Mass Spectra of 3-Nitro-2*H*-chromenes and 3-Nitrochromans

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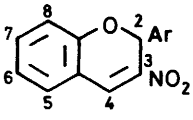
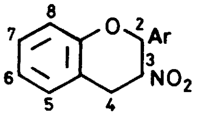
The 4 kV, 70 eV electron impact mass spectra (e.i.-m.s.) of eight 2-aryl-3-nitro-2*H*-chromenes and ten 2-aryl-3-nitrochromans of diverse functionality are reported and discussed. The peak due to the molecular ion is always appreciable and often intense in these spectra. Loss of NO_2 from $M^{+\cdot}$ is responsible for the base peak in the nitrochromene spectra. In contrast, $[M - HNO_2]^{+\cdot}$ is more abundant than $[M - NO_2]^+$ in the spectra of the nitrochromans; furthermore, this unusual HNO_2 loss persists even for metastable molecular ions. A diagnostically important ion, of nominal structure $[ArCH_2]^+$, accounts for the base peak in the chroman spectra; this ion, which defines the formula of the 2-aryl substituent, corresponds to elimination of benzofuran from $[M - NO_2]^+$.

All the compounds studied exhibited $[M]^{-\cdot}$ ions in their electron capture negative ion chemical ionisation (c.i.) spectra. Apart from $[M]^{-\cdot}$ and the base peak at $[M - NO_2]^-$, few ions were of considerable abundance in these spectra, although $[NO_2]^-$ ions were present in the nitrochroman series.

3-Nitro-2*H*-chromenes (**A**) constitute a class of biologically active oxygen heterocycles.[1–3] These compounds are conveniently synthesised by the condensation of *o*-hydroxybenzaldehydes with β-nitrostyrenes, in the presence of basic alumina, using sonic acceleration.[4] Interest in nitro-2*H*-chromenes reflects the reported[5] radioprotective properties of chromenes containing electron-attracting substituents at the 3-position. The corresponding saturated analogues, 3-nitrochromans (**B**), were first prepared only very recently by the reduction of 3-nitrochromenes with sodium borohydride in methanol–tetrahydrofuran.[6] In view of the biological activity of the 2*H*-chromenes and the novelty of the chromans, a study of the mass spectra (m.s.) of these heterocycles is timely.



(**A**)



(**B**)

Results and Discussion

The 4 kV, 70 eV e.i.-m.s. of eight 2-aryl-3-nitro-2*H*-chromenes and ten 2-aryl-3-nitrochromans are given in Tables 1 and 2, respectively. All the compounds show significant molecular ions, but the spectra of the 2*H*-chromenes and chromans contain many differences which are apparent on careful inspection.

First, the intensity of the molecular ion peak is greater for the 2*H*-chromenes than is the case in the analogous chromans. Thus, the relative abundances of $[M]^{+\cdot}$ in the spectra of the corresponding pairs (**1**) and (**9**), (**2**) and (**10**), (**3**) and (**12**), and (**4**) and (**13**) are 41 and 18, 45 and 28, 30 and 9, and 21 and 9%, respectively. This trend probably reflects a real difference in the stability of the ionised molecules, with respect to fragmentation, because the percentage of the total ion current carried by $[M]^{+\cdot}$ is systematically higher for chromenes (typically 3—8%) than for the analogous chromans (typically 1—5%). The relative abundance of $[M^{+\cdot}]$ in both classes of heterocycle is increased by the presence of electron-rich alkoxy substituents in the 2-aryl group or at the 8-position, but it is reduced by substitution of a 2-naphthyl group for the 2-phenyl group.

Loss of $^{\cdot}OH$ from $[M^{+\cdot}]$ produces only a small peak in the spectra of nitro-2*H*-chromenes and nitrochromans. This reaction, which is often of importance for ionised nitro compounds,[7] is of marginally greater significance in the nitrochromene series. Moreover, at the low internal energies appropriate to the decomposition of metastable ions,[8,9] $^{\cdot}OH$ elimination becomes the dominant reaction of ionised nitrochromenes. The corresponding nitrochroman radical-cations do not expel $^{\cdot}OH$ to any appreciable extent in metastable transitions.

