Formation of Azacyclopropenes by Pyrolysis of Vinyl Azides

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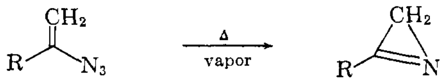
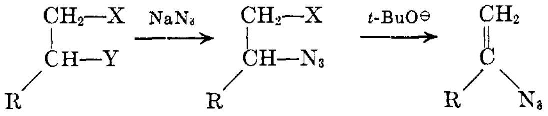
The syntheses of α-azidostyrene (I), α-azido-*o*-methylstyrene (II), and 2-azidohexene-1 (III) are described. The vapor phase pyrolysis of these azides leads to the formation of 2-phenyl-, 2-(*o*-tolyl)-, and 2-butylazirine, respectively. The possible mechanism of formation of the products is discussed.

In a preliminary communication[1] we reported that the vapor phase pyrolysis of α-azidostyrene (I) leads to the formation of 2-phenylazirine (IV). The present paper contains detailed information concerning the preparation, properties, and pyrolysis products of the three vinyl azides I, II (α-azido-*o*-methylstyrene), and III (2-azidohexene-1).



I $R = C_6H_5$ IV
II $R = o\text{-}CH_3C_6H_4$ V
III $R = n\text{-}C_4H_9$ VI

The vinyl azides were prepared as outlined below:

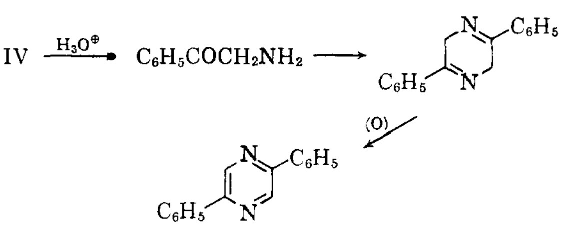


$R = C_6H_7$ or $o\text{-}CH_3C_6H_4$ then $X = Y = Br$
$R = n\text{-}C_4H_9$ then $X = Cl$, $Y = OTs$

In all three cases the pure azides were found to be pale yellow in color. The ultraviolet spectrum of III has a maximum at 243 mμ (ε 4600) but none at longer wave lengths. The infrared spectra of all three compounds show absorption in the region characteristic for the azide group[2]; however, in the case of I and II, there are three bands in this region in contrast to the usual one. The n.m.r. spectra of all three compounds are consistent with the assigned structures. Compounds I and II were reasonably stable at room temperature, while III readily polymerized giving a polyazido alkane as was evident from the infrared spectrum of the product.

Vapor phase pyrolysis of I, II, and III leads to the formation of IV, V [2-(*o*-tolyl)azirine], and VI (2-butylazirine), respectively, in yields of 50–60%. The infrared spectra of the freshly formed crude pyrolysate products all exhibited a sharp band in the region 4.9–5.0 μ. The intensity of this band diminished with time and completely vanished after an hour or two. A likely structure which would give rise to infrared absorption in this region is one such as VII.[3] Such a compound could have been formed by a shift of the R-group from carbon to nitrogen—a process similar to that observed in the Curtius rearrangement. It is estimated that products such as VII from each of the three azides account for no more than 5 or 6% of the pyrolysate. The azirenes, IV, V, and VI, have a characteristic, unpleasant odor and are extremely irritating to the skin. They appear to be reasonably stable if stored under nitrogen at −20°. 2-Butylazirine (VI) holds up somewhat better on standing than do the aryl substituted compounds IV and V. Treatment of IV with dilute alcoholic hydrochloric acid converts it to 2,5-diphenylpyrazine (VIII) presumably *via* hydrolysis to phenacylamine followed by self-condensation and air oxidation.

$$R{-}N{=}C{=}CH_2$$
VII



VIII

The C=N absorption in the infrared is found at 5.74 μ for the aryl substituted compounds IV and V and at 5.64 μ for the aliphatic azirine VI. These bands are moderately intense being somewhat weaker than carbonyl absorptions. Compound VI exhibits a low intensity maximum in the ultraviolet spectrum at 229 mμ (ε 112), but substitution of the butyl side chain by an aryl group as in IV and V gives rise to intense absorption in the 240-mμ region. The n.m.r. spectra of the azirines are consistent with the assigned structures.

Although azacyclopropanes have been postulated as intermediates in the Neber reaction,[4] only one such compound, 2-(2,4-dinitrophenyl)-3-methyl-2-azirine, has been isolated and its structure es-

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(1) G. Smolinsky, *J. Am. Chem. Soc.*, **83**, 4483 (1961).

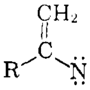
(2) E. Lieber, C. N. R. Rao, T. S. Chao, and C. W. W. Hoffman, *Anal. Chem.*, **29**, 9161 (1957).

