

PHOTOLYSIS OF 3-BROMOCHROMAN-4-ONES

M. Consuelo Jiménez, Miguel A. Miranda,* and Rosa Tormos

Departamento de Química/Instituto de Tecnología Química
UPV-CSIC, Universidad Politécnica de Valencia, Apartado
22012, E-46071-Valencia, Spain

Abstract- Photolysis of 3-bromochroman-4-ones (**1a-f**) leads to debrominated chromanones (**2a-f**) and chromones (**3a-f**) as major products. Their formation is accounted for in terms of primary cleavage of the carbon halogen bond to give α -carbonyl radicals (**I**) and/or cations (**II**). In the case of the 2,2-disubstituted compounds (**1d-f**), intermediates (**II**) undergo rearrangement with 1,2-shift of the phenyl or benzyl substituent prior to deprotonation. Minor by-products are the pentacyclic pyrone (**4e**) or 2-methylchromone (**3a**) (starting from **1e** and **1f**, respectively).

In connection with our previous studies on the photochemistry of benzopyran-derived compounds,¹⁻⁴ we were interested in the photofragmentation of 3-bromochromanones, as a potential source of the corresponding α -keto radicals and/or cations, which are key intermediates in the electron transfer processes undergone by 4-acetoxychromenes.⁴ Short lived species of this type are also relevant because they are thought to play an important role in some processes of biosynthetic interest in the field of flavonoids, such as the oxidation of the C₃ bridge of flavanones (to afford flavones or flavonols) and the flavone-isoflavone isomerization.^{5,6}

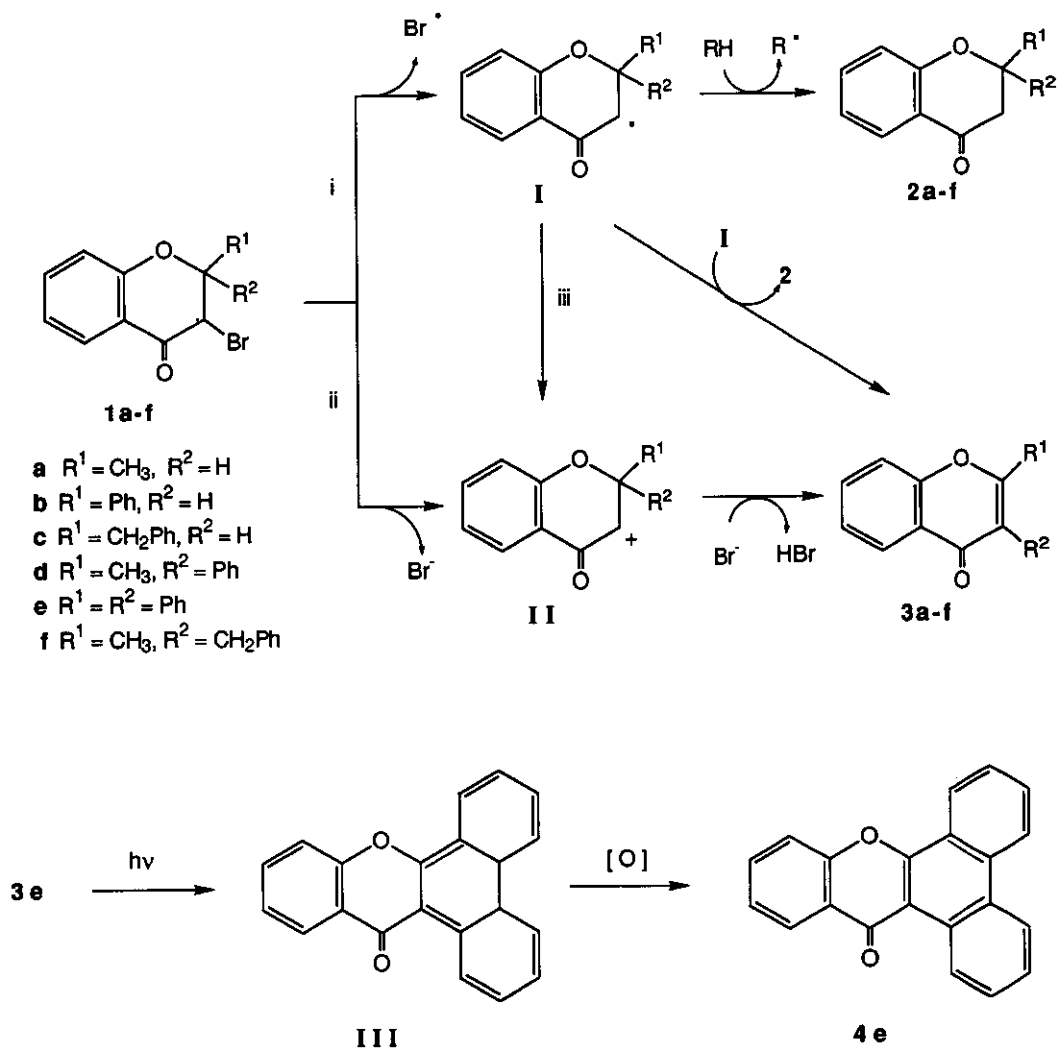
For this purpose, the compounds (1a-c) were selected as substrates. In addition to these 2-substituted derivatives, the 2,2-disubstituted analogues (1d-f) were also studied in order to determine the fate of the reaction when a direct dehydrohalogenation to flavone-like products is prevented.