A third difference between the spectra of nitro-2*H*-chromenes and nitrochromans concerns the intensity of the peaks produced by NO_2 and HNO_2 loss from $[M^{+\cdot}]$. The base peak in the spectra of each of the eight nitrochromenes is $[M - NO_2]^+$; only a much smaller peak is present at $[M - HNO_2]^{+\cdot}$, although there is often a peak at $[M - NO_2 - H_2]^+$ of sizeable intensity. In contrast, $[M - HNO_2]^{+\cdot}$ is the most abundant of the group of three ions at $[M - NO_2]^+$, $[M - HNO_2]^{+\cdot}$, and $[M - NO_2 - H_2]^+$ in the spectra of the nitrochromans. However, even in the cases of (**9**) and (**10**), $[M - HNO_2]^{+\cdot}$ is not the most abundant ion in the spectrum, though it rivals the base peak in intensity. The intensity of the peak at $[M - HNO_2]^{+\cdot}$ declines sharply on progressing to the 2-naphthyl-3-nitrochromans, or on adding substituents at the 6- or 8-position. Nevertheless, loss of HNO_2 remains of importance at low internal energies, as evidenced by the appearance of a metastable peak for the process $[M]^{+\cdot} \longrightarrow [M - HNO_2]^{+\cdot}$. This reaction is rare for ionised nitro compounds. It seems likely that HONO, rather than HNO_2, is lost, see equation (1). Hydrogen transfer from the 2-position of the ionised chroman (**19**) to the nitro group, leads to the stabilised cation-radical (**20**); expulsion of HONO from (**20**) produces an extremely stable daughter ion (**21**). This hypothesis is supported by the behaviour of the deuterium-labelled analogue (**22**) which expels specifically $[HNO_2]$ in metastable transitions, see equation (2). The only plausible alternative mechanism would involve hydrogen abstraction from the 4-position, but this would not yield a daughter ion having the stabilising structural features of (**24**).

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Table 1. 70 eV, 4 kV E.i.-m.s. of 2*H*-chromenes

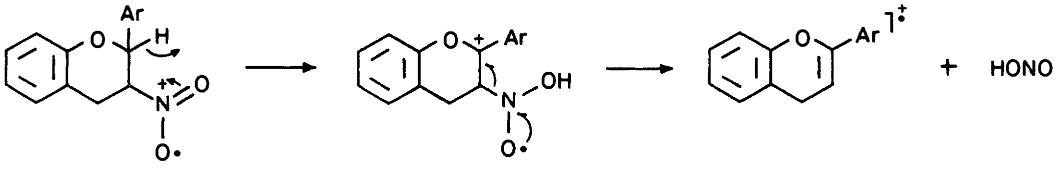
Compound	*m*/*z* and relative abundance[a]
3-Nitro-2-phenyl-2*H*-chromene (**1**)	254 (7%), 253 $[M^{+\cdot}]$ (41), 236 (19), 208 (16), 207 (100), 206 (30), 205 (12), 179 (19), 178 (74), 177 (16), 176 (28), 152 (15), 89 (16)
2-(4-Isopropylphenyl)-3-nitro-2*H*-chromene (**2**)	296 (10%), 295 $[M^{+\cdot}]$ (45), 278 (22), 250 (49), 249 (100), 248 (18), 235 (18), 234 (71), 233 (68), 220 (15), 207 (28), 205 (24), 179 (21), 178 (29), 176 (29)
2-(1-Naphthyl)-3-nitro-2*H*-chromene (**3**)	304 (4%), 303 $[M^{+\cdot}]$ (30), 258 (20), 257 (100), 256 (24), 255 (58), 229 (40), 228 (28), 227 (18), 226 (22)
2-(2-Naphthyl)-3-nitro-2*H*-chromene (**4**)	304 (4%), 303 $[M^{+\cdot}]$ (21), 258 (23), 257 (100), 256 (19), 255 (30), 249 (15), 229 (26), 228 (33), 227 (16), 226 (24)
2-(3,4-Diethoxyphenyl)-8-methoxy-3-nitro-2*H*-chromene (**5**)	372 (24%), 371 $[M^{+\cdot}]$ (84), 326 (35), 325 (100), 298 (15), 297 (72), 281 (19), 269 (39), 268 (20), 253 (16), 252 (18), 206 (28), 152 (20), 115 (16)
8-Methoxy-2-(1-naphthyl)-3-nitro-2*H*-chromene (**6**)	334 (11%), 333 $[M^{+\cdot}]$ (50), 316 (17), 288 (24), 287 (100), 286 (30), 285 (41), 272 (27), 271 (70), 259 (25), 255 (23), 244 (26), 243 (22), 228 (17), 227 (15), 226 (17), 216 (22), 215 (67), 213 (18), 189 (41), 165 (16), 152 (23), 107 (37)
6-Chloro-2-(1-naphthyl)-3-nitro-2*H*-chromene (**7**)	340 (2%), 339 (10), 338 (7), 337 $[M^{+\cdot}]$ (30), 293 (27), 292 (26), 291 (97), 290 (28), 289 (56), 256 (68), 255 (100), 228 (40), 227 (28), 226 (62), 223 (15), 128 (19), 113 (50), 101 (18)
3,6-Dinitro-2-phenyl-2*H*-chromene (**8**)	299 (5%), 298 $[M^{+\cdot}]$ (23), 281 (37), 253 (18), 252 (100), 251 (30), 207 (14), 206 (85), 205 (34), 178 (20), 177 (25), 176 (31), 165 (18), 152 (23), 151 (16), 102 (15), 76 (16)

