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AN ANOMALOUS REACTION IN BROMINATION OF 2-BENZYLAMINO-1-BUTANOL

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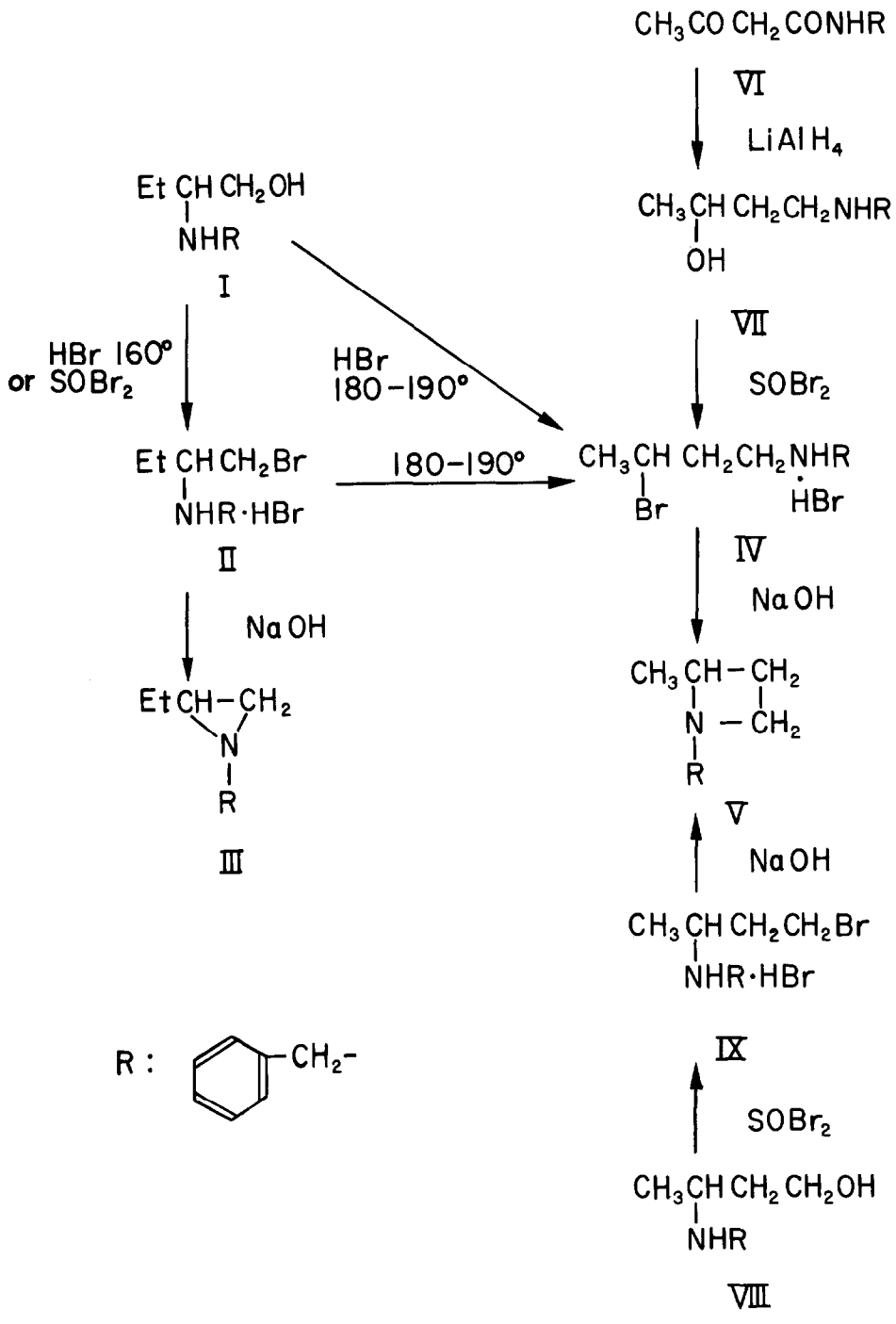
We wish to report an anomalous reaction of 2-benzylamino-1-butanol (I) with HBr whereby I can be converted into 1-benzylamino-3-bromobutane hydrobromide (IV).

The conversion of β-amino alcohols to β-haloamines followed by base-catalyzed cyclization (Gabriel synthesis) constitutes one of a more useful routes to aziridines. A possible modification of the Gabriel synthesis consists of the reaction of amino alcohol with HBr. Heating of optically active I (Ia, mp 74-75°, $[\alpha]_D^{15}$ + 26.60° (c 1.015, EtOH); Ia-HBr, mp 135-136°, $[\alpha]_{300}^{25}$ + 12.4° (c 1.129, EtOH)) with 48% HBr at 160° by the modified procedure of Cortese (1) gave the expected corresponding product (IIa) (mp 122-123°, $[\alpha]_D^{20}$ + 22.07° (c 1.495, EtOH)) in 22% yield. A mixture of Ia and HBr was heated under reflux and the water formed was distilled through a fractionation column. In this reaction, when the final heating was carried out until the temperature of the content reached 180-190°, an abnormal product, mp 223-225°, which had no optical rotation, was obtained exclusively in 46% yield. Reaction of the racemate of I (Ib, mp 59-60°; Ib-HCl, mp 125-126°) with HBr under the same condition yielded a product identical with the abnormal product in 38% yield, mixed mp 224°. A cyclic amine produced by the treatment of this compound with alkali also did not correspond to the desired aziridine (III), even by variation of the reaction condition.