Bromination of the known chromanones (2a-f)⁷⁻¹⁴ was easily achieved by treatment with bromine in CCl₄ solution. With the exception of 2e, two stereoisomers were obtained. Their relative ratio in the reaction mixtures was determined by gc and ¹H-nmr spectroscopy. For 1d and 1f chromatographic separation of their stereoisomers was achieved by hplc, with characterization purposes. This was not possible in the other cases.

Photolysis of the resulting 3-bromochromanones (stereoisomeric mixtures) was carried out in acetonitrile and acetone, using the Pyrex filtered light of a medium pressure mercury lamp. In general, the conversions were high, except for the flavanone (1b). Reductive dehalogenation to the precursor chromanones (2a-f) was always observed to occur, although the yields were higher when acetone was used as solvent. When the 2-position of the heterocyclic ring was monosubstituted, the corresponding dehydro derivatives (3a-c) were also found in the photomixtures, especially in acetonitrile solution. In the case of the 2,2-disubstituted compounds (1d-f), dehydrohalogenation was accompanied by 1,2-migration of the phenyl or benzyl group. Finally, minor amounts of photofragmentation products (2-methylchromone (3a) and benzyl bromide) or secondary photoreaction products (the pentacyclic pyrone (4e)) were obtained starting from the 3-bromochromanones (1f) or (1e), respectively.

The above results can be rationalized through primary photochemical cleavage of the carbon-halogen bond, to afford radical and/or ion pairs.¹⁵⁻²¹ The latter intermediates can be generated either directly (heterolysis, ii) or by initial homolysis (i) followed by electron transfer (iii). Obviously, routes (ii) and (iii) should be favoured in more polar solvents, like acetonitrile. However, the fact that more flavanone (2b) was obtained in acetone than in cyclohexane (data not

shown) suggested that the multiplicity of the involved excited states also plays some role in the type of product formed. Thus, generation of ion pairs appears to be favoured upon direct irradiation in acetonitrile (higher contribution of the singlet), while it is disfavoured upon triplet photosensitization with acetone.



Scheme 1

Table 1. Photolysis of Compounds (1a-f)

Substrate	Solvent	Conversion (%)	Mass Balance (%)	Products Yield (%)		
				2	3	Others
1 a	Acetonitrile	100	68	18	82	-
	Acetone	100	60	22	78	-
1 b	Acetonitrile	28	81	33	67	-
	Acetone	48	78	68	32	-
1 c	Acetonitrile	96	60	8	92	-
	Acetone	100	55	25	75	-
1 d	Acetonitrile	91	64	33	66	-
	Acetone	100	62	84	16	-
1 e	Acetonitrile	55	72	13	77	10 ^a
	Acetone	100	55	79	17	4 ^a
1 f	Acetonitrile	90	66	31	56	13 ^b
	Acetone	99	61	90	7	3 ^b

^aCompound 4e. ^bCompound 3a together with PhCH₂Br.

In order to determine the origin of hydrogen atoms abstracted in the last step of the radical pathway, irradiation of **1b** was performed in perdeuterated acetonitrile and acetone. No deuterium was incorporated to the obtained flavanone (**2b**), as evidenced by gc-ms analysis. Thus, the hydrogen source must be the substrate itself, partially by means of disproportionation. This also explains the formation of significant amounts of polymers, which results in corresponding reductions of the mass balances (see Table).

Concerning the secondary processes leading to chromones in the ionic pathway, direct deprotonation of the cations (II) obviously occurs with 2-monosubstituted bromo ketones (1a-c). However, the 2,2-disubstituted derivatives must undergo 1,2-migration to the very stable pyrylium cations prior to deprotonation.

