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A SIMPLE SYNTHESIS OF FLUORESCENT URIDINES BY PHOTOCHEMICAL METHOD[1]

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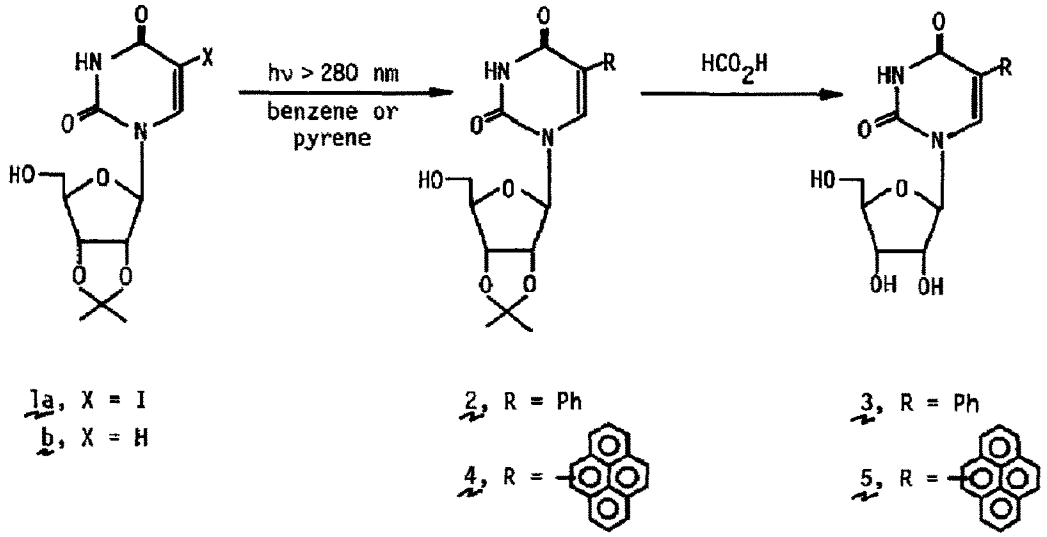
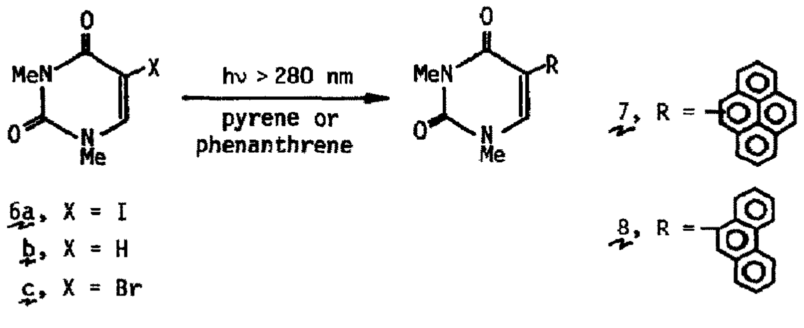
Summary: A strongly fluorescent 5-pyrenyluridine was prepared by the photoreaction of 2',3'-O-isopropylidene-5-iodouridine with pyrene. Several fluorescent analogues of uracil were synthesized by similar procedures.

Fluorescent analogues of nucleosides have been widely used as fluorescent probes for investigating the structure and function of nucleic acids.[2] The synthesis of strongly fluorescent nucleosides with long fluorescence lifetimes is highly desirable. In a continuation of our studies on the photochemistry of nucleic acid bases,[3] we have found that irradiation of 5-halouridines in the presence of aromatic compounds produces 5-aryluridines in fair yields. We report herein a simple synthesis of strongly fluorescent nucleoside, 5-pyrenyluridine, and other fluorescent analogues of uracil.

Irradiation of 2',3'-O-isopropylidene-5-iodouridine 1a[4] (3.1 mM) in acetonitrile-benzene (3 : 1) with a 400-W high-pressure mercury lamp (Pyrex filter) for 11 h gave 2 (59%). Treatment of 2 with formic acid followed by preparative TLC produced 5-phenyluridine (3, 41%). Under similar conditions irradiation of 1a (2.5 mM) and pyrene (22 mM) in acetonitrile followed by chromatographic separation (silica gel, $CHCl_3$-acetonitrile; 10 : 1) provided 1b (26%) and 4 (31%). A similar acid-treatment of 4 removed the protecting group to provide 5-pyrenyluridine 5 (55%) which appears to consist of a single isomer as evidenced by NMR and TLC analyses.[5] However, the substituted position on the pyrene ring is not known.

In order to know more details on the coupling reaction, irradiation of 5-iodo-1,3-dimethyluracil (6a, 5.6 mM) with pyrene (50 mM) was carried out in acetonitrile. In this case a 4 : 1 mixture of the isomeric coupled products 7 (45%) was isolated together with 6b (44%). In view of the observed highest reactivity of the 1 position on pyrene ring toward radical[6] and electrophilic[7] reactions, the major product is presumably 1,3-dimethyl-5-(1-pyrenyl)uracil. Likewise irradiation of 6a (3.6 mM) and phenanthrene (11.2 mM) in acetonitrile under the same conditions gave 6b (25%) and 8 (39%). The structure of 8 was rigorously established by its ^{1}H NMR spectrum (Table 1).





