Anal. Calcd. for $C_{20}H_{31}O_2N$: C, 75.67; H, 9.84; N, 4.41. Found: C, 76.01; H, 10.05; N, 4.61.

4,17α-Dimethyl-4-azaandrost-5-en-17β-ol-3-one (III) (Method B). A solution of 3.2 g. of 17α-methyl-3,5-seco-4-norandrostan-17β-ol-5-on-3-oic acid[7] (I) in 200 ml. of ethanol was saturated with methylamine. The solution was heated in a sealed tube for 8 hr. at 140°. The solvent was distilled and the residue crystallized from ethanol to yield 2.54 g. (80%) of III as white needles, m.p. 172–174°. This product was shown to be identical with that obtained by method A by a mixed melting point and a comparison of infrared spectra and specific rotation values.

4-(β-Hydroxyethyl)-17α-methyl-4-azaandrost-5-en-17β-ol-3-one (IV). A mixture of 15.0 g. of 17α-methyl-3,5-seco-4-norandrostan-17β-ol-5-on-3-oic acid[7] (I) and 60 ml. of ethanolamine was refluxed for 4 hr. After cooling, water was added and the mixture was extracted with benzene. The benzene extracts were washed with dilute hydrochloric acid and water, and then dried over sodium sulfate. The residue obtained, after evaporating the solvent, was crystallized from acetone to yield 4.8 g. (31%) of 4-(β-hydroxyethyl)-17α-methyl-4-azaandrost-5-en-17β-ol-3-one (IV) as white needles; m.p. 172–175°; $[\alpha]_D$ −137.4°; λ_{max} 235 mμ (log ε 4.06), and 6.14 μ with an inflection at 6.00 μ.

Anal. Calcd. for $C_{21}H_{33}O_3N$: C, 72.59; H, 8.46; N, 4.03. Found: C, 72.40; H, 9.26; N, 3.71.

4-Benzyl-17α-methyl-4-azaandrost-5-en-17β-ol-3-one (V). Lactam V was prepared from a mixture of 15.0 g. of the acid (I) and 60 ml. of benzylamine by a procedure similar to that used for IV. Crystallization of the product from ether yielded 13.0 g. (71%) of the lactam (V) as white needles; m.p. 104–106°; $[\alpha]_D$ −138°; λ_{max} 235 mμ (log ε 4.04), and 6.13 μ with an inflection at 6.00 μ.

Anal. Calcd. for $C_{26}H_{35}O_2N$: C, 79.33; H, 8.96; N, 3.56. Found: C, 79.53; H, 9.00; N, 3.53.

17α-Methyl-4-azaandrost-4-en-17β-ol (VI). Lactam II (6.07 g.) was reduced by lithium aluminum hydride in tetrahydrofuran following standard procedures.[6] The crude product, after two recrystallizations from methanol, yielded 3.6 g. (62%) of VI as white needles; m.p. 183–185°; $[\alpha]_D$ +53.2°; λ_{max} 6.03 μ (a sharp peak of moderately high intensity).

Anal. Calcd. for $C_{19}H_{31}ON$: C, 78.84; H, 10.80; N, 4.84. Found: C, 79.10; H, 10.70; N, 4.87.

4,17α-Dimethyl-4-azaandrost-5-en-17β-ol (VII). Lactam III (8.82 g.) was added to a slurry of lithium aluminum hydride in ether, by means of a Soxhlet extractor, and refluxed for 12 hr. After working up,[6] the product was crystallized from ether to obtain 8.14 g. (97%) of VII as white needles; m.p. 148–152°; λ_{max} 6.08 μ (weak absorption).

Anal. Calcd. for $C_{20}H_{33}ON$: C, 79.16; H, 10.96; N, 4.62. Found: C, 79.03; H, 10.70; N, 4.34.