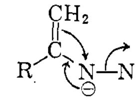
(3) R. Dijkstra and H. J. Backer, *Rec. trav. chim.*, **73**, 575 (1954); C. L. Stevens and J. C. French, *J. Am. Chem. Soc.*, **75**, 657 (1953).

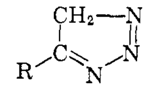
(4) P. W. Neber and A. Burgard, *Ann.*, **493**, 281 (1932); P. W. Neber and G. Huh, *ibid.*, **515**, 283 (1935).

tablished.[5] Thus the formation of azirines from vinyl azides is not only interesting in itself, but presumably by pyrolyzing suitably constituted vinyl azides one could prepare almost any azirine desired. It would seem that the synthetic value of this reaction is limited only by the availability of the requisite azide—unfortunately this can be a rather severe limitation. For example, several months were spent in trying to synthesize 1-cyclohexenyl azide to no avail.

The detailed mechanism of azacyclopropene formation from the azides is not as yet understood. One can postulate three essentially distinct routes to its formation; (1) intervention of a vinyl nitrene[6] intermediate, IX, which cyclizes *via* the singlet or triplet state; (2) a concerted process involving

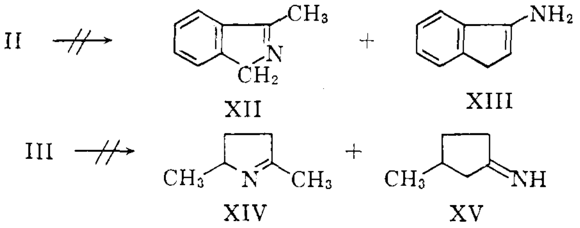

IX


X


XI

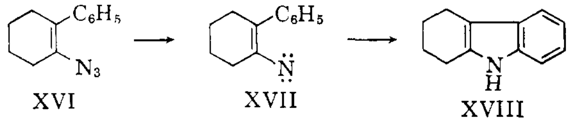
ring closure with concomitant loss of nitrogen (X); or (3) an initial cyclization to XI which then loses nitrogen.

It was thought that if pyrolysis of II and III had given rise to compounds such as XII or XIII, and XIV or XV, respectively, then one could have made a good case for a mechanism involving an


XII XIII XIV XV

nitrene (IX) which reacted either at the carbon or nitrogen end of the π-system with the nearby δ-carbon-hydrogen bond. The failure to detect any of these compounds does not necessarily exclude the formation of an azene intermediate. The ready formation of the azacyclopropene system from vinyl azides may be compared with the formation of cyclopropenes from alkenylcarbenes.[7]

We hoped to prepare 1-azido-2-phenylcyclohexene (XVI) in order to test the postulate of Wenkert and Barnett[8] that XVII is an intermediate in the synthesis of tetrahydrocarbazole (XVIII) from the pyrolysis of α-phenylcyclohexanone oxime. Since we were unable to prepare 1-azidocyclohexene, the synthesis of XVI was not attempted.


XVI XVII XVIII

Experimental[9]

α-Azidostyrene (I).—A solution of 26.4 g. (0.1 mole) of recrystallized commercial grade 1,2-dibromo-1-phenylethane and 6.5 g. (0.1 mole) of sodium azide in 150 ml. of dimethylformamide was stirred at ambient temperature overnight. In the morning the reaction mixture was diluted with water, extracted with hexane, and the organic phase separated and washed with water. After drying over anhydrous potassium carbonate, the organic phase was concentrated at reduced pressure (water aspirator) at 40–45°, leaving a residue of crude 1-azido-2-bromo-1-phenylethane which was taken up in 250 ml. of benzene. This solution was stirred for 5 hr. with 16 g. of potassium *t*-butylate, and then diluted with 500 ml. of hexane. The resulting mixture was washed well with water, the organic phase separated, dried over potassium carbonate, and concentrated at reduced pressure (water aspirator; 40–45°). The crude styryl azide was purified by dissolving it in petroleum ether (b.p. 30–60°) and passing the solution through 120 g. of Woelm neutral alumina (activity grade 1). The yield of pure, yellow styryl azide amounted to 11 g. (76%). The analytical sample was molecularly distilled at 0.6 mm. and had the following physical properties: infrared (neat), N_3 bands at 4.53 μ (m), 4.63 μ (s), and 4.73 μ (s); C=C band at 6.2 μ. The n.m.r. spectrum showed the non-equivalent methylene hydrogens as two single sharp lines at 5.68 and 4.68 τ and the phenyl hydrogens as a multiplet the region 2.7 τ.

Anal. Calcd. for $C_8H_7N_3$: C, 66.19; H, 4.86; N, 28.95. Found: C, 65.96; H, 4.87; N, 29.18.

