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NUCLEOSIDES. X. THE ACTION OF SODIUM ETHOXIDE ON 3'-O-TOSYL-2'-DEOXYADENOSINE

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Recently Robins and Robins (1) described the direct displacement of the secondary sulfonyloxy group of 3'-O-tosyl-2'-deoxyadenosine (I) by ethyl mercaptan in a sodium ethoxide-ethanol medium as part of a synthetic sequence leading to 2',3'-dideoxyadenosine (IV) (2). We wish to report that the base-solvent system alone effects both elimination and intramolecular displacement in I and thereby affords both a 2',3'-unsaturated nucleoside (III) and a 3',5'-oxetane derivative (II) in a ratio of ca. 4:1. The olefin provides a synthetic avenue to a number of difficultly accessible purine nucleosides which includes a more efficient route (3) to IV (vide infra).

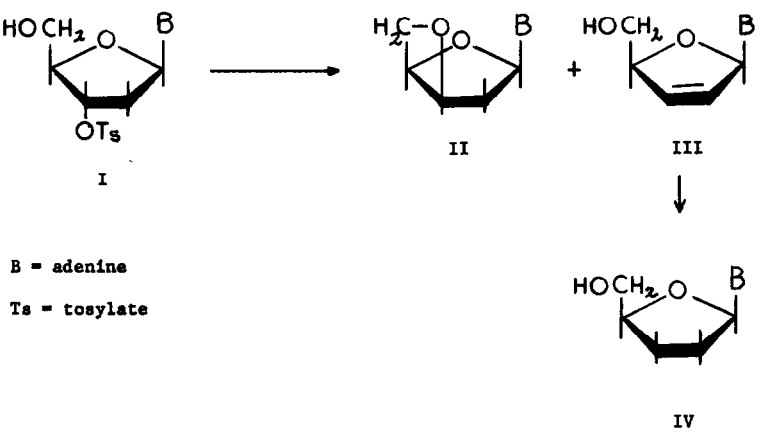
Treatment of I (1) with a slight excess (1.25 equiv.) of sodium ethoxide in ethanol under gentle reflux for 0.75 hr. afforded a mixture of nucleosides which was resolved by column chromatography over Dowex-1(OH^-)* according to the procedure described by Dekker (4). Two peaks of optical density at 260 mu developed an elution of the column with 30% methanol. The material comprising the first peak crystallized from ethanol in the form of colorless needles (14% yield), m.p. 260-262° dec. $[\alpha]_D^{24}$ - 95.2° (c 0.3, H_2O), $\lambda_{max,\ min}^{MeOH}$ 259 mu (ϵ 15200), 226 mu (ϵ 2200), and was assigned the structure 6-amino-9-(2-deoxy-3,5-epoxy-β-D-

* Bio-Rad AG 1-X8 (OH^-, 140-325 mesh).

threo-pentofuranosyl)purine (II). Anal. Calcd. for $C_{10}H_{11}N_5O_2$: C, 51.49; H, 4.75; N, 30.03. Found: C, 51.40; H, 4.96; N, 29.92.

The specific rotation of II is in accord, both in sign and order of magnitude, with the optical rotatory values of the 1-(2-deoxy-3,5-epoxy-β-D-threo-pentofuranosyl)pyrimidines (5). The proton magnetic resonance spectra of the latter show a complex multiplet at δ 2.6 to 2.8 which is assigned to the C'5 methylene protons of the oxetane ring. Virtually the same multiplet is seen in the high field portion of the spectrum (D_2O) of II.

The product derived from the second peak crystallized from ethyl acetate as colorless needles (52% yield), m.p. 190° (6), $[\alpha]_D^{24}$ + 22.5° (c 0.4, MeOH), and was assigned the isomeric structure 6-amino-9-(2,3-dideoxy-2-ene-β-D-glycero-pentofuranosyl)purine (III). Anal. Found: C, 51.43; H, 4.97; N, 29.85. Spectral data showed: $\lambda_{max,\ min}^{MeOH}$ 259 mμ (ε 15300), 226 mμ (ε 2900). Catalytic (10% Pd.C) reduction of III gave 2',3'-dideoxyadenosine (IV), m.p. 183-185°, $[\alpha]_D^{25}$ - 28.3° (c 0.5, H_2O) [lit. (1) 184-186°, $[\alpha]_D^{25}$ - 25.2° (H_2O)].



I II III

B = adenine

Ts = tosylate

IV

Recent studies (5,7) in this laboratory have demonstrated that the oxetane ring in, for example, 1-(2-deoxy-3,5-epoxy-β-D-threo-pentofuranosyl)thymine readily undergoes decyclization with concomitant introduction of 2',3'-unsaturation on treatment with potassium t-butoxide in dimethyl sulfoxide (t-BuOK-DMSO) at ambient temperatures. By contrast, the same linkage proved resistant to cleavage by either sodium methylate or sodium benzylate (8). The latter behavior was, as might be anticipated, seen also in II which was recovered unchanged following treatment with 1 equiv. of sodium ethoxide in ethanol at reflux for 5 hr. Accordingly, it may be concluded that II and III are the result of independent reactions with the process of elimination favored over cyclic ether formation. The latter transformation appears to be a relatively rare instance of displacement of a ring secondary sulfonate by a primary hydroxyl group which has only recently been observed (9) in the formation of a 2,6-anhydro-glycopyranoside derivative. However, the present example is distinguished by the fact that displacement is promoted under conditions which proved ineffective in the formation of the 2,6-anhydro sugar derivative.

The possibility of promoting the direct conversion of I to III in t-BuOK-DMSO is currently under study. The results of this phase of the investigation will be reported in the more detailed communication.

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6. The melt solidifies immediately and there is no further indication of a change in state up to 360°. A similar observation was recorded for the 2',3'-unsaturated pyrimidine nucleosides; see ref. 5.

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