The NMR spectra of the abnormal product and the cyclic amine showed a doublet assignable to the methyl group. This means that they do not contain an ethyl group in their structure as a result of rearrangement during bromination. Their elemental analytical values and molecular weight were consistent with those of the expected compounds, II and III, but their spectral evidences suggested that their structures were different from II and III. This result, their mode of formation,


CH3CO CH2CONHR
VI
LiAlH4
CH3CH CH2CH2NHR
OH
VII
SOBr2
Et CH CH2OH
NHR
I
HBr 160°
or SOBr2
HBr
180-190°
Et CH CH2Br
NHR·HBr
II
180-190°
CH3CH CH2CH2NHR
Br
HBr
IV
NaOH
Et CH-CH2
N
R
III
NaOH
CH3CH-CH2
N-CH2
R
V
NaOH
CH3CH CH2CH2Br
NHR·HBr
IX
SOBr2
CH3CH CH2CH2OH
NHR
VIII
R : CH2-

their reactivities toward various reagents, and comparison with model compounds (v. i.) indicated them to possess respective structures of IV and V.

The authentic sample of IV, mp 223-224°, NMR (CF_3COOH), τ 2.51 (s, 5, aromatic), 5.59 (m, 3, $C\underline{H}_2Ph$, $C\underline{H}Br$), 6.50 (broad, 2, $C\underline{H}_2NR_2$), 7.58 (broad, 2, $CHC\underline{H}_2$), 8.23 (d, 3, $C\underline{H}_3$), was derived from N-benzylacetoacetamide (VI), mp 104-105°, IR (KBr) cm^{-1}, 3220 (NH), 1710 (C=O), 1635 and 1578 (amide C=O), which was prepared by treating diketene and benzylamine according to the reported procedure (2), by way of the reduction product (VII) (bp 121-123°/2 mm Hg, n_D^{20} 1.5237, the reduction was carried out with $LiAlH_4$ in tetrahydrofuran for 24 hr.). Treatment of VII with $SOBr_2$ by the reported procedure (3) for 1-amino-2-bromopropane hydrobromide afforded a product identical with IV, mp 225°, showing no depression in mixed melting point determination.

The reaction of Ia or Ib with $SOBr_2$ also gave the normal brominated product IIa (86%) or IIb (67%, mp 130-133°), which was converted into the corresponding 1-benzyl-2-ethylaziridine (III) by treatment with alkali (IIIa, bp 89-90°/9 mm Hg, n_D^{20} 1.5077, $[\alpha]_D^{15}$ + 22.12° (c 1.130, benzene), NMR (CCl_4) τ 2.80 (s, 5, aromatic), 6.70 (q, 2, $C\underline{H}_2Ph$), 8.45-8.86 (m, 5, $CH_3C\underline{H}_2C\underline{H}C\underline{H}_2$), 9.17 (t, 3, $C\underline{H}_3CH_2$)).

1-Benzyl-2-methylazetidine (V) (4), bp 86-87/9 mm Hg, [lit. 106-108°/23 mm Hg], n_D^{20} 1.5116, NMR (CCl_4) τ 2.84 (s, 5, aromatic), 6.53 (q, 2, $C\underline{H}_2Ph$), 6.79 (m, 2, $C\underline{H}_2N$), 7.00-7.55 (m, 1, $C\underline{H}$), 7.90-8.50 (m, 2, $CHC\underline{H}_2$), 9.01 (d, 3, $C\underline{H}_3$), was also synthesized in a good yield (67%) from 1-bromo-3-benzylaminobutane hydrobromide (IX), mp 151-152°, which was obtained in 86% yield by the treatment of 3-benzylamino-1-butanol (VIII) (4) with HBr under milder reaction condition or with $SOBr_2$, but IX had a structure different from that of IV. In the NMR spectra, the chemical shift of the methyl protons in IV (τ 8.24, CF_3COOH) was observed in a lower magnetic field than that of IX (τ 8.43, CF_3COOH).

Heating of IIa or IIb at 180-190° for 10 min. or the reaction of Ia-HBr with PBr_3 in the manner described by Leffler for monoethanolamine (5) also gave a product identical with IV. Under such a drastic condition, therefore, II formed by the first stage of bromination seems to undergo a rapid transformation. A similar thermal treatment of the compound IX or bromination of VIII with HBr under drastic conditions (200-215°) afforded only a mixture of IX and benzylamine hydrobromide

(mp 218-219°). This result seems to be a normal, thermal decomposition in the presence of HBr.

Various mechanisms can be considered for the transformation of II to IV. The most likely route appears to be (i) formation of an aziridinium ion (ii) ring opening of the aziridinium ion at the secondary carbon atom accompanying formation of a double bond between C_2 and C_3, and (iii) selective addition of HBr to the double bond. Further studies on the mechanism of this anomalous reaction is in progress.

All the compounds synthesized gave satisfactory elemental analyses.

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