HETEROCYCLES, Vol. 29, No. 1, 1989

PHOTOSENSITIZED DEHYDROGENATION OF FLAVANONES TO FLAVONES USING 2,4,6-TRIPHENYLPYRYLIUM TETRAFLUOROBORATE (TPT)

María J. Climent,[a] Hermenegildo García,[a] Sara Iborra,[a] Miguel A. Miranda,[b*] and Jaime Primo[a]

[a] Departamento de Química, ETSII, Universidad Politécnica de Valencia, Apartado 22012, 46071 Valencia, Spain

[b] Departamento de Química Orgánica, Facultad de Farmacia, Av. Blasco Ibañez 13, 46010 Valencia, Spain

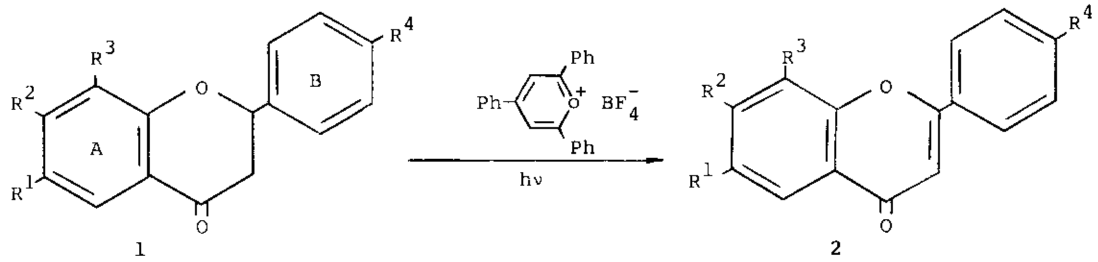
Abstract-Irradiation of flavanones **1a-c,e** using TPT as photosensitizer leads to the corresponding flavones **2a-c,e** in yields ranging between 50 and 69%. 4-Nitroflavanone (**1d**) remains unchanged under the same conditions. These results are consistent with a single electron-transfer (SET) occurring from the flavanone B ring to the excited pyrylium salt to give the radical cation intermediate **3**.

There is an increasing activity in the field of photosensitized electron-transfer reactions of organic compounds, including their exploitation in the design of new synthetic methodologies.[1-5] The preparation of 4H-benzopyrones from their corresponding dihydro derivatives is an important process in natural products chemistry,[6,7] which has attracted our attention in the course of recent studies on the synthesis of flavonoid compounds.[8-10] The fact that similar dehydrogenation processes can be achieved by ceric ammonium nitrate[11] or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[12,13] which are thought to operate via electron-transfer processes,[14,15] led us to try the triphenylpyrylium tetrafluoroborate (TPT) photosensitized reaction[16] as a conceptually different approach to achieve the transformation of flavanones into flavones.

The required substrates **1a-e** were prepared by a Claisen-Schmidt condensation of suitable o-hydroxyacetophenones with aromatic aldehydes and subsequent basic cyclization of the resulting chalcones following standard procedures.[7]

Irradiations of the flavanones **1** were carried out in CH_2Cl_2 solutions with catalytic amounts of TPT, using a Pyrex immersion well photoreactor provided with a 125 W medium pressure mercury lamp. The reaction time was always 4 h.

In this way, **1a-c,e** afforded the corresponding flavones **2a-c,e** in preparative yields ranging between 50 and 69%, while 4-nitroflavanone (**1d**) was recovered unchanged. Additionally in the case of **1e** a 13% of 6-formyl-8-methylflavanone (**1f**) was isolated from the photolysis mixture.