4-(β-Hydroxyethyl)-17α-methyl-4-azaandrost-5-en-17β-ol (VIII). Lactam IV (3.48 g.) was reduced with lithium aluminum hydride in tetrahydrofuran. The crude product was crystallized from methanol to obtain 3.10 g. (93%) of VIII as white needles; m.p. 175–176°; $[\alpha]_D$ −152°; λ_{max} 6.08 μ (weak absorption).

Anal. Calcd. for $C_{21}H_{35}O_2N$: C, 75.65; H, 10.58; N, 4.20. Found: C, 75.90; H, 10.69; N, 4.23.

4-Benzyl-17α-methyl-4-azaandrost-5-en-17β-ol (IX). Lactam V (3.30 g.) was reduced in the same manner as lactam III above. The product was crystallized from acetone to yield 3.09 g. (97%) of IX as white needles; m.p. 122–126°; $[\alpha]_D$ −175°; λ_{max} 6.08 μ (weak).

Anal. Calcd. for $C_{26}H_{37}ON$: C, 82.27; H, 9.83; N, 3.69. Found: C, 82.30; H, 10.02; N, 3.80.

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The Vapor Phase Pyrolysis of Several Substituted Azidobenzenes

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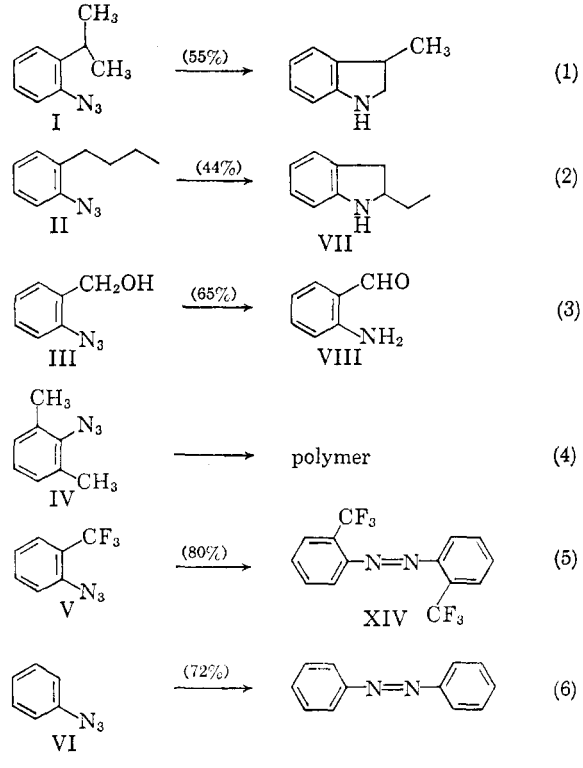
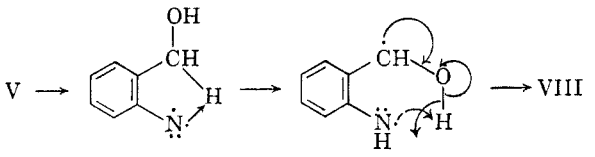
In two previous papers in this series[1] it was reported that pyrolysis of properly constituted aromatic azides resulted in attack of the azene intermediate upon the C–H bond of a saturated carbon atom with insertion of the nitrogen atom into the bond. Moreover, evidence was presented[1b] which indicated that the azene was most likely an imino radical (—$\dot{N}$:). These earlier pyrolyses were accomplished in solution and suffered from the disadvantage of affording the azene an opportunity of reacting with the solvent. Thus, it was decided to study the decompositions of several azides in the vapor phase, as in this way one would preclude reaction with solvent and would provide the maximum opportunity for intramolecular reaction of the azene.