[a] Abundances normalised to a value of 100 units for the base peak; ions of relative abundance below 15 units generally were omitted.

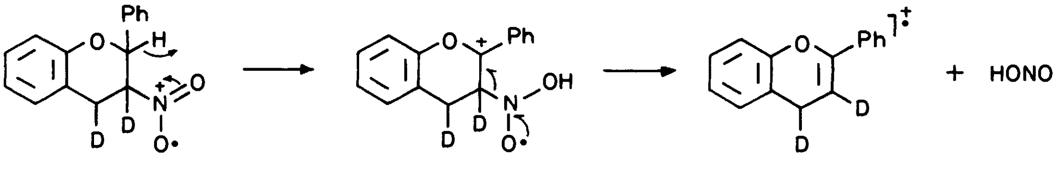
Table 2. 70 eV, 4 kV E.i.-m.s. of chromans

Compound	*m*/*z* and relative abundance[a]
3-Nitro-2-phenylchroman (**9**)	256 (3%), 255 $[M^{+\cdot}]$ (18), 209 (20), 208 (95), 207 (86), 131 (38), 115 (25), 91 (100), 78 (15), 77 (27)
2-(4-Isopropylphenyl)-3-nitrochroman (**10**)	298 (6%), 297 $[M^{+\cdot}]$ (28), 251 (29), 250 (97), 249 (64), 235 (26), 208 (17), 207 (70), 134 (15), 133 (100), 131 (37), 118 (40), 117 (30), 115 (33), 107 (19), 105 (36), 103 (15), 91 (39), 77 (29)
8-Methoxy-3-nitro-2-phenylchroman (**11**)	286 (8%), 285 $[M^{+\cdot}]$ (48), 239 (11), 238 (43), 237 (23), 149 (21), 136 (15), 115 (19), 91 (100), 77 (14)
2-(1-Naphthyl)-3-nitrochroman (**12**)	306 (2%), 305 $[M^{+\cdot}]$ (9), 258 (27), 257 (13), 165 (30), 152 (21), 141 (100), 131 (16), 128 (19), 127 (19), 107 (33), 77 (14)
2-(2-Naphthyl)-3-nitrochroman (**13**)	306 (2%), 305 $[M^{+\cdot}]$ (9), 259 (14), 258 (57), 257 (27), 165 (15), 156 (18), 155 (20), 141 (100), 131 (19), 127 (27)
2-(3,4-Diethoxyphenyl)-3-nitrochroman (**14**)	344 (13%), 345 $[M^{+\cdot}]$ (55), 297 (10), 296 (34), 239 (15), 180 (14), 179 (100), 165 (19), 152 (18), 151 (94), 131 (73), 123 (90), 118 (21), 107 (16), 77 (28)
6-Chloro-3-nitro-2-phenylchroman (**15**)	291 (2%), 290 (1), 289 $[M^{+\cdot}]$ (6), 244 (7), 243 (9), 242 (20), 241 (16), 91 (100), 89 (17), 77 (20)
8-Methoxy-2-(1-naphthyl)-3-nitrochroman (**16**)	336 (3%), 335 $[M^{+\cdot}]$ (14), 289 (4), 288 (9), 165 (22), 152 (18), 141 (100), 137 (19), 91 (32)
2-Nitro-3-phenyl-2,3-dihydro-1*H*-benzo[*h*]chromene (**17**)	306 (3%), 305 $[M^{+\cdot}]$ (18), 259 (14), 258 (62), 257 (35), 181 (38), 152 (15), 128 (29), 115 (37), 91 (100), 77 (21)
2-Nitro-3-(1-naphthyl)-2,3-dihydro-1*H*-benzo[*h*]chromene (**18**)	356 (6%), 355 $[M^{+\cdot}]$ (24), 309 (11), 308 (44), 307 (17), 181 (19), 165 (48), 153 (24), 152 (42), 141 (100), 128 (23), 127 (17), 115 (17)