α-Azido-*o*-methylstyrene (II).—Crude 1,2-dibromo-1-(*o*-tolyl)ethane[10] (~ 0.136 mole) was converted to II essentially as described above except that the potassium *t*-butylate treatment required about 12 rather than 5 hr. The pure yellow azide weighed 11.1 g. (~60%) and had the following physical properties: infrared (neat), N_3 bands at 4.59 μ (m), 4.67 μ (s), and 4.76 μ (s); C=C band at 6.13 μ. The n.m.r. spectrum exhibited the phenyl hydrogens as a multiplet in the region 2.8 τ, the non-equivalent methylene hydrogens as two single lines at 4.95 and 5.28 τ and the *ortho*-methyl hydrogens as a singlet at 7.62 τ.

Anal. Calcd. for $C_9H_9N_3$: C, 67.90; H, 5.70; N, 26.40. Found: C, 68.13; H, 5.90; N, 26.24.

1-Chlorohexanol-2[11] was prepared from propylmagnesium bromide and epichlorohydrin using the procedure described for the preparation of 1-chloropentanol-2.[12]

Tosylate of 1-Chlorohexanol-2.—Commercial grade tosyl chloride (150 g.) was added in small portions to a cold, stirred solution of 1-chlorohexanol-2 (86 g.) in 600 ml. of pyridine at such a rate as to maintain a temperature below 5°. When all the tosyl chloride had dissolved the reaction was placed in a refrigerator overnight (~ 0°). In the morning the solution was poured onto 600 g. of cracked ice, an

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(5) D. J. Cram and M. L. Hatch, *J. Am. Chem. Soc.*, **75**, 33 (1953).

(6) (a) G. Smolinsky, *ibid.*, **82**, 4717 (1960); (b) *ibid.*, **83**, 2489 (1961); (c) *J. Org. Chem.*, **26**, 4108 (1961); (d) D. H. R. Barton and L. R. Morgan, Jr., *J. Chem. Soc.*, 622 (1962).

(7) G. L. Closs and L. E. Closs, *J. Am. Chem. Soc.*, **83**, 2015 (1961).

(8) E. Wenkert and B. F. Barnett, *ibid.*, **82**, 4671 (1960).

(9) Infrared spectra were determined with a Perkin-Elmer Infracord, ultraviolet spectra with a Beckman DK-2 recording spectrophotometer, and n.m.r. spectra in carbon tetrachloride solution with a Varian 60-Mc. high resolution instrument. All reactions were run in a nitrogen atmosphere unless otherwise stated.

(10) This compound was obtained by bromination of *o*-methylstyrene in carbon tetrachloride solution. The styrene was prepared by reaction of *o*-tolylmagnesium bromide with acetaldehyde in ether, followed by dehydration over potassium hydrogen sulfate–*p*-*t*-butylcatechol.

(11) P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **79**, 482 (1928).

(12) C. F. Koelsch and S. M. McElvain, *J. Am. Chem. Soc.*, **51**, 3390 (1929).

equal volume of cold water added, and the mixture extracted with methylene chloride. The organic phase was washed well with ice water, cold dilute sulfuric acid, cold dilute sodium bicarbonate, dried over sodium sulfate, and concentrated at reduced pressure (water aspirator, 25–30°). The yield of crude tosylate was approximately 80%.

2-Azidohexene-1 (III).—To a mixture of sodium azide (30 g., 0.46 mole) and 1-chlorohexyl-2-tosylate (135 g., 0.463 mole) in 550 ml. of boiling methanol was added just sufficient water to effect complete solution. After 24 hr. at reflux, the reaction solution was poured onto cracked ice, the resulting mixture was extracted with methylene chloride, the organic phase washed with water, dried over potassium carbonate, and concentrated at reduced pressure (water aspirator). A distillation of the residue yielded 26.2 g. (36%) of 2-azido-1-chlorohexane as the fraction boiling 70–76° (9 mm.). The infrared and ultraviolet spectra of this material indicated that it was free of any tosylates.

Potassium *t*-butylate (40 g., 0.36 mole) was added to a stirred solution of chloroazide (43 g., 0.27 mole) in 700 ml. of dry ether. The reaction was at first cooled in an ice bath but after about 0.5 hr. was allowed to warm to room temperature. After 17 hr. the dark brown reaction mixture was poured onto cracked ice, the yellow ether layer separated, washed with water, dried over sodium sulfate, and concentrated at reduced pressure (water aspirator). The orange-yellow residue was taken up in petroleum ether (b.p. 30–60°) and passed through a column of 120 g. of Woelm neutral alumina (activity grade 1). The yellow vinyl azide thus obtained weighed 26.4 g. (80%) and was suitable for pyrolysis without additional purification.

A fractionation of 18.2 g. of vinyl azide, III, through a 2-ft. spinning band column gave 4 g. of essentially pure 2-azidohexene-1 (III) [b.p. 55° (39 mm.)]. The pot residue still showed N_3 absorption in the infrared but no C=C absorption.