The products obtained from the decomposition of 2-isopropylazidobenzene (I), 2-butylazidobenzene (II), and *o*-azidobenzyl alcohol (III) are consistent with the view that the azene intermediate reacts as a radical[1] (Equations 1, 2, and 3). The fact



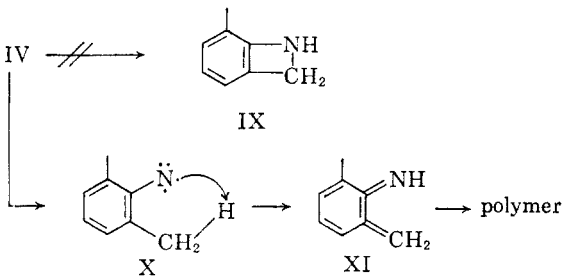
(1)(a) G. Smolinsky, *J. Am. Chem. Soc.*, **82**, 4717 (1960); (b) *J. Am. Chem. Soc.*, **83**, 2489 (1961).

that II did not lead to 2-methyl-1,2,3,4-tetrahydroquinoline can be rationalized as being due to the more facile formation of a six-membered cyclic transition state than the seven-membered transition state. Furthermore, the formation of *o*-aminobenzaldehyde (VIII) from the decomposition of III

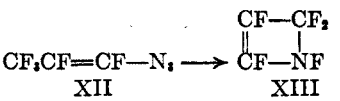


is best explained as a radical reaction, although a hydride transfer cannot be definitely ruled out.

In view of the results obtained in the preceding three cases, it was thought that the decomposition of IV might lead to the formation of IX; however, as only polymeric material was obtained in this reaction, it may be that the azene intermediate X formed the quinoid compound XI, which then polymerized.

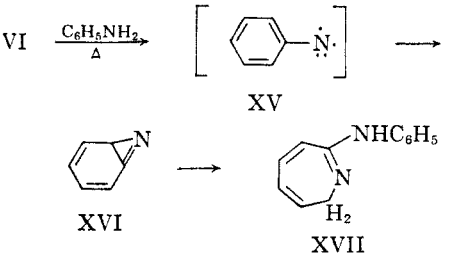


An investigation of the pyrolysis of 2-(trifluoromethyl)azidobenzene (V) was prompted by a recent report claiming that the decomposition of XII led to the formation of XIII.[2] However, when V was pyrolyzed in the vapor phase, an 80% yield of azobenzene XIV was obtained. This result is consistent with the view that the azene intermediate reacts as a diradical[1b] as it is unlikely that



a C—F bond would undergo radical cleavage. It may be that the reaction reported by Knunyants and Bykhovskaya[2] does not involve an azene intermediate, but proceeds through some sort of concerted process. Some weight is lent to this argument by the fact that XII loses nitrogen at room temperature, while in most known azene reactions, decomposition of the azide is not appreciable until a temperature of 140–160° is reached.[1]

Huisgen and co-workers[3] found that when azidobenzene (VI) was decomposed in aniline at 165°, a 54% yield of azepine XVII could be achieved. Huisgen postulated that XVI was formed directly from VI without the intercession of XV.



This conclusion is supported by the work of Bertho, who found that heating azidobenzene (VI) in *p*-xylene gave some azobenzene, aniline and 1,2-di-*p*-tolylethane[4]; and further supported by the observation that heating VI in benzenethiol gave diphenyldisulfide (60%) and aniline (52%).[5] Both of the preceding results can be readily explained as the logical products of an imino radical intermediate such as XV.

If, indeed, XVI is formed in Huisgen's reaction, whether *via* XV or not, then a vapor phase reaction might shed some light on the nature of such a species. However, a vapor phase decomposition of VI gave only azobenzene.

Thus it appears that in Huisgen's reaction, the aniline must participate before any rearrangement occurs; otherwise, it is difficult to explain why azepine is formed only in its presence. This point is presently under investigation.

EXPERIMENTAL[6]

o-Butylaniline. A commercial sample of pure butylbenzene was nitrated according to the procedure of Read and Mullin[7] and the product twice fractionated through a 2-ft. spinning bond column. The fraction boiling 136.2–138.2°/16 mm. (lit. value[6] 131–133°/15 mm.) was hydrogenated in ethanol with a 5% palladized carbon catalyst.

(2) I. L. Knunyants and E. G. Bykhovskaya, *Doklady Akad. Nauk. S.S.S.R.*, 131, 1338 (1960).

