Studies on Flavonoids. Part-III. Synthesis and Physiological Studies of some New 3-Bromoflavones†

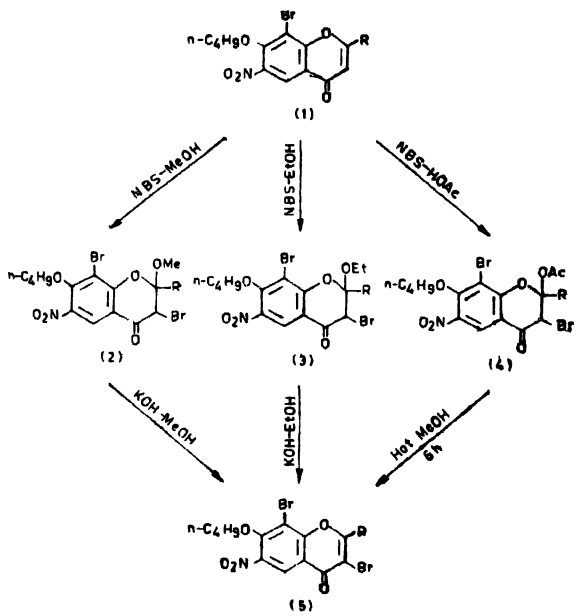
M. D. ANKHIWALA

Department of Chemistry, R. R. Mehta College of Science, Palanpur-385 002

Manuscript received 21 December 1990, revised 23 May 1991, accepted 17 July 1991

FLAVONES have been found to be associated with diverse biological activities[1]. It was therefore, thought interesting to synthesise the title compounds with the object of ascertaining whether presence of 3-bromo group in flavones could augment their physiological activity.

The present work reports the synthesis of 3,8-dibromo-6-nitro-7-n-butoxyflavones (**5**). These are derived from previously synthesised[2] 8-bromo-7-n-butoxy-6-nitroflavones and tested for their antimicrobial activity[2]. The reaction[3] of the flavones (**1**) with *N*-bromosuccinimide in methanol gave 2-methoxy-3-bromoflavanones (**2**). The said reaction[3] of the flavones (**1**) with *N*-bromosuccinimide in ethanol gave 2-ethoxy-3-bromoflavanones (**3**). These flavanones (**2** and **3**), on treatment with alcoholic potassium hydroxide at room temperature easily lost a molecule of alcohol to give the 3-bromoflavones (**5**). The reaction[3] of flavones (**1**) with *N*-bromosuccinimide in acetic acid–acetic anhydride gave good yields of the 2-acetoxy-3-bromoflavanones (**4**). Elimination of acetic acid from these compounds occurred easily. Boiling a solution of 2-acetoxy-3-bromoflavanone (**4**) in methanol gave 3-bromoflavones (**5** ; Scheme 1) whose structures have been confirmed by elemental analysis, ir and pmr spectra. The compounds have been screened for their antibacterial activity.



R = Aryl

Scheme 1

Antibacterial activity : Compounds **5** were screened for antibacterial activity at a concentration of 50 μg by cup-plate method[4] against gram-positive bacteria *Staphylococcus aureus* and gram-negative bacteria *Escherichia coli*. The activity of the compounds was compared with chloromycetin and penicillin G at the same concentration level. The compounds **5** showed strong activity (zone of inhibition, 15–30 mm) against *S. aureus* and medium activity (8–14 mm) against *E. coli*. It is concluded from the results that some of the compounds containing chlorine atom(s) introduced in aryl part of the flavone molecule are active while others possessed moderate activity against both the bacteria. Moreover, the bromine atom in position-3 of flavone enhanced the antibacterial activity.

Experimental

All m.ps. were determined by open capillary method and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 577 spectrophotometer and pmr spectra on a XL-100A (100.1 MHz) spectrometer using TMS as internal reference. The purity of the compounds was checked by tlc.

