min. $ED_{+300\%}$ values are recorded in Table I. $ED_{+300\%}$ is defined as the dose at which the average sleeping time of the animals in a test group is increased by 300% in comparison to that of a control group.

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Structure and Anticoccidial Activity of a New Series of 4-Hydroxyquinoline-3-carboxylates

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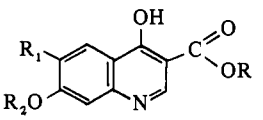
A new group of broad-spectrum coccidiostats, the 4-hydroxyquinoline-3-carboxylates (**1**), was first described by Spencer, *et al.*[1] The activity of these compounds was later confirmed in several publications.[2-4] Decoquinate[3] (**1a**),

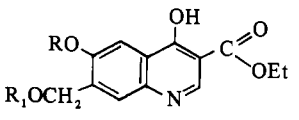


1

1a, decoquinate	**1b**, nequinate	**1c**, buquinolate
R = Et	R = Me	R = Et
$R_1 = OC_{10}H_{21}$	R_1 = *n*-Bu	R_1 = *i*-BuO
R_2 = Et	$R_2 = CH_2C_6H_5$	R_2 = *i*-Bu

nequinate[2] (**1b**), and buquinolate[1] (**1c**) are among the most effective coccidiostats known at present. These compounds all have an alkoxy substituent in position 7 and an alkyl or alkoxy substituent in position 6.

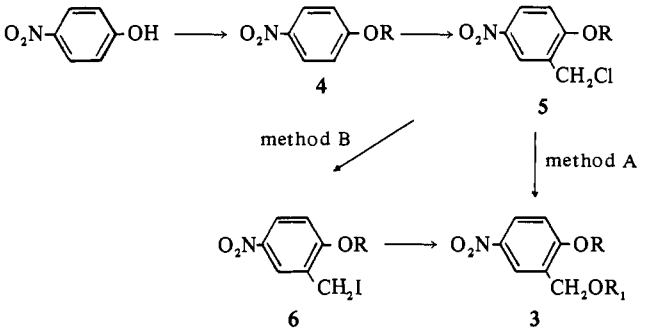
In contrast, the compounds **2** described here are ethyl 6-alkoxy-4-hydroxyquinoline-3-carboxylates with an alkoxymethyl or an aralkoxymethyl substituent in the 7 position. These compounds are also potent coccidiostats.



2

Chemistry. Nitro compounds **3** were used to initiate the synthetic pathways leading to the formation of compounds **2**. These nitro compounds themselves are synthesized as outlined in Scheme I. The reaction of *p*-nitrophenol with

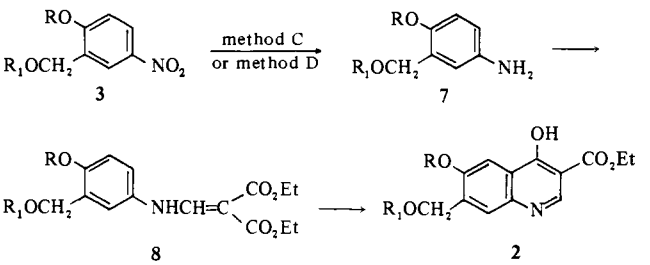
Scheme I



an appropriate alkyl halide in the presence of a base, *e.g.*, NaOH or NaOMe, yields the *p*-nitrophenoxyalkanes **4**. These alkoxynitrobenzenes may be chloromethylated using paraform, $ZnCl_2$, and gaseous HCl to produce the benzyl chlorides **5**. The desired nitro compounds **3** may be formed by the reaction of sodium alcoholates with benzyl chlorides (method A) although various side products and tars are frequently obtained. Therefore, the more usual procedure is to have the chlorides react with NaI in acetone to obtain benzyl iodides **6** (method B). High yields of the desired benzyl ethers **3** may be readily obtained by addition of appropriate alcohols to the system. Most of the benzyl halides, summarized in Table I, are novel.

The pathway starting with benzyl ethers **3**, as outlined in Scheme II, is used for the final synthesis of compounds

Scheme II

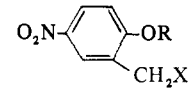


2. The nitro compounds **3** may be reduced to their corresponding anilines **7** by two different methods: either catalytic reduction with PtO_2 in ethanol (method C) or reduction with ammonium chloride and iron (method D). These anilines are condensed with diethyl methoxymethylenemalonate in boiling ethanol or 2-propanol.