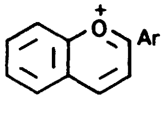
[a] For significance of footnote, see Table 1.



(**19**) (**20**) (**21**) (1)



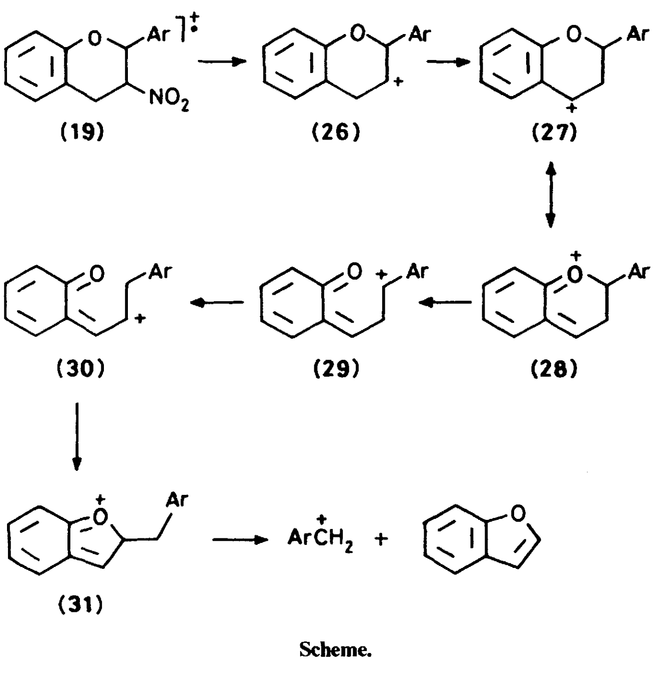
(**22**) (**23**) (**24**) (2)



(25)

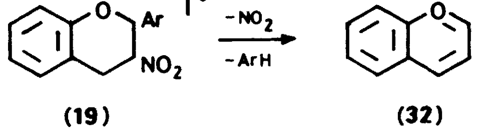
Elimination of a hydrogen radical from $[M - HNO_2]^{+\cdot}$ would lead to the formation of the benzopyrylium cation (**25**), which would be expected to be extremely stable. However, other routes to the ion at $[M - H_2 - NO_2]^+$ are possible, including H_2 loss from $[M - NO_2]^+$. Despite this uncertainty, the greater abundance of the ions at $[M - HNO_2]^{+\cdot}$ and $[M - H_2 - NO_2]^+$ in the spectra of the chromans can be interpreted in terms of the enhanced stability of these ions compared with the corresponding species in the 2*H*-chromene spectra.

The fourth contrast between the spectra of the 2*H*-chromenes and those of the chromans is the appearance of a structurally informative ion of nominal structure $[ArCH_2]^+$ as the base peak in the spectra of the chromans. The constitution of this ion as $[ArCH_2]^+$ was confirmed by accurate mass measurements at high resolving power. Consequently, the formula of the 2-aryl substituent in these nitrochromans is defined by this peak. A possible mechanism for production of the ion at $[ArCH_2]^+$ is given in the Scheme. Following NO_2 loss from (**19**) the derived ion (**26**) undergoes a hydride shift to form the stabilised ion (**27**) ⟷ (**28**). Ring opening of (**28**) to (**29**), and a subsequent hydride shift leads to (**30**), which cyclises to (**31**); cleavage of the exocyclic C–C bond in (**31**) then results in expulsion of benzofuran and the formation of $[ArCH_2]^+$. Other mechanisms are feasible, including a modification of the Scheme to allow for production of the isomeric tropylium cation as the daughter ion. When 3,4-dideuterio-3-nitro-2-phenylchroman was investigated, the relative abundances of the ions at *m*/*z* 91, 92, and 93 were 15:100:18%. The preponderance of $C_7H_6D^+$ (*m*/*z* 92) can be explained using the Scheme on the assumption that the hydride (or deuteri-ide) shifts are largely irreversible. In the absence of an isotope effect, the expected relative abundances of *m*/*z* 91, 92, and 93 are 33:100:8%; thus, it would seem that some exchange of hydrogen and deuterium atoms occurs prior to the formation of these ions. Unfortunately, it was not possible to probe this process more deeply by investigating metastable ions because the reaction did not give rise to a significant metastable peak. Consequently, the possibility that the $[ArCH_2]^+$ ion arises by another mechanism cannot be rigorously excluded. Notwithstanding this limitation, it is logical to associate the $[ArCH_2]^+$ peak with benzofuran loss from $[M - NO_2]^+$. The absence of a comparable peak in the nitrochromene spectra would be expected since there is no parallel mechanism for its formation by expulsion of a stable neutral species from $[M - NO_2]^+$.



