

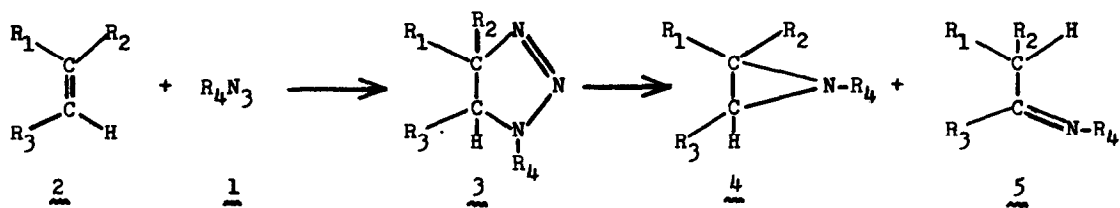
THE REACTION OF PHENYL AZIDE WITH OLEFINS

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The reaction between organic azides (1) and olefins (2) has recently come under close scrutiny.^(1,2,3) At elevated temperatures the 1,2,3-triazolines (3), which are the initially formed products at lower temperatures, have been observed to undergo pyrolytic elimination of nitrogen with the subsequent formation of the aziridine (4), the Schiff base (5) or, in most cases, a mixture of these products (CHART 1).


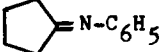

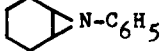

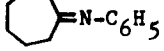

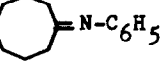
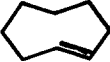

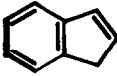
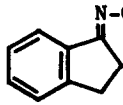

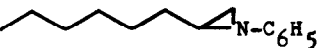
CHART 1



The present communication reports the reaction of phenyl azide (1a, $R_4=C_6H_5$) with a series of olefins at intermediate temperatures. The temperature was chosen to permit the smooth pyrolytic elimination of nitrogen to occur. The olefin, temperature of reaction, isolated products, percent yield and approximate relative reactivity are presented in TABLE I.

The products of these reactions were isolated by careful fractional distillation. Only in the case of the reaction of 1-octene with phenyl azide was there any indication that any of the isomeric product was being formed. In this case infrared analysis of the reaction mixture indicated the presence of a small amount, which was not isolated but was estimated to be less than five percent, of the isomeric anil. It is possible that small amounts of the isomeric product were present in other reactions but remained undetected by this isolation procedure.

TABLE I
Decomposition of Phenyl Azide in Olefins

Olefin	Temp. (°C)	Rel. React. (a)	Product	Yield (%) (b)
	42	-		75
	80	2.4		79
	80	3.3		80
	80	3.0		87
 (trans) (c)	80	Too fast to measure	 (d)	85
	91	1.4		79
	80	1.0		63

(a) The relative reactivities were measured by competitive reaction at 90°C.

(b) The yields are of purified, isolated products and are based on the percent reaction as determined from the nitrogen evolution. When allowed to proceed for extended periods of time, all reactions evolved greater than 95% of the theoretical quantity of nitrogen.

(c) Prepared by the method of E. J. Corey, F. A. Carey and R. A. E. Winter, *J. Am. Chem. Soc.*, **87**, 934 (1965). We thank Prof. E. J. Corey, Harvard University, for kindly supplying the details of this preparation.

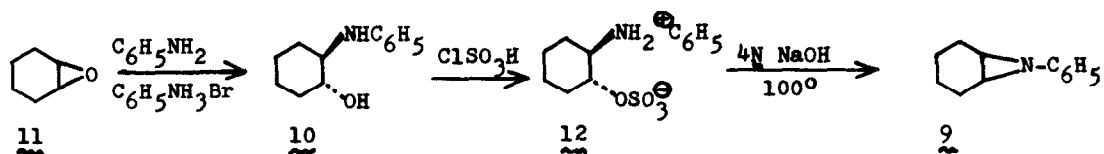
(d) We suspect that this is the cis-isomer, however, unequivocal structure proof is not now available.

The structure of the products was established by elemental analysis, and by infrared and nuclear magnetic resonance spectral analysis. In several instances these compounds were synthesized by alternate routes and subjected to direct comparison with the reaction products.

N-Phenyliminocyclopentane (6), N-phenyliminocycloheptane (7) and N-phenyliminocyclooctane (8) were prepared by the acid-catalyzed condensation of aniline with the appropriate ketone in benzene solution. The water was removed from the reaction mixture by azeotropic distillation.