Only a limited number of condensation products **8** were isolated, the majority being used in their crude form for the last stage of the synthesis. Ring closure of compounds **8** was effected by heating in diphenyl ether or diphenylmethane, both solvents being equally suitable (Table II).

Chemotherapy. For screening purposes, 18-day-old male Hisex chickens weighing between 100 and 120 g were housed in individual cages for the duration of the experiment. Feed, known not to contain coccidiostat, was available at will. On day 0, the chickens were divided into three groups: four noninfected, nontreated birds; four infected, nontreated birds; two infected, treated birds. Coccidiosis was induced by inoculation of the test animals with approximately two million sporulated oöcysts of *Eimeria Acervulina*. For 6 days, the treated birds were given the compounds **2** at will at a dose of 0.01% of their feed. On the seventh day, the medicated feed was replaced by normal feed for five subse-

Table I



Compd	R	X	Yield, purified, %	Mp or bp (mm), °C	Formula	Analyses[a]
9	Me	Cl	84	78.5	$C_8H_8ClNO_2$[b]	Cl
10	Me	I	81	103	$C_8H_8INO_3$[c]	I, N
11	Et	Cl	73	69.5	$C_9H_{10}ClNO_3$[d]	Cl
12	Et	I	85	88	$C_9H_{10}INO_3$	I, C, H, N
13	*n*-Bu	Cl	87	170–173 (1)	$C_{11}H_{14}ClNO_3$	Cl, C, H, N
14	*n*-Bu	I	72	57	$C_{11}H_{14}INO_3$	I, C, H, N
15	*n*-C_7H_{15}	Cl	63	215–219 (2, 5)	$C_{14}H_{20}ClNO_3$[e]	Cl
16	*n*-$C_{10}H_{21}$	Cl	87	*f*	$C_{17}H_{26}ClNO_3$	Cl
17	*n*-$C_{10}H_{21}$	I	83	63	$C_{17}H_{26}INO_3$	I, C, H, N

[a]Gc analysis gave a purity of at least 94% for all compounds. [b]R. Quelet and H. Coudanne, *C. R. Acad. Sci., Paris, Ser. C*, **252**, 894 (1961). [c]G. Bendz, *et al., J. Chem. Soc.*, 1130 (1950). [d]M. Wakae, *et al., Chem. Abstr.*, **54**, 10921*h* (1960). [e]R. Collins and M. Davis, *J. Chem. Soc. C*, 873 (1966). [f]Crude residue was used in the next step.

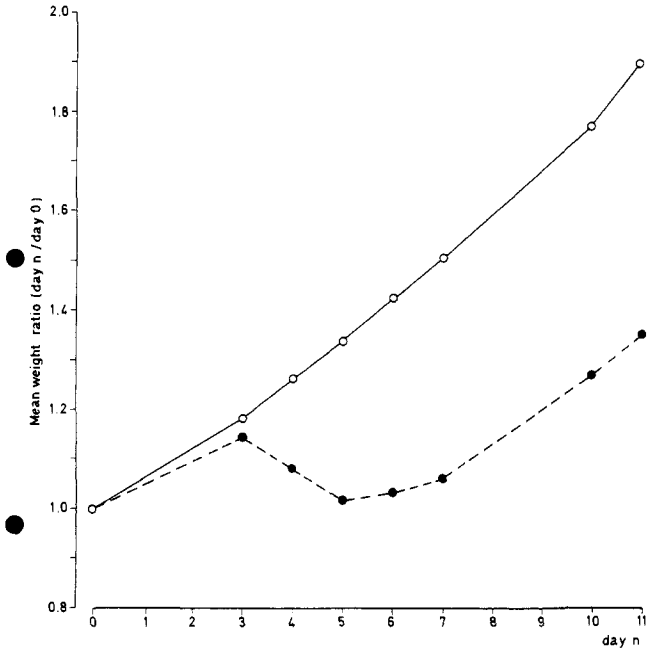


Figure 1. Growth rate for noninfected (○—○) and for infected (●- - -●) chicks.

quent days. During the experiment, all birds were weighed eight times, their fecal consistency was recorded three times, and a fecal count for oocysts was carried out once. All birds were sacrificed on the eleventh day of the experiment. Comparison of the growth rates of the control groups (Figure 1) shows a marked decrease in weight gain for the infected chickens. The main weight ratio (day 5/day 0) for these birds is 1.02. The anticoccidial activity of a compound can be determined by comparing the mean weight ratio (day *n*/day 0) from day 3 to day 7 with that of the two control groups. The results obtained on day 5 are presented in Table III, together with those of three leading coccidiostats.

