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PHOTOTRANSFORMATION OF 2,4-DIMETHOXY-6-CHLOROPYRIMIDINE

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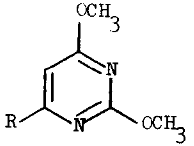
In a recent investigation of the photoisomerization of diazines, we have discovered that 2,4-dimethoxy-6-chloropyrimidine (I) does not undergo isomerization to analogous pyrazines or pyridazines but yields instead a mixture of three pyrimidine photoproducts. Irradiation of a 1% solution of I in methanol with 2537 or 3130A light afforded products involving reduction (II), nucleophilic displacement (III) and alkylation (IX) at the originally chlorinated 6-position. The structures of the photoproducts attained were confirmed by comparison of physical properties with authentic samples. Table I summarizes the product distribution for irradiation in various alcoholic and hydrocarbon solvents. The nucleophilic displacement product III is a true photoproduct and not a simple ground state solvolysis product since II could not be detected when I was heated to reflux in a neutral or acidic alcoholic solution for extended periods of time.

It is important to note that the ratio of reduction to displacement product varies with the hydrogen atom donating ability of the irradiation solvent. Addition of triethylamine, which is known to be an excellent source of hydrogen atoms (3), greatly increased the yield of the reduction product while the photosolvolysis product yield remained unchanged. One possible explanation of this solvent effect would be that both products are formed from a common intermediate which arises via initial photohomolysis of the carbon-chlorine bond to yield a pyrimidine free radical (IV). Depending on the hydrogen atom donating capacity of the solvent, this free radical could partition itself between abstraction of a hydrogen atom from the solvent and elimination of a hydrogen atom to form 2,4-dimethoxy-5-pyrimidyne (V). Subsequent solvolysis of (V) would yield the observed photodisplacement product. However, the pyrimidyne intermediacy was ruled out when I was irradiated in deuteriomethanol and mass spectral analysis indicated no incorporation of deuterium in the 2,4,6-trimethoxypyrimidine isolated from this photolysis. In

Table I

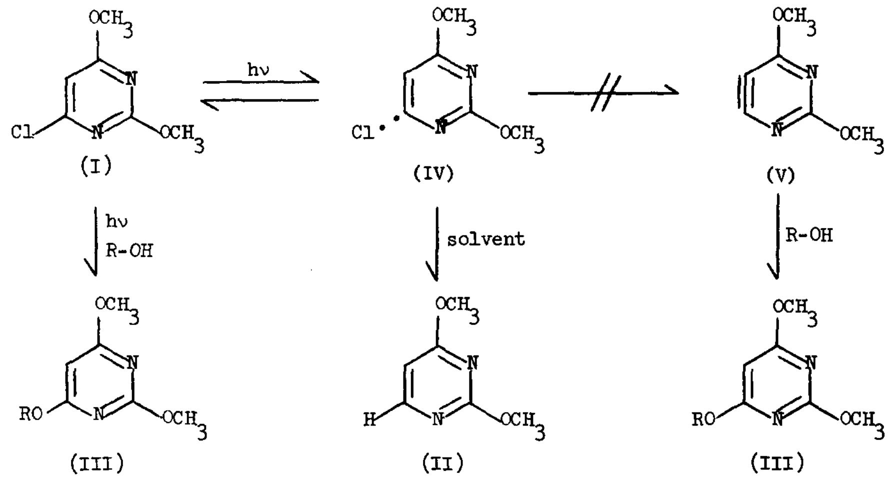
Irradiation of 2,4-Dimethoxy-6-chloropyrimidine Products

