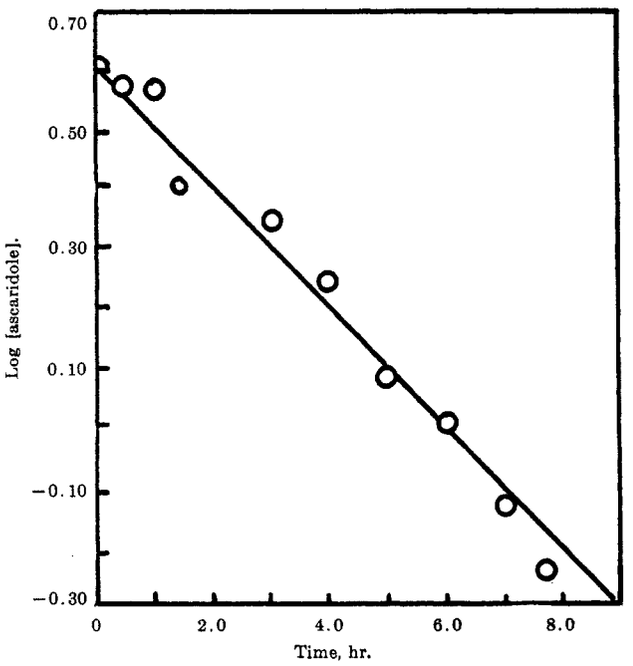


Figure 1.—Isomerization of ascaridole at 131°.

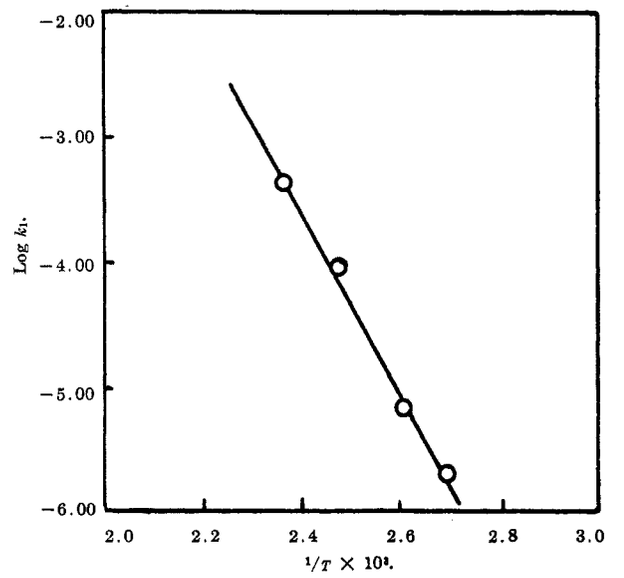
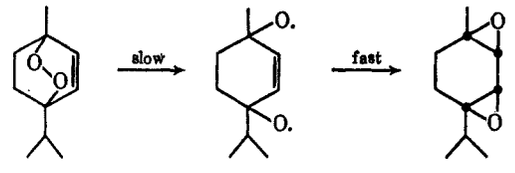


Figure 2.—Arrhenius plot for the thermal isomerization of ascaridole.

in a slow step followed by rapid addition of oxygens to the double bond. The value of $\Delta H^{\pm}$ is entirely consistent with this mechanism. Bond strengths of acyclic peroxides are in the range of 33 kcal/mol,[7] and, because of strain, the peroxide bond of ascaridole would be expected to be weaker by several kcal/mol. The entropy of activation for a unimolecular cleavage, as proposed, would be expected to be small.[8]



(7) "Selected Values of Chemical Thermodynamic Properties," National Bureau of Standards Circular 500, U. S. Government Printing Office, Washington, D. C., 1950.

Experimental Section

Materials.—Ascaridole was obtained from chenopodium oil by fractional vacuum distillation and further purified on an aluminum oxide column. Toluene was purified by distillation.

Sample Preparation.—Stock solutions of toluene and ascaridole were made up gravimetrically. After mixing, aliquots were sealed into vials made from 5-mm soft-glass tubing. Sets of sample tubes were immersed in a suitable refluxing solvent, and tubes were periodically removed, cooled, and analyzed. Initial concentrations of ascaridole in separate kinetic runs were 4.14 and 4.60 *M*.