A more detailed investigation into the activity of different concentrations of compound **88** was conducted with the aid of three different strains of *Eimeria*. Administration of the active compound was initiated on the day of inoculation (*i.e.*, simultaneous treatment) or two days before (*i.e.*, prophylactic treatment). Apart from this, the experimental procedure was as previously described.

The mean weight ratios are given in Table IV together with data on compound **1b** (nequinate) for comparative purposes. The results indicate that compound **88** is at least as effective as nequinate and has therefore been selected for further investigation.

Experimental Section†

2-Butoxy-α-chloro-5-nitrotoluene (13). Gaseous HCl was passed through a mixture of 50.7 g (0.26 mol) of 4-O_2N-C_6H_4-OBu, 28.2 g (0.94 mol) of $(CH_2O)_3$, and 61.3 g (0.45 mol) of anhydrous $ZnCl_2$ for 3 hr at a temperature of 80°. The reaction mixture was cooled and poured into H_2O and $CHCl_3$. The organic layer was separated, washed with $NaHCO_3$ solution and with H_2O, dried ($MgSO_4$), and evaporated. The residue was distilled giving 54 g (87%) of **13**, bp 170–173° (1 mm). *Anal.* ($C_{11}H_{14}ClNO_3$) C, H, N, Cl.

2-Butoxy-α-iodo-5-nitrotoluene (14). A mixture of 24.3 g (0.1 mol) of **13**, 17 g (0.113 mol) of NaI, and 125 ml of Me_2CO was refluxed for 1 hr, after which time the reaction mixture was poured into H_2O and extracted with *i*-Pr_2O. The organic layer was dried ($MgSO_4$) and evaporated. Crystallization from EtOH yielded 24 g (72%) of **14**, mp 57°. *Anal.* ($C_{11}H_{14}INO_3$) C, H, N, I.

Method A. 2-Butoxy-α-heptyloxy-5-nitrotoluene (57). A solution of 4.2 g (0.18 g-atom) of Na in 120 ml of *n*-$C_7H_{15}OH$ was added dropwise, at a temperature of 40°, to a mixture of 29.3 g (0.12 mol) of **13** in 40 ml of $C_7H_{15}OH$. The mixture was stirred for 72 hr at room temperature, after which time 200 ml of Et_2O was added. The organic layer was washed with H_2O, dried ($MgSO_4$), and evaporated. The residue was distilled to give 25 g (64%) of **57**, bp 184–188° (0.2 mm). *Anal.* ($C_{18}H_{29}NO_4$) C, H, N.

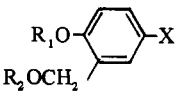
Method B. 2-Ethoxy-α-undecyloxy-5-nitrotoluene (48). A solution of 6.9 g (0.3 g-atom) of Na in 160 g of *n*-$C_{11}H_{21}OH$ was added dropwise, at a temperature between 45 and 50°, to a stirred mixture of 61 g (0.2 mol) of **12** in 80 g of *n*-$C_{11}H_{21}OH$. Stirring was continued for 2 days at room temperature. The reaction mixture was poured into H_2O and extracted with Et_2O. The extract was dried ($MgSO_4$) and evaporated. The solid residue was crystallized from petroleum ether yielding 41.3 g (59%) of **48**, mp 50°. *Anal.* ($C_{20}H_{33}NO_4$) C, H, N.

Method C. 3-(Octyloxymethyl)-*p*-phenetidine (43). A mixture of 47 g (0.15 mol) of **42**, 300 ml of EtOH, and 1 g of PtO_2 was hydrogenated at normal pressure and room temperature. After the calculated volume of H_2 was taken up, the catalyst was removed by filtration and the filtrate concentrated. The residue was distilled to give 36.5 g (87%) of **43**, bp 164–168° (0.15 mm). *Anal.* ($C_{17}H_{29}NO_2$) N.

Method D. 3-(Heptyloxymethyl)-*p*-phenetidine (40). **39** (101 g, 0.34 mol) was added gradually to a stirred and refluxing mixture of 65 g (1.16 g-atom) of Fe and 650 ml (0.78 *N*) of NH_4Cl solution. The reaction mixture was refluxed for an additional 8 hr, cooled, and extracted with PhMe; the organic layer was dried ($MgSO_4$) and evaporated. The residue was distilled giving 70 g (79%) of **40**, bp 155–158° (0.4 mm). *Anal.* ($C_{16}H_{27}NO_2$) N.