2-Methoxy-3,8-dibromo-6-nitro-7-n-butoxyflavanone (**2a**) : It was prepared by the reported method[3], (90%), m.p. 146° (Found : C, 45.32 ; H, 3.62 ; N, 2.70. $C_{20}H_{19}O_6NBr_2$ calcd. for : C, 45.37 ; H, 3.59 ; N, 2.65%) ; ν_{max} (KBr) 1 690 (C=O), 1 110 (C–O–C) and 565 cm^{-1} (C–Br) ; δ (TMS ; DMSO-d_6) 7.01–8.03 (6H, m, ArH), 4.40 (1H, s, 3-H) and 3.02 (3H, s, OMe). Similarly, other flavanones (77–92%) were prepared (Table 1).

3,8-Dibromo-6-nitro-7-n-butoxyflavone (**5a**) : It was prepared by the reported method[3], (86%), m.p. 132° (Found : C, 45.82 ; H, 3.10 ; N, 2.85. $C_{19}H_{15}O_5NBr_2$ calcd. for : C, 45.88 ; H, 3.02 ; N, 2.82%) ; ν_{max} (KBr) 1 640 (C=O), 1 560 (C=C), 1 140 (C–O–C) and 560 cm^{-1} (C–Br) ; δ 7.0–7.9 (6H, m, ArH) and the signals due to 3-H and OMe observed in **2a** were found absent in **5a**. Similarly, other 3-bromoflavones (75–92%) were prepared (Table 1).

2-Ethoxy-3,8-dibromo-6-nitro-7-n-butoxyflavanone (**3a**) : It was prepared by the reported method[3], (88%), m.p. 152° (Found : C, 46.36 ; H. 3.82 ; N, 2.64. $C_{21}H_{21}O_6NBr_2$ calcd. for : C, 46.41 ; H, 3.87 ; N, 2.58%) ; ν_{max} (KBr) 1 695 (C=O), 1 115 (C–O–C) and 570 cm^{-1} (C–Br) ; δ 7.0–8.13 (6H, m, ArH), 4.44 (1H, s, 3-H), 3.30 (2H, q, OCH_2CH_3) and 0.9 (3H, t, OCH_2CH_3). Similarly, other flavanones (76–92%) were prepared (Table 1).

3,8-Dibromo-6-nitro-7-n-butoxyflavone (**5a**) : It was prepared by the reported method[3], (92%), m.p. 132°. The crystalline product obtained was identical with the 3-bromoflavone prepared by the previous route. Similarly, other 3-bromoflavones were prepared (Table 1).

† Presented at the 26th Annual Convention of Chemists held at Indore, 1989.