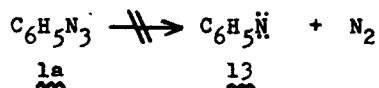
The synthesis of 7-phenyl-7-azabicyclo [4.1.0] heptane (9) was accomplished by the route outlined in CHART 2. trans-2-Anilincyclohexanol (10) was prepared by the acid-catalyzed ring-cleavage of cyclohexene oxide (11) according to a

CHART 2



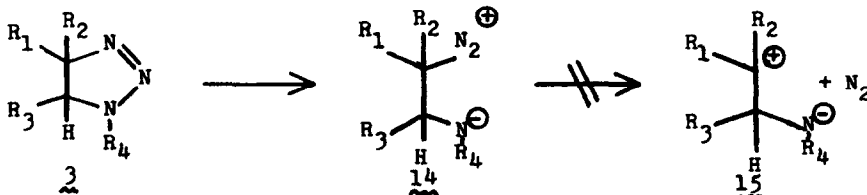
modification of the procedure of Browne and Lutz.⁽⁴⁾ The aminoalcohol was converted to the internal salt of the o-sulfonic acid (12) by the procedure of Stogryn and Brois.⁽⁵⁾ Ring closure to the aziridine (9) was effected by treatment with aqueous alkali.

In the reaction of phenyl azide with olefins, the reaction mixture could be satisfactorily analyzed for olefin and phenyl azide by gas-liquid partition chromatography (g.l.p.c.).⁽⁶⁾ When the reaction was carried out in the presence of an excess of the olefinic reagent, comparison of the rate of disappearance of phenyl azide, as determined by g.l.p.c. analysis, with the overall reaction rate, as measured by volumetric determination of the nitrogen evolution, pointed unequivocally to a multistep reaction mechanism in which the initial step, almost certainly the bimolecular 1,3-dipolar addition⁽¹⁾ of the azide to the olefin to provide the 1,2,3-triazoline, is not rate limiting. In all reactions the phenyl azide had diminished to an amount which could not be detected by g.l.p.c. analysis when only 40-60% of the theoretical quantity of the nitrogen had been evolved. Thus, it is probable that under the conditions used in this study, the mechanistic course is the initial, relatively rapid formation of the 1,2,3-triazoline (3, $R=C_6H_5$) by 1,3-dipolar addition of the azide (1a, $R=C_6H_5$) to the olefin (2), followed by a rate-controlling elimination of nitrogen to provide the products 4 ($R_4=C_6H_5$) or 5 ($R_4=C_6H_5$) as outlined in CHART 1; the cyclic olefins afforded a single product and 1-octene gave over 95% of one product (TABLE I). That the reaction between phenyl azide (1a) and the olefin does not proceed by way of initial unimolecular loss of nitrogen from the azide to form the highly-reactive electron-deficient phenylnitrene (13) was also indicated by the observation that the phenyl azide was inert to the reaction conditions in the absence of any olefin using either cyclohexane or benzene as solvent.



The relative reactivities of the various olefins presented in TABLE I were determined by measurement of the relative rate of disappearance of the olefin in competitive experiments by using pairs of olefins, and thus, this represents the relative rate of 1,3-dipolar addition. The olefin analysis was carried out by g.l.p.c. As is expected, ⁽¹⁾ with the exception of trans-cyclooctene which contains 9.2 kcal/mole more strain energy than cis-cyclooctene, ⁽⁷⁾ the rate of reaction is quite insensitive to structural variation in the olefin. Both N-Phenyliminocyclohexane and the isomeric 7-phenyl-7-azabicyclo [4.1.0] heptane were stable to the reaction conditions and there was no aziridine-imine tautomerization occurring.

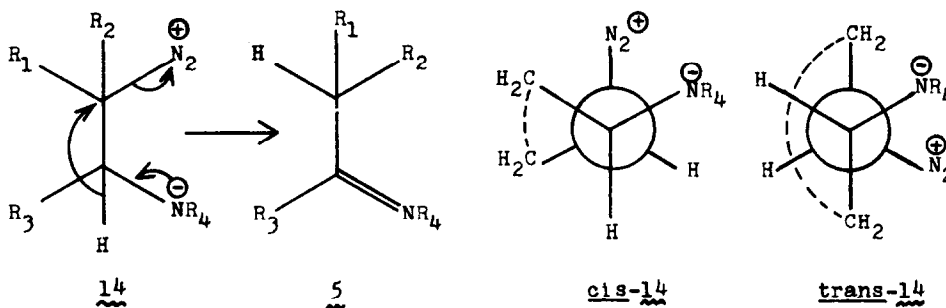
The most distinctive result which bears on the mechanistic course of the thermal decomposition of the 1,2,3-triazolines ⁽³⁾ is the markedly different behavior of the phenyl azide adducts of cis- and trans-cyclooctene. This observation strongly suggests that the relative stereochemistry of the substituents surrounding the two carbon atoms forming the junction of the bicyclic ring system plays a predominant role in determining the course of reaction. Recent work ⁽⁸⁾ on the solvent dependence of the rate of thermal decomposition of 1,2,3-triazolines indicates that the initial step in the thermolysis involves the heterolytic cleavage of the N₁-N₂ bond of the triazoline with the formation of zwitterion 14. It is apparent that this intermediate does not undergo unassisted loss of nitrogen to form the free 1,3-dipolar ion 15 since the same ion, and hence the same product(s) should be obtained from both cis- and trans-cyclooctene-phenyl azide adducts.



