ALKYLATION OF TETRAZOLES BY n-PROPYL- AND ISOBUTYL ALCOHOLS

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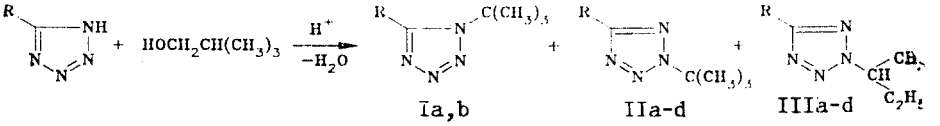
We have recently shown [1] that tetrazole and 5-substituted tetrazoles are alkylated by isopropyl, *tert*-butyl, and cyclohexyl alcohols in concentrated H_2SO_4 (~20°C) selectively at the ring 2 position. High yield (80-100%), short duration of the reaction (30-70 min), and its simplicity allow us to propose it as a convenient method for preparing 2- and 2,5-substituted tetrazoles [2]. It was of interest to consider the reaction of tetrazoles with other alcohols, in particular the primary alcohols *n*-PrOH and *i*-BuOH which might undergo isomerization of the carbon skeleton under the conditions used.

As might be expected, alkylation by these alcohols proceeds much more slowly. The only reaction products of the tetrazole or 5-methyltetrazole with *n*-PrOH in 96% sulfuric acid are the corresponding 2-isopropyltetrazole (yield 36%) and 2-isopropyl-5-methyltetrazole (20%). Upon alkylation of tetrazole and 5-methyltetrazole by isobutyl alcohol under the same conditions there are formed the corresponding 2-*tert*- and 2-*sec*-butyl derivatives IIa, b and IIIa, b together with the unexpected 1-*tert*-butyltetrazoles Ia (62%) and Ib (13%). The 1-isomers are not found in the reaction of 5-phenyl- and 5-trifluoromethyltetrazoles with isobutyl alcohol. The content of the 2-*tert*-butyltetrazoles in the mixtures are: 8 (IIa), 65 (IIb), 80 (IIc), and 86% (IId), the remainder being the 2-*sec*-butyltetrazoles IIIa-d.



a R=H, b R=CH_3, c R=C_6H_5, d R=CF_3

Formation of the 1-*tert*-butyltetrazoles by alkylation with isobutyl alcohol is sensitive to the content and electronic character of the 5-substituent and also to the reaction time. Thus the reaction mechanism, in this case, differs from that proposed earlier [1] for *sec*- and *tert*-alcohols.

The alcohol (27 mmoles) was added dropwise to a solution of the 5-R-tetrazole (25 mmoles) in 96% H_2SO_4 (17-18 ml), held for 18 h at ~20°C, and worked up as described in method [1]. The composition of the reaction mixture was determined by PMR and ^{13}C NMR spectroscopy. The mixture composition was calculated from the integrated intensities of the PMR spectral signals. The melting points of the 1-*tert*-butyltetrazoles Ia and Ib, after distillation of the 2-isomers and recrystallization, agreed with literature data [1, 3].

LITERATURE CITED

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