†All melting points were measured with a "Mettler FP 1" melting point apparatus and are uncorrected. Where analyses are indicated by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values unless otherwise stated.

Table II



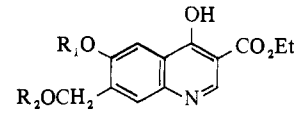
Compd	R_1	R_2	X	Yield, %	Method[a]	Mp or bp (mm),[b] °C	Formula	Analyses
18	Me	Et	NO_2	70	A	66.6	$C_{10}H_{13}NO_4$[c]	N
19	Me	Et	NH_2	47	D	109 (0.4)	$C_{10}H_{15}NO_2$	N
20	Me	Et	$NHCH=C(CO_2Et)_2$	90		47	$C_{18}H_{25}NO_6$	C, H, N
21	Me	*i*-Bu	NO_2	57	B	35	$C_{12}H_{17}NO_4$	C, H, N
22	Me	*i*-Bu	NH_2	90	C		$C_{12}H_{19}NO_2$	
23	Me	*i*-Bu	$NHCH=C(CO_2Et)_2$	90			$C_{20}H_{29}NO_6$	
24	Me	*n*-C_7H_{15}	NO_2	51	A	50	$C_{15}H_{23}NO_4$	C, H, N
25	Me	*n*-C_7H_{15}	NH_2	53	D	163–164 (0.5)	$C_{15}H_{25}NO_2$	N
26	Me	*n*-C_7H_{15}	$NHCH=C(CO_2Et)_2$	91			$C_{23}H_{35}NO_6$	N
27	Me	*n*-C_8H_{17}	NO_2	82	B	54	$C_{16}H_{25}NO_4$	C, H, N
28	Me	*n*-C_8H_{17}	NH_2	27	D	174–176 (0.5)	$C_{16}H_{27}NO_2$	N
29	Me	*n*-C_8H_{17}	$NHCH=C(CO_2Et)_2$	90			$C_{24}H_{37}NO_6$	N
30	Me	$CH_2C_6H_5$	NO_2	82	B	83	$C_{15}H_{15}NO_4$	C, H, N
31	Me	$CH_2C_6H_5$	NH_2	95	C		$C_{15}H_{17}NO_2$	
32	Me	$CH_2C_6H_5$	$NHCH=C(CO_2Et)_2$	95			$C_{23}H_{27}NO_6$	
33	Et	*i*-Bu	NO_2	79	B	84.5	$C_{13}H_{19}NO_4$	C, H, N
34	Et	*i*-Bu	NH_2	80	C		$C_{13}H_{21}NO_2$	
35	Et	*i*-Bu	$NHCH=C(CO_2Et)_2$	95			$C_{21}H_{31}NO_6$	
36	Et	*n*-C_6H_{13}	NO_2	87	B		$C_{15}H_{23}NO_4$	N
37	Et	*n*-C_6H_{13}	NH_2	68	D	163–166 (1.2)	$C_{15}H_{25}NO_2$	N
38	Et	*n*-C_6H_{13}	$NHCH=C(CO_2Et)_2$	95			$C_{23}H_{35}NO_6$	N
39	Et	*n*-C_7H_{15}	NO_2	84	B		$C_{16}H_{25}NO_4$	N
40	Et	*n*-C_7H_{15}	NH_2	79	D	155–158 (0.4)	$C_{16}H_{27}NO_2$	N
41	Et	*n*-C_7H_{15}	$NHCH=C(CO_2Et)_2$	90		46.5	$C_{24}H_{37}NO_6$	C, H, N
42	Et	*n*-C_8H_{17}	NO_2	88	B	198–200 (0.8)	$C_{17}H_{27}NO_4$	N
43	Et	*n*-C_8H_{17}	NH_2	87	C	164–168 (0.15)	$C_{17}H_{29}NO_2$	N
44	Et	*n*-C_8H_{17}	$NHCH=C(CO_2Et)_2$	80		64	$C_{25}H_{39}NO_6$	C, H, N
45	Et	*n*-C_9H_{19}	NO_2	67	B	37	$C_{18}H_{29}NO_4$	C, H, N
46	Et	*n*-C_9H_{19}	NH_2	70	C		$C_{18}H_{31}NO_2$	
47	Et	*n*-C_9H_{19}	$NHCH=C(CO_2Et)_2$	83			$C_{26}H_{41}NO_6$	