Analysis.—Analysis of samples were performed on a Varian A-60 A spectrometer. Peak integrations of the aromatic protons of toluene (τ 3.1) and the C-2, C-3 protons in ascaridole (τ 3.9) were made. The peak areas of the C-2 and C-3 protons in the isomerized product (τ 7.2) and the methyl protons of toluene were also recorded. The isomerization was followed to about 80% completion in each run. The moles of ascaridole and rearrangement product present in each sample were calculated from the following equations.

$$[\text{ascaridole}] = {}^5/_2(\tau\ 3.9\ \text{area}/\tau\ 3.1\ \text{area})\ (\text{moles of toluene})$$

$$[\text{rearrangement product}] = {}^3/_2(\tau\ 7.2\ \text{area}/\tau\ 7.9\ \text{area})\ (\text{moles of toluene})$$

Calculations.—Rate constants were determined both from the concentration of ascaridole present in the samples and the concentration of diepoxide formed. The rate constants determined from the concentration of starting material and product were consistent with each other. Because of the proximity of absorbtion of other protons, the ratio of peak areas for the C-2 and C-3 protons of the diepoxide and methyl protons of toluene could not be established as precisely as the ratio between the C-2 and C-3 protons of ascaridole and the aromatic protons of toluene. The data listed in Table I was calculated from the ascaridole/toluene ratios.

Registry No.—I, 512-85-6.

(8) Several examples of first-order isomerization and first-order decompositions with small entropies of activation are listed and discussed in A. A. Frost and R. G. Pierson, "Kinetics and Mechanism," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1961, pp 109–112.

The Thermal Decomposition of *o*-Azidodiphenylmethane Leading to Azepino[2,1-*a*]-1H-indole

LEROY KRBECHEK[1] AND HIDEYO TAKIMOTO

Chemical Propulsion Department, Laboratories Division, Aerospace Corporation, El Segundo, California 90045

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The thermal decomposition of *ortho*-substituted phenyl azides, where possible, generally leads to five-membered-ring structures. Examples of such thermolyses are *o*-azidobiaryls,[2] *o*-azidobenzylidenamines,[3] benzylidene-*o*-azidoanilines,[4] *o*-azidobenzophenone,[5] and diazidoazobenzene.[6] On the other hand, the

(1) International Minerals and Chemical Corp., Growth Sciences Center, Libertyville, Ill.

(2) (a) P. A. S. Smith and J. H. Boyer, *J. Amer. Chem. Soc.*, **73**, 2626 (1951); (b) P. A. S. Smith and J. H. Hall, *ibid.*, **84**, 480 (1962); (c) B. Coffin and R. F. Robbins, *J. Chem. Soc.*, 1252 (1965).

(3) L. Krbechek and H. Takimoto, *J. Org. Chem.*, **29**, 1150 (1964).

(4) (a) L. Krbechek and H. Takimoto, *ibid.*, **29**, 3630 (1964); (b) J. H. Hall and D. R. Kamm, *ibid.*, **30**, 2092 (1965).

(5) P. A. S. Smith, B. B. Brown, R. K. Putney, and R. F. Reinisch, *J. Amer. Chem. Soc.*, **75**, 6335 (1953).

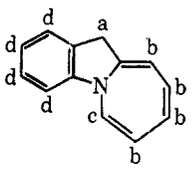
(6) (a) R. A. Carboni and J. E. Castle, *ibid.*, **84**, 2453 (1962); (b) R. A. Carboni, J. C. Kauer, W. R. Hatchard, and R. J. Harder, *ibid.*, **89**, 2626 (1967).

formation of six-membered-ring structures is also reported[5] in the *o*-azidobiaryl systems where the two aryl groups are separated by O, S, or SO_2. The yields in the latter cases, however, are much lower than the former. In the cases where cyclization is not possible, the ring enlargement of the phenyl to form seven-membered azepine structures have also been reported. Thus, 2-anilino-7H-azepine[7] is formed from the decomposition of phenyl azide in aniline. The present report describes the thermal decomposition of *o*-azidodiphenylmethane, where the aryl groups are separated by a methylene group, resulting in a ring enlargement.

