (55 g, 0.29 mol) was added a solution of 600 mL of *N*,*N*-dimethylformamide and 60 mL of pyridine. The mixture went into solution after 2.0 h and the solution was stirred overnight. The solution was poured into water (3 L) and a light yellow solid precipitated. The solid was collected by filtration and washed with ethanol and ether. The product was dried in a 60 °C oven and recrystallized from acetic acid (500 mL) to give 46 g (55%) of a light yellow product: mp 248–253 °C; IR (Nujol) 1725, 1670, 1640 cm^{-1} (carbonyls); NMR (Me_2SO-d_6) δ 3.90 (s, 2, imidazolidinedione CH_2), 4.30 (d, 2, CH_2, collapses to singlet upon exchange), 6.70 (s, 1, CH), 7.0–7.7 (m, 7, aromatics), 7.88 (t, 1, exchanges to s, amide NH), 11.5 (br s, 1, exchanges, NH); MS, *m/e* 289 (MH^+), 189, 154, 105.

1-[[(5-Phenyl-2-oxazolyl)methylene]amino]-2,4-imidazolidinedione (6a). A mixture of **5a** (30 g, 0.10 mol) and phosphorus oxychloride (520 mL) was stirred and refluxed for 0.5 h. An additional 180 mL of phosphorus oxychloride was added to the very thick mixture. The mixture was stirred and refluxed for another 15 min. The solid was collected and added to a mixture of ice and water (4 L).

The solid was collected and recrystallized from acetic acid (800 mL). The product **6a** (23 g) was collected in two crops (78%): mp 279–282 °C; IR (Nujol) 1775, 1725 cm^{-1} (imidazolidinedione carbonyls); NMR (Me_2SO-d_6) δ 4.45 (s, 2, CH_2), 7.35–7.90 (m, 7, aromatics), 11.47 (br s, 1, exch); MS, *m/e* 270 (M^+), 172, 170, 157, 105, 103.

1-[[(5-Phenyl-2-oxazolyl)methylene]amino]-2,4-imidazolidinedione Sodium Salt Monohydrate (6b). To a stirred mixture of **6a** (5 g, 0.018 mol) and methanol (150 mL) was added a solution of sodium hydroxide (1.0 g, 0.025 mol) in methanol (40 mL). After being stirred (1.0 h), the mixture was filtered and the collected solid was allowed to air-dry. The collected solid was recrystallized from SDA-30 (300 mL) and exposed to ambient conditions for 3 days to give 3.1 g (56%) of **6b**: mp 180 °C; IR (Nujol) 1700, 1600 cm^{-1} (br, imidazolidinedione anion); NMR (Me_2SO-d_6) δ 3.90 (s, 2, CH_2), 7.41–7.91 (m, 7, aromatics); MS, *m/e* 293 (MH^+), 315 (MNa^+), 271.

Alternate Synthesis of 6f. To a solution of ethyl 5-(4-chlorophenyl)-2-oxazolecarboxylate (**7**) (19.1 g, 0.076 mol) in methylbenzene (700 mL) at −70 °C was added diisobutylaluminum hydride (68 mL, 0.084 mol) over 20 min. After being stirred 1.0 h at −70 °C, the solution was allowed to warm to −20 C°, and 100 mL of methanol/water (1:1) was introduced over 30 min. Then 1.0 N HCl (100 mL) was added and the mixture was filtered. The methylbenzene layer was separated and dried (Na_2SO_4). Evaporation yielded 14.1 g of crude aldehyde, which was dissolved in SDA-30 (200 mL). To this alcoholic solution was added 1-amino-2,4-imidazolidinedione hydrochloride (0.070 mol, 10.6 g) in water (100 mL). The mixture was heated on a steam bath, precipitation occurred, and water (500 mL) was added. Filtration yielded a yellow solid. Recrystallization from nitromethane (3.0 L) allowed isolation of 14.0 g (60% yield) of **6f**: mp 290–293 °C; IR (Nujol) 1780, 1725 cm^{-1} (imidazolidinedione carbonyls); NMR (Me_2SO-d_6) δ 4.37 (s, 2, CH_2), 7.42–7.90 (m, 6, aromatics), 11.5 (s, 1, br exch, NH); MS, *m/e* 304 (MH^+), 206, 204, 139.