Formation of the pentacyclic pyrone (4e) starting from 1e can be accounted for in terms of the well-known stilbene-phenanthrene photocyclization of 2,3-diphenylchromone (3e).²²⁻²³ This was confirmed by independent irradiation of 3e, which afforded 4e as a single product. Finally, formation of benzyl bromide and 2-methylchromone (3a) upon photolysis of 1f formally requires two cleavages (C₃-bromine and C₂-benzyl bonds), as well as combination of the two lost fragments. Most probably, this is a two step reaction with the α -carbonyl cation (II) as an intermediate; however, other routes (including concerted processes) can be envisaged.

EXPERIMENTAL

Melting points are uncorrected. Combustion analyses were performed at the Instituto de Química Bio-Orgánica del Consejo Superior de Investigaciones Científicas (CSIC) in Barcelona. Ir Spectra were determined with a gc/ftir Hewlett-Packard 5965; absorptions (ν , cm⁻¹) are given for all the bands. ¹H-Nmr spectra were recorded in CDCl₃ with a 400 MHz Varian VXR-400S Instrument; chemical shifts are reported as δ (ppm) values relative to TMS. Ms were obtained under electron impact using a Hewlett-Packard 5988A spectrometer; the ratios and relative abundances (in brackets) are given only for the most important peaks. Purification of chromanones (2a-f) and bromochromanones (1a-f) was carried out by column chromatography on silica gel Merck 60 (0.063-0.200 mm), using dichloromethane or mixtures hexane/dichloromethane as eluent.

Preparation of 3-bromo-4-chromanones (1a-f)

A solution of Br₂ (1.0 g, 6.25 mmol) in 30 ml of CCl₄ was added to a well stirred solution of the corresponding 4-chromanone (6.25 mmol) in CCl₄ (30 ml). After 2 h, the reaction mixture was evaporated *in vacuo* and products (1a-f) were isolated by column chromatography.

Irradiations

Solutions of 1a-f (0.06 mmol) in acetonitrile or acetone (2 ml) were irradiated at room temperature in Pyrex test tubes surrounding an immersion well photoreactor equipped with a HQL 125 W medium pressure mercury lamp and a quartz cooling jacket. After 1 h, the photomixtures were analyzed by gc, gc-ms and ¹H-nmr. The structures of the photoproducts were confirmed by comparison with retention times and fragmentation patterns of authentic samples obtained by known procedures.²⁴⁻²⁷

Products

Z-3-Bromo-2-methylchroman-4-one (Z-1a). (45%). Oil. Exact Mass Calcd for C₁₀H₉O₂⁷⁹Br, 239.9786. Found 239.9784; gc/ftir 3082, 2997, 2946, 2854, 1715, 1609, 1466, 1388, 1307, 1230, 1154, 1124, 1024, 958, 882, 757, 633; ¹H-nmr 7.96-6.99 (m, 4H, Ar-H), 4.37 (dq, J_a= 1.7 Hz, J_b= 6.2 Hz, 1H, OCHCH₃), 4.36 (d, J_a= 1.7 Hz, 1H, COCHBr), 1.59 (d, J_b= 6.2 Hz, 3H, CH₃); ms 240 (17), 161 (31), 121 (19), 120 (100), 115 (6), 105 (6), 92 (23), 65 (6), 63 (10).

E-3-Bromo-2-methylchroman-4-one (E-1a). (15%). Oil. Exact Mass Calcd for C₁₀H₉O₂⁷⁹Br, 239.9786. Found 239.9789; gc/ftir 3082, 2990, 2943, 2891, 1715, 1609, 1466, 1387, 1297, 1229, 1151, 1123, 1070, 951, 759, 631; ¹H-nmr 7.96-6.99 (m, 4H, Ar-H), 4.71 (dq, J_a= 8.1 Hz, J_b= 6.5 Hz, 1H, OCHCH₃), 4.52 (d, J_a= 8.1 Hz, 1H, COCHBr), 1.63 (d, J_b= 6.5 Hz, 3H, CH₃); ms 240 (9), 161 (37), 121 (17), 120 (100), 117 (8), 115 (8), 105 (8), 92 (27), 64 (10), 63 (14).

Z-2-Benzyl-3-bromochroman-4-one (Z-1c). (32%). Oil. Exact Mass Calcd for $C_{17}H_{15}O_2^{79}Br$, 315.9922. Found 315.9826; gc/ftir 3075, 3036, 2937, 2851, 1714, 1607, 1467, 1306, 1227, 1149, 1116, 1039, 959, 864, 757. 1H -nmr 7.96-7.00 (m, 9H, Ar-H), 4.83 (dt, $J=6.9$ Hz, 1H, $OCHCH_2$), 4.50 (d, $J=6.9$ Hz, 1H, $COCHBr$), 3.30 (m, 2H, CH_2); ms 318 (100), 316 (94), 237 (24), 209 (21), 146 (22), 121 (24), 120 (68), 118 (25), 115 (34), 91 (16).