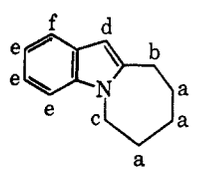
Thermolysis of *o*-azidodiphenylmethane in decalin at 160° resulted in a hydrogen-abstraction reaction with the formation of *o*-aminodiphenylmethane. However, the decomposition of this azide, in 1,2,4-trichlorobenzene at 160°, resulted in a loss of nitrogen and yielded a compound (66%) having the empirical formula $C_{13}H_{11}N$ (I), mp 91–95.5°. This compound was not dihydroacridine, the product that would result from six-membered-ring closure during the decomposition of *o*-azidodiphenylmethane. The ultraviolet spectrum of I in ethanol exhibited absorption bands at 314 mμ (log ε 3.79), 272 (4.23), and 227 (4.40). Hydrogenation of I with 10% Pd–C in ethanol resulted in an uptake of 2 mol of hydrogen to yield (79.5%) a second compound, $C_{13}H_{15}N$ (II). Absorptions at 292 mμ (log ε 3.83), 283 (3.92), 277 (3.89) shoulder, and 224 (4.62) were observed for II in ethanol.

The nmr spectrum of I in CCl_4 exhibited absorptions at δ 3.33 (2 H, a), 5.93–5.40 (4 H, b), 7.32 (1 H, c), and 7.10–6.78 (4 H, d). Compound II, also in CCl_4, had absorptions at δ 1.74 (6 H, a), 2.76 (2 H, b), 3.97 (2 H, c), 6.08 (1 H, d), 6.98 (3 H, e), 6.32 (1 H, e), and 7.32 (1 H, f).

Based on the above information, the following structures were assigned.



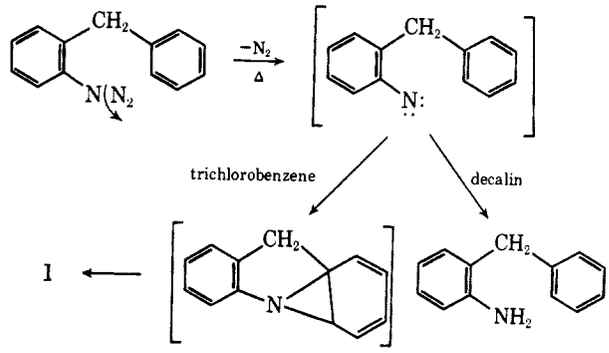
I



II

The ultraviolet absorptions for I at 227 and 272 mμ are attributed to the nitrogen attached to a benzene ring similar to that found in aniline. The latter compound has absorptions at 230 mμ (log ε 3.93) and 280 (3.16)[8] in water. The absorption at 314 mμ for I is attributed to the azepine structure, since many azepines exhibit bands at approximately 300 mμ. For example, 2-diethylamino-3H-azepine has an absorption maximum at 297 mμ (log ε 3.90),[9] 2-benzylamino-7H-azepine shows absorptions at 210 mμ (log ε 4.32) and 287 (3.88),[7b] 2-(*o*-tolylamino)-7H-azepine exhibits maxima at 205 mμ (log ε 4.37) and 290 (4.03),[7c] and 2-(diisopropylamino)-7H-azepine has maxima at 213 mμ (log ε 4.45) and 297 (4.28).[7c] The reduction of I by the uptake of 2 mol of hydrogen resulted in the saturation of the azepine and the shift of one of the unsaturated bonds into conjugation with the benzene ring to form the indole structure. Thus, the longer wavelength absorption of I assigned to the azepine disappeared, and the spectrum of II is consistent with the indole structure. Indole has absorptions at 287 mμ (log ε 3.6), 280 (3.7), 265 (4.4) broad band, in cyclohexane.[10]

The decomposition of *o*-azidodiphenylmethane in 1,2,4-trichlorobenzene appears to proceed by the elimination of nitrogen and the attack of the nitrene (univalent uncharged nitrogen) on the neighboring phenyl group. The elimination of nitrogen and the attack may occur either *via* a concerted or a stepwise reaction. The stepwise reaction is favored since *o*-aminodiphenylmethane was obtained in decalin by the hydrogen abstraction from the solvent by the nitrene.[11] The decalin, being a better donor of hydrogen than trichlorobenzene, traps the nitrene and prevents the azepine formation. The rearrangement of the resulting intermediate leads to I.



The formation of I leading to ring enlargement of the phenyl group is similar to the decomposition reaction of 2-(β-phenylethyl)-phenyldiazomethane reported by Gutsche, *et al.*[12] In this case the phenyls are separated by two methylene groups, and a carbene is generated instead of a nitrene. The addition of the carbene to the phenyl followed by rearrangement, leads to the product 6,6a-dihydro-5H-cyclohepta[*a*]naphthalene.