48	Et	*n*-$C_{11}H_{23}$	NO_2	59	B	50	$C_{20}H_{33}NO_4$	C, H, N
49	Et	*n*-$C_{11}H_{23}$	NH_2	73	C	69	$C_{20}H_{35}NO_2 \cdot HCl$	C, H, N, Cl
50	Et	*n*-$C_{11}H_{23}$	$NHCH=C(CO_2Et)_2$	91			$C_{28}H_{45}NO_6$	
51	Et	$CH_2CH_2C_6H_5$	NO_2	26	B	220–225 (2)	$C_{17}H_{19}NO_4$	N
52	Et	$CH_2CH_2C_6H_5$	NH_2	89	C		$C_{17}H_{21}NO_2$	
53	Et	$CH_2CH_2C_6H_5$	$NHCH=C(CO_2Et)_2$	92			$C_{25}H_{31}NO_6$	N
54	*n*-Bu	*n*-Pr	NO_2	76	A		$C_{14}H_{21}NO_4$	N
55	*n*-Bu	*n*-Pr	NH_2	81	C		$C_{14}H_{23}NO_2$	
56	*n*-Bu	*n*-Pr	$NHCH=C(CO_2Et)_2$	91			$C_{22}H_{33}NO_6$	N
57	*n*-Bu	*n*-C_7H_{15}	NO_2	64	A	184–188 (0.2)	$C_{18}H_{29}NO_4$	C, H, N
58	*n*-Bu	*n*-C_7H_{15}	NH_2	88	C		$C_{18}H_{31}NO_2$	
59	*n*-Bu	*n*-C_7H_{15}	$NHCH=C(CO_2Et)_2$	64			$C_{26}H_{41}NO_6$	N
60	*n*-Bu	*n*-C_8H_{17}	NO_2	71	A	192–194 (0.2)	$C_{19}H_{31}NO_4$	C, H, N
61	*n*-Bu	*n*-C_8H_{17}	NH_2	91	C		$C_{19}H_{33}NO_2$	
62	*n*-Bu	*n*-C_8H_{17}	$NHCH=C(CO_2Et)_2$	50			$C_{27}H_{43}NO_6$	N
63	*n*-Bu	*n*-C_9H_{19}	NO_2	64	A	204–208 (0.2)	$C_{20}H_{33}NO_4$	C, H, N
64	*n*-Bu	*n*-C_9H_{19}	NH_2	87	C		$C_{20}H_{35}NO_2$	
65	*n*-Bu	*n*-C_9H_{19}	$NHCH=C(CO_2Et)_2$	67			$C_{28}H_{45}NO_6$	N
66	*n*-C_7H_{15}	Et	NO_2	49	A	173–176 (0.4)	$C_{16}H_{25}NO_4$	N
67	*n*-C_7H_{15}	Et	NH_2	91	C		$C_{16}H_{27}NO_2$	
68	*n*-C_7H_{15}	Et	$NHCH=C(CO_2Et)_2$	82			$C_{24}H_{37}NO_6$	N
69	*n*-C_7H_{15}	$CH_2C_6H_5$	NO_2	67	A	243–244 (0.7)	$C_{21}H_{27}NO_4$	N
70	*n*-C_7H_{15}	$CH_2C_6H_5$	NH_2	83	C		$C_{21}H_{29}NO_2$	
71	*n*-C_7H_{15}	$CH_2C_6H_5$	$NHCH=C(CO_2Et)_2$	87			$C_{29}H_{39}NO_6$	N
72	*n*-$C_{10}H_{21}$	Et	NO_2	67	A	196 (0.3)	$C_{19}H_{31}NO_4$	N
73	*n*-$C_{10}H_{21}$	Et	NH_2	81	C		$C_{19}H_{33}NO_2$	
74	*n*-$C_{10}H_{21}$	Et	$NHCH=C(CO_2Et)_2$	91			$C_{27}H_{43}NO_6$	
75	*n*-$C_{10}H_{21}$	*n*-Pr	NO_2	80	B	33	$C_{20}H_{33}NO_4$	C, H, N
76	*n*-$C_{10}H_{21}$	*n*-Pr	NH_2	83	C		$C_{20}H_{35}NO_2$	
77	*n*-$C_{10}H_{21}$	*n*-Pr	$NHCH=C(CO_2Et)_2$	89			$C_{28}H_{45}NO_6$	
78	*n*-$C_{10}H_{21}$	*n*-C_5H_{11}	NO_2	82	B		$C_{22}H_{37}NO_4$	
79	*n*-$C_{10}H_{21}$	*n*-C_5H_{11}	NH_2	91	C		$C_{22}H_{39}NO_2$	
80	*n*-$C_{10}H_{21}$	*n*-C_5H_{11}	$NHCH=C(CO_2Et)_2$	93			$C_{30}H_{49}NO_6$	

