J. Indian Chem. Soc.,
Vol. LXI, November, December 1984, pp. 996-997

Syntheses of 3-Bromochromones

A. K. D. MAZUMDAR, G. C. SAHA, T. K. SINHA and K. D. BANERJI*

Chemical Laboratory, Bhagalpur University, Bhagalpur-812 007

Fifteen 3-bromochromones have been prepared by brominating the corresponding hydroxyaroyl aroyl/heteroyl methanes and cyclization. Direct bromination of chromones to yield 3-bromochromones has been studied by three different reagents, (i) bromine, (ii) *N*-bromosuccinimide and (iii) cupric bromide. Cupric bromide gives the best result. The chromone structures have been established by analysis, spectral data and their conversion to the corresponding coumaran-3-ones.

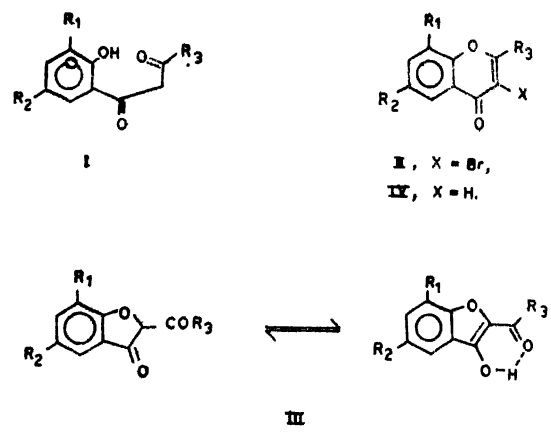
BROMINATION of chromones using bromine in different solvents produce 3-bromochromones but the products are contaminated with other derivatives and the yields are not very satisfactory. Prior to 1978, *N*-bromosuccinimide has been used to brominate 2-methylchromones by two sets of workers[1,2]. A reinvestigation by Rastogi *et al.*[3] showed that the 3-bromochromone is the major product and two other isomeric compounds are often simultaneously produced. Wadodkar and Doifode[4] have recently converted 2-hydroxybenzoylbenzoylmethanes into 3-bromochromones by brominating the diketones using molecular bromine and dioxane when the intermediate bromo derivatives get directly converted into 3-bromochromones.

Since these authors have used only six diketones of the type $R_1COCH_2COR_2$ (where R_1 and R_2 are both benzenoid) it was considered worthwhile to investigate if the route is of general application. For the purpose five diketones were chosen, where R_1 and R_2 are both aromatic, while in ten others the R_2 moiety is either furyl or thineyl (Chart 1)

All the fifteen diketones **I** (**a-o**) were brominated with bromine in dioxane at room temperature and gave the corresponding 3-bromochromones, **II** (**a-o**), in 60-80% yield. All the 3-bromochromones were analysed correctly for carbon and hydrogen. The 3-bromochromones, on refluxing with alcoholic KOH, easily gave the 2-aroyl (**III, a-e**) or 2-heteroyl (**III, f-o**) coumaran-3-ones.

The coumaran-3-ones (**III**) were found to be identical with samples prepared by earlier workers[5,6] in this laboratory and whose structures had thoroughly been established by elemental analysis, chemical properties, ir and pmr data. Chromones and their heterocyclic analogues invariably show signal[7] for the proton at 3-position δ 6.63-6.67, which is indeed characteristic of chromones. In the 3-bromochromones this proton signal was missing, thus confirming the structure of 3-bromochromones.

The study was extended to find how far it was possible to prepare satisfactorily 3-bromo derivatives directly from the chromones or their heterocyclic analogues. The latter set of compounds are prone to substitution by bromine while in chromones the



I

II, X = Br,
IV, X = H.

III

Chart 1

a R_1=CH$_3$, R_2=Br, R_3=4′-Bromophenyl
b R_1=H, R_2=CH$_3$, R_3=4′-Bromophenyl
c R_1=Br, R_2=CH$_3$, R_3=4′-Bromophenyl
d R_1=H, R_2=Cl, R_3=4′-Bromophenyl
e R_1=Br, R_2=Cl, R_3=4′-Bromophenyl
f R_1=CH$_3$, R_2=Br, R_3=2-Furyl
g R_1=H, R_2=CH$_3$, R_3=2-Furyl
h R_1=Br, R_2=CH$_3$, R_3=2-Furyl
i R_1=H, R_2=Cl, R_3=2-Furyl
j R_1=Br, R_2=Cl, R_3=2-Furyl
k R_1=CH$_3$, R_2=Br, R_3=2-Thienyl
l R_1=H, R_2=CH$_3$, R_3=2-Thienyl
m R_1=Br, R_2=CH$_3$, R_3=2-Thienyl
n R_1=H, R_2=Cl, R_3=2-Thienyl
o R_1=Br, R_2=Cl, R_3=2-Thienyl

substituent in benzenoid ring at 2-position may affect the course of bromination. Bromination of fifteen chromones (**IV, a-o**), therefore, was undertaken and the substituent at 2-position was varied from phenyl to furyl to thienyl. Three brominating agents were used, namely (i) bromine in acetic acid, (ii) NBS in chloroform and (iii) cupric bromide.