Pharmacology. All compounds were tested by using the pithed rat gastrocnemius muscle preparation method described by Ellis and Wessels.[2]

Adult male Charles River rats (385–400 g) were anesthetized with ether. After a tracheotomy, the rat was pithed, immediately connected to a rodent respirator (Harvard), and bilaterally vagotomized. One carotid artery was ligated and the other was cannulated for recording arterial blood pressure. Blood pressure recordings were made with a pressure transducer (Statham P23D) connected to a polygraph (Gross Model 7B). One jugular vein was ligated and the other was cannulated for drug administration.

The gastrocnemius muscle was prepared by cutting the Achilles tendon free and attaching it to a force-displacement transducer (Grass FT 03C). Stimulating electrodes (Grass E-2 subdermal) were inserted in the belly (anode) and tendon (cathode) of the muscle. A stimulator (Grass-S88) with isolation units (Grass SIU5) was used to generate supramaximal electrical impulses (50% above the voltage that gave a maximum contraction). Tubocurarine chloride, 0.075 mg/kg iv, was administered to produce neuromuscular blockade. This procedure was used to detect direct skeletal muscle inhibition induced by drug actions on the muscle itself at a site beyond the neuromuscular junction. Many of these compounds exhibit a low aqueous solubility and therefore were dissolved in an organic solvent (tetrahydro-2-furanmethanol or dimethyl sulfoxide) for intravenous administration at a cumulative dose of 36.6 mg/kg (sequential doses of 0.83, 2.5, 8.3, and 25 mg/kg). Confidence limits were calculated by using polynomial regression.[9]

To detect muscle relaxant activity following oral drug administration, a gross observation method in mice similar to that described by Irwin[8] was used. The test compounds were suspended in 0.5% methylcellulose 4000 and orally administered at doses of 50, 200, 400, and 800 mg/kg. The muscle relaxant activity was scored during a 2.0-h observation period after drug administration. Activity was rated according to a four-point scale: 0 = none, 1 = slight, 2 = moderate, 3 = marked, and 4 = severe muscle relaxation. Acute toxicity was assessed over a 72-h period after drug administration. Table III presents the results of this testing.

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Registry No. 1, 2827-56-7; **2**, 64748-89-6; **3**, 64748-90-9; **4a**, 5468-37-1; **4b**, 5425-81-0; **4c**, 23082-65-7; **4d**, 5467-71-0; **4e**, 5467-72-1; **4f**, 456-00-8; **4g**, 3883-94-1; **4h**, 5467-70-9; **4i**, 61062-56-4; **4j**, 41995-19-1; **4k**, 51084-83-4; **5a**, 64748-75-0; **5b**, 64748-77-2; **5c**, 105336-07-0; **5d**, 64769-69-3; **5e**, 64748-80-7; **5f**, 64748-82-9; **5g**, 64748-78-3; **5h**, 64748-84-1; **5i**, 64748-88-5; **5j**, 64748-91-0; **5k**, 105336-08-1; **6a**, 64748-74-9; **6b**, 105336-09-2; **6c**, 64748-76-1; **6d**, 105336-10-5; **6e**, 105336-11-6; **6f**, 64748-85-2; **6g**, 105336-12-7; **6h**, 105336-13-8; **6i**, 64748-79-4; **6j**, 105336-14-9; **6k**, 64748-81-8; **6l**, 105336-15-0; **6m**, 64748-92-1; **6n**, 105336-16-1; **6o**, 64748-83-0; **6p**, 105336-17-2; **6q**, 64748-86-3; **6r**, 105336-18-3; **6s**, 64748-73-8; **6t**, 105336-19-4; **7**, 2082-14-6; 8, 105336-20-7; $OHCCO_2H$, 298-12-4.

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