Reactions of Sodium Hydrogentelluride with α-Azido Ketones and α-Azido Bromides

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(Received August 15, 1985)

Synopsis. When treated with sodium hydrogentelluride in ethanol at room temperature, α-azido ketones are easily converted to pyrazines via the self-condensation of initially formed α-amino ketones followed by aerobic oxidation during work-up. On a similar treatment, activated α-azido bromide such as 1,2-diphenyl-1-azido-2-bromoethane suffers E2-type β-elimination to give the corresponding olefin as the sole product, while ordinary α-azido bromides afford complicated mixtures containing amino and olefinic compounds among other products.

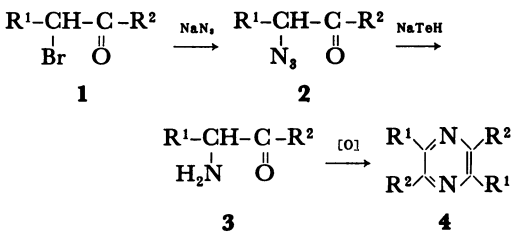
On heating with an excess of sodium borohydride in ethanol under nitrogen, elemental tellurium is reduced to form sodium hydrogentelluride as a wine-colored

$$Te + NaBH_4 + 3C_2H_5OH \xrightarrow[N_2,\,\Delta]{} NaHTe + B(OC_2H_5)_3 + 3H_2$$

solution. This reagent was first introduced by Barton in 1975,[1] but, in spite of its versatility as a selective reagent for reduction of a variety of organic compounds,[2] it has received little attention until recently. In a recent paper,[3] we have reported that sodium hydrogentelluride has an excellent ability to reduce alkyl and aryl azides to the corresponding amines under mild conditions. The reaction proceeds rapidly to completion and products are usually obtained in high state of purity. As an extension of this work, we have examined the reactions of sodium hydrogentelluride with polyfunctional azides, α-azido ketones and α-azido bromides, with an intent to see if the reaction can be used as a means to construct some nitrogen-containing heterocycles under mild conditions.

α-Azido ketones (**2**), readily prepared from α-bromo ketones (**1**) by standard procedure, was reacted with sodium hydrogentelluride in ethanol under nitrogen. The reaction occurred with immediate liberation of nitrogen and precipitation of free tellurium. After a while, the reaction mixture was exposed to air, freed from insoluble matter by filtration over a thin layer of Celite, and evaporated under reduced pressure to afford pyrazines (**4**). Several substituted pyrazines prepared by utilizing this procedure are summarized in Table 1, together with spectral data of the products. Yields shown do not represent optimized values.

Although the present method worked quite well with ordinary secondary azido ketones, it is not of a general nature. Thus, treatment of some primary azido ketones



such as α-azidoacetophenone and azidoacetone with sodium hydrogentelluride led to complicated mixtures of unidentified products. Azido ketone activated by adjacent electron-withdrawing group also failed to yield pyrazine; ethyl α-azidoacetoacetate gave only polymeric materials.

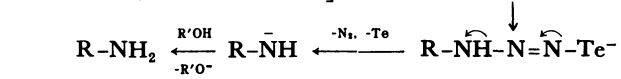
Reported procedures for converting carbonyl compounds into pyrazines include the reaction of 1,2-diketones with 1,2-diamines[4,5] or α-amino amides,[6] ammonolysis of α-halo ketones,[7,8] oxidation of ketones with alkaline hexacyanoferrate(III),[9] reduction of α-azido ketones with hydrogen over catalyst[10] or triphenylphosphine,[11] and reaction of ketones with iodine azide.[12]

Conversion of azide to amine may be explained to occur via a pathway which involves the attachment of hydrogentelluride anion to the terminal nitrogen atom of the azido group, followed by the fragmentation of the resulting triazene-type adduct in a way as

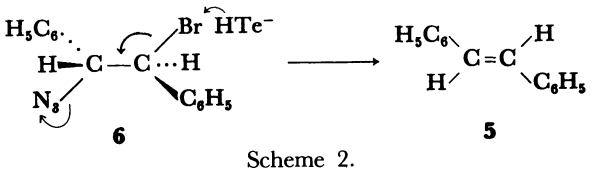
Table 1. Preparation of Pyrazines **4** from α-Azido Ketones **2**