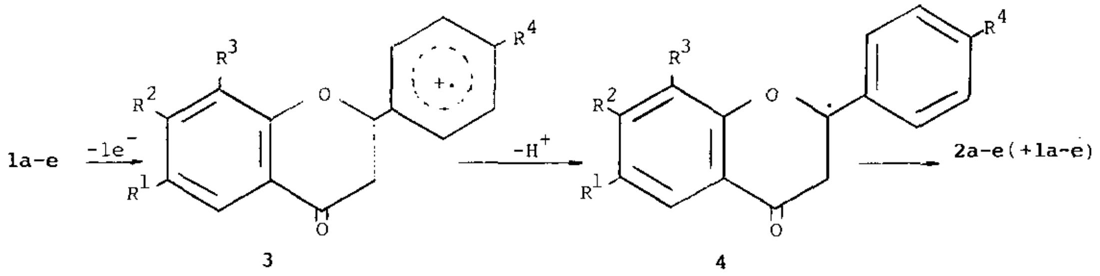


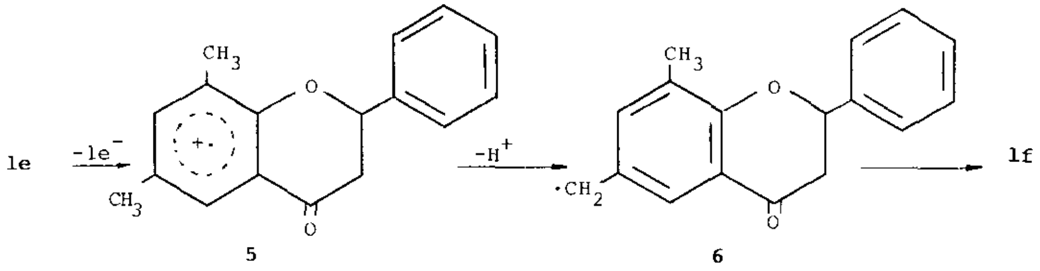
	R^1	R^2	R^3	R^4	Yield of **2**(%)	Ref
a	H	H	H	H	59	17
b	H	OCH_3	H	H	68	17
c	H	H	H	OCH_3	69	17
d	H	H	H	NO_2	0	18
e	CH_3	H	CH_3	H	52*	8,9

* **1f** (13%) was also obtained (R^1=CHO, R^2=R^4=H, R^3=CH_3).

These results could be rationalized in terms of an initial single electron-transfer process occurring from the aromatic B ring of the flavanone **1** to the excited pyrylium salt to give the radical cation **3** which would lose a proton to form the benzylic radical **4** from which the flavone would be finally formed after disproportionation.[19] The effects of the substitution on this ring strongly support our mechanistic proposals. Thus the electron withdrawing nitro group prevents the reaction, while the electron donating methoxy substituent enhances the flavone yields.

Finally, the formation of **1f** is in agreement with the general behaviour of methylarenes which undergo an oxidation to aromatic aldehydes under electron-transfer conditions.[3,5] In this case, the dimethyl substitution in the A ring compensates the deactivating effect of the carbonyl group, and therefore electron-transfer to excited TPT from this ring competes with that occurring from the 2-phenyl group.





In conclusion, our results are relevant in the finding and development of synthetic applications of photosensitized electron-transfer processes. They show that *dehydrogenation of flavanones using* TPT as photosensitizer constitutes a facile method for the preparation of flavones in moderate to good yields. The scope of this transformation appears to be limited to substrates where no electron withdrawing substituents are present on the flavanone B ring.

EXPERIMENTAL

Melting points are uncorrected. Combustion analysis of **1f** was performed at Instituto de Química Bio-Orgánica of the CSIC (Barcelona). Ir spectra were determined in CCl_4, with a Perkin-Elmer 781 spectrophotometer; absorptions (ν, cm^{-1}) are given only for the carbonyl bands. ^1H-Nmr spectra were recorded with a Varian 360 EM instrument, using CCl_4 as solvent; chemical shifts are reported in ppm downfield (δ) from TMS. The flavanone uv spectrum was determined in ethanol with a Varian *634* spectrophotometer; *absorbed radiation* is defined by its wavelength (λ_{max}, nm) and log ϵ (in brackets). Mass spectrum of **1f** was measured with a GC/MS Hewlett-Packard 5988 A spectrometer; m/z ratio and their relative abundances in percentages (in brackets) are given only for the main bands.

Preparation of 2,4,6-triphenylpyrylium tetrafluoroborate (TPT)

A solution of chalcone (208 g, 1 mol) and acetophenone (60 g, 0.5 mol) in

1,2-dichloroethane (350 ml) was warmed at 70°C. Then, a 50% ethereal solution of fluoroboric acid (160 ml) was slowly added under continous stirring during 30 min. After the addition was completed, the mixture was heated at reflux temperature for 1 h. Then, the suspension was cooled at 0°C and the resulting crystalline solid was collected and washed with ether. More product could be obtained from the mother liquor by addition of ethyl ether (250 ml). The TPT was recrystallized from 1,2-dichloroethane (700 ml) before its use as photosensitizer. The total yield was 68%.

