Tetrahedron Letters No.32, pp. 2157-2160, 1964. Pergamon Press Ltd.
Printed in Great Britain.

ON THE BROMINATION OF ACENAPHTO-2-ISOXAZOLINES

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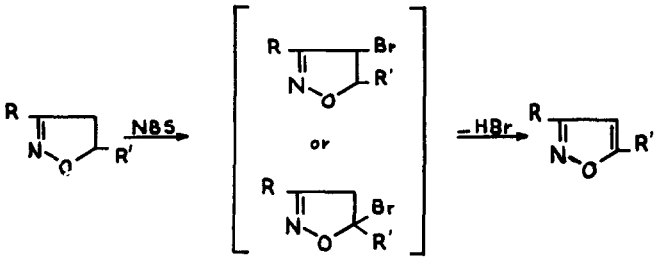
(Received 22 June 1964)

The dehydrogenation of 2-isoxazolines, readily available by condensation of nitrile oxides with double bond compounds, via N-bromosuccinimide bromination and subsequent dehydrobromination has been proved to represent a convenient and general route to isoxazoles (1):

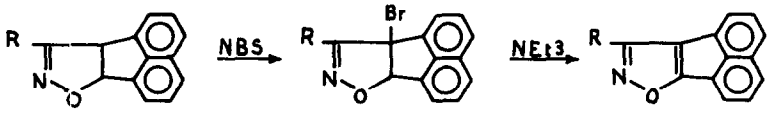


Usually the intermediate bromoderivative is too unstable to be isolated. However, we wish to report now the results obtained with 2-isoxazolines derived from acenaphtylene, where the bromoderivatives are stable and readily isolable.

3-Methyl-acenaphto [1,2,d] -2-isoxazoline (I, R = CH_3)(2) in CCl_4 solution reacts rapidly with N-bromosuccinimide in the presence of some α, α'-azoisobutyronitrile; filtration and solvent evaporation leaves with 88 % yield a product m.p. 111° (colorless prisms from methanol)(+).

(+) Satisfactory analyses were obtained for all compounds reported herein.

The structure (II) of isoxazoline-4-bromoderivative is supported by n. m. r. spectroscopy (+). The n. m. r. spectrum of 3-methyl-acenaphto [1, 2, d] -2-isoxazoline shows, besides the signals of naphthalenic protons (multiplet between 2.50 and 2.67 τ) and the CH_3 protons (7.97τ), two doublets at 3.64 resp. 5.08 τ , typical for an AB system with J = 9.1 c. p. s. From a systematic study on n. m. r. spectroscopy of several 2-isoxazoline derivatives, whose substituents in 4 and 5 position are known unequivically, it has been possible to allocate the doublet at 3.64 τ to the 5-proton of 2-isoxazoline ring, and the doublet at 5.08 to the 4-proton. In bromoderivative m. p. 111° (II, R = CH_3) the



I II III

doublet at 5.08 τ disappears, and the 5-proton appears as a singlet at a slightly shifted position (Δτ - 0.05 p. p. m.)

, 3-Methyl-4-bromo-acenaphto [1, 2, d] -2-isoxazoline (II, R = CH_3) dehydrobrominates easily by prolonged heating (8-9 hrs.) with NEt_3 or by shorter heating (1hr.) in methanolic KOH, yielding quantitatively 3-methyl-acenaphto [1, 2, d] isoxazole m. p. 82-82, 5° (deep yellow needles from methanol).

Likewise 3-phenyl-acenaphto [1, 2, d] -2-isoxazoline (I, R = C_6H_5)(3), treated with N-bromosuccinimide, gave (96 % yield) the 4-bromoderivative (II, R = C_6H_5) m. p. 159° (white tables from ethanol). Its structure has

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(+) The n. m. r. spectra were recorded in saturated CCl_4 solution at 55° on a Varian Assoc. Model DP-60 high resolution spectrometer (60 Mc/sec), equipped with variable temperature kit. Chemical shifts were determined by the audiofrequency side-band technique with tetramethylsilane as an internal reference (10.0 τ) and are accurate to at least ± 0.04 τ .

been confirmed by comparison of its n. m. r. spectrum with that of the parent isoxazoline (I, R = C_6H_5), which, besides the multiplet due to naphthalenic and phenyl protons at 2.5 0 - 2.90 τ , shows the 5-proton doublet at 3.71 τ and the 4-proton doublet at 4.70 τ ($\underline{J}$ = 9.10 c.p.s.). The n. m. r. spectrum of 4-bromoderivative lacks of 4-proton signal and shows a singlet at 3.45 τ .