Experimental Section[13–15]

o-Azidodiphenylmethane.—A solution of 3.6 g (0.02 mol) of *o*-aminodiphenylmethane was diazotized[16] in 8 ml of concentrated hydrochloric acid and 80 ml of water cooled to −10°. To the cold solution, 1.4 g (0.02 mol) of sodium nitrite in 10 ml of water was slowly added. A solution of 1.5 g of sodium azide in 10 ml of water was added to the diazonium salt. The solution was extracted twice with 100 ml of ether. The ethereal extract was washed with 5% sodium hydroxide solution and dried with sodium sulfate. The solvent was removed under reduced pressure. The residue was chromatographed on alumina. Petroleum

(7) (a) R. Huisgen, D. Vossius, and M. Appl, *Angew. Chem.*, **67**, 756 (1955); (b) R. Huisgen, D. Vossius, and M. Appl, *Ber.*, **91**, 1 (1958); (c) M. Appl and R. Huisgen, *ibid.*, **92**, 2961 (1959).

(8) A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold Ltd., London, 1957, p 140.

(9) W. von E. Doering and R. A. Odum, *Tetrahedron*, **22**, 81 (1966).

(10) R. A. Friedel and M. Orchin, "Ultraviolet Spectron of Aromatic Compounds," John Wiley & Sons, Inc., New York, N. Y., 1951, Spectra No. 192.

(11) The preference of the nitrene mechanism was suggested by one of the referees.

(12) C. D. Gutsche, E. F. Jason, R. C. Coffey, and H. E. Johnson, *J. Amer. Chem. Soc.*, **80**, 5756 (1958).

(13) All melting points are uncorrected.

(14) Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

(15) The nmr spectra were taken and interpreted by Wilbur Simon, Simon Research Laboratory, Elgin, Ill., on a Varian A-60 MC instrument with tetramethylsilane as an internal standard.

(16) C. L. Hewett, L. J. Lermit, H. T. Oppenshaw, A. R. Todd, A. H. Williams, and F. N. Woodward, *J. Chem. Soc.*, 292 (1948).

ether (bp 60–90°) eluted 3.8 g (92%) of *o*-azidodiphenylmethane.

Anal. Calcd for $C_{13}H_{11}N_3$: C, 74.61; H, 5.30; N, 20.09. Found: C, 74.84; H, 5.37; N, 19.96.

Decomposition of *o*-Azidodiphenylmethane. A.—To 150 ml of decalin preheated to 160°, 4.5 g of *o*-azidodiphenylmethane was added. After 5 hr at 160–165°, all gas evolution had ceased. A total of 480 ml of gas at standard conditions were collected (theoretical, 475 ml). The solvent was removed at <5-mm pressure. The residue was dissolved in a mixture of benzene and petroleum ether and put on an alumina chromatographic column. Petroleum ether eluted the first fraction. This fraction yielded 1.6 g (41%) of *o*-aminodiphenylmethane upon distillation. No other products were isolated.

B.—A solution of 2.0 g of *o*-azidodiphenylmethane in 100 ml of 1,2,4-trichlorobenzene was heated to 160° and maintained at this temperature for 4 hr. The solvent was removed at <5-mm pressure, and the residue subjected to steam distillation. The steam distillate was extracted twice with 150 ml of ether. The etheral extracts were dried with sodium sulfate. Removal of the ether at reduced pressure left 1.1 g (66%) of crude azepino-[2,1-*a*]-11H-indole (I), mp 80–87°. This solid was recrystallized from hexane to yield white crystals, mp 91°. An analytical sample was sublimed at 80° (0.1 mm), mp 91–91.5°.

Anal. Calcd for $C_{13}H_{11}N$: C, 86.15; H, 6.12; N, 7.73. Found: C, 86.05; H, 6.20; N, 7.62.

1,2,3,4,5-Pentahydroazepino[2,1-*a*]indole (II).—A solution of 0.8 g of I in 200 ml of ethanol was catalytically hydrogenated with 0.4 g of 10% palladium on charcoal on a Parr shaker. The sample was filtered free of catalyst, and the solvent was removed at reduced pressure. The solid residue was recrystallized from a hexane–cyclohexane mixture to yield 0.65 g (79.5%) of 1,2,3,4,5-pentahydroazepino[2,1-*a*]indole, mp 82–88°. An analytical sample was prepared by sublimation at 80° (0.1 mm) to yield white crystals, mp 88°.

