A Facile Synthesis of 9*H*-Pyrimido[4,5-*b*]indole *via* Photolysis of 4-Azido-5-phenylpyrimidine

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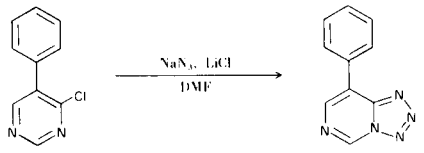
Our interest in the photochemistry of 2-substituted biphenyls (2a-d) led us to extend our efforts into heterocyclic biaryl systems. The facile synthesis of 4-substituted-5-phenyl pyrimidines (3a-c) prompted us to initiate our studies with this ring system. We report here the high yield route to 9*H*-pyrimido[4,5-*b*]indole (IV) from photolysis of 4-azido-5-phenylpyrimidine (III).

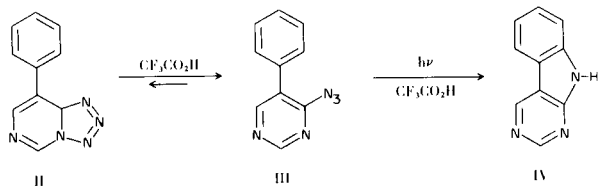
The high yield photolysis of 2-azidobiphenyls to carbazoles suggested an analogous transformation in the pyrimidine systems. The reaction of 4-chloro-5-phenylpyrimidine (I) with sodium azide-lithium chloride in *N*,*N*-dimethylformamide afforded a 96% yield of a compound analyzing for $C_{10}H_7N_5$, which showed no azide band in the ir (2120-2160 cm^{-1} region) either in the solid state or *N*,*N*-dimethylformamide solution. The presence of a sharp band at 1070 cm^{-1} in the ir, characteristic of the tetrazole ring (4), led to the structure assignment for this compound as 8-phenyltetrazolo[1,5-*c*]pyrimidine (II).



I II

The photolysis of dilute solutions of II in either tetrahydrofuran or acetonitrile proceeded sluggishly to yield one isolable compound (IV) in low yield in addition to highly colored polymeric material (*vide infra*). Since the photolysis of the tetrazole II was of little synthetic value, we sought to study the photolysis of the corresponding azide. It has been noted that certain *N*-heterocyclic fused tetrazole rings are capable of tautomeric conversion to azides (5) and that acid media favors the azide tautomer (6a,b) (Scheme I). Accordingly, the ir spectrum of II in trifluoroacetic acid shows loss of the 1070 cm^{-1} tetrazole band and formation of the azide band (2140 cm^{-1}) of 4-azido-5-phenylpyrimidine (III). That the acid had effected no molecular rearrangement was verified by removal of the trifluoroacetic acid and recovery of unchanged II.

Scheme I



II III IV

In contrast to the complex photolysis of II in ordinary solvents, irradiation in trifluoroacetic acid led to rapid formation of a single photoproduct (IV) in 91% yield. The structure of the photoproduct (IV) was assigned as 9*H*-pyrimido[4,5-*b*]indole (7a,b) on the basis of its melting point and spectroscopic properties. The mass spectrum (70 ev) showed in addition to the parent mass at 169, prominent peaks at m/e = 142 and 115 (loss of HCN) confirming the integrity of the pyrimidine ring (8). The nmr [DMSO-d_6] of IV shows: τ 2.48 (m, 3H, H_5, H_6, H_7); 1.76 (d, 1H, J = 7 Hz, H_8); 1.06 (s, 1H, H_4); 0.52 (s, 1H, H_2); -2.25 (br, s, 1H, N-H). The two high-field resonances may be compared to carbazole [2.48 (m, 6H) and 1.80 (d, 2H, J = 8 Hz)]; while the lower field signals are typical of pyrimidine C-H's. The ultraviolet spectrum of IV in ethanol is very similar to γ-carboline (9a,b), showing maxima at 207.5 (ϵ = 31,000), 232.7 (22,000), 253.0 (24,000), and 287.5 (10,000) nm.

In view of the high yield of this photolysis and the availability of the starting materials, this route should suffice as a general route to 9*H*-pyrimido[4,5-*b*]indoles. Further studies in this and related systems are in progress.