Anal. Calcd. for $C_6H_{11}N_3$: C, 57.57; H, 8.86; N, 33.57. Found[13]: C, 58.26; H, 9.25; N, 32.66.

The vinyl azide exhibited the following physical properties: infrared (neat); N_3 band at 4.75 μ, C=C band at 6.19 μ. Ultraviolet (cyclohexane); a maximum at 243 mμ (4600) and a minimum at 217 mμ (1250). The n.m.r. spectrum showed the vinyl hydrogens absorbing at 5.45 τ as a single sharp line.

Pyrolysis of the Azides.—The azides were pyrolyzed in a manner described in an earlier paper,[6c] with but minor modifications: The products were trapped at ice–methanol temperatures instead of at Dry Ice temperatures, and in the case of III the pressure in the apparatus was maintained at about 20 mm. rather than the usual 0.1–0.3 mm.

A. **α-Azidostyrene** (I, 6.8 g.) on pyrolysis gave crude 1-phenylazirine (IV, 4.4 g., 80%). The combined produce from several runs was fractionated through a 2-ft. spinning band column and gave analytically pure material boiling at 80° (10 mm.). This material showed C=N absorption in the infrared (carbon tetrachloride) at 5.74 μ. The ultraviolet spectrum in cyclohexane had one minimum (ϵ_{217} 6300), a maximum (ϵ_{239} 13,000) and six shoulders (ϵ_{243} 12,600; ϵ_{249} 10,500; ϵ_{255} 7100; ϵ_{261} 3800; ϵ_{278} 1200; ϵ_{287} 750); in ethanol the spectrum had a minimum (ϵ_{218} 6000), a maximum (ϵ_{242} 13,000), an inflection at 278 mμ and a shoulder (ϵ_{287} 1000). The n.m.r. had a singlet at 8.35 τ and two sets of multiplets centered at 2.1 and 2.4 τ in the ratio 2:3:2.

Anal. Calcd. for C_8H_7N: C, 82.02; H, 6.02; N, 11.96, mol. wt., 117. Found: C, 81.87; H, 6.23; N, 11.64; mol. wt., 126.[14]

B. **α-Azido-*o*-methylstyrene** (II, 9.34 g.) gave 6 g. (78%) of crude 2-(*o*-tolyl)azirine. Fractionation through a 2-ft. spinning band column gave analytically pure material of b.p. 65° (2.3 mm.). This material had C=N absorption in the infrared (carbon tetrachloride) at 5.74 μ. The ultraviolet spectrum in cyclohexane had a minimum (ϵ_{222} 4200) a maximum (ϵ_{243} 13,300) and two shoulders (ϵ_{285} 1700; ϵ_{294} 1200). The n.m.r. exhibited the methylene hydrogens and methyl hydrogen absorptions as singlets at 8.46 τ and 7.34 τ, respectively. The phenyl hydrogens exhibited a multiplet in the region 2.65 τ. The ratio of these peaks in the order stated were 2:3:4.

Anal. Calcd. for C_9H_9N: C, 82.40; H, 6.92; N, 10.68. Found: C, 82.11; H, 6.84; N, 10.60.

C. **2-Azidohexene-1** (III) mainly polymerized when pyrolysis was attempted and thus from a total of about 40 g. of vinyl azide only 9 g. of crude 2-butylazirine (VI) was obtained. This material upon fractionation through a 2-ft. spinning band column gave an analytically pure compound boiling at 57° (54 mm.). This substance had C=N absorption in the infrared (carbon tetrachloride) at 5.64 μ. The ultraviolet spectrum in cyclohexane had a minimum at 213 mμ (ϵ 81) and a maximum at 229 mμ (ϵ 112).

Anal. Calcd. for $C_6H_{11}N$: C, 74.17; H, 11.41; N, 14.42. Found: C, 73.94; H, 11.22; N, 14.27.

Hydrolysis of 2-Phenylazirine (IV).—A solution of 576 mg. (4.92 mmole) of IV in 5 ml. of 95% ethanol containing 1 drop of concentrated hydrochloric acid was maintained at reflux for 5 hr. The reaction was then opened to the air 2 ml. of concentrated ammonium hydroxide added, and heating continued an additional 12 hr. On concentrating the solution to a small volume, crystals separated (172 mg., 30%) which after recrystallization from ethanol had a m.p. of 195–196°. A mixed melting point determination with authentic 2,5-diphenylpyrazine[15] did not depress and further the infrared spectra of the two compounds were identical.

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[13] These results can be rationalized by assuming a 4.6% contamination of 2-butylazirine.

[14] Cryoscopic determination in cyclohexane.

[15] L. Wolff, *Ber.*, **20**, 432 (1887).