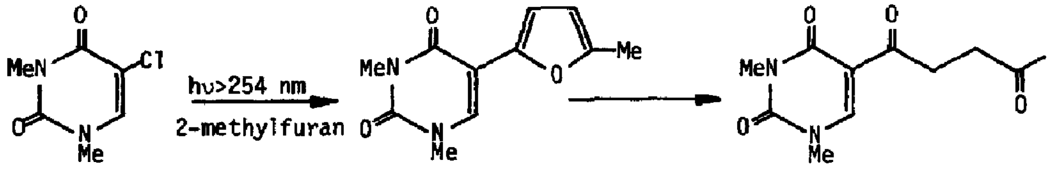
We have previously reported that acetone-sensitized irradiation of 5-bromo-1,3-dimethyluracil (6c) and indoles gives the corresponding coupled products via an electron-transfer process.[3a,g] However, neither 6a nor 6c produced the coupled products with other heteroaromatics, *e.g.*, furans, upon sensitized and direct irradiations. In contrast, direct irradiation of 5-chloro-1,3-dimethyluracil[8] (9, 12 mM) with excess 2-methylfuran in acetonitrile containing aqueous K_2CO_3 afforded 10 (28%). Refluxing of 10 in acetic acid-aqueous H_2SO_4 produced 5-substituted uracil 11 (52%).

Table 1. Spectral Data[a]

	Mp (°C)	^{1}H NMR	UV λ_{max}, nm (log ε) in CH_3CN	Em λ_{max}, nm (excitation, nm) in CH_3CN
3	179 - 181	δ 3.75 (A part of ABX, 1 H, J_{AB} = 12.0, J_{AX} = 2.8 Hz), 3.91 (B part of ABX, 1 H, J_{AB} = 12.0, J_{BX} = 2.6 Hz), 4.06 (m, 1 H), 4.24 (dd, 1 H, J = 4.1, 5.0 Hz), 4.30 (dd, 1 H, J = 4.1, 3.8 Hz), 6.01 (d, 1 H, J = 3.8 Hz), 7.24 - 7.70 (m, 5 H), 8.33 (s, 1 H) in CD_3OD.	235 (4.57) 280 (4.57)	417 (310)
5	214 - 217	δ 3.58 (A part of ABX, 1 H, J_{AB} = 12.2, J_{AX} = 2.8 Hz), 3.75 (B part of ABX, 1 H, J_{AB} = 12.2, J_{BX} = 2.6 Hz), 4.04 (m, 1 H), 4.20 (dd, 1 H, J = 4.5, 4.4 Hz), 4.37 (dd, 1 H, J = 4.4, 4.5 Hz), 6.10 (d, 1 H, J = 4.4 Hz), 7.84 - 8.42 (m, 10 H) in CD_3OD.	241 (4.65)[b] 265 (4.40) 276 (4.55) 324 (4.28) 338 (4.43)	460 (360)[b]
7	235 - 238 (Major isomer)	δ 3.43 (s, 3 H), 3.49 (s, 3 H), 7.30 (s, 1 H), 7.79 - 8.24 (m, 9 H) in $CDCl_3$.	242 (4.62) 267 (4.31) 277 (4.47) 327 (4.26 342 (4.40)	404 (359)
	226 - 228 (Minor isomer)	δ 3.57 (s, 6 H), 7.40 (s, 1 H), 7.78 - 8.28 (m, 9 H) in $CDCl_3$.	242 (4.73) 267 (4.42) 276 (4.58) 326 (4.36) 341 (4.50)	404 (344)
8	176 - 177	δ 3.32 (s, 3 H), 3.39 (s, 3 H), 7.24 (s, 1 H), 7.43 - 7.89 (m, 6 H), 7.59 (br s, 1 H, C_{10}-H), 8.58 - 8.77 (m, 2 H) in $CDCl_3$.	220 (4.58)[b] 253 (4.70) 297 (4.45)	377 (307)
10	161 - 162	δ 2.31 (d, 3 H, J = 1.3 Hz), 3.40 (s, 3 H), 3.46 (s, 3 H), 6.04 (td, J = 3.0, 1.3 Hz), 6.94 (d, 1 H, J = 3.0 Hz), 7.59 (s, 1 H) in $CDCl_3$.	254 (4.50) 321 (4.45)	417 (346)
11	145 - 145.5	δ 2.21 (s, 3 H), 2.79 (t, 2 H , J = 6.2 Hz), 3.32 (t, 2 H, J = 6.2 Hz), 3.38 (s, 3 H), 3.50 (s, 3 H), 8.16 (s, 1 H) in $CDCl_3$.	225 (4.36) 286 (4.43)	

[a] Satisfactory elemental analyses and mass spectral data were obtained.

[b] In methanol.



9 **10** **11**

The results described here demonstrate that photoreaction of 5-halouracils provides a convenient method for the introduction of aromatic and heteroaromatic systems into the 5-position of uracil nucleus in one-step. By this method a strongly fluorescent nucleoside such as **5** (Em λ_{max} 460 nm excited at 360 nm) of potential utility as a fluorescence probe has been synthesized.

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