Bromination using bromine invariably gave products which were gummy masses and from which crystals were difficult to obtain. This route, therefore, did not seem to be of much use from preparative point of view and was not investigated further.

Bromination by NBS gave the bromo derivatives in 50-70% yield, except in the case of 8-methyl-6-bromo-2-(2′-furyl)chromone, where the yield was *ca* 40%.

Cupric bromide has been used as a brominating agent in this laboratory and elsewhere[8], for brominating hydroxyacetophenones, coumarins[9] with good results but the reagent has not so far been used in this area. Addition of chromones, IV(a-o) to a refluxing solution of cupric bromide in dry ethyl acetate-chloroform and continuation of refluxing for several hours gave the 3-bromochromones in 50-80% yield. However, if a furan ring is present at 2-position of the chromone the yield is generally lower (*ca* 40%). In the pmr spectra, the chromone protons at 3-position show in the region δ 6.63 to 6.68, the furyl protons in the region 6.60 to 7.61, the thienyl protons in the region 7.15 to 7.75 and the benzenoid protons in the region 7.40 to 8.10.

Experimental

Melting points were recorded in open capillary and are uncorrected. The ir spectra were recorded in Beckman IR-20 spectrophotometer, using KBr or nujol mull.

3-Bromochromones (II) *:* (Procedure A). The diketone[7] (I, 0.01 mol) was dissolved in anhydrous dioxane (20 ml) and molecular bromine (0.05 ml) was added to the stirred solution in drops. Stirring was continued for 3 h. The reaction mixture on pouring in a large volume of water yielded a white precipitate, which was filtered, washed and crystallised from suitable solvent (Table 1).

Preparation of 3-bromochromones (II) *by bromination of chromones* IV *:* (Procedure B). To a solution of chromone IV[7] (0.01 mol) in chloroform (25 ml), *N*-bromosuccinimide (0.01 mol) was added. The mixture was refluxed for 12 h. A further amount of NBS (0.004 mol) was added over a period of 4 h, followed by refluxing for another 20 h. The mixture was then filtered and concentrated. The crystals, thus obtained, were filtered, washed and recrystallised (Table 1).

Procedure C : To a solution of cupric bromide (1 g) in ethyl acetate-chloroform mixture (2 : 1) was added chromone IV(a-o) (0.3 mol) and the solution was refluxed for 4-12 h. The grey-white precipitate of cuprous bromide, thus obtained, was filtered and the filtrate was evaporated to dryness. The solid residue, thus obtained, was crystallised. In some cases, a gummy mass was obtained which was extracted with benzene and passed over silica gel. The resulting solution was evaporated to dryness and the residue was crystallised (Table 1).

TABLE 1—3-BROMOCHROMONES (II)*

Compd. no.	M.p. °C	Solvent of crystallisation	Yield % A	B	C
a	171-72	Acetic acid	70	60	62
b	198-99	Acetic acid	76	70	75
c	211-12	Acetic acid	75	75	81
d	191-92	Acetic acid	78	70	76
e	198	Acetic acid	83	78	80
f	163-64	Acetic acid	63	49	42
g	133	Ethanol	69	58	50
h	193-95	Methanol	65	62	52
i	174-75	Methanol	62	60	55
j	148-49	Methanol	72	61	56
k	198-99	Ethanol	62	58	60
l	246-47	Ethanol	68	68	63
m	268-69	Ethanol	72	72	65
n	198-99	Ethanol	65	65	75
o	268-69	Ethanol	76	76	72

* Satisfactory C and H analyses, ν_{max} 1625-1645 cm^{-1} (C=O).

Preparation of 2-aroyl- or 2-heteroyl-coumaran-3-ones (III)[5,6] *:* A 3-bromochromone II(a-o) (0.01 mol) was dissolved in ethanol (30 ml) and ethanolic KOH (10 ml, 25%) was added to it. The mixture was gently refluxed for 2 h. The solution was then poured over ice-cold HCl (2 *N*). The solid, thus obtained, was filtered, washed and crystallised. The yields of III(a-o) were in the range of 70-90%.

Acknowledgement

The authors express their deep sense of indebtedness to Prof. J. N. Chatterjea, Patna University for his valuable suggestion and fruitful discussion and to the authorities of Bhagalpur University for facilities.

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