	Pyrazine **4**		Mp	Yield/%	IR (KBr)	^{1}H NMR ($CDCl_3$)
	R^1	R^2	θ_m/°C		ν/cm^{-1}	δ/ppm
a	$-(CH_2)_4-$		105—106	87	1455, 1440, 1420, 1335, 1190, 1130, 980, 875, 820	1.4—2.2 (br. 8H), 2.4—3.1 (br. 8H)
b	CH_3	CH_3	85—86	82	1460, 1410, 1220, 1200, 1180, 985, 800	2.45 (s, 12H)
c	CH_3	C_3H_7	oil	98	1460, 1410, 1195, 1160, 1050, 975	0.95 (t, 6H, J=7 Hz), 1.3—1.9 (m, 4H), 2.40 (s, 6H), 2.60 (t, 4H, J=7 H)
d	H	$(CH_3)_3C$	105—107	50	1485, 1360, 1320, 1165, 1140, 1030	1.42 (s, 18H), 8.54 (s, 2H)
e	CH_3	C_6H_5	122—124	40	1440, 1400, 1230, 1160, 1065, 1025, 965, 775, 750, 700	2.61 (s, 6H), 7.2—7.6 (m, 10H)

shown in Scheme 1. In a protic solvent such as ethanol, amide anion is protonated to give amine. It was therefore of interest for us to see if the amide anion generated from α-azido bromide might undergo an intramolecular nucleophilic displacement of bromine atom by adjacent negative nitrogen, leading to the nitrogen-containing cyclic system, i.e. aziridine. Thus, *erythro*-1-azido-2-bromo-1,2-diphenylethane (**6**) was prepared from *trans*-stilbene (**5**) and added to an ethanolic solution of sodium hydrogentelluride at room temperature. Tellurium immediately precipitated with effervescence and the original olefinic hydrocarbon **5** was obtained in nearly quantitative yield. The absence of amino compound in the product mixture and preservation of the original stereochemistry at carbon-carbon double bond suggest that this conversion involves the E2-type β-elimination as shown in Scheme 2.



Scheme 1.



Scheme 2.

On a similar treatment, 3-azido-2-bromo-2-methylbutane and 1-azido-2-bromocyclohexane afforded complicated mixtures containing amino and olefinic compounds among other products, but the expected azacyclic compounds could not be detected.

Experimental

Melting points were determined on a hot stage apparatus and are not corrected. ^{1}H NMR spectra were obtained at 60 MHz on a JEOL model JMN-60 spectrometer for solutions in carbon tetrachloride. IR spectra were recorded as potassium bromide disks on a Hitachi EPI-3G spectrophotometer.

Powdered tellurium was a commercial product of 99.99% purity and used as received. Azido ketones were prepared from the corresponding bromo ketones by treatment with an excess of sodium azide in acetone. Bromo azides were obtained by treating olefins with bromine azide, generated in situ from bromine and sodium azide in dichloromethane/30% hydrochloric acid.[14] Products were identified by ^{1}H NMR, IR and mass spectra as well as by comparison with authentic specimens. All compounds obtained are known.

Conversion of α-Azido Ketones (2) to Pyrazines (4); Typical Procedure: Sodium hydrogentelluride was prepared by heating powdered tellurium (0.65 g, 5.1 mmol) and sodium borohydride (0.45 g, 11.9 mmol) in ethanol (20 ml) for 1 h under a nitrogen atmosphere. To the resulting dark red solution, 2-azidocyclohexanone (**2a**; 0.278 g, 2.0 mmol) in ethanol (5 ml) was added with stirring. The color instantly turned black and was followed by evolution of nitrogen. After stirring for a while, the mixture was left open to air to destroy excess reagent and oxidize a dihydropyrazine formed via self-condensation of α-amino ketone (**3a**). Removal of metallic tellurium by filtration over Celite followed by evaporation of solvent afforded crude 1,2,3,4,6,7,8,9-octahydrophenazine (**4a**) as a solid residue, which was purified by chromatography over silica gel or recrystallization from methanol. Yield, 0.164 g (87%). Mp 105—106 °C (lit,[15] 106—108 °C).

Reaction of *erythro*-1-Azido-2-bromo-1,2-diphenylethane (6) with Sodium Hydrogentelluride. To a solution of sodium hydrogentelluride, prepared from tellurium (0.26 g, 2.0 mmol), sodium borohydride (0.19 g, 5.0 mmol) and ethanol (20 ml), was added α-azido bromide **6** (0.60 g, 2.0 mmol) in ether (2 ml) under nitrogen and the resulting black mixture was stirred for 2 h at room temperature. Addition of water (20 ml) followed by extraction of the product with dichloromethane afforded *trans*-stilbene (0.35 g, 98%). Mp 122—124 °C (lit,[16] 123—124 °C).

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