A Versatile High Yield Photochemical Synthesis of 5-Substituted 6-Azauracils.

John S. Swenton (1) and Robert J. Balchunis

Department of Chemistry, Ohio State University, Columbus, Ohio 43210

Received March 18, 1974

Sir:

There has been extensive interest in *as*-triazines (often referred to as 6-azapyrimidines) as antiviral agents and as antimetabolites of pyrimidine bases (2). In spite of the biological interest in these systems, most syntheses of substituted 6-azauracils (*as*-triazine-3,5-(2*H*,4*H*)diones) are limited to ring closure processes of α-ketoacid derivatives (3); synthetic routes to functionalized 5-substituted 6-azauracils are uncommon. In connection with photochemical studies of azapyrimidine systems (4), we have noted a mild, facile conversion of the parent 6-azauracil to functionalized 5-substituted derivatives which we wish to report here. Appropriate reactions at the 5-substituent should provide easy access to a wide variety of 5-substituted 6-azauracils.

Acetone sensitized irradiation of 6-azauracil (**1a**) or 1,3-dimethyl-6-azauracil (**1b**) in the presence of vinyl acetates (**2a** or **2b**) produces good yields of the corresponding azetidines (**3a-d**). While these epimeric adducts can be isolated by careful silica gel chromatography, it is more convenient to treat the crude product with water and obtain the dihydro derivatives (**4a-d**) in overall yields of 66-83%. Oxidation of the dihydro derivatives (**4a-d**) affords the respective 5-substituted 6-azauracils.

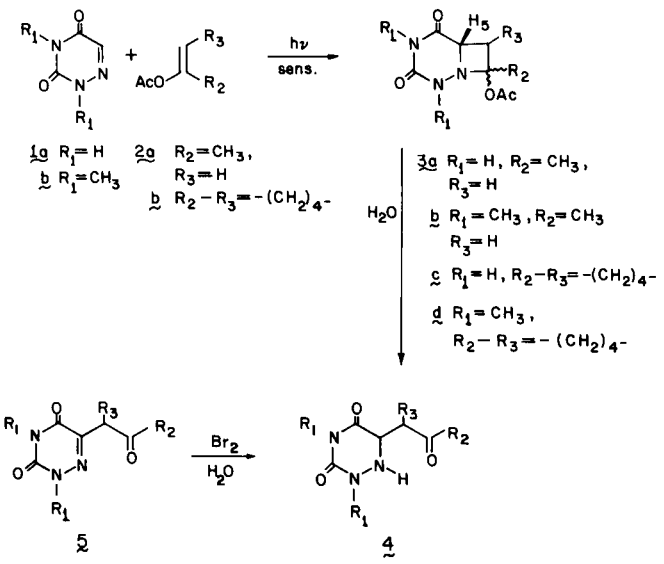
There are two possible orientations for the bicyclic azetidine adducts produced from these reactions, the acetate moiety being either at the 7- or the 8-position of the 1,2,4-triazabicyclo[4.2.0]octa-3,5-dione skeleton. To rigorously establish the orientation for one of these reactions, the major cycloadduct from 1,3-dimethyl-6-azauracil and isopropenyl acetate was isolated by column chromatography (65% yield, m.p. 99-102°). This material, which decomposed rapidly at room temperature liberating acetic acid, showed an nmr spectrum consistent only with the orientation shown: nmr (deuteriochloroform, 60 Mz): 4.28 (doublet of doublets, J = 6.5, 3.0 Hz, 1H), 3.18 (s, 3H), 3.13 (s, 3H), 2.8-2.5 (m, 2H), 1.94 (s, 3H), and 1.71 (s, 3H) δ. The appearance of H_5 as a doublet of doublets at 4.28 δ rigorously excludes the product with the acetate and methyl group at position 7 as this would have shown H_5 as a singlet. The azetidines formed in the remaining systems were not rigorously characterized but decomposed with water to yield the corresponding dihydro compounds (**4a-d**). This same orientation is strongly supported for these compounds by their facile hydrolyses under mild conditions and the formation of corresponding dihydro compounds. The structures of the dihydro compounds

TABLE I

Acetone Sensitized Addition of 6-Azauracils to Vinyl Acetates (a,b,c)

6-Azauracil Derivative (moles)	Olefin (moles)	Yield of **4**	M.p., °C **4**	M.p., °C **5**
1a (0.019)	isopropenyl acetate (0.30)	83%	191-193	174-176
1b (0.0071)	isopropenyl acetate (0.018)	70%	90-92	102-103
1b (0.0142)	isopropenyl acetate (0.20)	80%		
1a (0.0088)	cyclohexenyl acetate (0.142)	70%	224-226	239-240
1a (0.0095)	cyclohexenyl acetate (0.021)	70%		
1b (0.0071)	cyclohexenyl acetate (0.107)	66%	112-114	128-130

(a) Corex-filtered light from a 450-watt Hanovia medium-pressure source was utilized for all irradiations; (b) In a typical run the indicated amount of reactants in 70% acetone-water (**1a**) or 10% acetone-acetonitrile (**1b**) was irradiated for 2-4 hours to effect complete reaction; (c) All compounds reported here gave acceptable combustion analyses, ± 0.3%.



(**4a-d**) and the 6-azauracils (**5a-d**) are supported by their combustion analyses, ir, nmr, and mass spectra (5).

The photochemical route described here makes potentially available a wide range of 5-substituted 6-azauracil derivatives. As this sequence offers an extremely mild, high yield procedure for carbon-carbon bond formation, it may be exceedingly useful in functionalizing nucleoside derivatives of 6-azauracil as well as other conjugated imine systems. Studies along these lines are currently in progress and will be the subject of future publications.

REFERENCES

(1) Camille and Henry Dreyfus Teacher-Scholar (1972-1977).

(2) For leading references see J. Elis and H. Raskova, *Europ. J. Clin. Pharmacol.*, **4**, 77 (1972); J. Skoda, *Progress in Nucleic Acid Research and Molecular Biology*, **2**, 197 (1963).

(3) For leading references see J. Gut, *Adv. in Heterocyclic Chemistry*, 1, 189 (1963).

(4) J. A. Hyatt and J. S. Swenton, *J. Chem. Soc., Chem. Commun.*, 1144 (1972).

(5) Complete spectroscopic data will be reported in our full manuscript.