SYNTHESIS AND REARRANGEMENTS OF 2-AZIDOVINYL

KETONES

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The information in the literature on unsaturated azides in which the azido group is adjacent to an ethylenic bond is sparse and is concerned mainly with the synthesis of these compounds. Forster and Newman [1] have described the preparation of the simplest compound of this type, namely vinyl azide, and they state that they were unable to bring about the rearrangement of this into a triazole [1]. Azido-substituted cinnamic acid [2], 4-phenyl-3buten-2-one [3, 4], and chalcone have also been prepared [5]. The position of the azido group in these compounds was not established, and their properties have received scarcely any investigation.

The high mobility of the chlorine atom in alkyl [6] and aryl [7] 2-chlorovinyl ketones has enabledus to make use of them in the synthesis of the heretofore unknown 2-azidovinyl ketones. We have developed two variants of the synthesis of these compounds. In the first variant we used the 2-chlorovinyl ketones themselves, which readily react with sodium azide in an aqueous-alcoholic medium:

$$ArCOCH = CHCl + NaN_3 \rightarrow ArCOCH = CHN_3$$
$$Ar = C_0H_5 -, o - ClC_6H_4 -, p - ClC_6H_4 -, p - BrC_6H_4 - .$$

A drawback of this variant is the difficulty in the purification of the labile 2-azidovinyl ketones from the original ketones. The second variant envisages reaction in aqueous solution with use of the ammonium salts obtained from 2-chlorovinyl ketones and tertiary amines [8, 9]:

$$\begin{aligned} \text{RCOCH} &= \text{CHN}^+ (\text{CH}_3)_3 \text{ Cl} + \text{NaN}_3 \rightarrow \text{RCOCH} = \text{CHN}_3 + \text{N} (\text{CH}_3)_3 + \text{NaCl} \\ \text{R} &= \text{CH}_3 - , \ C_6 \text{H}_5, \ o\text{-ClC}_6 \text{H}_4 - , \ p\text{-ClC}_6 \text{H}_4, \ p\text{-Br} - C_6 \text{H}_4 - . \end{aligned}$$

In the preparation of aryl 2-azidovinyl ketones from ammonium salts impurities are formed of 2-aroylvinyl-substituted aroylacetaldehydes of structure:

$$ArCOCH - CHO$$
$$\downarrow$$
$$CH = CHCOAr$$

These substances, however, are very sparingly soluble in comparison with the aryl 2-azidovinyl ketones themselves and the impurities are easily removed in recrystallization. The ammonium salt obtained from 2-chlorovinyl methyl ketone is scarcely hydrolyzed at all under the experimental conditions, so that 2-azidovinyl methyl ketone is more conveniently prepared by the use of this variant of the synthesis because the azide may be used in further work without purification. 2-Azidovinyl methyl ketone is a heavy liquid with a pungent odor; it explodes violently (!) when heated, and great care must be taken when working with it. We did not succeed in carrying out its elementary analysis for carbon and hydrogen, and therefore confined ourselves to analysis for nitrogen. Aryl 2-azidovinyl ketones are crystalline substances which decompose when melted in a capillary with vigorous evolution of nitrogen. When kept, particularly in the light, all azides decompose with formation of a viscous red mass which gradually congeals into a glass.

It is known that the azido group has weak electron-donating properties [10]; in 2-azidovinyl ketones it is mobile and may be readily replaced in reactions with more strongly nucleophilic groups.

$$C_{6}H_{5}-C-CH=CH-N_{3}$$

$$X^{-} (X = NH, OCH_{3})$$

$$C_{6}H_{5}-C-CH=CH-X \xrightarrow{CH_{3}OH} C_{6}H_{5}COCH_{2}CH(OCH_{3})_{2}$$
for X = OCH_{3}

On reaction of 2-azidovinyl phenyl ketone with two molecules of piperidine a good yield is obtained of the previously known phenyl 2-piperidinovinyl ketone. On treatment with a solution of sodium hydroxide in anhydrous methanol 2-azidovinyl phenyl ketone probably gives 2-methoxyvinyl phenyl ketone, which under these conditions reacts further with methanol with formation of benzoylacetaldehyde dimethyl acetal. These transformations indicate that the compounds obtained are 2-azidovinyl ketones and not the isomeric triazones, whose formation might be supposed to occur. Moreover, despite several attempts we did not succeed in bringing about their rearrangement into triazoles. It should be noted that the question of the rearrangement of alkenyl azides into triazoles has been given special consideration in the literature, and such rearrangement is placed under doubt [11].