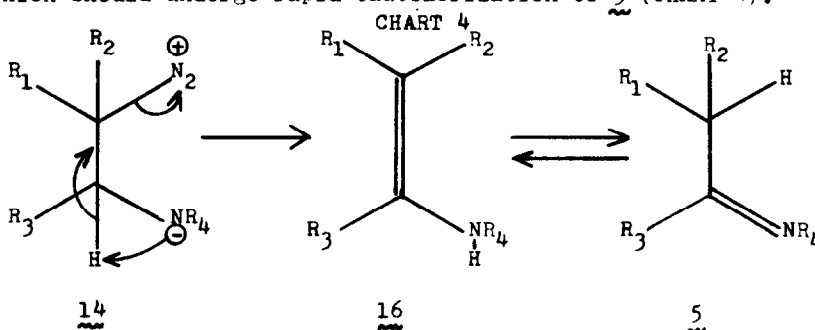
Thus, the ring closure to provide the aziridine or the hydrogen shift to provide the anil must occur to some degree in concert with the expulsion of nitrogen.

There are two conceivable pathways for the hydrogen shift to follow, both of which ultimately result in the formation of the observed anil: (1) the direct

shift of a hydride ion in 14 with expulsion of nitrogen (CHART 3), or (2) a
CHART 3



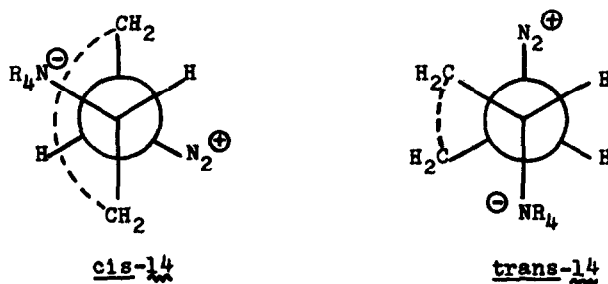
1,2-shift of a proton to the nitrogen bearing the negative charge to provide the enamine 16 which should undergo rapid tautomerization to 5 (CHART 4).



The proton shift (CHART 4) is less consistent with the postulate that the stereochemistry is the governing factor as this should take place with nearly equal facility in the zwitterions 14 derived from either cis- or trans-cyclooctene-phenyl azide adducts. This point is, however, not rigorously established by the evidence presently available. A careful inspection of Dreiding models reveals that the anti arrangement of the hydride and diazonium moieties, which is the most favorable for concerted 1,2-hydride migrations,⁽⁹⁾ is possible only in the case of the cis-zwitterion 14; the eight-membered ring may contain anti-butane segments, but only with considerable difficulty (CHART 3).⁽¹⁰⁾

The conformations of cis- and trans-zwitterions 14, necessary for aziridine ring formation, are shown in CHART 5. The trans displacement of nitrogen by the amide anion can readily achieve the anti coplanar conformation only in the case of trans-14; the phenyl azide adduct from trans-cyclooctene would then yield a cis-fused aziridine.

CHART 5



Thus, the course of pyrolytic decomposition of 1,2,3-triazolines is apparently, under conditions used in this study, primarily governed by the relative orientation of substituents about the carbon-carbon bond of the triazoline ring system. At higher temperatures, where a mixture of products is generally observed, this "conformational selectivity" is apparently lost.

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REFERENCES

1. R. Huisgen, Angew. Chem. Int. Ed., **2**, 565, 633 (1963).
2. A. L. Logothetis, J. Am. Chem. Soc., **87**, 749 (1965).
3. P. Scheiner, J. H. Schomaker, S. Deming, W. J. Libbey and G. P. Nowack, ibid., **87**, 306 (1965).
4. C. L. Browne and R. E. Lutz, J. Org. Chem., **17**, 1187 (1952).
5. E. L. Stogryn and S. J. Brois, ibid., **30**, 88 (1965).
6. G.l.p.c. analyses were carried out on a 2-meter x 6.25 mm column packed with 10% of a saturated solution of silver nitrate in Carbowax-1000 supported on 60-80 mesh F & M Diatoport S. We thank Prof. E. Wilkins Reeve for the use of this column.
7. C. T. Mortimer, Reaction Heats and Bond Strengths, p. 38, Pergamon Press, New York (1962).
8. A. L. Logothetis, J. Am. Chem. Soc., **87**, 749 (1965).
9. M. Chérest, H. Felkin, J. Sicher, F. Šipoš and M. Tichy, J. Chem. Soc., 2513 (1965).
10. E. L. Eliel, Stereochemistry of Carbon Compounds, p. 257, McGraw-Hill, New York (1962).