Preparation of flavanones **1a-e**

To an ethanolic (10 ml) solution of the corresponding o-hydroxyacetophenone (5 mmol) and the aromatic aldehyde (5 mmol) was added lithium hydroxide (70 mg, 15 mmol) and the mixture was warmed at 50°C under magnetic stirring. The progress of the reaction was periodically followed by GC until no changes were observed. Then, the solution was neutralized with aqueous hydrochloric acid and the resulting suspension filtered, the solid washed with cold water and recrystallized from ethanol.

Cyclization of o-hydroxychalcones to flavanones was accomplished by treating a solution of the chalcone (1 mmol) in benzene (50 ml) with an aqueous solution of 20% of tetraethylammonium hydroxide (20 ml) under continous magnetic stirring for 5 h. After this time, the organic layer was separated, washed with water, dried over anhydrous sodium sulfate and finally concentrated in vacuo. The residue was submitted to purification affording the expected flavanone.

Irradiations

A solution of flavanone (200 mg) and TPT (40 mg) in methylene chloride (450 ml) was irradiated for 4 h at room temperature with a 125 W medium pressure mercury lamp inside a pyrex immersion well, using a potassium chromate solution (100 mg/ml) as filter. After removal of the solvent, the photolysis mixture was submitted to purification by flash column chromatography on silica gel Merck 60, 70-230 mesh, using hexane as eluent.

Products

Flavanone (**1a**), mp 74-76° (lit.[20] 75-76°), ir 1695, ^{1}H-nmr 8.20-6.80 (m, 9H, Ar$\underline{H}$), 5.50 (dd, J_{cis}=6Hz, J_{trans}=12Hz, 1H, H at C-2), 3.21-2.72 (m, 2H, $C\underline{H}_2$), uv 320 (3.53).

7-Methoxyflavanone (**1b**), mp 86-88° (lit.[20] 90-91°), ir 1695, ^{1}H-nmr 7.79 (d, J=9Hz, 1H, H at C-8), 7.41 (s, 5H, $C_6\underline{H}_5$), 6.57 (dd, J_{ortho}=9Hz, J_{meta}=1Hz, 1H, H at C-6), 6.40 (d, J=1Hz, 1H, H at C-8), 5.30 (dd, J_{cis}=5Hz, J_{trans}=11Hz, 1H, H at C-2), 3.80, (s, 3H, $OC\underline{H}_3$), 3.00-2.65 (m, 2H, $C\underline{H}_2$), uv 310 (3.69)

4´-Methoxyflavanone (**1c**), mp 86-88° (lit.[17] 87-88°), ir 1695, ^{1}H-nmr 8.00-6.60 (m, 8H, Ar$\underline{H}$), 5.25 (dd, J_{cis}=4.5Hz, J_{trans}=12Hz, 1H, H at C-2), 3.78 (s, 3H, $OC\underline{H}_3$), 3.00-2.60 (m, 2H, $C\underline{H}_2$), uv 320 (3.32).

4´-Nitroflavanone[18] (**1d**), mp 161-163°, ir 1690, ^{1}H-nmr 8.55-6.80 (m, 8H, Ar$\underline{H}$), 5.50 (dd, J_{cis}=8Hz, J_{trans}=12Hz, 1H, H at C-2), 3.10-2.80 (m, 2H, $C\underline{H}_2$), uv 306 (3.52).

6,8-Dimethylflavanone (**1e**), mp 69-71° (lit.[8] 69-71°), ir 1710, ^{1}H-nmr 7.52-6.82 (m, 7H, Ar$\underline{H}$), 5.23 (dd, J_{cis}=6Hz, J_{trans}=10Hz, 1H, H at C-2), 2.94-2.69 (m, 2H, $C\underline{H}_2$), 2.23 (s, 3H, $C\underline{H}_3$), 2.19 (s, 3H, $C\underline{H}_3$), uv 337 (3.41).

6-Formyl-8-methylflavanone (**1f**), *Anal. Calcd for* $C_{17}H_{14}O_3$: *C, 76.68; H, 5.30;* Found: C, 76.35; H, 5.17 , ir 1695, ^{1}H-nmr 9.94 (s, 1H, C$\underline{H}$O), 8.28 (d, J=1Hz, 1H, H at C-5), 7.97 (d, J=1Hz, 1H, H at C-7), 7.50 (s, 5H, $C_6\underline{H}_5$), 5.52 (dd, J_{cis}=6Hz, J_{trans}=8Hz, 1H, H at C-2), 3.19-2.90 (m, 2H, $C\underline{H}_2$), 2.40 (s, 3H, $C\underline{H}_3$), ms 266 (100), 265 (40), 189 (35), 162 (100), 134 (85), 104 (80), 77 (55).

