SELECTIVE ALKYLATION OF 5-AMINOURACIL DERIVATIVES

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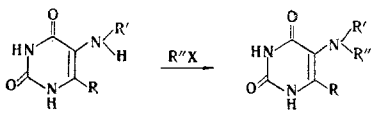
We have found that the direct selective alkylation of the amino group of 5-aminouracils (I-IV) with alkyl halides to give 5-N-alkyl- and 5-N,N-dialkylaminouracils (II-XIII) is possible. Alkylation proceeds readily in solvents with high ionizing capacity in the presence of a small molar excess of the alkyl halide and if the alkaline agent is fed in uniformly (with allowance for the reaction rate and without permitting the accumulation of excess base). The reaction time was established by titration of the halide ion.

A mixture of 28.2 g (0.2 mole) of Ib and 150 ml of dimethylformamide was heated to 90°, 32 g (0.25 mole) of bromofluoroethane was added and the mixture was neutralized with equal portions of triethylamine [four 5.08-g (0.2-mole) portions] every 2 h for 8 h. The mixture was then cooled and filtered, and the filtrate was vacuum evaporated. The residue was washed with methylene chloride and recrystallized from nitromethane to give 26 g (70%) of Vb with mp 185-187° and R_f 0.38. UV spectrum, λ_{max} (log ε), pH 7 270 nm (3.77); pH 1 262 nm (3.84); pH 13 285 nm (3.76). Found, %: C 45.0; H 5.4; F 10.0; N 22.6. $C_7H_{10}FN_3O_2$. Calculated, %: C 44.9; H 5.4; F 10.2; N 22.5.

The compounds presented in Table 1 were similarly synthesized.



I-IV V-VIII

I R′=H; II R′=CH_3; III R′=C_2H_5; IV R′=CH_2CH_2OH; V R′=H, R″=CH_2CH_2F; VI R′=R″=CH_3; VII R′=R″=C_2H_5; VIII R′=R″=CH_2CH_2OH; IX R′=R″=CH_2CH_2F; X R′=CH_2CH_2OH, R″=CH_3; XI R′=CH_2CH_2OH, R″=C_2H_5; XII R′=C_2H_5, R″=CH_3CH_2F; XIII R′=CH_2CH_2OH, R″=CH_2CH_2F; I—XIII a R=H; b R=CH_3; X=Br, I

Satisfactory analytical results were obtained for all of the compounds. The R_f values for chromatography on Silufol in chloroform–methanol (9 : 1) are given. The IR spectra of V-VIII contain absorption bands at 3100 (ring NH) and 1630-1730 cm^{-1} (C=O). The PMR spectra contain two N_1H and N_3H signals at 10.5-11.5 ppm. Absorption maxima at 260-263 nm (pH 1) and at 285-293 nm (pH 13) are characteristic in the UV spectra of V-VIII.

TABLE 1. Characteristics of the Compounds Obtained

Compound	Mp (dec.), °C	R_f	Yield, %
VIa	305—307	0,30	65
VIIb	193—195	0,56	73
VIIIb	195—196	0,16	77
IXb	172—173	0,57	39
Xa	223—225	0,27	60
XIa	208—209	0,32	75
XIb	169—171	0,36	85
XIIb	175—177	0,64	79
XIIIa	149—151	0,30	57
XIIIb	122—124	0,34	72

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