Scheme.

A fifth distinction between the spectra of the 2*H*-chromenes and the chromans is the presence of an ion at $[M - (NO_2 + ArH)]^+$ for some nitrochromans. This ion, which is of only occasional importance [for example, *m*/*z* 131 in the spectrum of (**14**) at a relative abundance of 73%], is probably produced by consecutive loss of NO_2 and ArH. The likely structure of the daughter ion is the benzopyrylium cation (**32**), see equation (3).



(19) **(32)** (3)

In the benzochroman series, the peak corresponding to this dissociation appears at *m*/*z* 181, as would be predicted on the basis of the shift rule.[10,11] However, the abundance of these $[M - (NO_2 + ArH)]^+$ ions is not always sufficiently high to permit their use as reliable source of structural information.

Similar remarks apply to the ion which is present at $[M - HNO_2 - CO]^+$ in the spectra of a number of 2*H*-chromenes. This peak is very intense (74% relative intensity) in the spectrum of (**1**); it persists at reduced importance in the spectra of the 2-(4-isopropylphenyl) and 2-(naphthyl) compounds (15—33%), but it is of only minor significance in the spectra of the remaining chromenes. Loss of CO from $[M - HNO_2]^+$ clearly requires extensive rearrangement; this reaction presumably competes effectively with more direct dissociations because it produces very stable daughter ions. In the case of the parent chromene (**1**) likely structures for the resultant $[C_{14}H_{10}]^{+\cdot}$ ions are ionised anthracene, phenanthrene, or 1,2-diphenylacetylene. However, the present data do not allow the mechanism of this unusual process to be defined. The corresponding chromans do not show appreciable $[M - HNO_2 - CO]^+$ ions in their spectra. This contrast between the spectra of the 2*H*-chromenes and chromans is particularly striking for the 2-phenyl derivatives (Figure), but it is less obvious for the higher homologues.

Other interesting features in the mass spectra include the successive loss of two NO_2 groups from the ionised dinitro-2*H*-chromene (**8**) and the elimination of HCl from $[M - NO_2]^+$ in the spectrum of the chloronitro-2*H*-chromene (**7**). The former process constitutes a violation[12] of the even-electron rule;[13] however, consecutive loss of NO_2 radicals from ionised dinitro compounds is not particularly unusual. In addition, there are the characteristic successive losses of neutral species having a mass of 28 daltons (C_2H_4, by accurate mass measurement at high resolution) from fragments containing the diethoxyphenyl substituent in the spectra of (**5**) and (**14**). In the case of (**14**), these peaks [*m*/*z* 151 (94%) and 123 (90%)] provide further information on the nature of the 2-aryl group, whose gross structure is defined by the $[ArCH_2]^+$ peak at *m*/*z* 179. Apart from these instances, there are relatively few fragmentations of high abundance which are associated with the presence of specific functional groups in the nitrochromenes or nitrochromans.