Flavone (**2a**), mp 95-97° (lit.[21] 96-97°), ir 1650, ^{1}H-nmr 8.20-7.18 (m, 9H, Ar$\underline{H}$), 6.79 (s, 1H, H at C-3).

7-Methoxyflavone (**2b**), mp 110-113° (lit.[21] 110-112°), ir 1676, ^{1}H-nmr 8.23-6.96 (m, 8H, Ar$\underline{H}$), 6.85 (s, 1H, H at C-3), 3.80 (s, 3H, $OC\underline{H}_3$).

4´-Methoxyflavone (**2c**), mp 155-158° (lit.[21] 157-158°), ir 1677, ^{1}H-nmr 8.50-6.98 (m, 8H, Ar$\underline{H}$), 6.89 (s, 1H, H at C-3), 3.90 (s, 3H, $OC\underline{H}_3$).

6,8-Dimethylflavone (**2e**), mp 163-164° (lit.[8] 163-164°), ir 1650, ^{1}H-nmr 8.50-7.24 (m, 7H, Ar$\underline{H}$), 6.70 (s, 1H, H at C-3), 2.55 (s, 3H, $C\underline{H}_3$), 2.40 (s, 3H, $C\underline{H}_3$).

ACKNOWLEDGEMENTS

Financial support by the Comisión Asesora de Investigación Científica y Técnica (CAICYT) is gratefully acknowledged.

REFERENCES

1. G.J. Kavarnos and N.J. Turro, *Chem. Rev.*, 1986, **86**, 401.
2. M. Julliard and M. Chanon, *Chem. Rev.*, 1983, **83**, 425.
3. M.A. Fox, *Adv. Photochem.*, 1986, **13**, 237.
4. S.L. Mattes and S. Farid in: "Organic Photochemistry", ed. by A. Padwa, Marcel Dekker, New York, 1986, vol. 6, p. 233.
5. P.S. Mariano and J.L. Stavinoha in: "Synthetic Organic Photochemistry", ed. by W.M. Horspool, Plenum Press, New York, 1984, p. 145.
6. G.P. Ellis, "Chromenes, Chromanones and Chromones", Wiley-Interscience, New York, 1977.
7. J.B. Harborne, T.J. Mabry, and H. Mabry, "The Flavonoids", Academic Press, New York, 1976.
8. H. García, S. Iborra, M.A. Miranda, and J. Primo, *Heterocycles*, 1985, **23**, 1983.
9. H. García, S. Iborra, M.A. Miranda, and J. Primo, *Heterocycles*, 1986, **24**, 2511.
10. H. García, S. Iborra, M.A. Miranda, and J. Primo, *J. Org. Chem.*, 1986, **51**, 4432.
11. M.P. Doyle, L.J. Zuidema, and T.R. Bade, *J. Org. Chem.*, 1975, **40**, 1454.
12. Ch.G. Shankar, B. Mallaiah, and G. Srimannarayama, *Synthesis*, 1983, 310.
13. K. Imafuku, M. Honda, and J.F.W. McOmie, *Synthesis*, 1987, 199.
14. I.P. Beletskaya and Makhon´kov, *Russ. Chem. Rev.*, 1981, **50**, 1007.
15. A.B. Turner in: "Synthetic Reagents", ed. by J.S. Pizey, Ellis Horwood Pub., Chilchester, 1977, vol. 3, p. 193.
16. W. Adam and M. Dörr, *J. Am. Chem. Soc.*, 1987, **109**, 1570.
17. N. Takeno, T. Fukushima, S. Takeda, and K. Kishimoto, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 1599.
18. A. Grouiller, P. Thomassery, and H. Pacheco, *Bull. Soc. Chim. Fr.*, 1973, 3448.

19. Obviously, the radical formed from the pyrylium cation as a consequence of the electron transfer process must be able to lose an electron if one has to explain the requirement of only catalytic amounts of TPT. In this context, the generation of active oxygen species such as superoxide ion, could play an important role. In fact, oxygen must be involved in these reactions, as indicated by the formation of the aldehyde **1f**. Further work is currently being carried out in order to confirm this point.

20. A. Kasuhara, T. Izumi, and M. Ooshima, Bull. Chem. Soc. Jpn., 1974, **47**, 2526.
21. P.K. Jain, J.K. Makrandi, and S.K. Grover, Synthesis, 1982, 220.

Received, 11th July, 1988