TABLE 1—PHYSICAL DATA OF COMPOUNDS*

Compd. no.	R	Molecular formula	M.p. °C
2a	Phenyl	$C_{20}H_{19}O_6NBr_2$	146
2b	2'-Chlorophenyl	$C_{20}H_{18}O_6NClBr_2$	117
2c	4'-Chlorophenyl	$C_{20}H_{18}O_6NClBr_2$	109
2d	2',4'-Dichlorophenyl	$C_{20}H_{17}O_6NCl_2Br_2$	157
2e	4'-Methylphenyl	$C_{21}H_{21}O_6NBr_2$	175
2f	3',4'-Methylenedioxyphenyl	$C_{21}H_{19}O_8NBr_2$	160
2g	3',4',5'-Trimethoxyphenyl	$C_{23}H_{25}O_9NBr_2$	134
2h	3',4'-Dimethoxyphenyl	$C_{22}H_{23}O_8NBr_2$	111
2i	4'-Methoxyphenyl	$C_{21}H_{21}O_7NBr_2$	125
2j	2'-Methoxyphenyl	$C_{21}H_{21}O_7NBr_2$	105
3a	Phenyl	$C_{21}H_{21}O_6NBr_2$	152
3b	2'-Chlorophenyl	$C_{21}H_{20}O_6NClBr_2$	128
3c	4'-Chlorophenyl	$C_{21}H_{20}O_6NClBr_2$	114
3d	2',4'-Dichlorophenyl	$C_{21}H_{19}O_6NCl_2Br_2$	166
3e	4'-Methylphenyl	$C_{22}H_{23}O_6NBr_2$	133
3f	3',4'-Methylenedioxyphenyl	$C_{22}H_{21}O_8NBr_2$	170
3g	3',4',5'-Trimethoxyphenyl	$C_{24}H_{27}O_9NBr_2$	122
3h	3',4'-Dimethoxyphenyl	$C_{23}H_{25}O_8NBr_2$	155
3i	4'-Methoxyphenyl	$C_{22}H_{23}O_7NBr_2$	148
3j	2'-Methoxyphenyl	$C_{22}H_{23}O_7NBr_2$	117
4a	Phenyl	$C_{21}H_{19}O_7NBr_2$	124
4b	2'-Chlorophenyl	$C_{21}H_{18}O_7NClBr_2$	147
4c	4'-Chlorophenyl	$C_{21}H_{18}O_7NClBr_2$	152
4d	2',4'-Dichlorophenyl	$C_{21}H_{17}O_7NCl_2Br_2$	173
4e	4'-Methylphenyl	$C_{22}H_{21}O_7NBr_2$	160
4f	3',4'-Methylenedioxyphenyl	$C_{22}H_{19}O_9NBr_2$	141
4g	3',4',5'-Trimethoxyphenyl	$C_{24}H_{25}O_{10}NBr_2$	137
4h	3',4'-Dimethoxyphenyl	$C_{23}H_{23}O_9NBr_2$	155
4i	4'-Methoxyphenyl	$C_{22}H_{21}O_8NBr_2$	108
4j	2'-Methoxyphenyl	$C_{22}H_{21}O_8NBr_2$	98
5a	Phenyl	$C_{19}H_{15}O_6NBr_2$	132
5b	2'-Chlorophenyl	$C_{19}H_{14}O_6NClBr_2$	160
5c	4'-Chlorophenyl	$C_{19}H_{14}O_6NClBr_2$	172
5d	2',4'-Dichlorophenyl	$C_{19}H_{13}O_6NCl_2Br_2$	178
5e	4'-Methylphenyl	$C_{20}H_{17}O_6NBr_2$	151
5f	3',4'-Methylenedioxyphenyl	$C_{20}H_{17}O_7NBr_2$	122
5g	3',4',5'-Trimethoxyphenyl	$C_{22}H_{21}O_8NBr_2$	148
5h	3',4'-Dimethoxyphenyl	$C_{21}H_{19}O_7NBr_2$	140
5i	4'-Methoxyphenyl	$C_{20}H_{17}O_6NBr_2$	108
5j	2'-Methoxyphenyl	$C_{20}H_{17}O_6NBr_2$	120

*All compounds gave satisfactory C, H and N analyses.

2-Acetoxy-3,8-dibromo-6-nitro-7-n-butoxyflavanone (**4a**) *:* It was prepared by the reported method[3], (90%), m.p. 124° (Found : C, 45.20 ; H, 3.45 ; N, 2.46. $C_{21}H_{19}O_7NBr_2$ calcd. for : C, 45.24 ; H, 3.41 ; N, 2.51%) ; ν_{max} (KBr) 1 705 (C=O), 1 100 (C−O−C) and 580 cm^{-1} (C−Br) ; δ 7.04−8.01 (6H, m, ArH), 4.5 (1H, s, 3-H) and 1.85 (3H, s, OAc). Similarly, other flavanones (75−92%) were prepared (Table 1).

3,8-Dibromo-6-nitro-7-n-butoxyflavone (**5a**) *:* It was prepared by the reported method[3], (88%), m.p. 132°. The crystalline product was identical with the 3-bromoflavone prepared by the previous two routes. Similarly, other 3-bromoflavones were prepared (Table 1).

Acknowledgement

The author is garteful to the college authority for facilities and thankful to U.G.C., New Delhi, for financial assistance.

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