The electron-attracting nature of the nitro group would be expected to make the nitro-2*H*-chromenes and nitrochromans

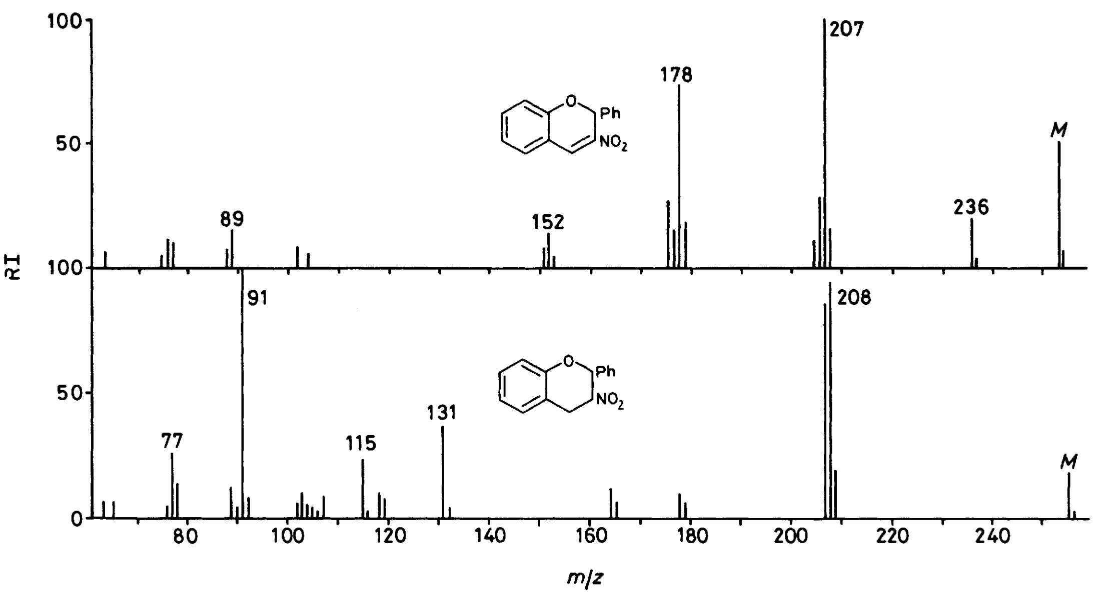


Figure.

yield abundant $[M]^{-\bullet}$ ions by electron capture, at a high level of sensitivity, when subjected to negative ion chemical ionisation.[14] This expectation was fully realised when ammonia was employed as the buffer gas. The resultant electron attachment spectra contain $[M]^{-\bullet}$ peaks of moderate abundance (typically 10—20%) and intense signals corresponding to $[M - NO_2]^-$ as the base peak. Ions other than $[M]^{-\bullet}$ and $[M - NO_2]^-$ (or related ions, such as $[M - HNO_2]^{-\bullet}$, at very similar *m*/*z*) are rare. However, some loss of CH_2O occurs from $[M]^{-\bullet}$ and $[M - NO_2]^-$ in the spectrum of the methoxynitro-2*H*-chromene (**6**). The only major difference between the spectra of the 2*H*-chromenes and chromans is the appearance of a significant peak at *m*/*z* 46 $[NO_2]^-$ in the nitrochroman spectra. This divergence of behaviour could reflect the greater ability of $[M - NO_2]$ to retain the electron in the unsaturated series, perhaps because the charge is formally located in an sp^2 orbital, rather than in an sp^3 orbital as is necessary in the chroman series. The abundance of $[NO_2]^-$ in the nitrochroman spectra is occasionally very high, and some peaks arising from $[NO_2]^-$ attachment to the parent nitrochroman can appear in these circumstances.

Conclusion

3-Nitro-2*H*-chromenes and 3-nitrochromans are amenable to analysis by mass spectrometry. Electron impact and electron capture spectra give complementary information on both types of compound. Several characteristic fragmentations exist in the electron impact spectra, and there are clear differences between the behaviour of nitrochromenes and nitrochromans under these conditions. Unambiguous determination of the molecular masses of these heterocycles can be achieved using either electron impact or electron capture mass spectrometry.

Experimental

The syntheses of the compounds studied in this work have been described previously.[4,6] 3,4-Dideuterio-3-nitro-2-phenylchroman was prepared by reduction of 3-nitro-2-phenyl-2*H*-chromene with $NaBD_4$ in CH_3OD–tetrahydrofuran. All compounds had satisfactory analytical and spectroscopic properties.

Mass spectra were recorded using a KRATOS MS80 double-focusing mass spectrometer operating at an accelerating voltage of 4 kV. Electron impact spectra were obtained by ionisation with 70 eV electrons at a source pressure of *ca.* 2×10^{-6} Torr. Electron capture spectra were obtained by introduction of the sample into a plasma of 'thermalised' electrons with ammonia as the buffer gas at a total source pressure of *ca.* 1 Torr.

Acknowledgements

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