Like all azides, aryl 2-azidovinyl ketones are unstable in presence of mineral acids and undergo rearrangement with liberation of nitrogen. We considered it to be of interest to study this rearrangement, for it has been scarcely investigated at all in the case of unsaturated azides. A rearrangement in the reaction of dinitro olefins with sodium azide was examined by Emmons and Freeman; here they isolated furoxan, whose formation was explained by the authors on the basis of the rearrangement of the intermediate unsaturated azide, which was not isolated by them in the free state [12]

$$\begin{array}{c} \mathbf{R} - \mathbf{C} = \mathbf{C} - \mathbf{R} \\ | & | \\ \mathbf{NO}_2 \ \mathbf{NO}_2 \end{array} + \mathbf{NaN_3} \rightarrow \begin{bmatrix} \mathbf{R} - \mathbf{C} = \mathbf{C} - \mathbf{R} \rightarrow \mathbf{R} - \mathbf{C} = \mathbf{C} - \mathbf{R} \\ | & | \\ \mathbf{NO}_2 \ \mathbf{N}_3 \end{array} \begin{bmatrix} \mathbf{R} - \mathbf{C} = \mathbf{C} - \mathbf{R} \\ | & | \\ \mathbf{NO}_2 \ \mathbf{N}_3 \end{array} \end{bmatrix} \rightarrow \begin{bmatrix} \mathbf{R} - \mathbf{R} - \mathbf{R} \\ \mathbf{N} \\ \mathbf$$

Knunyants and Bykhovskaya observed an interesting rearrangement of perfluoropropenyl azide, which according to their results gives perfluoroazacyclobut-2-ene [13]. However, perfluoropropenyl azide was also not isolated in the free state.

$$\begin{bmatrix} CF_{2}CF = CF - N \\ \end{bmatrix} \rightarrow \begin{bmatrix} CF_{2} - CF \\ \parallel \\ F - N - CF \end{bmatrix}$$

When the 2-azidovinyl phenyl ketone that we obtained was decomposed in a glacial acetic acid medium under the action of concentrated hydrochloric acid, we isolated and identified benzoylacetonitrile (82%) and 5-phenylisoxazole (7%):

$$C_{6}H_{5}COCH = CHN_{3} \rightarrow C_{6}H_{5}COCH_{2}CN +$$

$$C_{6}H_{5} O$$

It is known that the decomposition of azides gives an intermediate rapidly rearranging particle called azene

(RN <). In the recent literature there has been a discussion of the electronic nature of this particle. On analogy

to carbenes, azenes are considered to have either a singlet state of electrons (RN: - an electrophilic particle) or a triplet state (RN· - a diradical). Some examples are found to confirm one view and some the other, but most cases of the rearrangement of the azene can be explained on the basis of the diradical properties of the particle [14]. Formally, we could represent the formation of the products of the rearrangement of (2-benzoylvinyl)azene ($C_6H_5COCH =$

CH N <), both on the basis of the diradical and on the basis of the electrophilic properties of this particle. How-

ever, for the explanation of the mechanism it appears most convenient to us to adopt the scheme of the rearrange-

ment of
$$\begin{bmatrix} C_6H_5COCH = CH N \end{bmatrix}$$
 by coordinated cyclic electronic transfer [15].

The formation of benzoylacetonitrile by such a mechanism may be explained by three-center cyclic electronic transfer, as a result of which there is formed benzoylketene imine, a tautomeric form of benzoylacetonitrile, for which the tautomeric equilibrium is strongly displaced toward the nitrile side:

$$\begin{bmatrix} C_6H_5-CO-CH=C-NH & C_6H_5COCH=C=NH & C_6H_5COCH_2CN & H \end{bmatrix}$$

The formation of 5-phenylisoxazole may be represented as a five-center cyclic coordinated transfer occurring as a result of the conjugation of the azene group with the double bond and the carbonyl group.



EXPERIMENTAL

Synthesis of aryl 2-azidovinyl ketones. Variant 1. A solution of 0.018 mole of sodium azide in 50 ml of water was added with stirring to 0.01 mole of the aryl 2-chlorovinyl ketone in 50 ml of methanol. After two hours the reaction mixture was diluted with 300 ml of water, and the precipitate was filtered off, washed carefully with water on the filter, dried, and recrystallized. Analytical data for the substances synthesized are given in the table.

Variant 2. A solution of 0.015 mole of sodium azide in water was added to a rapidly filtered aqueous solution of the quaternary salt (0.01 mole) that had been prepared beforehand from the aryl 2-chlorovinyl ketone and trimethylamine [8, 9]; there was an immediate precipitate; after 30-40 minutes the precipitate was filtered off, washed with water, and dried.

Synthesis of 2-azidovinyl methyl ketone. Ether (100 ml) was added to a solution of 8.17 g (0.05 mole) of (2-acetylvinyl)trimethylammonium chloride in 8 ml of water, and the resulting mixture was cooled with ice water while 4.87 g (0.075 mole) of sodium azide in 22 ml of water was added. After 30 minutes the ethereal solution was separated, and the aqueous layer was extracted with ether. The combined ether extracts were dried over CaCl₂, and the ether was evaporated. The yield of 2-azidovinyl methyl ketone was 3 g (54%). The product was freed from traces of moisture by evacuation at 10⁻³ mm at room temperature; $n^{20}D$ 1.5442. The substance exploded violently when heated. Found: N 37.47%. C₄H₅ON₃. Calculated: N 37.82%.