Dehydrobromination of (II, R = C_6H_5) by heating with methanolic KOH for 30-40 minutes yielded (95 %) 3-phenyl-acenaphto [1,2,d] isoxazole (III, R = C_6H_5) m.p. 144-145° (yellow needles from ethanol).

The behaviour of 3-ethyl-acenaphto [1,2,d] -2-isoxazoline (I, R = C_2H_5) (2) towards N-bromosuccinimide is noteworthy: column chromatography allowed to separate two isomers m.p. 111,5-112,5° resp. m.p. 108° in almost equivalent quantities. The former product (colorless plates from methanol) is the 4-bromoderivative (II, R=C_2H_5), as demonstrated by its n. m. r. spectrum with signals at 3.60 (5-proton), 7.65 (-CH_2-) and 8.90 τ (CH_3-), and by ist easy conversion with bases to 3-ethyl-acenaphto (1,2,d isoxazole (III, R = C_2H_5) m.p. 78° (yellow tablets from methanol).

The product m.p. 108° (colorless needles from methanol) is thought to be 3-α.bromoethyl-acenaphto [1,2,d] -2-isoxazoline (I, R = CH_3CHBr), whose structure is consistent both with u.v. and n. m. r. evidence: u.v. spectrum (see Table I) is very similar to the spectra of 3-alkyl-acenaphto [1,2,d] -2-isoxazolines, whereas 4-bromoderivatives (II) present only one absorption maximum at about 290 mμ instead of the three maxima at 276, 286, 298 mμ typical of former compounds. N. m. r. spectrum of 3-ethyl-acenaphto [1,2,d] -2-isoxazoline shows, besides naphthalenic protons at 2.64-2.80 τ and 5-proton resp. 4-proton at 3.82 resp. 5.15 τ ($\underline{J}$ = 9.10 c.p.s.), the -CH_2- quartet at 7.68 τ and the CH_3- triplet at 8.89 τ ($\underline{J}_{CH_2-CH_3}$ = 7.5 c.p.s.). In n. m. r. spectrum of bromoderivative m.p. 108°, whereas both 5-proton and 4-proton appear, although chemically shifted (3.63 resp. 4.67 τ with unchanged $\underline{J}$ = 9.1 c.p.s.), the ethyl signals are deeply altered. The original -CH_2- signal shifts towards a lower field with $\Delta\tau \geq$ - 2.3 p.p.m. and its relative intensity is reduced to

TABLE I - U.V. Spectra (in EtOH)

Compound	λ_{max} (mμ)	log ε
I, R = CH_3	224, 276, 286, 298	4.74, 3.44, 3.54, 3.37
I, R = C_2H_5	225, 276, 286, 298	4.73, 3.75, 3.85, 3.67
I, R = C_6H_5	225, 266, 275, 286, 298	4.86, 4.06, 4.08, 4.03, 3.78
I, R = CH_3CHBr	223, 276, 286, 298	4.83, 3.78, 3.87, 3.70
II, R = CH_3	224, 292, 324.5	4.75, 3.81, 3.16
II, R = C_2H_5	224, 292, 325	4.73, 3.80, 3.17
II, R = C_6H_5	222, 285	4.97, 3.76
III, R = CH_3	231, 266, 276, 318, 340	4.69, 3.96, 3.98; 3.98, 3.76
III, R = C_2H_5	231, 266, 276, 318, 340	4.71, 3.97, 3.99, 3.98, 3.76
III, R = C_6H_5	230, 277, 287, 319, 344	4.65, 4.18, 4.18, 3.97, 3.68

one half, whereas the CH_3- signal appears as a doublet (8.08 τ), indicating that only one proton remains on adjacent α-carbon atom of ethyl group.

Consistently with structure (I, R = CH_3CHBr), the bromoderivative m. p. 108° does not dehydrobrominate to isoxazole by heating with KOH or NEt_3.

Further experiments in this field actually going on are confirming that isolation of a stable 4-bromoderivative by bromination with N-bromo-succinimide is general for 3-aryl (or methyl)-2-isoxazolines condensed with a five-membered ring in 4,5-position.

The authors gratefully acknowledge the financial assistence of the Consiglio Nazionale delle Ricerche.

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