

7. TLC analysis of the product was carried out on Quanta precoated silica gel, Q6 plates (developed with cyclohexane and visualized by charring with sulfuric acid) indicates a pure material. M^+ 370 ($C_{27}H_{46}$); $[\alpha]_D^{24} = +19.6^\circ$; IR: 831, 783, and 678 cm^{-1} ; NMR ($CDCl_3$), δ 0.66 (s, 3H, C-18 CH_3), 0.94 (s, 3H, C-19 CH_3), 5.23-5.75 (m, 2H, vinyl). The oily product crystallized after long standing, mp. $48-50^\circ$, lit.³ $48-49^\circ$. The dibromo derivative, 3 α ,4 β -dibromo-5 β -cholestane melted at $98-99^\circ$, [lit. $98-100^\circ$: A. Nickon, N. Schwartz, J. Digiorgio and D. Widdowson, J. Org. Chem., 30, 1711 (1965).].

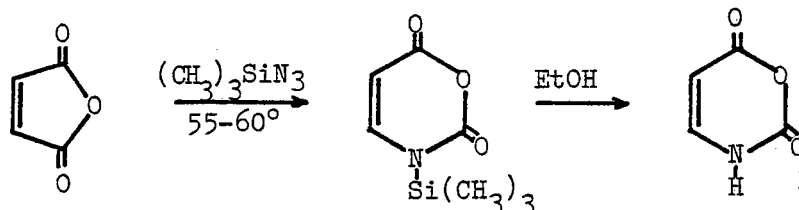
IMPROVED PROCEDURE FOR THE PREPARATION OF "OXAUACIL",

2H-1,3(3H)-OXAZINE-2,6-DIONE

Submitted by John H. Macmillan
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Department of Chemistry
Temple University
Philadelphia, Pennsylvania 19122

The 3-oxa derivative of uracil, 2H-1,3(3H)-oxazine-2,6-dione (I) has been under investigation as an antimetabolite due to its demonstrated activity vs. E. Coli¹ and L1210 leukemia cells.² Published procedures for the synthesis of I³⁻⁵ suffer from low and irreproducible yields. The product obtained by heating maleic anhydride with trimethylsilyl azide to reflux in non-polar solvents is also usually severely contaminated with a difficultly separable brown polymer. Since we required large quantities of I in reasonable purity, a study of the optimum conditions for its synthesis was undertaken. A procedure for the synthesis of I in 60-80% yields with little polymeric contamination from trimethylsilyl azide and maleic anhydride in the absence of solvent has been developed.



PROCEDURE

All glassware should be washed with dilute acid and distilled water then oven dried. Trimethylsilyl azide (Petrarch Systems) and maleic anhydride (Aldrich lumps, freshly pulverized) were used as received. All reactions and workups should be carried out in an efficient hood.

2H-1,3(3H)-Oxazine-2,6-Dione (I).- A flame-dried 50 ml three-neck flask was charged under nitrogen with 4.9 g (50 mmoles) of maleic anhydride and 14 ml (100 mmoles) of trimethylsilyl azide. A thermometer was inserted and the slurry gently heated with stirring. At $\sim 40^\circ$ the anhydride dissolved and gas evolution commenced. The reaction gently exothermed at this point and the external heat was discontinued. Gas evolution became moderate at $\sim 55-60^\circ$. The reaction was alternatively heated and cooled with a water bath so as to maintain a temperature range of $55-60^\circ$. The temperature must not be allowed to go above 60° or a substantially colored product will result. After 3 hrs., gas evolution had ceased. The reaction was cooled to room temperature, diluted with 30 ml chloroform and treated with 2.5 g (54 mmoles) of absolute ethanol. Cooling to 0° gave copious white microcrystals of I which were collected and washed with ether; yield 3.2 g (57%), mp. $158-62^\circ$ (dec.), lit.⁴ mp. $158-9^\circ$ (dec.). The IR and NMR spectra were identical to those reported.⁴ Partial concentration of the filtrate and cooling gave a second crop, 1.2 g, mp. $153-6^\circ$ (dec.), slightly tan microcrystals: total yield 4.4 g (78%). The resulting product is sufficiently pure for most purposes but may be crystallized from ethyl acetate.

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