Ar	Yield (%)		Decomp.	Found (%)				Calculated (%)			
	vari- ant 1	vari- and 2	temp. in °C (solvent)	C	н	N	Hal	С	н	N	Hal
C ₆ H ₅	. 90	93	85—86 (Petroleum ether)	62,43	4,12	24,00		62,41	4,07	24,27	_
o-ClC ₆ H ₄ —	88	83	86-87 (alcohol)	52, 32	2,99	20,07	17,37	52,07	2,91	20,24	17,09
$o\operatorname{-BrC_6H_4}$	94	87	68-70	42,70	2,51	-	31,67	42,88	2,40		31,30
<i>p</i> -B1C ₆ H ₄ -	97		96-97 (alcohol)	43,06	2,53		31,44	42,88	2,40		31,30

Ar $COCH = CHN_3$

<u>Reaction of 2-azidovinyl phenyl ketone with piperidine</u>. To a suspension of 1.73 g (0.01 mole) of 2-azidovinyl phenyl ketone in 15 ml of dry ether 1.72 g (0.02 mole) of piperidine in 5 ml of dry ether was added dropwise with cooling. The reaction mixture was then left for 30 minutes at room temperature. When nitrogen ceased to be evolved, the contents of the flask were treated with water; the precipitate formed was filtered off, washed carefully on the filter with water, and dried. Recrystallization from petroleum ether gave 1.88 g (87%) of phenyl 2-piperidinovinyl ketone, m. p. 91-92°, undepressed by admixture of a known sample [16]. When 0.01 mole of piperidine was used under similar conditions, phenyl 2-piperidinovinyl ketone was obtained in 40% yield.

<u>Reaction of 2-azidovinyl phenyl ketone with alcoholic sodium hydroxide</u>. A solution of 0.45 g of sodium hydroxide in 20 ml of absolute methanol was added to a stirred solution of 2 g of 2-azidovinyl phenyl ketone in 100 ml of absolute methanol. After 15-20 minutes the reaction mixture was poured into water and extracted with ether. The ether extracts were washed with water and saturated calcium chloride solution and were dried over sodium sulfate. Vacuum distillation gave 1.2 g (54%) of benzoylacetaldehyde dimethyl acetal; b. p. 143-145° (13 mm); $n^{20}D$ 1.5110. The literature [17] gives: b. p. 111-115° (2 mm); $n^{20}D$ 1.5103.

Rearrangement of 2-azidovinyl phenyl ketone. Concentrated hydrochloric acid (2 ml) was added dropwise to a stirred suspension of 17.3 g (0.1 mole) of 2-azidovinyl phenyl ketone in 80 ml of glacial acetic acid contained in a wide-necked Erlenmeyer flask. A few minutes after the addition of the hydrochloric acid very vigorous evolution of nitrogen set in and it was necessary to apply cooling to prevent the ejection of the reaction mixture. When vigorous evolution of nitrogen had stopped, a further 1 ml of concentrated HCl was added, and the whole was set aside for 4.5 hours at room temperature. The reaction mixture was then diluted with 400 ml of ice water and carefully neutralized with sodium bicarbonate solution (calculated on the amount of acetic acid taken). The mixture obtained was extracted with ether. The ether extracts were extracted with 5% sodium hydroxide solution until the alkaline layer ceased to turn bright orange (the treatment with alkali should not be continued beyond the point at which the color of the alkaline layer changes from orange to light yellow, because on prolonged treatment with sodium hydroxide 5-phenylisoxazole is decyclized into benzoylacetonitrile). The alkaline solution was acidified with 15% sulfuric acid and extracted with ether. The yield of benzoylacetonitrile was 12 g (82%); m. p. 80-81°; the literature [18] gives m. p. 81°. A mixture with a known sample melted without depression.

After the alkaline treatment the ethereal solution was washed with water and dried over sodium sulfate; ether was distilled off. To the residue a saturated solution of cadmium chloride was added. The resulting precipitate of the complex of 5-phenylisoxazole with cadmium chloride was filtered off, washed on the filter with ether, and transferred to a Wurtz flask. A little water was added, and 5-phenylisoxazole was steam-distilled off. 5-Phenylisoxazole was extracted with ether and dried over sodium sulfate. Distillation gave 1 g (7%) of 5-phenylisoxazole: b. p. 128-130° (13 mm); $n^{20}D$ 1.5850. The literature [19] gives b. p. 96° (2 mm). 5-Phenylisoxazole was treated with alcoholic sodium ethoxide, then acidified, and so converted into benzoylacetonitrile, m. p. 80-81°, undepressed by admixture of a known sample.

SUMMARY

1. A method was developed for the synthesis of the previously unknown 2-azidovinyl ketones from 2-chlorovinyl ketones.

2. Under the action of hydrochloric acid 2-azidovinyl phenyl ketone undergoes rearrangement with the liberation of nitrogen; as a result benzoylacetonitrile and 5-phenylisoxazole were prepared and identified.

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