(3) R. Huisgen, *Angew. Chem.*, 67, 756 (1955); R. Huisgen and D. Vossius and M. Appl, *Chem. Ber.*, 91, 1 (1958); R. Huisgen and M. Appl, *Chem. Ber.*, 91, 12 (1958).

(4) A. Bertho, *Ber.*, 57, 1138 (1924).

(5) VI was heated at 165° in a 10-mole excess of benzenethiol until nitrogen evolution ceased (*ca.*, three quarters of an hour). The residue from the vacuum distillation of the reaction solution was shown to be diphenyldisulfide while the aniline was extracted with 1*M* hydrochloric acid from an ether solution of the distillate.

(6) All melting points are corrected; boiling points are uncorrected. Ultraviolet spectra were taken on a Beckman DK-2 recording spectrophotometer.

(7) R. R. Read and D. B. Mullin, *J. Am. Chem. Soc.*, 50, 1763 (1928).

Azidobenzenes. The amines[8] were converted to the corresponding azides using procedure A or B of Smith and Brown[9] with the following modifications: When procedure B was employed, sodium nitrite was used in place of amyl nitrite. Furthermore, in each case, the azide was isolated from the aqueous mixture by extraction with a suitable solvent. The extracts were washed with water and carbonate solution, dried and evaporated at reduced pressure at 40–45°. All the azides were purified by chromatography on Woelm alumina, activity grade one (wt. ratio 10:1).

2-Isopropylazidobenzene (I) was formed in 68% yield by procedure B. The crude product was extracted with petroleum ether (b.p. 30–60°) and chromatographed in the same solvent.

Anal. Calcd. for $C_9H_{11}N_3$: C, 67.05; H, 6.88; N, 26.07. Found: C, 67.01; H, 6.75; N, 26.28.

2-Butylazidobenzene (II) was prepared, using procedure B, in 62% yield. The product was extracted with petroleum ether and chromatographed in this solvent.

Anal. Calcd. for $C_{10}H_{13}N_3$: C, 68.58; H, 7.48; N, 23.98. Found: C, 68.52; H, 7.36; N, 24.21.

o-Azidobenzyl alcohol (III) was obtained in 73% yield using procedure A. The product was extracted with benzene and purified by sublimation (60°/1 mm.); m.p. 52–53°.

Anal. Calcd. for $C_7H_7N_3O$: C, 56.37; H, 4.73; N, 28.18. Found: C, 56.60; H, 4.81; N, 27.98.

2,6-Dimethylazidobenzene (IV) was obtained in 62% yield by procedure A. The crude product was extracted with petroleum ether and chromatographed.

Anal. Calcd. for $C_8H_9N_3$: C, 65.28; H, 6.16; N, 28.55. Found: C, 65.51; H, 6.42; N, 28.50.

2-(Trifluoromethyl)azidobenzene (V) was prepared in 68% yield using procedure B and was extracted with petroleum ether and chromatographed with this solvent.

Anal. Calcd. for $C_7H_4N_3F_3$: C, 44.93; H, 2.15; N, 22.46. Found: C, 45.10; H, 2.11; N, 22.42.

Azidobenzene (VI) was prepared in 90% yield using procedure A. The crude product was extracted with petroleum ether and chromatographed with the same solvent. Its infrared spectrum (neat) showed absorption characteristic of the N_3 group at 4.70–4.75 μ.[10]

Pyrolysis of the azides. The azides were vaporized at ambient temperatures and reduced pressure (0.1–0.3 mm.) in a stream of nitrogen. (The nitrogen was introduced by means of a fine capillary tube, and in the case of the liquid azides was bubbled through the liquid.) The vapors passed through a 3″ section of 15 mm. tubing packed with 1/8″ pyrex helices and maintained at 350–360° by means of an externally heated coil of nichrome wire. The products from the reactions were trapped in a cold finger at Dry Ice temperatures.