Anal. Calcd for $C_{13}H_{15}N$: C, 84.27; H, 8.16; N, 7.56. Found: C, 84.29; H, 8.00; N, 7.59.

Registry No.—I, 17691-63-3; II, 17691-64-4; *o*-azidodiphenylmethane, 17691-65-5.

Acknowledgments.—The authors are deeply indebted to Dr. L. Schieler and Professor P. A. S. Smith for their helpful interest in this work and to Mr. S. Hotta for spectral measurements and valuable preparative assistance.

Synthesis of New Chlorine-Substituted Derivatives of 2-Tetralone[1,2]

ANDRE ROSOWSKY, JOSEPHINE BATTAGLIA, KATHERINE K. N. CHEN, AND EDWARD J. MODEST

The Children's Cancer Research Foundation and the Departments of Biological Chemistry and Pathology, Harvard Medical School, Boston, Massachusetts 02115

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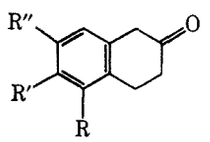
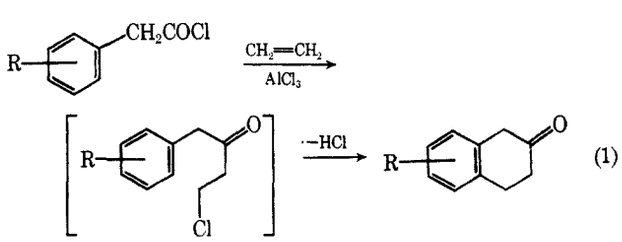
2-Tetralones containing one or more chlorine substituents on the aromatic ring have not been described in the chemical literature to date. Such compounds are of interest, in this laboratory, as points of departure for the synthesis of various chlorine-substituted condensed ring systems of potential biological interest. In the present Note, we should like to report the preparation of 6-chloro-2-tetralone (**1**), 7-chloro-2-tetralone (**2**), 5,7-dichloro-2-tetralone (**3**), and 6,7-dichloro-2-tetralone (**4**) *via* the Darzens reaction,[3] as modified by Burckhalter and Campbell.[4]



1, R = R″ = H; R′ = Cl
2, R = R′ = H; R″ = Cl
3, R = R″ = Cl; R′ = H
4, R = H; R′ = R″ = Cl

Methods of synthesis of 2-tetralone and its substituted analogs have been reviewed recently.[5] The approach favored by most workers during the past 25 years has involved reduction of substituted 2-methoxynaphthalene derivatives with sodium in alcohol. Catalytic, electrolytic, and sodium–liquid ammonia reductions have also been reported. This general plan appeared to be unsuitable for the synthesis of chlorinated 2-tetralones because of (1) the possibility of base-catalyzed dehalogenation, and (2) the relative inaccessibility of the required 2-methoxynaphthalene intermediates. Multistep sequences have been devised to transform substituted 1-tetralones into the corresponding 2-tetralones. However, such methods offer no particular advantage in this case because chlorinated 1-tetralones are themselves not readily obtained. The condensation of substituted phenylacetyl chlorides with ethylene under the influence of aluminum chloride (eq 1), according to the convenient



(1)

one-step procedure of Burckhalter and Campbell,[4] appeared to be an attractive alternative to the use of preformed naphthalene precursors. 2-Tetralones containing alkyl substituents in the saturated ring were prepared as early as 1947 by this approach in a two-step procedure.[6] However, little work has been done to define either the precise mechanism or the synthetic scope of this interesting reaction.

(1) This investigation was supported in part by Research Contract DA-49-193-MD-3008 from the U. S. Army Medical Research and Development Command, Office of the Surgeon General, and by Research Career Development Award K3-CA-22,151 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service. This is publication number 342 from the Army Research Program on Malaria.

(2) Presented in part before the Division of Medicinal Chemistry at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 4, 1968.

(3) L. F. Fieser and M. Fieser, "Topics in Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1963, p 548.

(4) J. H. Burckhalter and J. R. Campbell, *J. Org. Chem.*, **26**, 4232 (1961).

(5) V. F. Schner and N. M. Przhiyalgovskaya, *Russ. Chem. Rev.*, **35**, 523 (1966).

(6) J. Colonge and J. Chambion, *Compt. Rend.*, **224**, 128 (1947); J. Colonge and J. Chambion, *Bull. Soc. Chim. Fr.*, 1002 (1947).