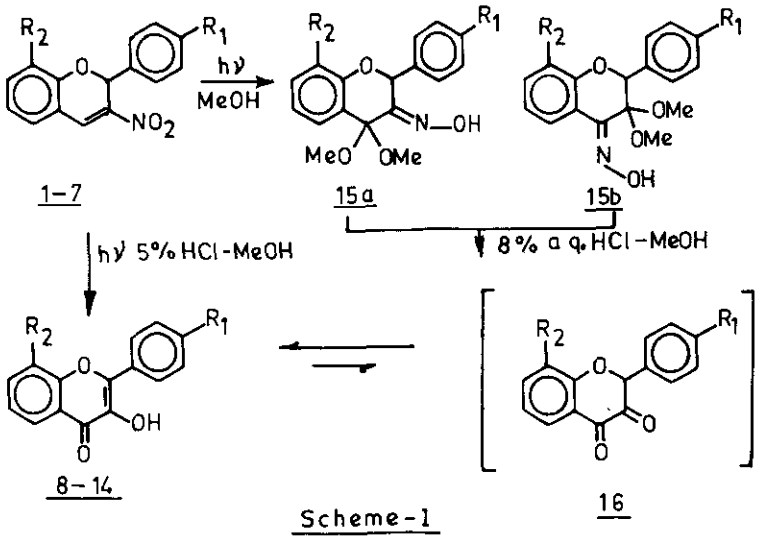
A NOVEL PHOTOCHEMICAL METHOD FOR THE SYNTHESIS OF FLAVONOLS

T. Sudhakar Rao, Anil Kumar Singh and Girish Kumar Trivedi*
Department of Chemistry, Indian Institute of Technology,
Bombay-400 076, India

Abstract —— Photolysis of the nitrochromenes followed by acidic hydrolysis of the photoproducts yields the corresponding flavonols in high yields.

Flavonols are important biomolecules possessing antiviral, antitumor and antibiotic properties[1]. However, there are only a few methods reported[2-5] for their synthesis. Herein we wish to report a method for the preparation of flavonols in high yields. The method is based on a novel photochemical reaction of the nitrochromenes. Nitrochromenes 1-7 can be prepared[6,7] by condensing the appropriate O-hydroxybenzaldehydes with appropriately substituted nitrostyrenes. Photolysis[8] followed by the acidic hydrolysis of these nitrochromenes gave the flavonols 8-14 (Scheme 1). It is believed that the photolysis product is an oxime (15) which is hydrolysed to the diketone (16) and then tautomerized to the flavonol (Table 2).

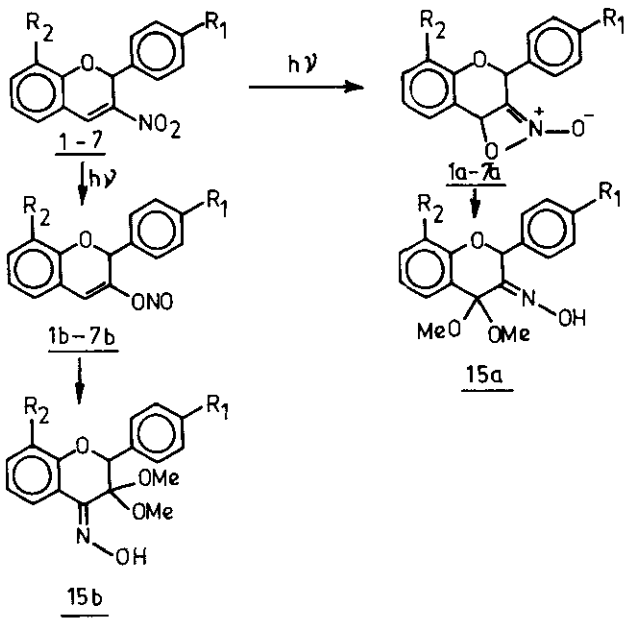


Scheme-1

Photolysis of nitrochromenes in acidic methanol (5% HCl-MeOH) followed by keeping the reaction mixture overnight at room temperature also resulted in the formation of flavonols. However, the yields were slightly lower in this case as compared to the photolysis in non-acidic medium.

The structure 15a or 15b for the photoproduct oxime was arrived at on the basis of their nmr and mass spectral data (Table 1). Further studies regarding the mechanistic details of this photoreaction and for the unambiguous assignment of structure of the photoproducts are in progress.

Though the spectral data are in accordance with the structures 15a and 15b for the oxime, structure 15b seems more probable, because aromatic nitro compound phototautomerizes[9,10] to O-NO(1b-7b), the subsequent Barton[11] type reaction and ketalization would give oxime 15b[12]. However, the possibility of oxime 15a cannot be ruled out since its formation is possible from the oxazete(1a-7a). (Scheme 2).



