ketones is reported in this paper. A series of 2-arylidene-1-indanones (**5–14**) was prepared by the reaction of 1-indanone (**1**) with the appropriate aromatic aldehydes. The same reaction of 7-methoxy-1-tetralone (**2**) afforded 2-arylidene-7-methoxy-1-tetralones **15–17**. Three new 3-arylidenechroman-4-ones (**18–20**) were synthesized by the condensation of the chroman-4-one (**3**) with aromatic aldehydes. 3-Arylideneflavanones (termed flavindogenides) are frequently studied substances and, therefore, various procedures have been developed for their synthesis [5–11].

Formerly we also synthesized a series of such compounds by the piperidine-catalyzed condensation of flavanone (**4**) with aromatic aldehydes [2]. This method has now been used to obtain novel 3-arylideneflavanones (**21–32**). Structure of all new compounds (**5–32**) has been elucidated by IR and ^{1}H NMR spectroscopy.

Experimental

1. Equipment

The NMR spectra were recorded on Varian Gemini-200 and Bruker WP 200 SY spectrometers in $CDCl_3$ (internal standard **TMS**, δ 0.0 ppm) at room temperature. IR spectra were measured for KBr discs with a Perkin-Elmer 283 instrument.

2. General procedure for the preparation of compounds **5–32**

A mixture of compounds **1–4** (10 mmol), aromatic aldehyde (10 mmol), and piperidine (0.1 ml) was heated at 150 °C for 1 h, then cooled to room temperature and crystallized from CH_3OH to afford substances **5–32** (Table).

Table Physical constants of compounds prepared

Compound	Ar	M.p. [°C]	Yield [%]	Formula
5	4-$CH(CH_3)_2$-C_6H_4	90–91	51.4	$C_{19}H_{18}O$
6	4-OH-C_6H_4	226–227	58.7	$C_{16}H_{12}O_2$
7	3-OCH_3-C_6H_4	137–138	75.0	$C_{17}H_{14}O_2$
8	3,4-OCH_2O-C_6H_3	179–180	84.7	$C_{17}H_{12}O_3$
9	3-OH,4-OCH_3-C_6H_3	186–187	84.6	$C_{17}H_{14}O_3$
10	4-OH,3-OCH_3-C_6H_3	190–191	68.6	$C_{17}H_{14}O_3$
11	3,4,5-$(OCH_3)_3$-C_6H_2	162–163	54.8	$C_{19}H_{18}O_4$
12	3-Cl-C_6H_4	137–138	76.8	$C_{16}H_{11}ClO$
13	4-CH_3CONH-C_6H_4	259–260	48.7	$C_{18}H_{15}NO_2$
14	2-naphthyl	187–188	57.8	$C_{20}H_{14}O$
15	C_6H_5	121–122	49.2	$C_{18}H_{16}O_2$
16	4-OCH_3-C_6H_4	150–151	52.5	$C_{19}H_{18}O_3$
17	4-Cl-C_6H_4	141–142	41.3	$C_{18}H_{15}ClO_2$
18	1-naphthyl	118–119	58.4	$C_{20}H_{14}O_2$
19	2-naphthyl	131–132	68.5	$C_{20}H_{14}O_2$
20	2-thienyl	125–126	48.5	$C_{14}H_{10}O_2S$
21	2-CH_3-C_6H_4	116–117	62.5	$C_{23}H_{18}O_2$
22	2-OCH_3-C_6H_4	108–109	78.6	$C_{23}H_{18}O_3$
23	3-OCH_3-C_6H_4	97–98	66.5	$C_{23}H_{18}O_3$
24	4-OC_2H_5-C_6H_4	181–182	48.1	$C_{24}H_{20}O_3$
25	2-Cl-C_6H_4	137–138	44.5	$C_{22}H_{15}ClO_2$
26	3-Cl-C_6H_4	131–132	31.8	$C_{22}H_{15}ClO_2$
27	2-Br-C_6H_4	142–143	54.9	$C_{22}H_{15}BrO_2$
28	3-Br-C_6H_4	127–128	49.5	$C_{22}H_{15}BrO_2$
29	1-naphthyl	153–154	48.3	$C_{26}H_{18}O_2$
30	2-naphthyl	115–116	61.3	$C_{26}H_{18}O_2$
31	2-thienyl	137–138	36.6	$C_{20}H_{14}O_2S$
32	5-Cl-2-thienyl	180–181	47.0	$C_{20}H_{13}ClO_2S$

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Nalidixic acid prodrugs: Amides from amino acid esters and nalidixic acid

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Nalidixic acid (**1**) is an antibacterial agent used against infections due to gram negative organisms and specially in urinary tract infections [1]. The unique feature of **1** is that, unlike antibiotics and Furadantin®, it does not encourage the formation and spread of R-factor in bacteria [2]. It has recently been suggested as a potentially useful agent for the treatment of psoriasis on dermal delivery [3]. However, gastrointestinal disturbances on prolonged oral use is its major drawback. Also, high plasma protein binding and rapid conjugation lead to higher dose. Thus, the objective of this study was to investigate: a) whether amide derivatives of **1** would behave as prodrugs, b) to what extent the physical properties of the prodrugs vary with structure, c) to what degree the *in vitro* cleavage rates vary with structure and d) to seek prodrug derivatives of **1** which would be non-irritant, readily absorbed and rapidly hydrolyzed to release free drug, and have a greater half-life in the body [4].

A remarkable rise in activity was observed for **2** and **4** while **3** exhibited lower potency (Table). The availability factors revealed that **4** was most available. The prodrugs resisted hydrolysis in simulated gastric fluid but the rate of hydrolysis in simulated intestinal fluid was **3** > **4** > **2**. The m.p.'s. of **2**, **3** and **4** are lower than that of **1** owing to absence of intramolecular hydrogen bonding as in **1** [5]. The more active compounds, **2** and **4**, were the less hydrolyzed ones. Thus, slowly hydrolizable congeners of **1** will alter the rate of excretion of the drug and enhance the blood levels. The masking of the carboxylic group will not only eliminate ulcerogenicity but also decrease plasma protein binding with raised blood levels resulting in better activity and lower dose. The high partition values are presumable for greater absorption through the lipoidal cell membranes. The amino acids would have healing effect on the gastrointestinal lesions as well as essential dietary value. Thus, it would be fair to assume that compounds reported here would behave as ideal prodrugs of **1**.

Experimental

1. Materials and equipment

Nalidixic acid (**1**; Ranbaxy Laboratories, Dewas, India), L-arginine, L-cystine, L-histidine (Loba Chemie Indoaustranol Co., Bombay, India), pepsin, trypsin, octan-1-ol (E. Merck, Bombay, India). Microbiological media (Hi-Media, Bombay, India). Model VSU 2-P spetrophotometer (Carl Zeiss).