E-2-Benzyl-3-bromochroman-4-one (E-1c). (14%). Oil. Exact Mass Calcd for $C_{17}H_{15}O_2^{79}Br$, 315.9922. Found 315.9807; gc/ftir 3076, 3037, 2970, 2935, 1714, 1608, 1465, 1366, 1299, 1225, 1147, 1112, 1032, 756, 700, 629; 1H -nmr 7.96-7.00 (m, 9H, Ar-H), 4.34 (ddd, $J_a=1.5$ Hz, $J_b=5.8$ Hz, $J_c=8.5$ Hz, 1H, $OCHCH_2$ 1H, $COCHBr$); ms 318 (100), 316 (90), 237 (46), 290 (10), 146 (25), 121 (17), 120 (38), 118 (23), 115 (32), 91 (22).

Z-2-Benzyl-3-bromo-2-methylchroman-4-one (Z-1f). (38%). Oil. Anal. Calcd for $C_{17}H_{15}O_2Br$: C, 61.65; H, 4.56. Found: C, 61.45; H, 4.64; gc/ftir 3075, 3038, 2991, 2937, 1714, 1609, 1583, 1465, 1385, 1306, 1231, 1145, 1114, 1051, 937, 757, 703, 638; 1H -nmr: 7.00-7.93 (m, 9H, Ar-H), 4.33 (s, 1H, $COCHBr$), 3.34 (d, $J=12.4$ Hz, 1H, CH_2Ar), 3.26 (d, $J=12.4$ Hz, 1H, CH_2Ar), 1.35 (s, 3H, CH_3); ms 332 (1), 330 (1), 251 (11), 241 (20), 239 (22), 161 (44), 160 (64), 131 (12), 121 (36), 120 (21), 115 (12), 92 (30), 91 (100), 65 (16).

E-2-Benzyl-3-bromo-2-methylchroman-4-one (E-1f). (54%). Oil. Anal. Calcd for $C_{17}H_{15}O_2Br$: C, 61.65; H, 4.56. Found: C, 61.49; H, 4.56; gc/ftir 3075, 3039, 2993, 2945, 1714, 1608, 1465, 1386, 1306, 1234, 1112, 1050, 958, 755, 702, 635; 1H -nmr 7.00-7.96 (m, 9H, Ar-H), 4.50 (s, 1H, $COCHBr$), 3.22 (d, $J=14.0$ Hz, 1H, CH_2Ar), 3.01 (d, $J=14.0$ Hz, 1H, CH_2Ar), 1.55 (s, 3H, CH_3); ms 332 (1), 330 (1), 251 (10), 241 (19), 239 (20), 161 (93), 160 (53), 131 (11), 121 (26), 120 (15), 115 (10), 92 (27), 91 (100), 65 (14).

Z-3-Bromo-2-methyl-2-phenylchroman-4-one (Z-1d). (30%). Oil. Anal. Calcd for $C_{16}H_{13}O_2Br$: C, 60.59; H, 4.13; Found: C, 60.51; H, 4.08; gc/ftir 3075, 2991, 1714, 1610, 1581, 1465, 1381, 1307, 1236, 1146, 1116, 1048, 950, 911, 757, 697, 640;

^1H -nmr 6.92-7.97 (m, 9H, Ar-H), 4.65 (s, 1H, COCHBr), 1.75 (s, 3H, CH₃); ms 318 (19), 316 (21), 303 (50), 301 (47), 238 (34), 237 (100), 198 (24), 196 (26), 121 (41), 120 (53), 115 (48), 92 (51), 91 (30).

E-3-Bromo-2-methyl-2-phenylchroman-4-one (*E*-1d), (50%). Oil. Anal. Calcd for C₁₆H₁₃O₂Br: C, 60.59; H, 4.13; Found: C, 60.64; H, 4.10; gc/ftir 3076, 3007, 2946, 1715, 1610, 1463, 1382, 1308, 1237, 1121, 1044, 956, 904, 717, 697, 639, 590; ^1H -nmr 6.98-7.76 (m, 9H, Ar-H), 5.03 (s, 1H, CHBr), 1.89 (s, 3H, CH₃); ms 319 (6), 318 (16), 317 (11), 316 (18), 303 (51), 301 (53), 237 (100), 198 (38), 196 (41), 121 (46), 120 (60), 115 (58), 92 (62), 91 (34).

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