EXPERIMENTAL

Melting points were determined in a Thomas-Hoover apparatus and are uncorrected. Ultraviolet spectra were determined in ethanol solution with a Cary Model 14 recording spectrophotometer. Infrared spectra were taken as Nujol mulls on a Perkin-Elmer Model 137 spectrophotometer. Nmr spectra were run in deuteriochloroform or DMSO-d_6 solution with a Varian A-60A instrument using tetramethylsilane as internal standard. Mass spectra were determined using an AEI MS-9 spectrometer. Microanalyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

8-Phenyltetrazolo[1,5-*c*]pyrimidine (II).

A solution of 10 g. (0.0525 mole) 4-chloro-5-phenylpyrimidine, 4 g. (0.0615 mole) sodium azide, and 2.5 g. (0.0615 mole) lithium chloride in 150 ml. of *N,N*-dimethylformamide was stirred for 24 hours at ambient temperature, with protection from moisture. The reaction mixture was poured into 1.5 liter of ice-water, and the precipitated crude product recrystallized from 95% ethanol to give 10.0 g. (96%) of light yellow needles, m.p. 164-165°. The analytical sample was prepared by sublimation *in vacuo*, m.p. 164.5-165°; ir, 6.21 (s), 8.10 (s), 9.31 (s), 10.10 (m), 10.15 (m), 10.75 (m), 12.85 (s), 13.10 (s), 13.20 (s), 14.40 (b); nmr δ 9.62, s (1H); 8.55, s (1H); 8.2, m (2H); 7.6, m (3H); uv λ max (ethanol) 2950 Å (ϵ = 1,400). The mass spectrum (70 ev) showed the parent m/e at 197 (calcd. 197).

Anal. Calcd. for $C_{10}H_7N_5$: C, 60.91; H, 3.58; N, 35.51. Found : C, 60.59; H, 3.66; N, 35.11.

9*H*-Pyrimido[4,5-*b*]indole (IV).

A solution of 1.0 g. (0.0051 mole) of 8-phenyltetrazolo[1,5-*c*]-pyrimidine (II) in 100 ml. of trifluoroacetic acid at *ca.* 20° was irradiated for two hours under a nitrogen atmosphere in a Rayonet photochemical reactor equipped with sixteen RPR-3000 Å lamps. Most of the solvent from the reaction mixture was removed at room temperature under reduced pressure and the residue diluted with 25 ml. of water. After the aqueous layer was rendered basic with 20% sodium hydroxide, it was extracted with diethyl ether (5 x 25 ml. portions). The washed and dried extracts were evaporated at reduced pressure to afford solid crude product which was recrystallized from benzene to give 0.77 g. (90%) of 9*H*-pyrimido[4,5-*b*]indole (IV), m.p. 232-235°. Sublimation *in vacuo* gave material of m.p. 236-237° [lit. (7a) 235-237°]; ir, 3.1-3.2 (m), 6.25 (s), 6.35 (s), 10.10 (m), 10.92 (m), 12.60 (s), 13.3-13.4 (b); nmr *vide supra;* uv, λ max (ethanol) 2075 Å (3.1×10^4), 2327 Å (2.2×10^4), 2530 Å (2.4×10^4), 2875 Å (1×10^4).

Photolysis of 8-Phenyltetrazolo[1,5-*c*]pyrimidine (II).

A solution of 100 mg. (0.0005 mole) of 8-phenyltetrazolo-[1,5-*c*]pyrimidine in 150 ml. of acetonitrile was irradiated 6.5 hours under nitrogen with a Pyrex-filtered 450-watt Hanovia source. The reaction mixture was stripped to dryness *in vacuo*, taken up in 2 ml. of methanol, and chromatographed on 50 g. of Merck (Darmstadt) No. 7734 silica gel. Elution with 5% methanol in chloroform gave 18 mg. (24%) of 9*H*-pyrimido[4,5-*b*]indole, m.p. 233-236° after recrystallization from benzene.

Irradiation of II in tetrahydrofuran and acetone solutions also gave ~20% IV as the only tractible product.

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