2-Isopropylazidobenzene (I, 235 mg.) gave 130 mg. of a liquid mixture which was separated by vapor phase chromatography[11] into two fractions. The major product (104 mg. 55%) was shown to be dihydroskatole by a comparison of its infrared spectrum (neat) with that of an authentic sample. The minor product could not be identified.

2-Butylazidobenzene (II, 1.15 g.) on pyrolysis gave 850 mg. of a pale yellow liquid having an infrared spectrum (neat) and ultraviolet spectrum in neutral (λ_{max} 293 mμ) and acidic (λ_{max} 249 mμ) ethanol consistent with that for an *o*-aminobenzene derivative.[12] This mixture was heated for 15 hr. at 200–210° with 60 mg. of 10% palladized carbon. The resulting mixture was taken up in ether and separated into neutral (427 mg.) and basic (246 mg.) fractions. The basic material was not 2-methylquinoline as shown by a comparison of its infrared spectrum with that of an authentic sample. The neutral product (2-ethylindole) was chromatographed on 15 g. of Merck acid-washed alumina in benzene. The colorless crystals thus obtained were recrystallized from petroleum ether and had a m.p. of 44–45° (lit.[13] m.p. 43°).

o-Azidobenzyl alcohol (III, 366 mg.) when pyrolyzed gave 130 mg. (65%) of a yellowish oil having an infrared spectrum (neat) consistent with that for *o*-aminobenzaldehyde (N—H: 2.85 μ, 2.95 μ; CO—H: 3.65 μ; and C = O: 6.0 μ). The phenylhydrazone derivative of this material had a m.p. of 223–224°. The reported m.p. of *o*-aminobenzaldehyde phenylhydrazone is 222°.[14]

2,6-Dimethylazidobenzene (IV, 289 mg.) when pyrolyzed formed an amorphous solid (154 mg.) having an infrared spectrum (carbon tetrachloride) exhibiting N-H absorption.

2-(Trifluoromethyl)azidobenzene (V, 353 mg.) formed a solid which when sublimed (60°/0.1 mm.) yielded 240 mg. (80%) of 2,2′-bis(trifluoromethyl)azobenzene (XVII). This material was recrystallized readily from methanol; m.p. 129–130°; the electronic absorption spectrum in cyclohexane exhibited three maxima and two shoulders, λ in mμ(ϵ): 230 (13,500); 307 (18,000); 318 (19,600); 330 (16,700); 453 (274).

Azidobenzene (VI, 411 mg.) yielded a dark oil which on sublimation (80°/0.3 mm.) gave 225 mg. (72%) of an orange solid of m.p. 65–67°. This material was shown to be azobenzene by a comparison of its melting point, mixed melting point and infrared spectrum (carbon tetrachloride solution) with that of an authentic sample.

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(8) Aniline, 2,6-dimethylaniline, and 2-(trifluoromethyl)-aniline are available commercially. The preparation of *o*-aminobenzyl alcohol has been described by A. Reissert and K. Crämer [*Ber.*, **61**, 2558 (1928)] and that of 2-isopropylaniline by G. Smolinsky (*J. Am. Chem. Soc.*, **83**, 2489 (1961)).

(9) P. A. S. Smith and B. B. Brown, *J. Am. Chem. Soc.*, **73**, 2438 (1951).

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

(11) A. Beckman GC-2 gas chromatograph having a 10′ column packed with Uconpolar on Fluoropak was used. A temperature of 210° and pressure of 30 p.s.i. gave good separation.

(12) T. Masamune, *J. Am. Chem. Soc.*, **79**, 4418 (1957).

(13) A. Verley and J. Beduivé, *Bull. soc. chim. France*, [4] **37**, 190 (1925).

(14) J. Eliasberg and P. Friedlander, *Ber.*, **25**, 1753 (1892).

2-Mercapto-2-phenylethylamine[1,2]

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In recent years there has been much interest in mercaptoethylamine and related compounds that contain mercapto and amino groups on

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(2) Presented before the Division of Medicinal Chemistry at the 138th Meeting of the American Chemical Society, N. Y., September 1960.