[a] Methods refer to the Experimental Section. [b] When no physical data are given, compounds were used in their crude form. [c] R. Quelet and H. Coudanne, *Bull. Soc. Chim. Fr.*, 2445 (1963).

Diethyl [3-(Heptyloxymethyl)-*p*-phenetidinomethylene]malonate (41). A solution of 13.3 g (0.05 mol) of **40** and 11.9 g (0.055 mol) of diethyl methoxymethylenemalonate in 100 ml of *i*-PrOH was refluxed for 24 hr. After evaporation of the reaction mixture, the residue was crystallized from petroleum ether to give 19.5 g (90%) of **41**, mp 46.5°. *Anal.* ($C_{24}H_{37}NO_6$) C, H, N.

Ethyl 6-Ethoxy-7-heptyloxymethyl-4-hydroxy-3-quinolinecarboxylate (88). **41** (13 g, 0.03 mol) was added to 100 g of Ph_2O preheated to 230°. The resulting mixture was heated at 245° for 15 min. After cooling to 70° Me_2CO was added. The precipitate was

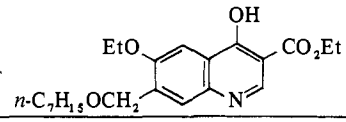
Table III



Compd	R_1	R_2	Yield purified, %	Mp, °C	Formula[a]	Weight ratio (day 5/day 0)[b] 0.01%	Weight ratio (day 5/day 0)[b] 0.001%	Oocyst count (day 7)[c] 0.01%	Oocyst count (day 7)[c] 0.001%	Fecal score (day 5)[d] 0.01%	Fecal score (day 5)[d] 0.001%
81	Me	Et	23	293.5	$C_{16}H_{19}NO_5$	1.18		1;1;0;0	1;1	1;1;1;1	3;3
82	Me	*i*-Bu	17	248	$C_{18}H_{23}NO_5$	1.17		1;1;1;1		2;1;2;3	
83	Me	*n*-C_7H_{15}	27	+300	$C_{21}H_{29}NO_5$	1.25		1;1;1;1	2;2;2;2	0;1;1;1	2;2;3;2
84	Me	*n*-C_8H_{17}	25	230	$C_{22}H_{31}NO_5$	1.25		0;0;0	3;2;2	1;1;1;1	2;2;1;3
85	Me	$CH_2C_6H_5$	29	231	$C_{21}H_{21}NO_5$	1.17		1;2;1;2		2;2;1;2	
86	Et	*i*-Bu	17	246	$C_{19}H_{25}NO_5$	1.24		1;2;2	2;2	1;1;1;0	1;2
87	Et	*n*-C_6H_{13}	31	222	$C_{21}H_{29}NO_5$	1.20		1;1;1;1	1;1;3;3	1;1;1;1	3;2;3;3
88	Et	*n*-C_7H_{15}	47	227	$C_{22}H_{31}NO_5$	1.24	1.23	0;0;1;1	0;0;2;2	1;0;1;1	1;1;1;1
89	Et	*n*-C_8H_{17}	31	226	$C_{23}H_{33}NO_5$	1.26	1.23	0;0;0;0	0;0;1;1	0;1;1;1	1;1;2;1
90	Et	*n*-C_9H_{19}	12	225	$C_{24}H_{35}NO_5$	1.22		1;1;0;0	0;0;2;2	1;1;0;0	1;1;3;3
91	Et	*n*-$C_{11}H_{23}$	31	222	$C_{26}H_{39}NO_5$	1.21		1;1;1;1	1;1;1;1	1;1;1;1	1;1;1;2
92	Et	$CH_2CH_2C_6H_5$	56	229	$C_{23}H_{25}NO_5$	1.25		1;1;2;2	1;1;2;2	0;0;2;1	2;1;1;2
93	*n*-Bu	*n*-Pr	33	227	$C_{20}H_{27}NO_5$	1.19		1;1;1;1	1;1;2;2	1;2;1;1	1;1;2;1
94	*n*-Bu	*n*-C_7H_{15}	28	217	$C_{24}H_{35}NO_5$	1.20		1;1;1;1	1;1;2;2	2;1;1;1	2;2;1;1
95	*n*-Bu	*n*-C_8H_{17}	32	215	$C_{25}H_{37}NO_5$	1.20		0;0;1;1	1;1;1;1	0;1;1;0	1;1;1;3
96	*n*-Bu	*n*-C_9H_{19}	25	213	$C_{26}H_{39}NO_5$	1.17		0;0;1;1	1;1;2;2	1;1;1;1	1;1;1;1
97	*n*-C_7H_{15}	Et	32	221	$C_{22}H_{31}NO_5$	1.18		1;2;2;2	1;1	1;3;1;1	3;3
98	*n*-C_7H_{15}	$CH_2C_6H_5$	27	219	$C_{27}H_{33}NO_5$	1.18		1;1;1;1	1;1;1;1	1;2;0;1	1;1;2;3
99	*n*-$C_{10}H_{21}$	Et	31	217	$C_{25}H_{37}NO_5$	1.30		1;1;1;1	1;1;1;1	0;0;1;1	1;1;1;1
100	*n*-$C_{10}H_{21}$	*n*-Pr	43	213	$C_{26}H_{39}NO_5$	1.19		2;1	3;3	3;1	3;3
101	*n*-$C_{10}H_{21}$	*n*-C_5H_{11}	23	205	$C_{28}H_{43}NO_5$	1.20		2;2;1;1	1;1;1;1	2;1;1;2	1;1;2;2
1a	Decoquinate (ethyl 6-*n*-decyloxy-7-ethoxy-4-hydroxy-3-quinoline-carboxylate)					1.24		0;0;0;0	0;0;1;1	1;0;1;1	1;1;1;0
1b	Nequinate (methyl 7-benzyloxy-6-*n*-butyl-4-hydroxy-3-quinoline-carboxylate)					1.24	1.19	0;0;1;0	0;1;2;1	0;1;1;0	0;0;2;1
1c	Amquinate (methyl 7-diethylamino-4-hydroxy-6-*n*-propyl-3-quinolinecarboxylate)					1.22		0;1;1;1	1;1;3;1	0;0;1;0	1;2;3;1