Scheme-2

TABLE I

Compound No.	R_1	R_2	NMR ($CDCl_3$/TMS_{int}) of the product[a] δ	ms m/e M^+
1	H	H	3.0(3H,s,OMe), 3.1(3H,s,OMe), 3.3(3H,s,OMe), 3.6(3H,s,OMe), 5.45 (1H,s,C_2-H), 5.55(1H,s,C_2-H), 7-7.9(18H,m,phenyl), 8.9(2H,s(br), OH)	299
2	Me	H	2.35(3H,s,Me), 2.4(3H,s,Me), 3.0(3H,s,OMe), 3.1(3H,s,OMe), 3.25(3H,s,OMe), 3.6(3H,s,OMe), 5.4(1H,s,C_2-H), 5.5(1H,s,C_2-H), 6.95-7.7 (16H,m,phenyl), 8.7(2H,s,(br), OH)	313
3	Cl	H	3.08(3H,s,OMe), 3.1(3H,s,OMe), 3.25(3H,s,OMe),3.56(3H,s,OMe), 5.46(1H,s,C_2-H),5.57(1H,s,C_2-H), 7-7.7(16H,m,phenyl),8.3(2H,s(br), OH)	333
4	OCH_3	H	3.06(3H,s,OMe), 3.1(3H,s,OMe), 3.26(3H,s,OMe),3.65(3H,s,OMe), 3.84(3H,s,4'-OMe), 3.87(3H,s,4'-OMe), 5.45(1H,s,C_2-H), 5.56(1H,s,C_2-H), 6.9-7.64(16H, m,phenyl), 8.16(1H,s, OH), 8.28(1H,s, OH)	329
5	Me	OMe	-	-
6	OMe	OMe	3.1(3H,s,OMe), 3.21(3H,s,OMe), 3.42(3H,s,OMe), 3.52 (3H,s,OMe), 3.56(3H,s,OMe), 3.65(3H,s,OMe), 3.88(3H,s,OMe), 3.9(3H,s,OMe), 5.34(1H,s,C_2-H), 5.54(1H,s,C_2-H) 6.8-8(14H,m,phenyl), 8.6(2H,s(br), OH)	359

Compound No.	R_1	R_2	NMR ($CDCl_3$/TMS$_{int}$) of the product[a] δ	ms m/e M^+
7	H	OMe	3.08(3H,s,OMe), 3.14(3H,s,OMe) 3.3(3H,s,OMe), 3.64(3H,s,OMe), 3.9(3H,s,C_8-OMe), 3.92(3H,s,C_8-OMe), 5.52(1H,s,C_2-H), 5.6(1H,s,C_2-H), 6.8-7.9(16H,m,phenyl), 8.4(2H,s(br),OH)	329

[a] The product was a mixture of two isomeric compounds which could not be separated by column chromatography.

The oxime of compound No.5 was not isolated.

TABLE 2

Compound No.	R_1	R_2	Yield[a,b] %	Mp °C	Molecular formula or lit. mp	ms m/e M^+	ν_{max} (nujol)
8	H	H	78	169-171	169-170	238	1635,3200(br)
9	Me	H	75	194-195	192-193	252	1630,3295(br)
10	Cl	H	73	198-199	198-199	272	1630,3290
11	OCH_3	H	84	229-230	230-231	268	1635,3200(br)
12	Me	OMe	73	187-188	187-188	282	1630,3240(br)
13	OMe	OMe	76	213-214	$C_{17}H_{14}O_5$	298	1635,3250(br)
14	H	OMe	69	197-198	197-198	268	1640,3300

a - Yields are calculated based on the conversion from chromene to flavonol.

b - Hydrolysis of oxime gave the flavonol in 98-99% yield.

EXPERIMENTAL

1. General procedure for photolysis

In a typical photolysis experiment a dilute solution (0.005 M) of nitrochromene in methanol was irradiated through a pyrex with 125 W Phillips mercury lamp till most of the starting material disappeared (tlc). Removal of methanol from the reaction mixture yielded an oil from which colorless compound was isolated

either by using column chromatography (silica gel, 10-15% ethyl acetate-hexane) or by crystallization from ethyl acetate-hexane.

2. General procedure for photolysis in acidic methanol

0.005 M 5% HCl-methanol solution of 3-nitrochromene was irradiated with a 125 W Phillips mercury lamp until most of the starting material disappeared (tlc). Then the reaction mixture was concentrated to 1/5 of the original volume under reduced pressure and kept at room temperature overnight. The flavonol which crystallized out from the reaction mixture was filtered. Further crystallization was achieved from methanol and the product characterised by physico-chemical data.

3. General procedure for hydrolysis of the oxime (15)

8% Aqueous HCl (10 ml) was added to a solution of oxime (0.5 mmol) dissolved in a mixture of chloroform-methanol (1:10). Then the reaction mixture was warmed on a steam bath to evaporate chloroform. The clear solution obtained was kept overnight (16 hr) at room temperature. The flavonol which crystallized out from the reaction mixture was filtered. Further crystallization from methanol yielded pure product which was characterized by its mp, mixed mp, uv, superimposable ir, nmr and mass spectral data.

REFERENCES

1. R. Bognar and M. Rakosi, Proc. 5th Hungarian Bioflavonoid Symp., Matrafured, Hungary, 1977, pp.138-142.
2. J. Allan and R. Robinson, J. Chem. Soc., 1924, 125, 2192.
3. J. Algar and J.P. Flynn, Proc.Royal Irish Acad., 1934, 42b, 1.
4. J. Oyamada, J. Chem. Soc. Japan, 1934, 55, 2156.
5. S.R. Deshpande, H.H. Mathur and G.K. Trivedi, Synthesis, 1983, 10, 835.
6. S.R. Deshpande, H.H. Mathur and G.K. Trivedi, Ind. J. Chem., 1983, 22B, 166.
7. Unpublished work.
8. T. Sudhakar Rao, Anil K. Singh and G. K. Trivedi, Chem. Lett., (Communicated for publication).
8a. S. T. Reid, J. K. Thomson and C. F. Mushambi, Tetrahedron Lett., 1983, 24(21), 2209.
9. O. L. Chapman, A. A. Griswold, E. Hoganson, G. Lenz and J. Reasoner, Pure Appl.Chem., 1964, 9, 585.

10. C. Kaneko, I. Yokoe and S. Yamada, Tetrahedron Lett., 1967, 775.

11. D. H. R. Barton and J. M. Beaton, J. Am. Chem. Soc., 1961, 83, 750.

12. We are thankful to one of the referees for this suggestion.

Received, 24th January, 1984