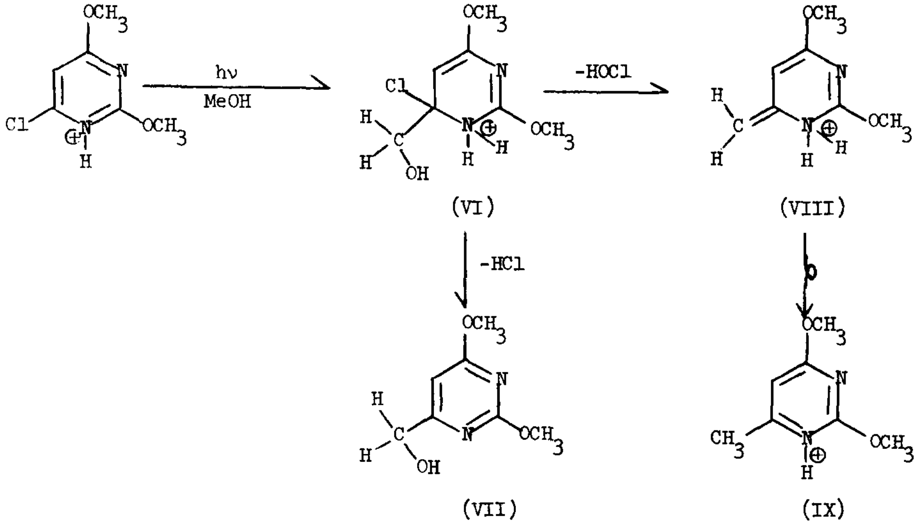


Solvent	Irradiation Time (hr.)	Recovered Starting Material (%)	R = H(%)	R = alkyl(%)	R = alkoxy(%)
Methanol	6 hr.	32	17	4	15
Methanol - 1 equ. triethylamine	6 hr.	12	40	0	16
Methanol - 1 equ. sodium methoxide	6 hr.	10	34	0	14
Ethanol	6 hr.	18	28	7	9
Ethanol - 1 equ. triethylamine	6 hr.	26	39	0	9
2-Propanol	6 hr.	33	24	4	5
2-Propanol - 1 equ. triethylamine	6 hr.	29	46	0	8
_t_-Butanol	6 hr.	37	13	0	32*
_t_-Butanol - 1 equ. triethylamine	6 hr.	38	31	0	5*
Hexane	6 hr.	89	3	--	--
Hexane - 1 equ. triethylamine	6 hr.	64	33	--	--

* Isolated as 2,4-dimethoxy-6-hydroxypyrimidine (X). It was found that 2,4-dimethoxy-6-_t_-butoxypyrimidine gave X and isobutylene upon work-up.

view of the lack of a common intermediate for these two photoproducts, the data can best be explained by a reversible homolytic cleavage of the carbon-chlorine bond to give a radical pair which can either recouple to regenerate starting material or abstract a hydrogen atom from the solvent to yield the reduction product. This homolytic cleavage reaction would be in competition with the direct nucleophilic displacement of the 6-chloro atom, and the hydrogen donating ability of the solvent would influence the ratio of the two photoproducts. In agreement with the direct photoassisted nucleophilic displacement mechanism for the formation of III, it was found that when 5-chloro-2,4-dimethoxypyrimidine was subjected to irradiation in methanol





no 2,4,5-trimethoxypyrimidine could be detected. It is well known that 5-halopyrimidines are much more resistant to nucleophilic attack than 6-halopyrimidines in ground-state reactions and the same order of reactivity appears to be prevalent in the excited states.

The nucleophilic displacement reaction could be completely circumvented and nearly quantitative yields of the reduction product could be realized when I was subjected to irradiation in hexane in the presence of one equivalent of triethylamine. These photolysis conditions are being further investigated as a synthetic method for selective dehalogenation of other heterocyclic systems and will be the subject of a future publication.

The photoalkylation product isolated in low yields when I is photolyzed in primary or secondary alcohols with or without added mineral acids appears to be another example of an acid-catalyzed imine photoalkylation reaction (4,5). Stermitz has proposed an imine photoreduction and subsequent rearrangement to account for photolakylation reaction of phenanthridines and pyrimidines. In agreement with this mechanism we have isolated in less than 1% yield 2,4-dimethoxy-6-hydroxymethylpyrimidine (VII) when I was photolyzed in methanol. The corresponding 6-hydroxyalkylpyrimidines were also isolated in low yields when ethanol and isopropyl alcohol were the irradiation solvents. These hydroxyalkylpyrimidines would arise by elimination of hydrogen chloride from the intermediate VI instead of by hypochlorus acid elimination to yield the corresponding alkylpyrimidines. Similar photoalkylation reactions did not occur when 2,4-dimethoxy-5-chloropyrimidine or 2,4-dimethoxypyrimidine were subjected to ultraviolet irridation. This lack of generality in the photoalkylation reaction is probably related to the reactivity indices of the various positions in the pyrimidine molecules (4).

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