[a] All compounds were analyzed for C, H, and N. Compound **97**, C: −0.54; **99**, C: −0.64; **100**, C: +0.47. [b] Refer to chemotherapy. [c] 0, no oocysts in feces; 1, 0-5 × 10^4 oocyst/g of feces; 2, 5 × 10^4-1 × 10^5 oocyst/g of feces; 3, 10^5-2 × 10^5 oocyst/g of feces; 4, more than 2 × 10^5 oocyst/g of feces. [d] 0, normal feces; 1, soft to normal feces; 2, fluid droppings with some mucous casts; 3, slimy, greyish, mucoid diarrhea.

Table IV. Chemotherapeutical Results of



Eimeria strain	Treatment	Mean weight ratio: Noninfected chicks	Infected chicks	Infected chicks treated with 0.01% of **88**	Infected chicks treated with 0.001% of **88**	Infected chicks treated with 0.001% of **1b**
Acervulina[a]	Simultaneous	1.33	1.04	1.24	1.23	1.19
	Prophylactic	1.60	1.16		1.50	1.50
Brunetti[b]	Simultaneous	1.42	1.14	1.40	1.42	1.41
	Prophylactic	1.65	1.14		1.66	1.62
Tenella[c]	Simultaneous	1.34	1.19	1.53	1.51	1.49
	Prophylactic	1.78	1.33	1.79	1.74	1.72

[a] Results of the 5th day. [b] Results of the 6th day. [c] Results of the 7th day.

filtered and triturated with Me_2CO for 1 hr. The precipitate was collected and dried *in vacuo* to give **5**.5 g (47%) of **88**, mp 227°. *Anal.* ($C_{22}H_{31}NO_5$) C, H, N.

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Synthesis and Antiviral Activity of Homologs of Noformycin

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In the past two decades, several papers have appeared on the antiviral activity of noformycin[1-7] (**1**) obtained from a culture of *Nocardia formica*. Among the viruses reportedly